Figure 15-57 Forest plot results Model IPTW QVA149 versus free LABA/LAMA with ICS – Total analysis population – Diabetes mellitus as endpoint

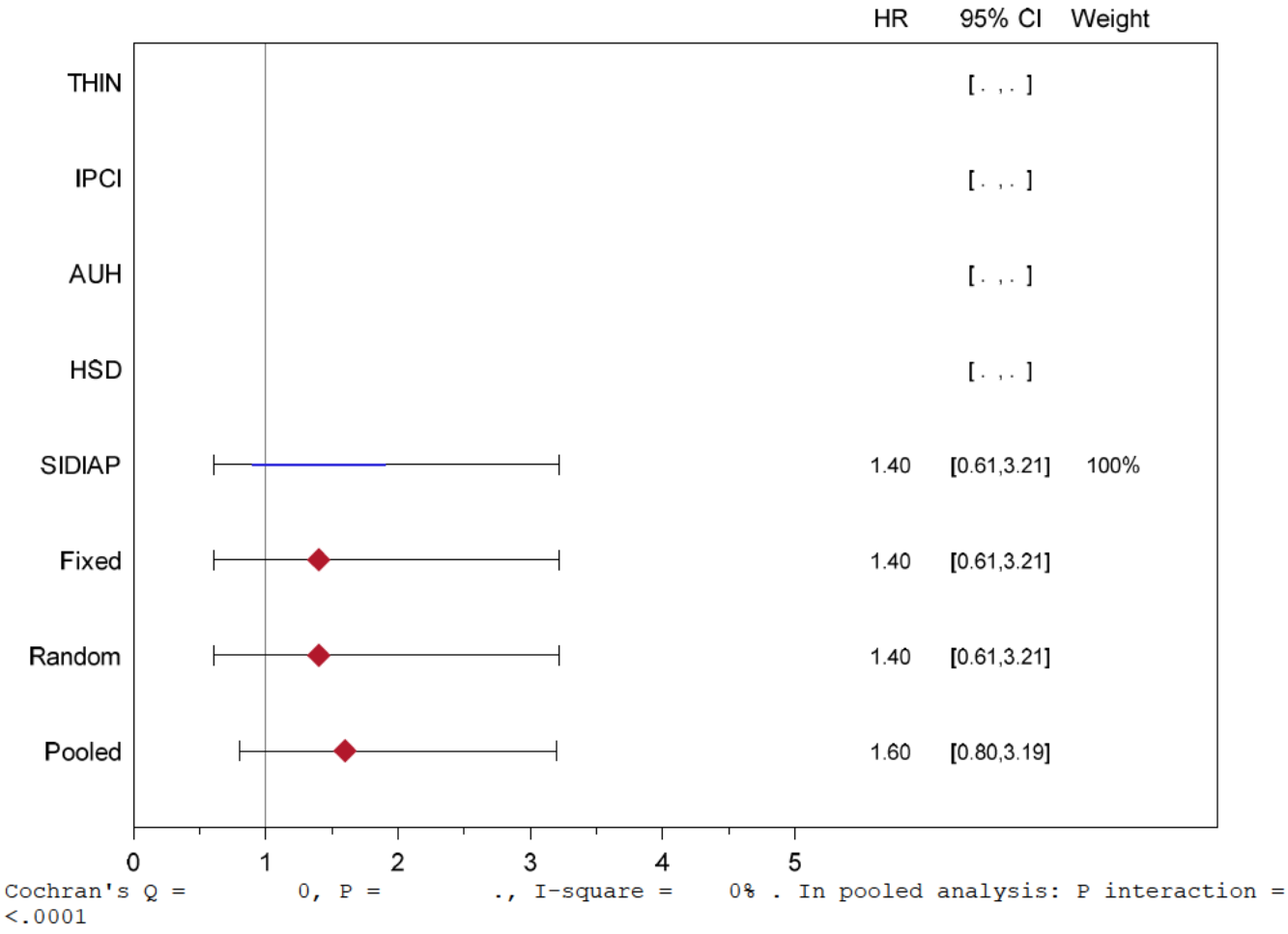
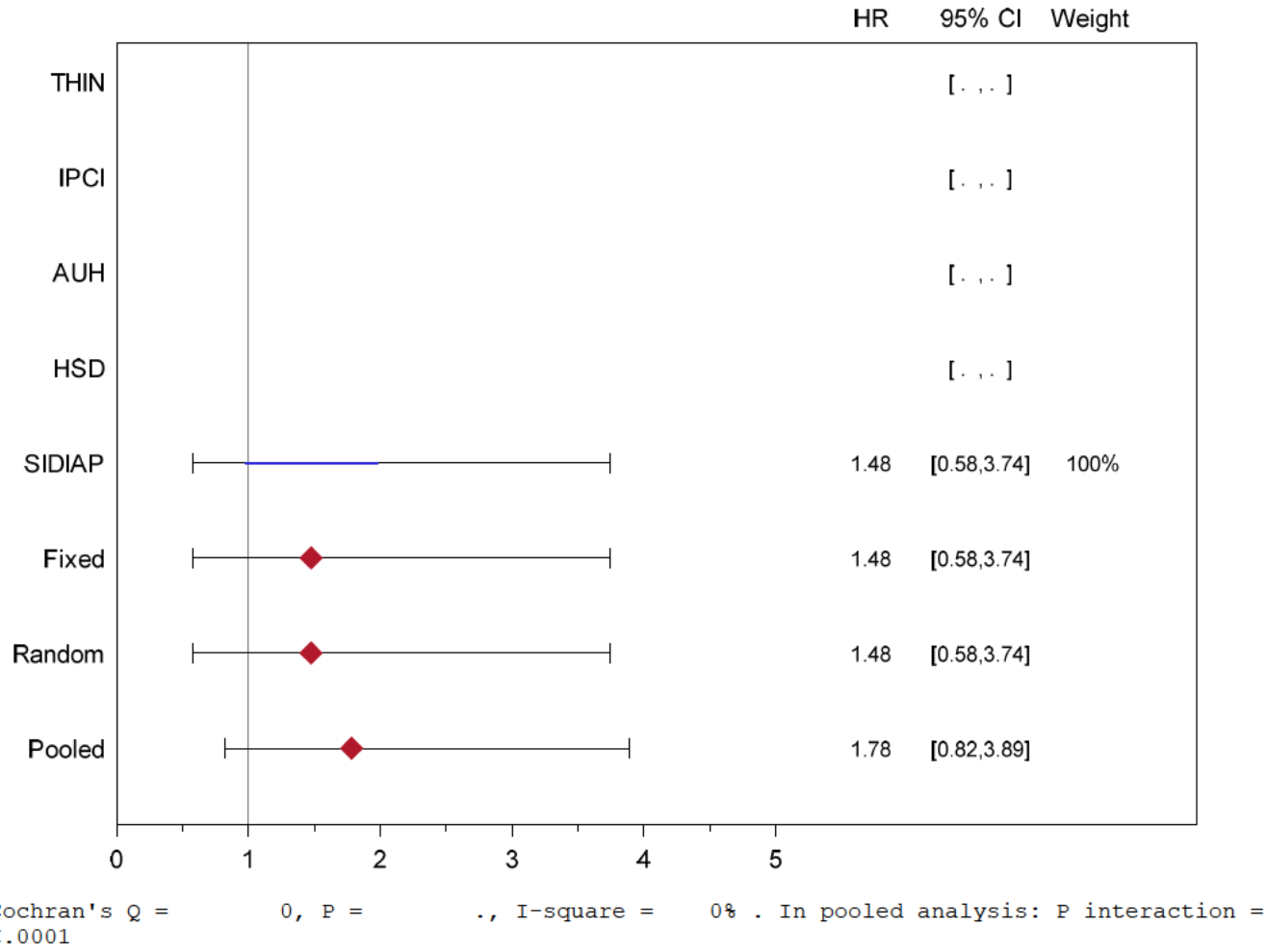
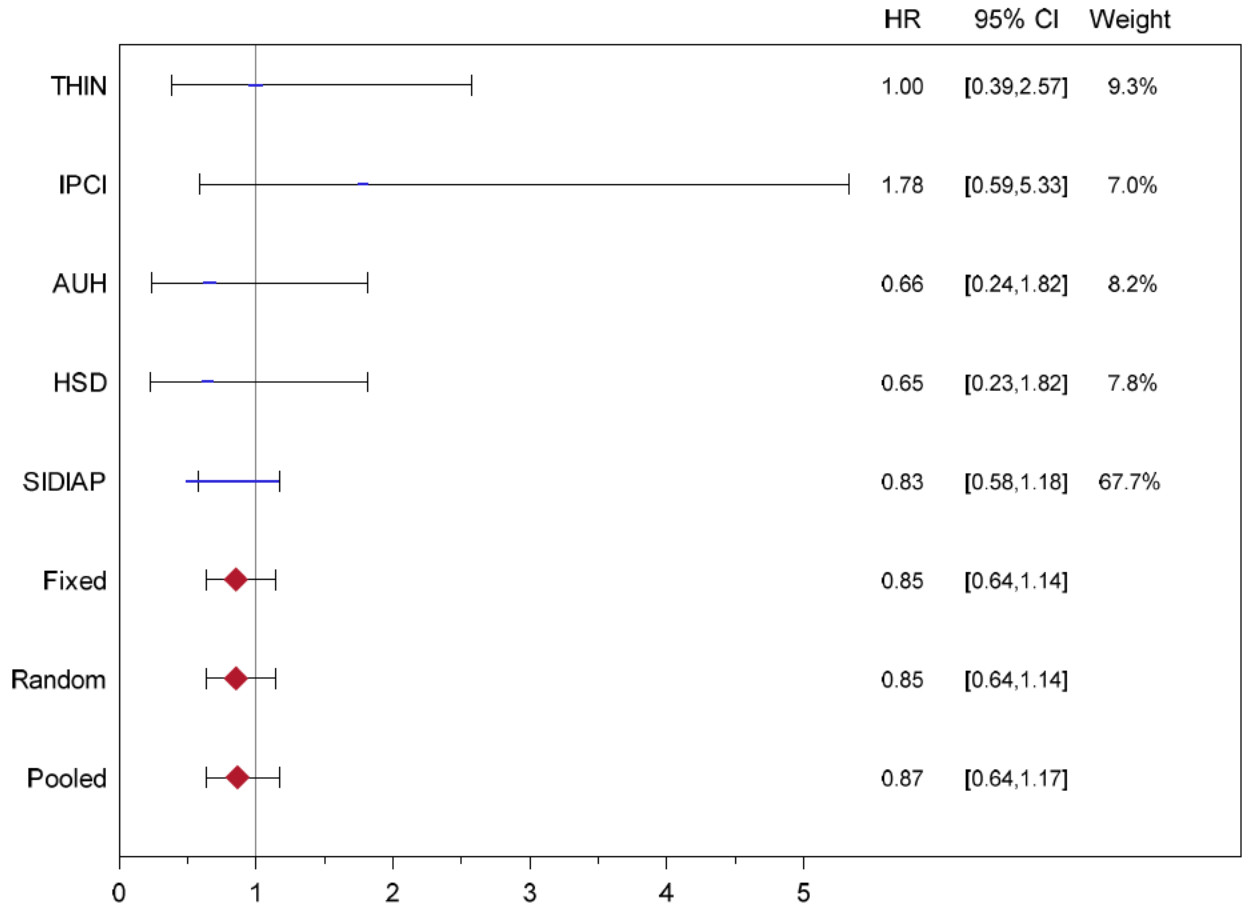


Figure 15-58 Forest plot results Model IPTW QVA149 versus Free LABA+ICS – Total analysis population – Diabetes mellitus as endpoint



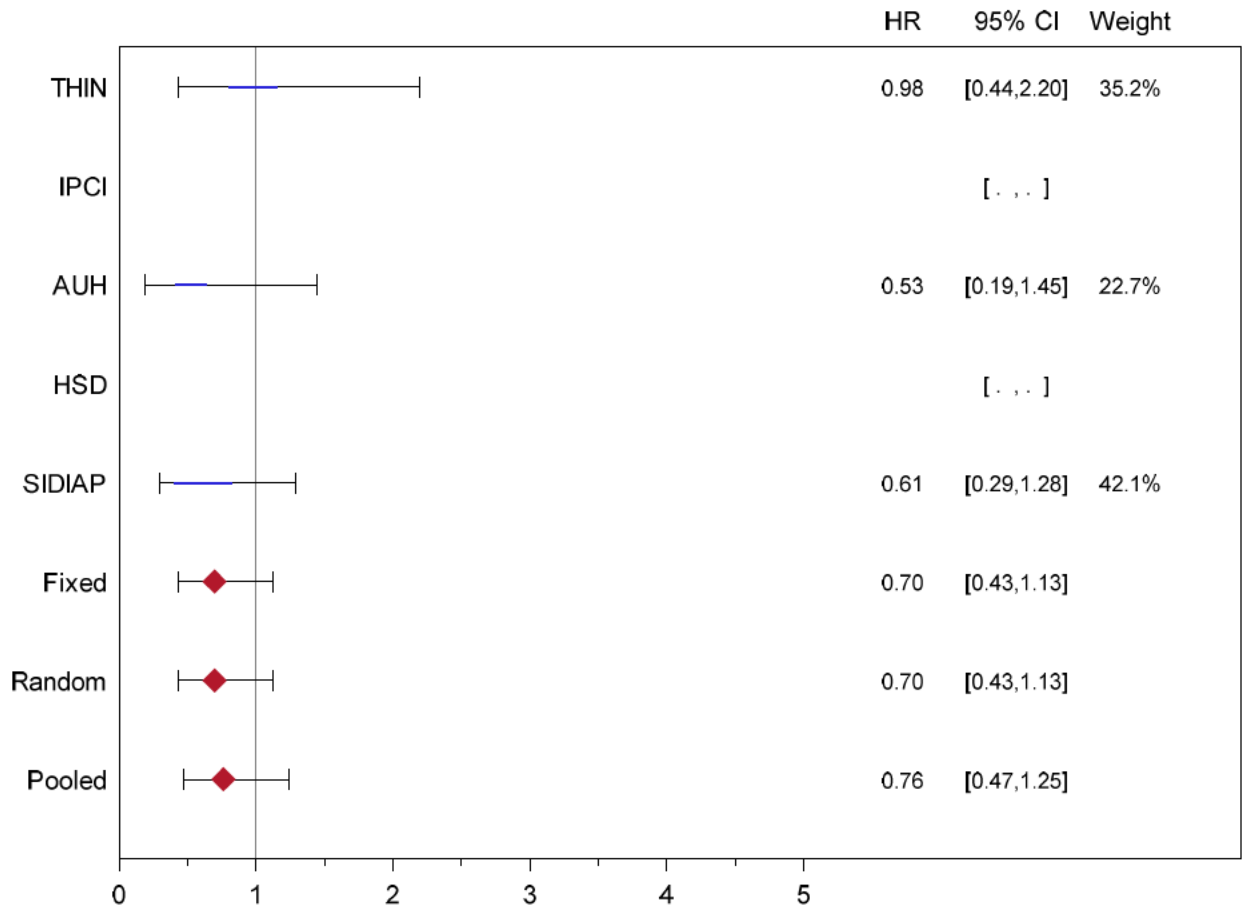
Cochran's Q = 0, P = ., I-square = 0% . In pooled analysis: P interaction = <.0001

Figure 15-59 Forest plot results Model IPTW QVA149 versus Fixed LABA/ICS – Total analysis population – Diabetes mellitus as endpoint



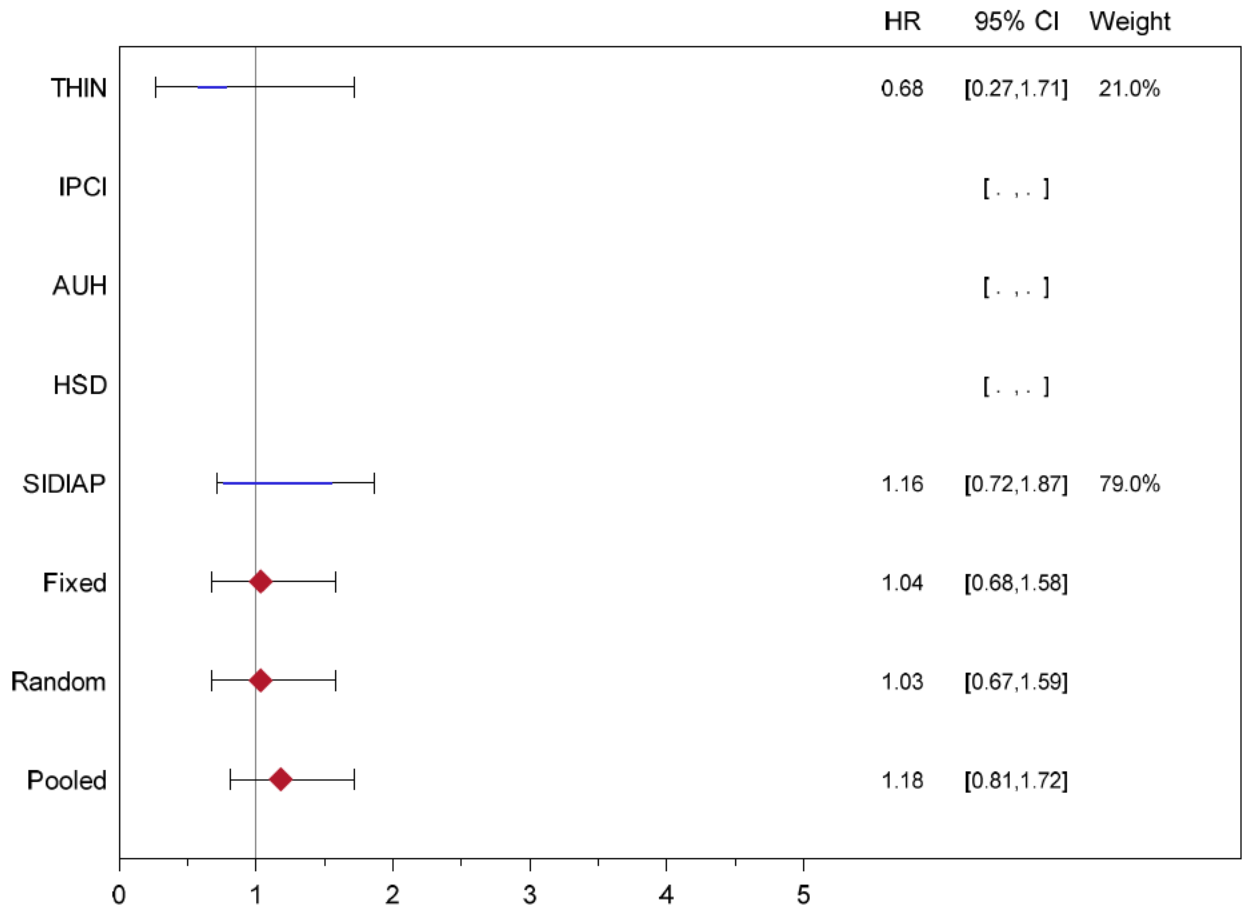
Cochran's Q = 2.371168, P = 0.667844, I-square = 0% . In pooled analysis: P interaction = 0.6352

Figure 15-60 Forest plot results Model IPTW QVA149 versus Fixed LABA/LAMA – Total analysis population – Diabetes mellitus as endpoint



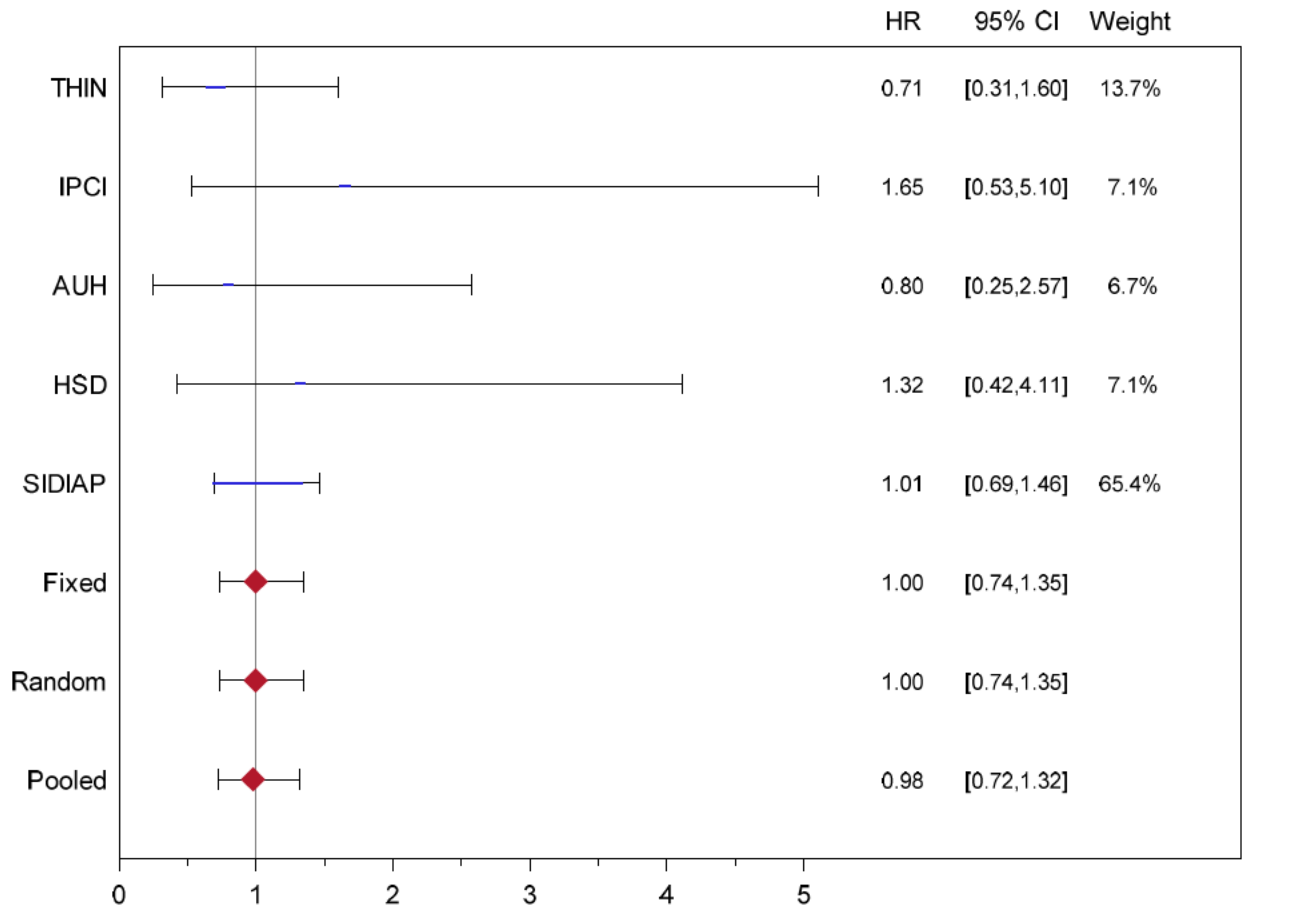
Cochran's Q = 1.083446, P = 0.581745, I-square = 0% . In pooled analysis: P interaction = 0.6790

Figure 15-61 Forest plot results Model IPTW QVA149 versus LABA – Total analysis population – Diabetes mellitus as endpoint



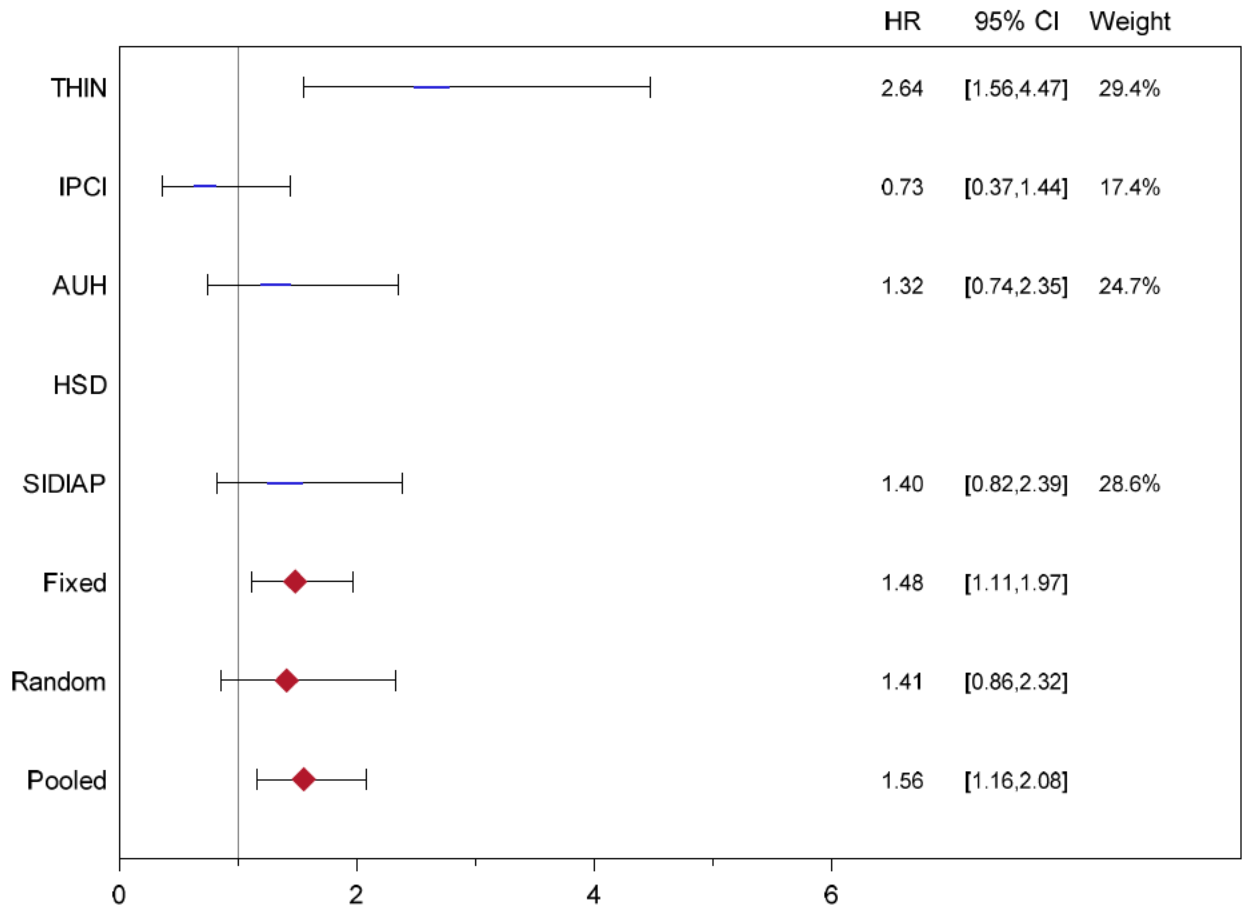
Cochran's Q = 1.006728, P = 0.315688, I-square = 1% . In pooled analysis: P interaction = 0.3805

Figure 15-62 Forest plot results Model IPTW QVA149 versus LAMA – Total analysis population – Diabetes mellitus as endpoint



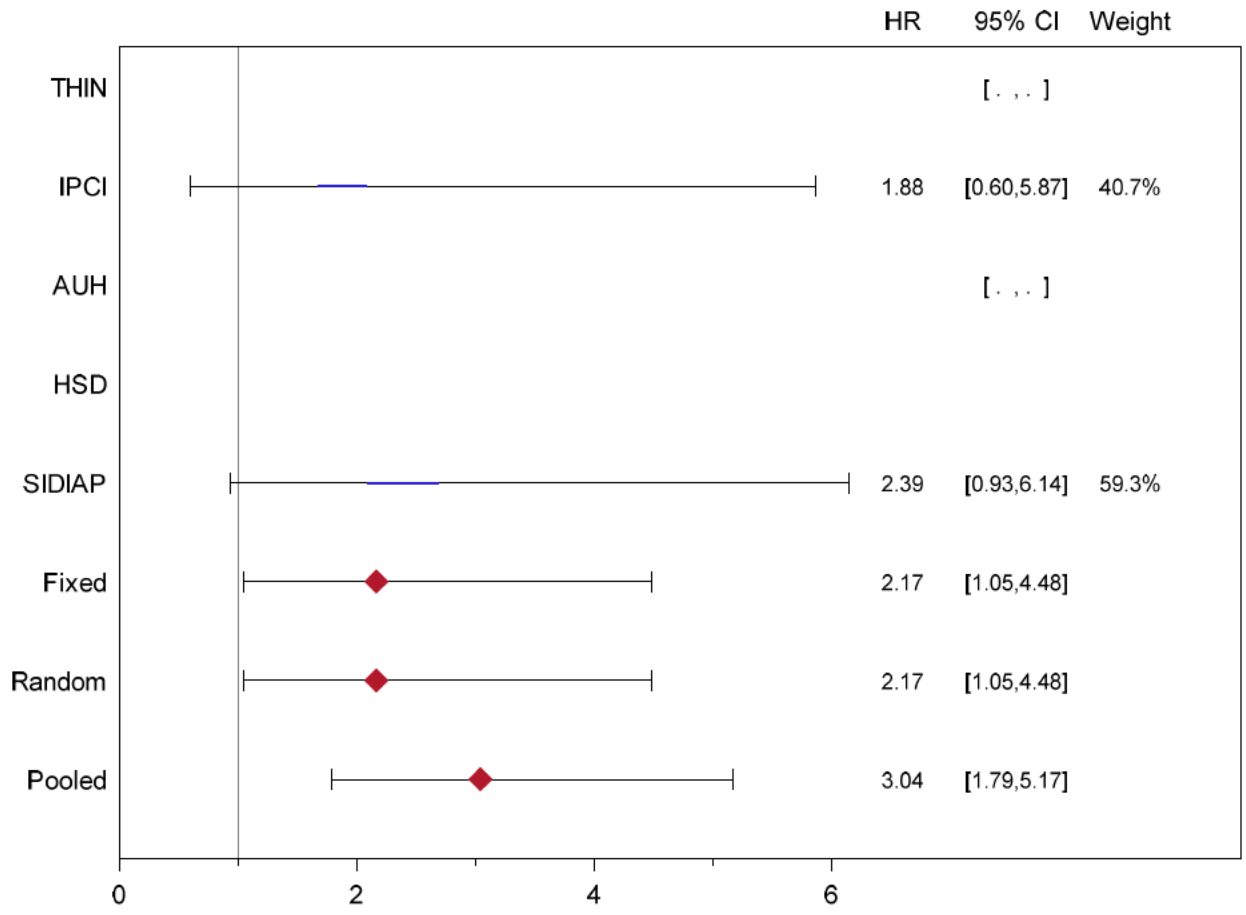
Cochran's Q = 1.827917, P = 0.767371, I-square = 0% . In pooled analysis: P interaction = 0.7328

Figure 15-63 Forest plot results Model IPTW QVA149 versus free LABA/LAMA without ICS – Total analysis population – Mortality as endpoint



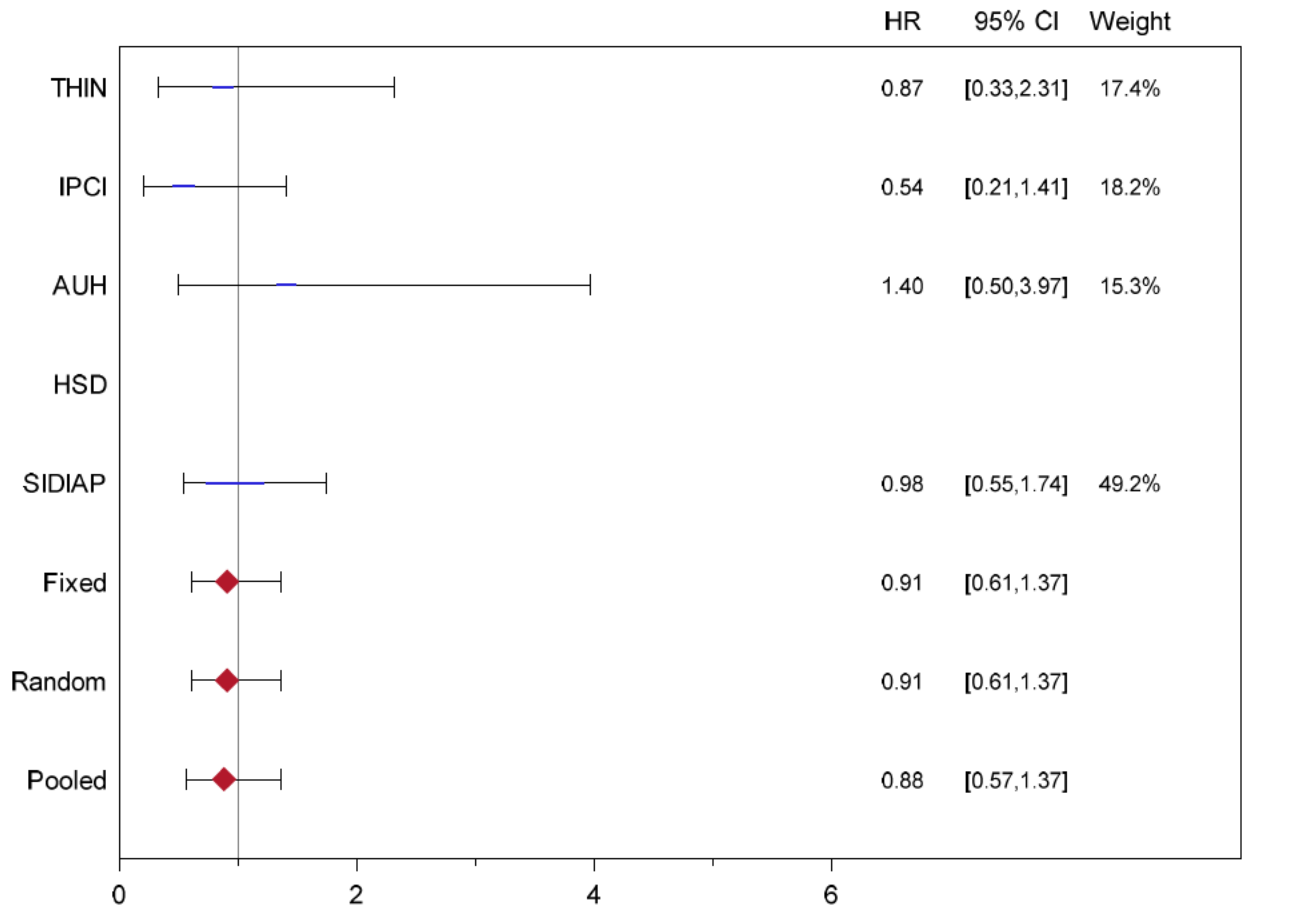
Cochran's Q = 8.942493, P = 0.030065, I-square = 66% . In pooled analysis: P interaction = 0.0552

Figure 15-64 Forest plot results Model IPTW QVA149 versus free LABA/LAMA with ICS – Total analysis population – Mortality as endpoint



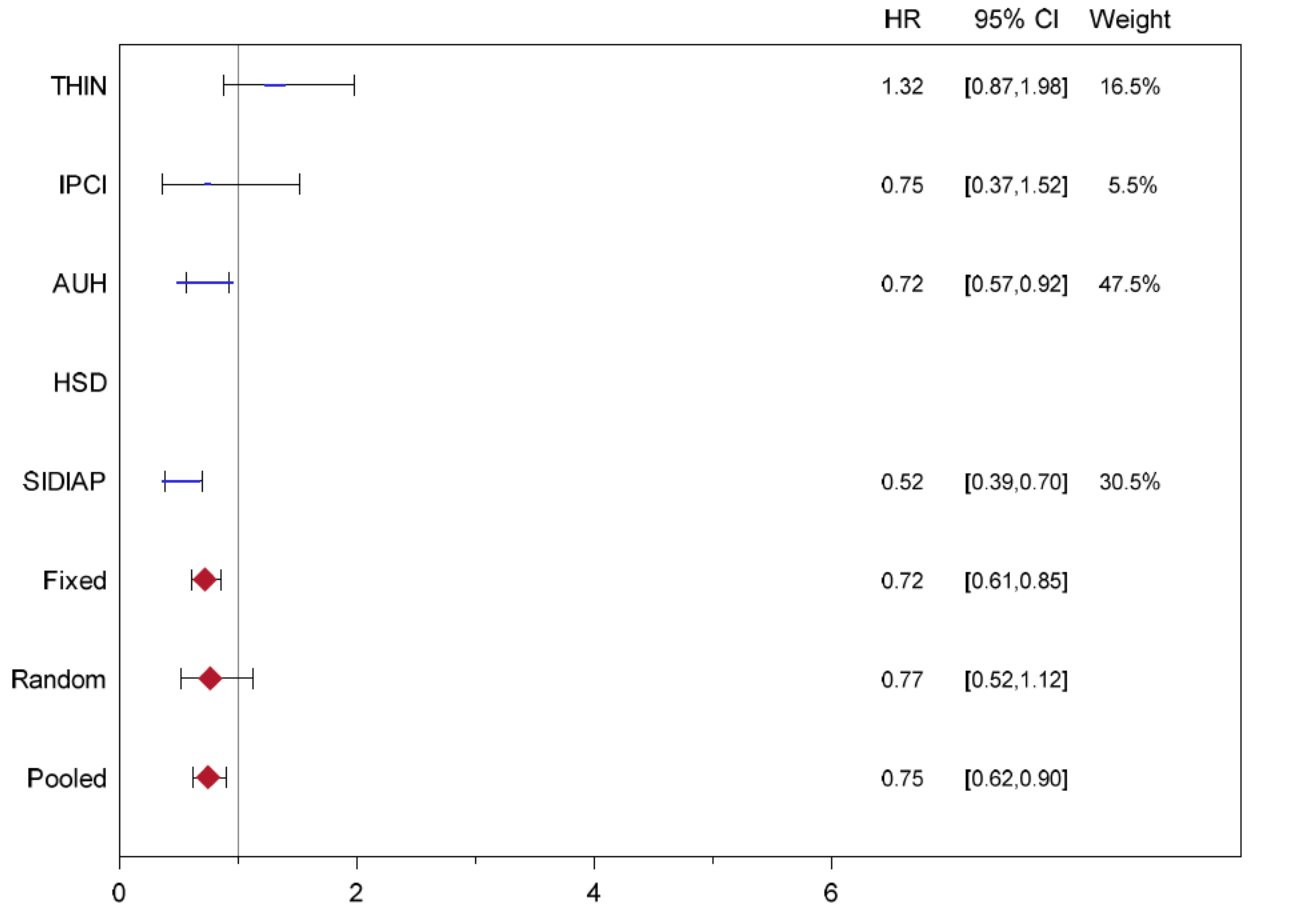
Cochran's Q = 0.103628, P = 0.747519, I-square = 0% . In pooled analysis: P interaction = 0.5228

Figure 15-65 Forest plot results Model IPTW QVA149 versus Free LABA+ICS – Total analysis population – Mortality as endpoint



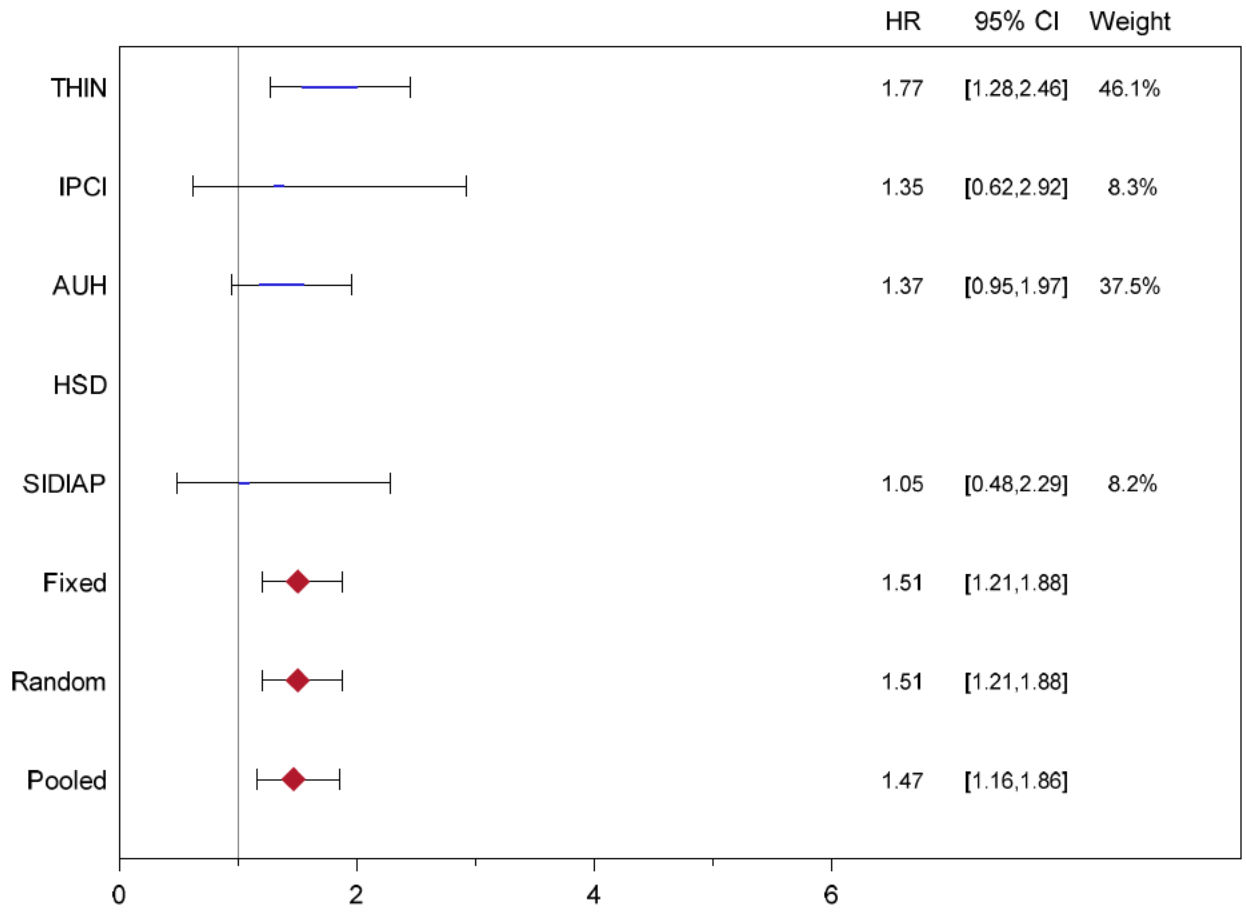
Cochran's Q = 1.861843, P = 0.60157, I-square = 0% . In pooled analysis: P interaction = 0.7035

Figure 15-66 Forest plot results Model IPTW QVA149 versus Fixed LABA/ICS – Total analysis population – Mortality as endpoint



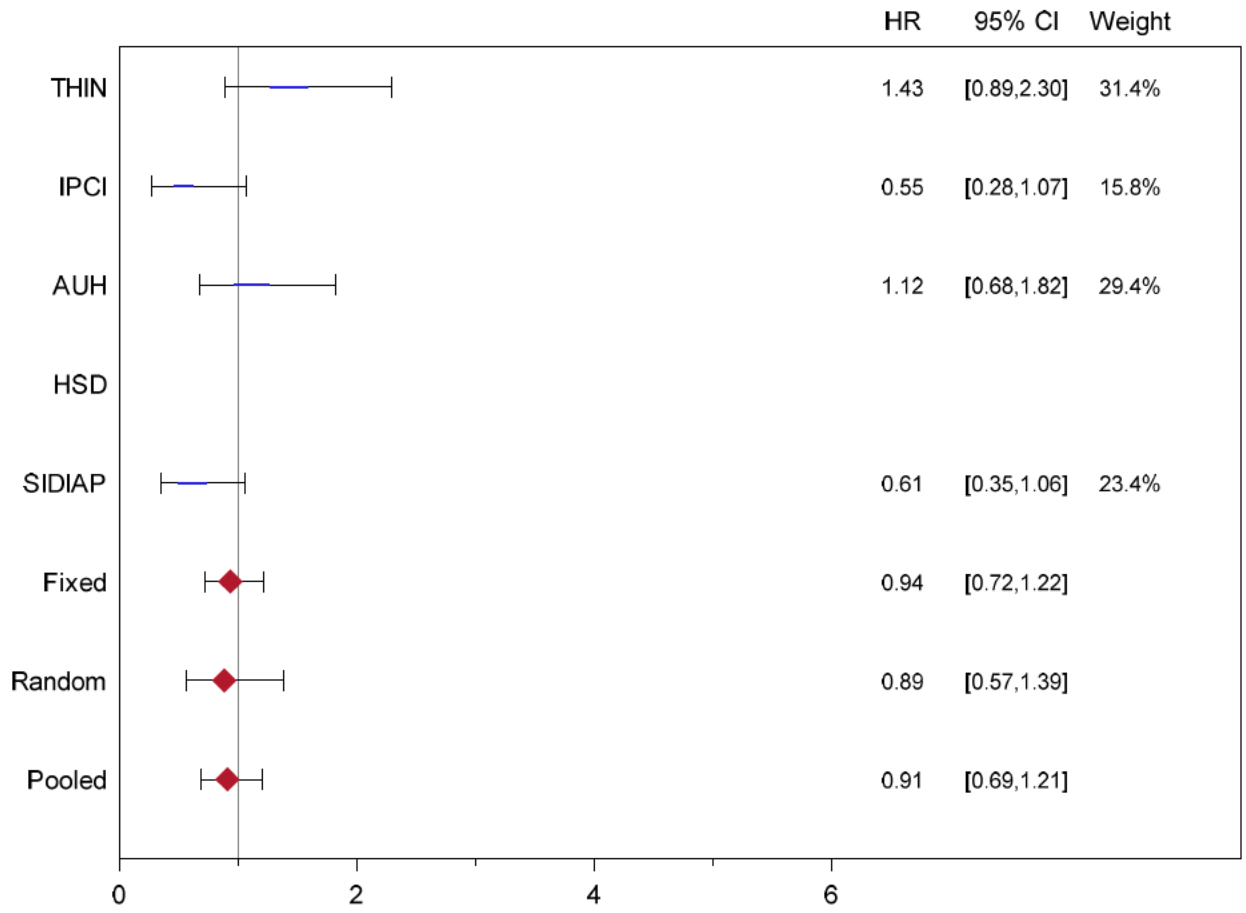
Cochran's Q = 12.79965, P = 0.005091, I-square = 77% . In pooled analysis: P interaction = 0.0111

Figure 15-67 Forest plot results Model IPTW QVA149 versus Fixed LABA/LAMA – Total analysis population – Mortality as endpoint



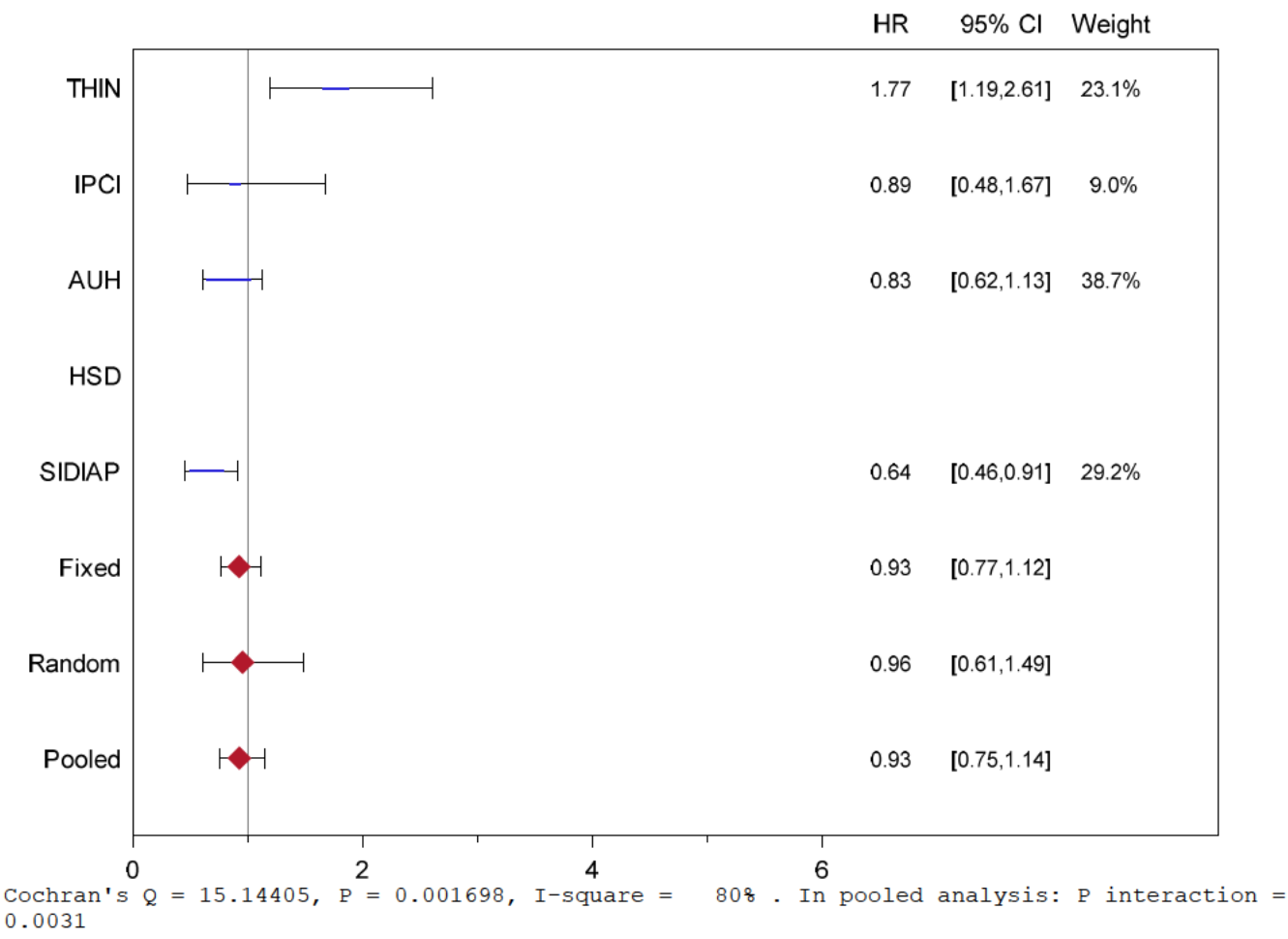
Cochran's Q = 2.112745, P = 0.549339, I-square = 0% . In pooled analysis: P interaction = 0.6707

Figure 15-68 Forest plot results Model IPTW QVA149 versus LABA – Total analysis population – Mortality as endpoint



Cochran's Q = 8.279083, P = 0.040583, I-square = 64% . In pooled analysis: P interaction = 0.0700

Figure 15-69 Forest plot results Model IPTW QVA149 versus LAMA – Total analysis population – Mortality as endpoint



Cochran's Q = 15.14405, P = 0.001698, I-square = 80% . In pooled analysis: P interaction = 0.0031

Table 15-1 Calendar year, gender and age distribution (pooled and by database)

POOLED	QVA N(%)	Free LABA+LAMA without ICS N(%)	Std Dif	Free LABA+LAMA with ICS N(%)	Std Dif
Total	9,798 (100.0%)	9,619 (100.0%)	0	3,192 (100.0%)	0
Year cohort entry			0.486		0.5548
2013	41 (0.4%)	685 (7.1%)	.	238 (7.5%)	.
2014	2,866 (29.3%)	3,918 (40.7%)	.	1,383 (43.3%)	.
2015	4,166 (42.5%)	3,307 (34.4%)	.	1,072 (33.6%)	.
2016	2,155 (22.0%)	1,452 (15.1%)	.	450 (14.1%)	.
2017	570 (5.8%)	257 (2.7%)	.	49 (1.5%)	.
Gender			-0.0571		-0.0386
Male	6,845 (69.9%)	6,465 (67.2%)	.	2,173 (68.1%)	.
Female	2,953 (30.1%)	3,154 (32.8%)	.	1,019 (31.9%)	.
Age at cohort entry			-0.0136		-0.0976
40-<60	1,462 (14.9%)	1,403 (14.6%)	.	394 (12.3%)	.
60-<80	6,275 (64.0%)	6,147 (63.9%)	.	2,023 (63.4%)	.
>=80	2,061 (21.0%)	2,069 (21.5%)	.	775 (24.3%)	.

POOLED	QVA N(%)	Free LABA+ICS N(%)	Std Dif	Fixed LABA ICS N(%)	Std Dif
Total	9,798 (100.0%)	4,628 (100.0%)	0	58332 (100.0%)	0
Year cohort entry			0.5683		0.3876
2013	41 (0.4%)	407 (8.8%)	.	3,623 (6.2%)	.
2014	2,866 (29.3%)	1,947 (42.1%)	.	21259 (36.4%)	.
2015	4,166 (42.5%)	1,538 (33.2%)	.	19628 (33.7%)	.
2016	2,155 (22.0%)	655 (14.2%)	.	10662 (18.3%)	.
2017	570 (5.8%)	81 (1.8%)	.	3,160 (5.4%)	.
Gender			-0.2188		-0.2633
Male	6,845 (69.9%)	2,752 (59.5%)	.	33425 (57.3%)	.
Female	2,953 (30.1%)	1,876 (40.5%)	.	24907 (42.7%)	.
Age at cohort entry			-0.051		0.0759
40-<60	1,462 (14.9%)	781 (16.9%)	.	11832 (20.3%)	.
60-<80	6,275 (64.0%)	2,649 (57.2%)	.	33903 (58.1%)	.
>=80	2,061 (21.0%)	1,198 (25.9%)	.	12597 (21.6%)	.

POOLED	QVA N(%)	Fixed LABA LAMA N(%)	Std Dif	LABA N(%)	Std Dif
Total	9,798 (100.0%)	9,150 (100.0%)	0	12364 (100.0%)	0
Year cohort entry			1.1755		0.4457
2013	41 (0.4%)		.	846 (6.8%)	.
2014	2,866 (29.3%)	139 (1.5%)	.	4,795 (38.8%)	.
2015	4,166 (42.5%)	2,284 (25.0%)	.	4,267 (34.5%)	.
2016	2,155 (22.0%)	4,665 (51.0%)	.	2,094 (16.9%)	.
2017	570 (5.8%)	2,062 (22.5%)	.	362 (2.9%)	.
Gender			-0.2772		-0.157
Male	6,845 (69.9%)	5,181 (56.6%)	.	7,722 (62.5%)	.
Female	2,953 (30.1%)	3,969 (43.4%)	.	4,642 (37.5%)	.
Age at cohort entry			0.0869		0.1108
40-<60	1,462 (14.9%)	1,513 (16.5%)	.	2,460 (19.9%)	.
60-<80	6,275 (64.0%)	6,031 (65.9%)	.	7,531 (60.9%)	.
>=80	2,061 (21.0%)	1,606 (17.6%)	.	2,373 (19.2%)	.

POOLED	QVA N(%)	LAMA	Std Dif
Total	9,798 (100.0%)	42972 (100.0%)	0
Year cohort entry			0.3736
2013	41 (0.4%)	2,509 (5.8%)	.
2014	2,866 (29.3%)	15132 (35.2%)	.
2015	4,166 (42.5%)	14045 (32.7%)	.
2016	2,155 (22.0%)	8,397 (19.5%)	.
2017	570 (5.8%)	2,889 (6.7%)	.
Gender			-0.19
Male	6,845 (69.9%)	26154 (60.9%)	.
Female	2,953 (30.1%)	16818 (39.1%)	.
Age at cohort entry			0.0971
40-<60	1,462 (14.9%)	8,369 (19.5%)	.
60-<80	6,275 (64.0%)	26168 (60.9%)	.
>=80	2,061 (21.0%)	8,435 (19.6%)	.

THIN	QVA N(%)	Free LABA+LAMA without ICS N(%)	Std Dif	Free LABA+LAMA with ICS N(%)	Std Dif
Total	1,346 (100.0%)	2,586 (100.0%)	0	394 (100.0%)	0
Year cohort entry			1.6375		1.7889
2013		151 (5.8%)	.	39 (9.9%)	.
2014		1,064 (41.1%)	.	166 (42.1%)	.
2015	290 (21.6%)	776 (30.0%)	.	110 (27.9%)	.
2016	555 (41.2%)	418 (16.2%)	.	56 (14.2%)	.
2017	501 (37.2%)	177 (6.8%)	.	23 (5.8%)	.
Gender			-0.0034		-0.1126
Male	694 (51.6%)	1,329 (51.4%)	.	181 (45.9%)	.
Female	652 (48.4%)	1,257 (48.6%)	.	213 (54.1%)	.
Age at cohort entry			0.0559		0.0514
40-<60	230 (17.1%)	450 (17.4%)	.	66 (16.8%)	.
60-<80	863 (64.1%)	1,727 (66.8%)	.	267 (67.8%)	.
>=80	253 (18.8%)	409 (15.8%)	.	61 (15.5%)	.
Age at cohort entry (years)			0.053		0.043
Mean (SD)	70.3 (10.4)	69.7 (10.1)	.	69.8 (10.0)	.

THIN	QVA N(%)	Free LABA+ICS N(%)	Std Dif	Fixed LABA ICS N(%)	Std Dif
Total	1,346 (100.0%)	583 (100.0%)	0	21315 (100.0%)	0
Year cohort entry			1.728		1.3116
2013		46 (7.9%)	.	1,144 (5.4%)	.
2014		260 (44.6%)	.	7,154 (33.6%)	.
2015	290 (21.6%)	150 (25.7%)	.	6,149 (28.9%)	.
2016	555 (41.2%)	81 (13.9%)	.	4,331 (20.3%)	.
2017	501 (37.2%)	46 (7.9%)	.	2,537 (11.9%)	.
Gender			-0.1397		-0.017
Male	694 (51.6%)	260 (44.6%)	.	10809 (50.7%)	.
Female	652 (48.4%)	323 (55.4%)	.	10506 (49.3%)	.
Age at cohort entry			0.1445		0.095
40-<60	230 (17.1%)	141 (24.2%)	.	4,544 (21.3%)	.
60-<80	863 (64.1%)	343 (58.8%)	.	13085 (61.4%)	.
>=80	253 (18.8%)	99 (17.0%)	.	3,686 (17.3%)	.
Age at cohort entry (years)			0.139		0.115
Mean (SD)	70.3 (10.4)	68.7 (11.8)	.	69.0 (11.1)	.

THIN	QVA N(%)	Fixed LABA LAMA N(%)	Std Dif	LABA N(%)	Std Dif
Total	1,346 (100.0%)	4,921 (100.0%)	0	3,006 (100.0%)	0
Year cohort entry			0.1763		1.435
2013			.	181 (6.0%)	.
2014		42 (0.9%)	.	1,118 (37.2%)	.
2015	290 (21.6%)	828 (16.8%)	.	835 (27.8%)	.
2016	555 (41.2%)	2,169 (44.1%)	.	575 (19.1%)	.
2017	501 (37.2%)	1,882 (38.2%)	.	297 (9.9%)	.
Gender			0.0418		-0.0013
Male	694 (51.6%)	2,640 (53.7%)	.	1,548 (51.5%)	.
Female	652 (48.4%)	2,281 (46.4%)	.	1,458 (48.5%)	.
Age at cohort entry			0.051		0.1106
40-<60	230 (17.1%)	882 (17.9%)	.	621 (20.7%)	.
60-<80	863 (64.1%)	3,222 (65.5%)	.	1,912 (63.6%)	.
>=80	253 (18.8%)	817 (16.6%)	.	473 (15.7%)	.
Age at cohort entry (years)			0.052		0.108
Mean (SD)	70.3 (10.4)	69.7 (10.2)	.	69.1 (10.8)	.

THIN	QVA N(%)	LAMA	Std Dif
Total	1,346 (100.0%)	18598 (100.0%)	0
Year cohort entry			1.2068
2013		946 (5.1%)	.
2014		5,786 (31.1%)	.
2015	290 (21.6%)	5,146 (27.7%)	.
2016	555 (41.2%)	4,174 (22.4%)	.
2017	501 (37.2%)	2,546 (13.7%)	.
Gender			0.0241
Male	694 (51.6%)	9,813 (52.8%)	.
Female	652 (48.4%)	8,785 (47.2%)	.
Age at cohort entry			0.0957
40-<60	230 (17.1%)	3,839 (20.6%)	.
60-<80	863 (64.1%)	11,672 (62.8%)	.
>=80	253 (18.8%)	3,087 (16.6%)	.
Age at cohort entry (years)			0.112
Mean (SD)	70.3 (10.4)	69.1 (10.8)	.

IPCI	QVA N(%)	Free LABA+LAMA without ICS N(%)	Std Dif	Free LABA+LAMA with ICS N(%)	Std Dif
Total	699 (100.0%)	1,148 (100.0%)	0	496 (100.0%)	0
Year cohort entry			0.1595		0.2113
2013	13 (1.9%)	53 (4.6%)	.	28 (5.7%)	.
2014	231 (33.1%)	357 (31.1%)	.	170 (34.3%)	.
2015	250 (35.8%)	416 (36.2%)	.	171 (34.5%)	.
2016	205 (29.3%)	322 (28.1%)	.	127 (25.6%)	.
Gender			-0.143		-0.2104
Male	425 (60.8%)	617 (53.8%)	.	250 (50.4%)	.
Female	274 (39.2%)	531 (46.3%)	.	246 (49.6%)	.
Age at cohort entry			-0.1175		-0.0738
40-<60	150 (21.5%)	217 (18.9%)	.	103 (20.8%)	.
60-<80	459 (65.7%)	732 (63.8%)	.	310 (62.5%)	.
>=80	90 (12.9%)	199 (17.3%)	.	83 (16.7%)	.
Age at cohort entry (years)			-0.125		-0.090
Mean (SD)	68.2 (10.1)	69.4 (10.2)	.	69.1 (10.2)	.

IPCI	QVA N(%)	Free LABA+ICS N(%)	Std Dif	Fixed LABA ICS N(%)	Std Dif
Total	699 (100.0%)	597 (100.0%)	0	7,001 (100.0%)	0
Year cohort entry			0.225		0.2232
2013	13 (1.9%)	36 (6.0%)	.	423 (6.0%)	.
2014	231 (33.1%)	190 (31.8%)	.	2,388 (34.1%)	.
2015	250 (35.8%)	189 (31.7%)	.	2,264 (32.3%)	.
2016	205 (29.3%)	182 (30.5%)	.	1,926 (27.5%)	.
Gender			-0.4068		-0.2037
Male	425 (60.8%)	244 (40.9%)	.	3,552 (50.7%)	.
Female	274 (39.2%)	353 (59.1%)	.	3,449 (49.3%)	.
Age at cohort entry			-0.0339		0.1114
40-<60	150 (21.5%)	141 (23.6%)	.	2,065 (29.5%)	.
60-<80	459 (65.7%)	352 (59.0%)	.	3,898 (55.7%)	.
>=80	90 (12.9%)	104 (17.4%)	.	1,038 (14.8%)	.
Age at cohort entry (years)			-0.075		0.114
Mean (SD)	68.2 (10.1)	69.0 (11.0)	.	66.9 (11.5)	.

IPCI	QVA N(%)	Fixed LABA LAMA N(%)	Std Dif	LABA N(%)	Std Dif
Total	699 (100.0%)	1,081 (100.0%)	0	1,526 (100.0%)	0
Year cohort entry			1.2041		0.2127
2013	13 (1.9%)		.	63 (4.1%)	.
2014	231 (33.1%)		.	402 (26.3%)	.
2015	250 (35.8%)	310 (28.7%)	.	520 (34.1%)	.
2016	205 (29.3%)	771 (71.3%)	.	541 (35.5%)	.
Gender			-0.1542		-0.1974
Male	425 (60.8%)	575 (53.2%)	.	779 (51.1%)	.
Female	274 (39.2%)	506 (46.8%)	.	747 (49.0%)	.
Age at cohort entry			-0.0177		0.0178
40-<60	150 (21.5%)	223 (20.6%)	.	383 (25.1%)	.
60-<80	459 (65.7%)	717 (66.3%)	.	902 (59.1%)	.
>=80	90 (12.9%)	141 (13.0%)	.	241 (15.8%)	.
Age at cohort entry (years)			-0.063		0.009
Mean (SD)	68.2 (10.1)	68.8 (10.0)	.	68.1 (11.3)	.

IPCI	QVA N(%)	LAMA	Std Dif
Total	699 (100.0%)	5,006 (100.0%)	0
Year cohort entry			0.1883
2013	13 (1.9%)	265 (5.3%)	.
2014	231 (33.1%)	1,618 (32.3%)	.
2015	250 (35.8%)	1,658 (33.1%)	.
2016	205 (29.3%)	1,465 (29.3%)	.
Gender			-0.1359
Male	425 (60.8%)	2,708 (54.1%)	.
Female	274 (39.2%)	2,298 (45.9%)	.
Age at cohort entry			0.0044
40-<60	150 (21.5%)	1,215 (24.3%)	.
60-<80	459 (65.7%)	3,004 (60.0%)	.
>=80	90 (12.9%)	787 (15.7%)	.
Age at cohort entry (years)			0.017
Mean (SD)	68.2 (10.1)	68.0 (10.8)	.

AARHUS	QVA N(%)	Free LABA+LAMA without ICS N(%)	Std Dif	Free LABA+LAMA with ICS N(%)	Std Dif
Total	1,807 (100.0%)	671 (100.0%)	0	242 (100.0%)	0
Year cohort entry			0.3969		0.4118
2013	28 (1.6%)	68 (10.1%)	.	26 (10.7%)	.
2014	735 (40.7%)	269 (40.1%)	.	96 (39.7%)	.
2015	565 (31.3%)	207 (30.9%)	.	74 (30.6%)	.
2016	479 (26.5%)	127 (18.9%)	.	46 (19.0%)	.
Gender			-0.0951		-0.2133
Male	953 (52.7%)	322 (48.0%)	.	102 (42.2%)	.
Female	854 (47.3%)	349 (52.0%)	.	140 (57.9%)	.
Age at cohort entry			-0.1153		0.0982
40-<60	247 (13.7%)	75 (11.2%)	.	38 (15.7%)	.
60-<80	1,189 (65.8%)	430 (64.1%)	.	163 (67.4%)	.
>=80	371 (20.5%)	166 (24.7%)	.	41 (16.9%)	.
Age at cohort entry (years)			-0.130		0.111
Mean (SD)	71.5 (10.0)	72.8 (9.8)	.	70.4 (10.1)	.

AARHUS	QVA N(%)	Free LABA+ICS N(%)	Std Dif	Fixed LABA ICS N(%)	Std Dif
Total	1,807 (100.0%)	273 (100.0%)	0	3,481 (100.0%)	0
Year cohort entry			0.3872		0.2439
2013	28 (1.6%)	29 (10.6%)	.	211 (6.1%)	.
2014	735 (40.7%)	103 (37.7%)	.	1,292 (37.1%)	.
2015	565 (31.3%)	75 (27.5%)	.	1,124 (32.3%)	.
2016	479 (26.5%)	66 (24.2%)	.	854 (24.5%)	.
Gender			-0.1025		-0.0937
Male	953 (52.7%)	130 (47.6%)	.	1,673 (48.1%)	.
Female	854 (47.3%)	143 (52.4%)	.	1,808 (51.9%)	.
Age at cohort entry			0.1609		0.0164
40-<60	247 (13.7%)	56 (20.5%)	.	688 (19.8%)	.
60-<80	1,189 (65.8%)	169 (61.9%)	.	1,916 (55.0%)	.
>=80	371 (20.5%)	48 (17.6%)	.	877 (25.2%)	.
Age at cohort entry (years)			0.182		0.053
Mean (SD)	71.5 (10.0)	69.6 (10.9)	.	70.9 (11.7)	.

AARHUS	QVA N(%)	Fixed LABA LAMA N(%)	Std Dif	LABA N(%)	Std Dif
Total	1,807 (100.0%)	1,758 (100.0%)	0	1,078 (100.0%)	0
Year cohort entry			1.0055		0.2714
2013	28 (1.6%)		.	74 (6.9%)	.
2014	735 (40.7%)	97 (5.5%)	.	395 (36.6%)	.
2015	565 (31.3%)	645 (36.7%)	.	340 (31.5%)	.
2016	479 (26.5%)	1,016 (57.8%)	.	269 (25.0%)	.
Gender			-0.0389		-0.0697
Male	953 (52.7%)	893 (50.8%)	.	531 (49.3%)	.
Female	854 (47.3%)	865 (49.2%)	.	547 (50.7%)	.
Age at cohort entry			-0.0137		0.0099
40-<60	247 (13.7%)	229 (13.0%)	.	159 (14.8%)	.
60-<80	1,189 (65.8%)	1,165 (66.3%)	.	693 (64.3%)	.
>=80	371 (20.5%)	364 (20.7%)	.	226 (21.0%)	.
Age at cohort entry (years)			-0.009		0.004
Mean (SD)	71.5 (10.0)	71.6 (9.8)	.	71.4 (10.7)	.

AARHUS	QVA N(%)	LAMA	Std Dif
Total	1,807 (100.0%)	2,095 (100.0%)	0
Year cohort entry			0.2825
2013	28 (1.6%)	151 (7.2%)	.
2014	735 (40.7%)	793 (37.9%)	.
2015	565 (31.3%)	654 (31.2%)	.
2016	479 (26.5%)	497 (23.7%)	.
Gender			-0.0629
Male	953 (52.7%)	1,039 (49.6%)	.
Female	854 (47.3%)	1,056 (50.4%)	.
Age at cohort entry			0.0075
40-<60	247 (13.7%)	359 (17.1%)	.
60-<80	1,189 (65.8%)	1,248 (59.6%)	.
>=80	371 (20.5%)	488 (23.3%)	.
Age at cohort entry (years)			0.029
Mean (SD)	71.5 (10.0)	71.2 (10.9)	.

HSD	QVA N(%)	Free LABA+LAMA without ICS N(%)	Std Dif	Free LABA+LAMA with ICS N(%)	Std Dif
Total	385 (100.0%)	995 (100.0%)	0	335 (100.0%)	0
Year cohort entry			1.1642		1.2544
2013		52 (5.2%)	.	20 (6.0%)	.
2014	2 (0.5%)	350 (35.2%)	.	128 (38.2%)	.
2015	144 (37.4%)	287 (28.8%)	.	90 (26.9%)	.
2016	170 (44.2%)	226 (22.7%)	.	71 (21.2%)	.
2017	69 (17.9%)	80 (8.0%)	.	26 (7.8%)	.
Gender			-0.0101		0.0139
Male	263 (68.3%)	675 (67.8%)	.	231 (69.0%)	.
Female	122 (31.7%)	320 (32.2%)	.	104 (31.0%)	.
Age at cohort entry			-0.0927		-0.141
40-<60	23 (6.0%)	71 (7.1%)	.	19 (5.7%)	.
60-<80	268 (69.6%)	625 (62.8%)	.	211 (63.0%)	.
>=80	94 (24.4%)	299 (30.1%)	.	105 (31.3%)	.
Age at cohort entry (years)			-0.084		-0.119
Mean (SD)	73.9 (8.8)	74.6 (9.1)	.	75.0 (9.3)	.

HSD	QVA N(%)	Free LABA+ICS N(%)	Std Dif	Fixed LABA ICS N(%)	Std Dif
Total	385 (100.0%)	437 (100.0%)	0	5,897 (100.0%)	0
Year cohort entry			1.2717		1.0791
2013		33 (7.6%)	.	326 (5.5%)	.
2014	2 (0.5%)	162 (37.1%)	.	1,887 (32.0%)	.
2015	144 (37.4%)	120 (27.5%)	.	1,621 (27.5%)	.
2016	170 (44.2%)	87 (19.9%)	.	1,440 (24.4%)	.
2017	69 (17.9%)	35 (8.0%)	.	623 (10.6%)	.
Gender			-0.1419		-0.2814
Male	263 (68.3%)	269 (61.6%)	.	3,229 (54.8%)	.
Female	122 (31.7%)	168 (38.4%)	.	2,668 (45.2%)	.
Age at cohort entry			-0.0567		0.045
40-<60	23 (6.0%)	32 (7.3%)	.	830 (14.1%)	.
60-<80	268 (69.6%)	281 (64.3%)	.	3,377 (57.3%)	.
>=80	94 (24.4%)	124 (28.4%)	.	1,690 (28.7%)	.
Age at cohort entry (years)			-0.036		0.111
Mean (SD)	73.9 (8.8)	74.2 (9.9)	.	72.8 (11.0)	.

HSD	QVA N(%)	Fixed LABA LAMA N(%)	Std Dif	LABA N(%)	Std Dif
Total	385 (100.0%)	426 (100.0%)	0	875 (100.0%)	0
Year cohort entry			0.7522		1.2374
2013			.	65 (7.4%)	.
2014	2 (0.5%)		.	308 (35.2%)	.
2015	144 (37.4%)	47 (11.0%)	.	262 (29.9%)	.
2016	170 (44.2%)	199 (46.7%)	.	175 (20.0%)	.
2017	69 (17.9%)	180 (42.3%)	.	65 (7.4%)	.
Gender			0.0458		-0.1927
Male	263 (68.3%)	300 (70.4%)	.	517 (59.1%)	.
Female	122 (31.7%)	126 (29.6%)	.	358 (40.9%)	.
Age at cohort entry			0.0331		0.1037
40-<60	23 (6.0%)	38 (8.9%)	.	115 (13.1%)	.
60-<80	268 (69.6%)	281 (66.0%)	.	542 (61.9%)	.
>=80	94 (24.4%)	107 (25.1%)	.	218 (24.9%)	.
Age at cohort entry (years)			0.093		0.170
Mean (SD)	73.9 (8.8)	73.1 (9.0)	.	72.2 (10.5)	.

HSD	QVA N(%)	LAMA	Std Dif
Total	385 (100.0%)	3,595 (100.0%)	0
Year cohort entry			1.1565
2013		229 (6.4%)	.
2014	2 (0.5%)	1,233 (34.3%)	.
2015	144 (37.4%)	963 (26.8%)	.
2016	170 (44.2%)	827 (23.0%)	.
2017	69 (17.9%)	343 (9.5%)	.
Gender			-0.182
Male	263 (68.3%)	2,143 (59.6%)	.
Female	122 (31.7%)	1,452 (40.4%)	.
Age at cohort entry			-0.0837
40-<60	23 (6.0%)	367 (10.2%)	.
60-<80	268 (69.6%)	2,075 (57.7%)	.
>=80	94 (24.4%)	1,153 (32.1%)	.
Age at cohort entry (years)			-0.026
Mean (SD)	73.9 (8.8)	74.1 (10.3)	.

SIDIAP	QVA N(%)	Free LABA+LAMA without ICS N(%)	Std Dif	Free LABA+LAMA with ICS N(%)	Std Dif
Total	5,561 (100.0%)	4,219 (100.0%)	0	1,725 (100.0%)	0
Year cohort entry			0.5315		0.5366
2013		361 (8.6%)	.	125 (7.3%)	.
2014	1,898 (34.1%)	1,878 (44.5%)	.	823 (47.7%)	.
2015	2,917 (52.5%)	1,621 (38.4%)	.	627 (36.4%)	.
2016	746 (13.4%)	359 (8.5%)	.	150 (8.7%)	.
Gender			0.0623		0.0149
Male	4,510 (81.1%)	3,522 (83.5%)	.	1,409 (81.7%)	.
Female	1,051 (18.9%)	697 (16.5%)	.	316 (18.3%)	.
Age at cohort entry			-0.0281		-0.1733
40-<60	812 (14.6%)	590 (14.0%)	.	168 (9.7%)	.
60-<80	3,496 (62.9%)	2,633 (62.4%)	.	1,072 (62.1%)	.
>=80	1,253 (22.5%)	996 (23.6%)	.	485 (28.1%)	.
Age at cohort entry (years)			-0.041		-0.221
Mean (SD)	71.3 (10.3)	71.7 (10.3)	.	73.5 (9.8)	.

SIDIAP	QVA N(%)	Free LABA+ICS N(%)	Std Dif	Fixed LABA ICS N(%)	Std Dif
Total	5,561 (100.0%)	2,738 (100.0%)	0	20638 (100.0%)	0
Year cohort entry			0.5671		0.4559
2013		263 (9.6%)	.	1,519 (7.4%)	.
2014	1,898 (34.1%)	1,232 (45.0%)	.	8,538 (41.4%)	.
2015	2,917 (52.5%)	1,004 (36.7%)	.	8,470 (41.0%)	.
2016	746 (13.4%)	239 (8.7%)	.	2,111 (10.2%)	.
Gender			-0.3144		-0.2907
Male	4,510 (81.1%)	1,849 (67.5%)	.	14162 (68.6%)	.
Female	1,051 (18.9%)	889 (32.5%)	.	6,476 (31.4%)	.
Age at cohort entry			-0.1197		-0.0024
40-<60	812 (14.6%)	411 (15.0%)	.	3,705 (18.0%)	.
60-<80	3,496 (62.9%)	1,504 (54.9%)	.	11627 (56.3%)	.
>=80	1,253 (22.5%)	823 (30.1%)	.	5,306 (25.7%)	.
Age at cohort entry (years)			-0.143		0.006
Mean (SD)	71.3 (10.3)	72.9 (11.4)	.	71.2 (11.6)	.

SIDIAP	QVA N(%)	Fixed LABA LAMA N(%)	Std Dif	LABA N(%)	Std Dif
Total	5,561 (100.0%)	964 (100.0%)	0	5,879 (100.0%)	0
Year cohort entry			1.2772		0.5005
2013			.	463 (7.9%)	.
2014	1,898 (34.1%)		.	2,572 (43.8%)	.
2015	2,917 (52.5%)	454 (47.1%)	.	2,310 (39.3%)	.
2016	746 (13.4%)	510 (52.9%)	.	534 (9.1%)	.
Gender			-0.0231		-0.1721
Male	4,510 (81.1%)	773 (80.2%)	.	4,347 (73.9%)	.
Female	1,051 (18.9%)	191 (19.8%)	.	1,532 (26.1%)	.
Age at cohort entry			0.074		0.1168
40-<60	812 (14.6%)	141 (14.6%)	.	1,182 (20.1%)	.
60-<80	3,496 (62.9%)	646 (67.0%)	.	3,482 (59.2%)	.
>=80	1,253 (22.5%)	177 (18.4%)	.	1,215 (20.7%)	.
Age at cohort entry (years)			0.046		0.119
Mean (SD)	71.3 (10.3)	70.8 (9.9)	.	70.0 (11.2)	.

SIDIAP	QVA N(%)	LAMA	Std Dif
Total	5,561 (100.0%)	13678 (100.0%)	0
Year cohort entry			0.4391
2013		918 (6.7%)	.
2014	1,898 (34.1%)	5,702 (41.7%)	.
2015	2,917 (52.5%)	5,624 (41.1%)	.
2016	746 (13.4%)	1,434 (10.5%)	.
Gender			-0.1149
Male	4,510 (81.1%)	10451 (76.4%)	.
Female	1,051 (18.9%)	3,227 (23.6%)	.
Age at cohort entry			0.0875
40-<60	812 (14.6%)	2,589 (18.9%)	.
60-<80	3,496 (62.9%)	8,169 (59.7%)	.
>=80	1,253 (22.5%)	2,920 (21.4%)	.
Age at cohort entry (years)			0.094
Mean (SD)	71.3 (10.3)	70.3 (10.9)	.

Table 15-2 Smoking status and GP contacts (pooled and by database)

POOLED	QVA N(%)	Free LABA+LAMA without ICS N(%)	Std Dif	Free LABA+LAMA with ICS N(%)	Std Dif
Smoking status			0.104		0.1641
Current smoker	3,089 (33.8%)	3,279 (35.9%)	.	804 (26.8%)	.
Past smoker	4,785 (52.4%)	4,814 (52.7%)	.	1,674 (55.7%)	.
Never smoker	1,265 (13.8%)	1,041 (11.4%)	.	527 (17.5%)	.
Unknown	659 (6.7%)	485 (5.0%)	.	187 (5.9%)	.
Smoking status (imputed)			0.0661		0.1686
Current smoker	(34.3%)	(36.2%)	.	(27.2%)	.
Past smoker	(52.1%)	(52.3%)	.	(55.3%)	.
Never smoker	(13.6%)	(11.5%)	.	(17.5%)	.
Number of contacts with GP at home			0.05		-0.0548
None	8,125 (82.9%)	8,153 (84.8%)	.	2,580 (80.8%)	.
1	813 (8.3%)	721 (7.5%)	.	296 (9.3%)	.
2	300 (3.1%)	260 (2.7%)	.	104 (3.3%)	.
3 or more	560 (5.7%)	485 (5.0%)	.	212 (6.6%)	.
Number of contacts with GP at practice			-0.0459		-0.1268
None	366 (3.7%)	222 (2.3%)	.	54 (1.7%)	.
1	365 (3.7%)	378 (3.9%)	.	97 (3.0%)	.
2	518 (5.3%)	493 (5.1%)	.	134 (4.2%)	.
3 or more	8,549 (87.3%)	8,526 (88.6%)	.	2,907 (91.1%)	.

POOLED	QVA N(%)	Free LABA+ICS N(%)	Std Dif	Fixed LABA ICS N(%)	Std Dif
Smoking status			0.3157		0.141

POOLED	QVA N(%)	Free LABA+ICS N(%)	Std Dif	Fixed LABA ICS N(%)	Std Dif
Current smoker	3,089 (33.8%)	1,128 (25.8%)	.	19980 (36.3%)	.
Past smoker	4,785 (52.4%)	2,099 (48.0%)	.	25405 (46.1%)	.
Never smoker	1,265 (13.8%)	1,144 (26.2%)	.	9,695 (17.6%)	.
Unknown	659 (6.7%)	257 (5.6%)	.	3,252 (5.6%)	.
Smoking status (imputed)			0.3236		0.1391
Current smoker	(34.3%)	(26.2%)	.	(36.5%)	.
Past smoker	(52.1%)	(48.0%)	.	(46.0%)	.
Never smoker	(13.6%)	(25.9%)	.	(17.6%)	.
Number of contacts with GP at home			-0.033		0.0203
None	8,125 (82.9%)	3,789 (81.9%)	.	48849 (83.7%)	.
1	813 (8.3%)	367 (7.9%)	.	4,455 (7.6%)	.
2	300 (3.1%)	132 (2.9%)	.	1,666 (2.9%)	.
3 or more	560 (5.7%)	340 (7.4%)	.	3,362 (5.8%)	.
Number of contacts with GP at practice			-0.0506		0.1167
None	366 (3.7%)	122 (2.6%)	.	2,765 (4.7%)	.
1	365 (3.7%)	180 (3.9%)	.	3,200 (5.5%)	.
2	518 (5.3%)	214 (4.6%)	.	3,888 (6.7%)	.
3 or more	8,549 (87.3%)	4,112 (88.9%)	.	48479 (83.1%)	.

POOLED	QVA N(%)	Fixed LABA LAMA N(%)	Std Dif	LABA N(%)	Std Dif
Smoking status			0.2817		0.1272
Current smoker	3,089 (33.8%)	3,373 (38.9%)	.	4,439 (38.0%)	.
Past smoker	4,785 (52.4%)	4,804 (55.5%)	.	5,430 (46.4%)	.
Never smoker	1,265 (13.8%)	485 (5.6%)	.	1,824 (15.6%)	.
Unknown	659 (6.7%)	488 (5.3%)	.	671 (5.4%)	.
Smoking status (imputed)			0.2721		0.1152
Current smoker	(34.3%)	(39.3%)	.	(38.2%)	.
Past smoker	(52.1%)	(55.0%)	.	(46.4%)	.
Never smoker	(13.6%)	(5.7%)	.	(15.4%)	.
Number of contacts with GP at home			0.0082		0.0829
None	8,125 (82.9%)	7,613 (83.2%)	.	10631 (86.0%)	.
1	813 (8.3%)	758 (8.3%)	.	822 (6.7%)	.
2	300 (3.1%)	285 (3.1%)	.	294 (2.4%)	.
3 or more	560 (5.7%)	494 (5.4%)	.	617 (5.0%)	.
Number of contacts with GP at practice			0.186		0.0627
None	366 (3.7%)	632 (6.9%)	.	469 (3.8%)	.
1	365 (3.7%)	508 (5.6%)	.	585 (4.7%)	.
2	518 (5.3%)	634 (6.9%)	.	799 (6.5%)	.
3 or more	8,549 (87.3%)	7,376 (80.6%)	.	10511 (85.0%)	.

POOLED	QVA N(%)	LAMA	Std Dif
Smoking status			0.1949
Current smoker	3,089 (33.8%)	17206 (41.8%)	.
Past smoker	4,785 (52.4%)	18841 (45.8%)	.
Never smoker	1,265 (13.8%)	5,095 (12.4%)	.
Unknown	659 (6.7%)	1,830 (4.3%)	.
Smoking status (imputed)			0.1563
Current smoker	(34.3%)	(41.8%)	.
Past smoker	(52.1%)	(45.7%)	.
Never smoker	(13.6%)	(12.5%)	.
Number of contacts with GP at home			0.0896
None	8,125 (82.9%)	37026 (86.2%)	.
1	813 (8.3%)	2,921 (6.8%)	.
2	300 (3.1%)	1,041 (2.4%)	.
3 or more	560 (5.7%)	1,984 (4.6%)	.
Number of contacts with GP at practice			0.108
None	366 (3.7%)	1,768 (4.1%)	.
1	365 (3.7%)	2,366 (5.5%)	.
2	518 (5.3%)	3,024 (7.0%)	.
3 or more	8,549 (87.3%)	35814 (83.3%)	.

THIN	QVA N(%)	Free LABA+LAMA without ICS N(%)	Std Dif	Free LABA+LAMA with ICS N(%)	Std Dif
Smoking status			0.0574		0.2923
Current smoker	526 (39.1%)	1,012 (39.1%)	.	120 (30.5%)	.

THIN	QVA N(%)	Free LABA+LAMA without ICS N(%)	Std Dif	Free LABA+LAMA with ICS N(%)	Std Dif
Past smoker	767 (57.0%)	1,494 (57.8%)	.	233 (59.1%)	.
Never smoker	52 (3.9%)	80 (3.1%)	.	41 (10.4%)	.
Unknown	1 (0.1%)		.		.
Smoking status (imputed)			0.0425		0.29
Current smoker	(39.1%)	(39.1%)	.	(30.5%)	.
Past smoker	(57.0%)	(57.8%)	.	(59.1%)	.
Never smoker	(3.9%)	(3.1%)	.	(10.4%)	.
Number of contacts with GP at home			0.0755		0.0174
None	1,101 (81.8%)	2,188 (84.6%)	.	324 (82.2%)	.
1	130 (9.7%)	213 (8.2%)	.	42 (10.7%)	.
2	43 (3.2%)	72 (2.8%)	.	11 (2.8%)	.
3 or more	72 (5.4%)	113 (4.4%)	.	17 (4.3%)	.
Number of contacts with GP at practice			-0.1077		-0.2193
None	63 (4.7%)	96 (3.7%)	.	13 (3.3%)	.
1	87 (6.5%)	123 (4.8%)	.	11 (2.8%)	.
2	110 (8.2%)	176 (6.8%)	.	21 (5.3%)	.
3 or more	1,086 (80.7%)	2,191 (84.7%)	.	349 (88.6%)	.

THIN	QVA N(%)	Free LABA+ICS N(%)	Std Dif	Fixed LABA ICS N(%)	Std Dif
Smoking status			0.3185		0.1428
Current smoker	526 (39.1%)	192 (32.9%)	.	8,497 (39.9%)	.
Past smoker	767 (57.0%)	320 (54.9%)	.	11329 (53.2%)	.
Never smoker	52 (3.9%)	71 (12.2%)	.	1,477 (6.9%)	.
Unknown	1 (0.1%)		.	12 (0.1%)	.
Smoking status (imputed)			0.3164		0.1428
Current smoker	(39.1%)	(32.9%)	.	(39.9%)	.
Past smoker	(57.0%)	(54.9%)	.	(53.2%)	.
Never smoker	(3.9%)	(12.2%)	.	(6.9%)	.
Number of contacts with GP at home			0.0382		0.0737
None	1,101 (81.8%)	486 (83.4%)	.	18051 (84.7%)	.
1	130 (9.7%)	47 (8.1%)	.	1,594 (7.5%)	.
2	43 (3.2%)	21 (3.6%)	.	580 (2.7%)	.
3 or more	72 (5.4%)	29 (5.0%)	.	1,090 (5.1%)	.
Number of contacts with GP at practice			-0.1086		0.0081
None	63 (4.7%)	21 (3.6%)	.	1,053 (4.9%)	.
1	87 (6.5%)	34 (5.8%)	.	1,450 (6.8%)	.
2	110 (8.2%)	33 (5.7%)	.	1,664 (7.8%)	.
3 or more	1,086 (80.7%)	495 (84.9%)	.	17148 (80.5%)	.

THIN	QVA N(%)	Fixed LABA LAMA N(%)	Std Dif	LABA N(%)	Std Dif
Smoking status			0.0435		0.0354
Current smoker	526 (39.1%)	1,948 (39.6%)	.	1,179 (39.2%)	.
Past smoker	767 (57.0%)	2,814 (57.2%)	.	1,692 (56.3%)	.
Never smoker	52 (3.9%)	158 (3.2%)	.	134 (4.5%)	.
Unknown	1 (0.1%)	1 (0.0%)	.	1 (0.0%)	.
Smoking status (imputed)			0.0356		0.0307
Current smoker	(39.1%)	(39.6%)	.	(39.3%)	.
Past smoker	(57.0%)	(57.2%)	.	(56.3%)	.
Never smoker	(3.9%)	(3.2%)	.	(4.5%)	.
Number of contacts with GP at home			0.1262		0.1157
None	1,101 (81.8%)	4,253 (86.4%)	.	2,588 (86.1%)	.
1	130 (9.7%)	353 (7.2%)	.	213 (7.1%)	.
2	43 (3.2%)	117 (2.4%)	.	81 (2.7%)	.
3 or more	72 (5.4%)	198 (4.0%)	.	124 (4.1%)	.
Number of contacts with GP at practice			0.0343		-0.0405
None	63 (4.7%)	258 (5.2%)	.	103 (3.4%)	.
1	87 (6.5%)	336 (6.8%)	.	168 (5.6%)	.
2	110 (8.2%)	422 (8.6%)	.	271 (9.0%)	.
3 or more	1,086 (80.7%)	3,905 (79.4%)	.	2,464 (82.0%)	.

THIN	QVA N(%)	LAMA	Std Dif
Smoking status			0.1378
Current smoker	526 (39.1%)	8,287 (44.6%)	.
Past smoker	767 (57.0%)	9,354 (50.3%)	.
Never smoker	52 (3.9%)	946 (5.1%)	.
Unknown	1 (0.1%)	11 (0.1%)	.
Smoking status (imputed)			0.1375
Current smoker	(39.1%)	(44.6%)	.
Past smoker	(57.0%)	(50.3%)	.
Never smoker	(3.9%)	(5.1%)	.
Number of contacts with GP at home			0.1412
None	1,101 (81.8%)	16174 (87.0%)	.
1	130 (9.7%)	1,236 (6.7%)	.
2	43 (3.2%)	456 (2.5%)	.
3 or more	72 (5.4%)	732 (3.9%)	.
Number of contacts with GP at practice			-0.0067
None	63 (4.7%)	810 (4.4%)	.
1	87 (6.5%)	1,218 (6.6%)	.
2	110 (8.2%)	1,524 (8.2%)	.
3 or more	1,086 (80.7%)	15046 (80.9%)	.

IPCI	QVA N(%)	Free LABA+LAMA without ICS N(%)	Std Dif	Free LABA+LAMA with ICS N(%)	Std Dif
Smoking status			0.1355		0.4215
Current smoker	337 (50.8%)	489 (44.4%)	.	147 (31.6%)	.

IPCI	QVA N(%)	Free LABA+LAMA without ICS N(%)	Std Dif	Free LABA+LAMA with ICS N(%)	Std Dif
Past smoker	302 (45.6%)	568 (51.6%)	.	273 (58.7%)	.
Never smoker	24 (3.6%)	44 (4.0%)	.	45 (9.7%)	.
Unknown	36 (5.2%)	47 (4.1%)	.	31 (6.3%)	.
Smoking status (imputed)			0.1358		0.442
Current smoker	(50.9%)	(44.2%)	.	(31.3%)	.
Past smoker	(45.4%)	(51.7%)	.	(58.8%)	.
Never smoker	(3.7%)	(4.1%)	.	(10.0%)	.
Number of contacts with GP at home			0.0449		-0.0275
None	504 (72.1%)	854 (74.4%)	.	353 (71.2%)	.
1	86 (12.3%)	120 (10.5%)	.	59 (11.9%)	.
2	30 (4.3%)	45 (3.9%)	.	20 (4.0%)	.
3 or more	79 (11.3%)	129 (11.2%)	.	64 (12.9%)	.
Number of contacts with GP at practice			-0.1434		-0.1395
None	31 (4.4%)	29 (2.5%)	.	18 (3.6%)	.
1	49 (7.0%)	60 (5.2%)	.	29 (5.9%)	.
2	57 (8.2%)	76 (6.6%)	.	23 (4.6%)	.
3 or more	562 (80.4%)	983 (85.6%)	.	426 (85.9%)	.

IPCI	QVA N(%)	Free LABA+ICS N(%)	Std Dif	Fixed LABA ICS N(%)	Std Dif
Smoking status			0.6039		0.2895
Current smoker	337 (50.8%)	140 (25.5%)	.	2,826 (43.4%)	.
Past smoker	302 (45.6%)	328 (59.6%)	.	2,994 (46.0%)	.
Never smoker	24 (3.6%)	82 (14.9%)	.	693 (10.6%)	.
Unknown	36 (5.2%)	47 (7.9%)	.	488 (7.0%)	.
Smoking status (imputed)			0.624		0.2877
Current smoker	(50.9%)	(25.3%)	.	(43.1%)	.
Past smoker	(45.4%)	(59.2%)	.	(46.2%)	.
Never smoker	(3.7%)	(15.5%)	.	(10.6%)	.
Number of contacts with GP at home			-0.0578		0.0802
None	504 (72.1%)	422 (70.7%)	.	5,327 (76.1%)	.
1	86 (12.3%)	56 (9.4%)	.	635 (9.1%)	.
2	30 (4.3%)	23 (3.9%)	.	264 (3.8%)	.
3 or more	79 (11.3%)	96 (16.1%)	.	775 (11.1%)	.
Number of contacts with GP at practice			-0.0973		0.0296
None	31 (4.4%)	25 (4.2%)	.	356 (5.1%)	.
1	49 (7.0%)	38 (6.4%)	.	491 (7.0%)	.
2	57 (8.2%)	30 (5.0%)	.	606 (8.7%)	.
3 or more	562 (80.4%)	504 (84.4%)	.	5,548 (79.3%)	.

IPCI	QVA N(%)	Fixed LABA LAMA N(%)	Std Dif	LABA N(%)	Std Dif
Smoking status			0.1676		0.1589
Current smoker	337 (50.8%)	437 (42.4%)	.	636 (44.0%)	.
Past smoker	302 (45.6%)	552 (53.5%)	.	722 (49.9%)	.
Never smoker	24 (3.6%)	42 (4.1%)	.	88 (6.1%)	.
Unknown	36 (5.2%)	50 (4.6%)	.	80 (5.2%)	.
Smoking status (imputed)			0.1757		0.1755
Current smoker	(50.9%)	(42.2%)	.	(43.6%)	.
Past smoker	(45.4%)	(53.4%)	.	(50.1%)	.
Never smoker	(3.7%)	(4.4%)	.	(6.4%)	.
Number of contacts with GP at home			-0.0071		0.0967
None	504 (72.1%)	779 (72.1%)	.	1,175 (77.0%)	.
1	86 (12.3%)	119 (11.0%)	.	126 (8.3%)	.
2	30 (4.3%)	56 (5.2%)	.	49 (3.2%)	.
3 or more	79 (11.3%)	127 (11.8%)	.	176 (11.5%)	.
Number of contacts with GP at practice			-0.0852		-0.0351
None	31 (4.4%)	35 (3.2%)	.	62 (4.1%)	.
1	49 (7.0%)	55 (5.1%)	.	107 (7.0%)	.
2	57 (8.2%)	89 (8.2%)	.	108 (7.1%)	.
3 or more	562 (80.4%)	902 (83.4%)	.	1,249 (81.9%)	.

IPCI	QVA N(%)	LAMA	Std Dif
Smoking status			0.1148
Current smoker	337 (50.8%)	2,319 (48.6%)	.
Past smoker	302 (45.6%)	2,159 (45.3%)	.
Never smoker	24 (3.6%)	290 (6.1%)	.
Unknown	36 (5.2%)	238 (4.8%)	.
Smoking status (imputed)			0.1206
Current smoker	(50.9%)	(48.4%)	.
Past smoker	(45.4%)	(45.3%)	.
Never smoker	(3.7%)	(6.2%)	.
Number of contacts with GP at home			0.1319
None	504 (72.1%)	3,921 (78.3%)	.
1	86 (12.3%)	391 (7.8%)	.
2	30 (4.3%)	178 (3.6%)	.
3 or more	79 (11.3%)	516 (10.3%)	.
Number of contacts with GP at practice			-0.0022
None	31 (4.4%)	229 (4.6%)	.
1	49 (7.0%)	346 (6.9%)	.
2	57 (8.2%)	400 (8.0%)	.
3 or more	562 (80.4%)	4,031 (80.5%)	.

AARHUS	QVA N(%)	Free LABA+LAMA without ICS N(%)	Std Dif	Free LABA+LAMA with ICS N(%)	Std Dif
Smoking status			0.2102		0.1799
Current smoker	551 (41.4%)	177 (40.8%)	.	64 (40.3%)	.
Past smoker	742 (55.7%)	237 (54.6%)	.	89 (56.0%)	.
Never smoker	39 (2.9%)	20 (4.6%)	.	6 (3.8%)	.
Unknown	475 (26.3%)	237 (35.3%)	.	83 (34.3%)	.
Smoking status (imputed)			0.068		0.0446
Current smoker	(41.2%)	(42.3%)	.	(40.5%)	.
Past smoker	(54.7%)	(52.3%)	.	(54.5%)	.
Never smoker	(4.1%)	(5.4%)	.	(5.0%)	.
Number of contacts with GP at home			0.0394		0.0452
None	1,257 (69.6%)	481 (71.7%)	.	173 (71.5%)	.
1	234 (13.0%)	73 (10.9%)	.	31 (12.8%)	.
2	104 (5.8%)	41 (6.1%)	.	12 (5.0%)	.
3 or more	212 (11.7%)	76 (11.3%)	.	26 (10.7%)	.
Number of contacts with GP at practice			-0.2459		-0.2715
None	152 (8.4%)	12 (1.8%)	.	4 (1.7%)	.
1	35 (1.9%)	14 (2.1%)	.	2 (0.8%)	.
2	33 (1.8%)	11 (1.6%)	.	6 (2.5%)	.
3 or more	1,587 (87.8%)	634 (94.5%)	.	230 (95.0%)	.

AARHUS	QVA N(%)	Free LABA+ICS N(%)	Std Dif	Fixed LABA ICS N(%)	Std Dif
Smoking status			0.3412		0.2643
Current smoker	551 (41.4%)	65 (37.6%)	.	1,085 (46.0%)	.
Past smoker	742 (55.7%)	90 (52.0%)	.	1,084 (45.9%)	.
Never smoker	39 (2.9%)	18 (10.4%)	.	192 (8.1%)	.
Unknown	475 (26.3%)	100 (36.6%)	.	1,120 (32.2%)	.
Smoking status (imputed)			0.2194		0.1906
Current smoker	(41.2%)	(37.7%)	.	(45.7%)	.
Past smoker	(54.7%)	(52.7%)	.	(46.9%)	.
Never smoker	(4.1%)	(9.6%)	.	(7.5%)	.
Number of contacts with GP at home			-0.0249		-0.0929
None	1,257 (69.6%)	188 (68.9%)	.	2,282 (65.6%)	.
1	234 (13.0%)	35 (12.8%)	.	463 (13.3%)	.
2	104 (5.8%)	11 (4.0%)	.	239 (6.9%)	.
3 or more	212 (11.7%)	39 (14.3%)	.	497 (14.3%)	.
Number of contacts with GP at practice			-0.2234		0.0142
None	152 (8.4%)	10 (3.7%)	.	276 (7.9%)	.
1	35 (1.9%)	3 (1.1%)	.	86 (2.5%)	.
2	33 (1.8%)	3 (1.1%)	.	82 (2.4%)	.
3 or more	1,587 (87.8%)	257 (94.1%)	.	3,037 (87.3%)	.

AARHUS	QVA N(%)	Fixed LABA LAMA N(%)	Std Dif	LABA N(%)	Std Dif
Smoking status			0.1615		0.2854
Current smoker	551 (41.4%)	569 (40.9%)	.	302 (43.8%)	.
Past smoker	742 (55.7%)	752 (54.0%)	.	336 (48.7%)	.
Never smoker	39 (2.9%)	71 (5.1%)	.	52 (7.5%)	.
Unknown	475 (26.3%)	366 (20.8%)	.	388 (36.0%)	.
Smoking status (imputed)			0.0517		0.154
Current smoker	(41.2%)	(41.8%)	.	(44.6%)	.
Past smoker	(54.7%)	(53.1%)	.	(48.5%)	.
Never smoker	(4.1%)	(5.1%)	.	(6.8%)	.
Number of contacts with GP at home			0.2046		0.114
None	1,257 (69.6%)	1,372 (78.0%)	.	806 (74.8%)	.
1	234 (13.0%)	190 (10.8%)	.	112 (10.4%)	.
2	104 (5.8%)	79 (4.5%)	.	58 (5.4%)	.
3 or more	212 (11.7%)	117 (6.7%)	.	102 (9.5%)	.
Number of contacts with GP at practice			0.3452		0.0431
None	152 (8.4%)	311 (17.7%)	.	99 (9.2%)	.
1	35 (1.9%)	73 (4.2%)	.	29 (2.7%)	.
2	33 (1.8%)	65 (3.7%)	.	19 (1.8%)	.
3 or more	1,587 (87.8%)	1,309 (74.5%)	.	931 (86.4%)	.

AARHUS	QVA N(%)	LAMA	Std Dif
Smoking status			0.3096
Current smoker	551 (41.4%)	662 (48.4%)	.
Past smoker	742 (55.7%)	598 (43.7%)	.
Never smoker	39 (2.9%)	109 (8.0%)	.
Unknown	475 (26.3%)	726 (34.7%)	.
Smoking status (imputed)			0.2167
Current smoker	(41.2%)	(47.9%)	.
Past smoker	(54.7%)	(44.9%)	.
Never smoker	(4.1%)	(7.2%)	.
Number of contacts with GP at home			0.0184
None	1,257 (69.6%)	1,478 (70.6%)	.
1	234 (13.0%)	253 (12.1%)	.
2	104 (5.8%)	121 (5.8%)	.
3 or more	212 (11.7%)	243 (11.6%)	.
Number of contacts with GP at practice			0.0616
None	152 (8.4%)	200 (9.6%)	.
1	35 (1.9%)	47 (2.2%)	.
2	33 (1.8%)	53 (2.5%)	.
3 or more	1,587 (87.8%)	1,795 (85.7%)	.

HSD	QVA N(%)	Free LABA+LAMA without ICS N(%)	Std Dif	Free LABA+LAMA with ICS N(%)	Std Dif
Smoking status			0.0991		0.2047
Current smoker	135 (40.9%)	311 (37.2%)	.	89 (33.0%)	.
Past smoker	139 (42.1%)	391 (46.8%)	.	131 (48.5%)	.
Never smoker	56 (17.0%)	134 (16.0%)	.	50 (18.5%)	.
Unknown	55 (14.3%)	159 (16.0%)	.	65 (19.4%)	.
Smoking status (imputed)			0.0751		0.1737
Current smoker	(41.0%)	(37.7%)	.	(32.7%)	.
Past smoker	(41.5%)	(44.9%)	.	(46.9%)	.
Never smoker	(17.6%)	(17.4%)	.	(20.5%)	.
Number of contacts with GP at home			-0.0789		-0.2591
None	333 (86.5%)	836 (84.0%)	.	258 (77.0%)	.
1	36 (9.4%)	83 (8.3%)	.	39 (11.6%)	.
2	4 (1.0%)	30 (3.0%)	.	14 (4.2%)	.
3 or more	12 (3.1%)	46 (4.6%)	.	24 (7.2%)	.
Number of contacts with GP at practice			0.0562		-0.0014
None	7 (1.8%)	29 (2.9%)	.	6 (1.8%)	.
1	7 (1.8%)	32 (3.2%)	.	8 (2.4%)	.
2	15 (3.9%)	28 (2.8%)	.	11 (3.3%)	.
3 or more	356 (92.5%)	906 (91.1%)	.	310 (92.5%)	.

HSD	QVA N(%)	Free LABA+ICS N(%)	Std Dif	Fixed LABA ICS N(%)	Std Dif
Smoking status			0.2747		0.2703
Current smoker	135 (40.9%)	103 (28.2%)	.	1,778 (37.6%)	.
Past smoker	139 (42.1%)	170 (46.6%)	.	1,674 (35.4%)	.
Never smoker	56 (17.0%)	92 (25.2%)	.	1,281 (27.1%)	.
Unknown	55 (14.3%)	72 (16.5%)	.	1,164 (19.7%)	.
Smoking status (imputed)			0.2755		0.2287
Current smoker	(41.0%)	(29.1%)	.	(37.1%)	.
Past smoker	(41.5%)	(45.1%)	.	(35.9%)	.
Never smoker	(17.6%)	(25.8%)	.	(27.0%)	.
Number of contacts with GP at home			-0.0967		-0.0063
None	333 (86.5%)	365 (83.5%)	.	5,103 (86.5%)	.
1	36 (9.4%)	33 (7.6%)	.	429 (7.3%)	.
2	4 (1.0%)	13 (3.0%)	.	120 (2.0%)	.
3 or more	12 (3.1%)	26 (6.0%)	.	245 (4.2%)	.
Number of contacts with GP at practice			0.0203		0.2171
None	7 (1.8%)	10 (2.3%)	.	310 (5.3%)	.
1	7 (1.8%)	11 (2.5%)	.	246 (4.2%)	.
2	15 (3.9%)	14 (3.2%)	.	267 (4.5%)	.
3 or more	356 (92.5%)	402 (92.0%)	.	5,074 (86.0%)	.

HSD	QVA N(%)	Fixed LABA LAMA N(%)	Std Dif	LABA N(%)	Std Dif
Smoking status			0.1326		0.1725
Current smoker	135 (40.9%)	138 (37.8%)	.	293 (40.0%)	.
Past smoker	139 (42.1%)	178 (48.8%)	.	266 (36.3%)	.
Never smoker	56 (17.0%)	49 (13.4%)	.	174 (23.7%)	.
Unknown	55 (14.3%)	61 (14.3%)	.	142 (16.2%)	.
Smoking status (imputed)			0.1238		0.1718
Current smoker	(41.0%)	(39.7%)	.	(39.5%)	.
Past smoker	(41.5%)	(46.5%)	.	(36.2%)	.
Never smoker	(17.6%)	(13.8%)	.	(24.3%)	.
Number of contacts with GP at home			0.0183		0.0026
None	333 (86.5%)	372 (87.3%)	.	759 (86.7%)	.
1	36 (9.4%)	29 (6.8%)	.	70 (8.0%)	.
2	4 (1.0%)	12 (2.8%)	.	11 (1.3%)	.
3 or more	12 (3.1%)	13 (3.1%)	.	35 (4.0%)	.
Number of contacts with GP at practice			-0.141		0.1146
None	7 (1.8%)	3 (0.7%)	.	37 (4.2%)	.
1	7 (1.8%)	6 (1.4%)	.	27 (3.1%)	.
2	15 (3.9%)	9 (2.1%)	.	29 (3.3%)	.
3 or more	356 (92.5%)	408 (95.8%)	.	782 (89.4%)	.

HSD	QVA N(%)	LAMA	Std Dif
Smoking status			0.2082
Current smoker	135 (40.9%)	1,127 (38.0%)	.
Past smoker	139 (42.1%)	1,091 (36.8%)	.
Never smoker	56 (17.0%)	749 (25.2%)	.
Unknown	55 (14.3%)	628 (17.5%)	.
Smoking status (imputed)			0.1931
Current smoker	(41.0%)	(37.7%)	.
Past smoker	(41.5%)	(36.9%)	.
Never smoker	(17.6%)	(25.4%)	.
Number of contacts with GP at home			-0.0369
None	333 (86.5%)	3,073 (85.5%)	.
1	36 (9.4%)	287 (8.0%)	.
2	4 (1.0%)	73 (2.0%)	.
3 or more	12 (3.1%)	162 (4.5%)	.
Number of contacts with GP at practice			0.1377
None	7 (1.8%)	160 (4.5%)	.
1	7 (1.8%)	124 (3.5%)	.
2	15 (3.9%)	123 (3.4%)	.
3 or more	356 (92.5%)	3,188 (88.7%)	.

SIDIAP	QVA N(%)	Free LABA+LAMA without ICS N(%)	Std Dif	Free LABA+LAMA with ICS N(%)	Std Dif
Smoking status			0.087		0.1782
Current smoker	1,540 (28.2%)	1,290 (30.9%)	.	384 (22.4%)	.
Past smoker	2,835 (51.8%)	2,124 (50.9%)	.	948 (55.2%)	.
Never smoker	1,094 (20.0%)	763 (18.3%)	.	385 (22.4%)	.
Unknown	92 (1.7%)	42 (1.0%)	.	8 (0.5%)	.
Smoking status (imputed)			0.0623		0.1398
Current smoker	(28.4%)	(30.9%)	.	(22.4%)	.
Past smoker	(51.7%)	(50.8%)	.	(55.2%)	.
Never smoker	(19.9%)	(18.3%)	.	(22.4%)	.
Number of contacts with GP at home			0.042		-0.0999
None	4,930 (88.7%)	3,794 (89.9%)	.	1,472 (85.3%)	.
1	327 (5.9%)	232 (5.5%)	.	125 (7.3%)	.
2	119 (2.1%)	72 (1.7%)	.	47 (2.7%)	.
3 or more	185 (3.3%)	121 (2.9%)	.	81 (4.7%)	.
Number of contacts with GP at practice			-0.0401		-0.1106
None	113 (2.0%)	56 (1.3%)	.	13 (0.8%)	.
1	187 (3.4%)	149 (3.5%)	.	47 (2.7%)	.
2	303 (5.5%)	202 (4.8%)	.	73 (4.2%)	.
3 or more	4,958 (89.2%)	3,812 (90.4%)	.	1,592 (92.3%)	.

SIDIAP	QVA N(%)	Free LABA+ICS N(%)	Std Dif	Fixed LABA ICS N(%)	Std Dif
Smoking status			0.2885		0.2567
Current smoker	1,540 (28.2%)	628 (23.3%)	.	5,794 (28.7%)	.
Past smoker	2,835 (51.8%)	1,191 (44.1%)	.	8,324 (41.3%)	.
Never smoker	1,094 (20.0%)	881 (32.6%)	.	6,052 (30.0%)	.
Unknown	92 (1.7%)	38 (1.4%)	.	468 (2.3%)	.
Smoking status (imputed)			0.2924		0.2539
Current smoker	(28.4%)	(23.3%)	.	(28.9%)	.
Past smoker	(51.7%)	(44.0%)	.	(41.2%)	.
Never smoker	(19.9%)	(32.7%)	.	(29.9%)	.
Number of contacts with GP at home			-0.1102		-0.0314
None	4,930 (88.7%)	2,328 (85.0%)	.	18086 (87.6%)	.
1	327 (5.9%)	196 (7.2%)	.	1,334 (6.5%)	.
2	119 (2.1%)	64 (2.3%)	.	463 (2.2%)	.
3 or more	185 (3.3%)	150 (5.5%)	.	755 (3.7%)	.
Number of contacts with GP at practice			-0.0142		0.111
None	113 (2.0%)	56 (2.1%)	.	770 (3.7%)	.
1	187 (3.4%)	94 (3.4%)	.	927 (4.5%)	.
2	303 (5.5%)	134 (4.9%)	.	1,269 (6.2%)	.
3 or more	4,958 (89.2%)	2,454 (89.6%)	.	17672 (85.6%)	.

SIDIAP	QVA N(%)	Fixed LABA LAMA N(%)	Std Dif	LABA N(%)	Std Dif
Smoking status			0.0878		0.2153
Current smoker	1,540 (28.2%)	281 (29.5%)	.	2,029 (34.9%)	.
Past smoker	2,835 (51.8%)	508 (53.3%)	.	2,414 (41.5%)	.
Never smoker	1,094 (20.0%)	165 (17.3%)	.	1,376 (23.7%)	.
Unknown	92 (1.7%)	10 (1.0%)	.	60 (1.0%)	.
Smoking status (imputed)			0.0701		0.2063
Current smoker	(28.4%)	(29.7%)	.	(34.9%)	.
Past smoker	(51.7%)	(53.1%)	.	(41.5%)	.
Never smoker	(19.9%)	(17.2%)	.	(23.6%)	.
Number of contacts with GP at home			-0.0556		0.0501
None	4,930 (88.7%)	837 (86.8%)	.	5,303 (90.2%)	.
1	327 (5.9%)	67 (7.0%)	.	301 (5.1%)	.
2	119 (2.1%)	21 (2.2%)	.	95 (1.6%)	.
3 or more	185 (3.3%)	39 (4.1%)	.	180 (3.1%)	.
Number of contacts with GP at practice			0.0272		0.0831
None	113 (2.0%)	25 (2.6%)	.	168 (2.9%)	.
1	187 (3.4%)	38 (3.9%)	.	254 (4.3%)	.
2	303 (5.5%)	49 (5.1%)	.	372 (6.3%)	.
3 or more	4,958 (89.2%)	852 (88.4%)	.	5,085 (86.5%)	.

SIDIAP	QVA N(%)	LAMA	Std Dif
Smoking status			0.2033
Current smoker	1,540 (28.2%)	4,811 (35.8%)	.
Past smoker	2,835 (51.8%)	5,639 (41.9%)	.
Never smoker	1,094 (20.0%)	3,001 (22.3%)	.
Unknown	92 (1.7%)	227 (1.7%)	.
Smoking status (imputed)			0.2028
Current smoker	(28.4%)	(35.8%)	.
Past smoker	(51.7%)	(41.9%)	.
Never smoker	(19.9%)	(22.3%)	.
Number of contacts with GP at home			0.0628
None	4,930 (88.7%)	12380 (90.5%)	.
1	327 (5.9%)	754 (5.5%)	.
2	119 (2.1%)	213 (1.6%)	.
3 or more	185 (3.3%)	331 (2.4%)	.
Number of contacts with GP at practice			0.0984
None	113 (2.0%)	369 (2.7%)	.
1	187 (3.4%)	631 (4.6%)	.
2	303 (5.5%)	924 (6.8%)	.
3 or more	4,958 (89.2%)	11754 (85.9%)	.

Table 15-3 COPD characteristics – COPD severity (pooled and by database)

POOLED	QVA N(%)	Free LABA+LAMA without ICS N(%)	Std Dif	Free LABA+LAMA with ICS N(%)	Std Dif
Total	9,798 (100.0%)	9,619 (100.0%)	.	3,192 (100.0%)	.
COPD severity assessed by spirometry			0.1639		-0.0022
Mild	730 (11.4%)	958 (14.3%)	.	229 (10.9%)	.
Moderate	3,370 (52.5%)	3,961 (59.1%)	.	1,104 (52.6%)	.
Severe	2,045 (31.9%)	1,611 (24.0%)	.	662 (31.5%)	.
Very severe	274 (4.3%)	175 (2.6%)	.	104 (5.0%)	.
Unknown	3,379 (34.5%)	2,914 (30.3%)	.	1,093 (34.2%)	.
COPD severity assessed by spirometry (imputed)			0.2015		0.0095
Mild	(11.5%)	(14.6%)	.	(11.6%)	.
Moderate	(52.6%)	(58.8%)	.	(53.1%)	.
Severe	(31.7%)	(24.1%)	.	(30.7%)	.
Very severe	(4.2%)	(2.5%)	.	(4.5%)	.

POOLED	QVA N(%)	Free LABA+ICS N(%)	Std Dif	Fixed LABA ICS N(%)	Std Dif
Total	9,798 (100.0%)	4,628 (100.0%)	.	58332 (100.0%)	.
COPD severity assessed by spirometry			0.0662		0.0321
Mild	730 (11.4%)	669 (24.0%)	.	7,719 (22.0%)	.
Moderate	3,370 (52.5%)	1,566 (56.2%)	.	18977 (54.0%)	.
Severe	2,045 (31.9%)	509 (18.3%)	.	7,599 (21.6%)	.
Very severe	274 (4.3%)	44 (1.6%)	.	850 (2.4%)	.
Unknown	3,379 (34.5%)	1,840 (39.8%)	.	23187 (39.8%)	.
COPD severity assessed by spirometry (imputed)			0.4463		0.3809
Mild	(11.5%)	(24.2%)	.	(22.8%)	.
Moderate	(52.6%)	(56.2%)	.	(55.0%)	.
Severe	(31.7%)	(18.1%)	.	(20.0%)	.
Very severe	(4.2%)	(1.6%)	.	(2.2%)	.

POOLED	QVA N(%)	Fixed LABA LAMA N(%)	Std Dif	LABA N(%)	Std Dif
Total	9,798 (100.0%)	9,150 (100.0%)	.	12364 (100.0%)	.
COPD severity assessed by spirometry			0.2083		0.1843
Mild	730 (11.4%)	1,034 (15.5%)	.	1,908 (24.0%)	.
Moderate	3,370 (52.5%)	3,666 (55.0%)	.	4,812 (60.5%)	.
Severe	2,045 (31.9%)	1,732 (26.0%)	.	1,126 (14.2%)	.
Very severe	274 (4.3%)	237 (3.6%)	.	110 (1.4%)	.
Unknown	3,379 (34.5%)	2,481 (27.1%)	.	4,408 (35.7%)	.
COPD severity assessed by spirometry (imputed)			0.1581		0.5296
Mild	(11.5%)	(15.5%)	.	(24.8%)	.
Moderate	(52.6%)	(55.1%)	.	(59.4%)	.
Severe	(31.7%)	(26.0%)	.	(14.4%)	.
Very severe	(4.2%)	(3.5%)	.	(1.4%)	.

POOLED	QVA N(%)	LAMA	Std Dif
Total	9,798 (100.0%)	42972 (100.0%)	.
COPD severity assessed by spirometry			0.1581
Mild	730 (11.4%)	6,126 (22.2%)	.
Moderate	3,370 (52.5%)	16430 (59.6%)	.
Severe	2,045 (31.9%)	4,592 (16.7%)	.
Very severe	274 (4.3%)	431 (1.6%)	.
Unknown	3,379 (34.5%)	15393 (35.8%)	.
COPD severity assessed by spirometry (imputed)			0.462
Mild	(11.5%)	(23.1%)	.
Moderate	(52.6%)	(58.9%)	.
Severe	(31.7%)	(16.5%)	.
Very severe	(4.2%)	(1.6%)	.

THIN	QVA N(%)	Free LABA+LAMA without ICS N(%)	Std Dif	Free LABA+LAMA with ICS N(%)	Std Dif
Total	1,346 (100.0%)	2,586 (100.0%)	.	394 (100.0%)	.
COPD severity assessed by spirometry			0.1184		0.0459
Mild	215 (19.2%)	426 (19.3%)	.	47 (13.3%)	.
Moderate	582 (51.8%)	1,309 (59.3%)	.	202 (57.1%)	.
Severe	288 (25.7%)	421 (19.1%)	.	85 (24.0%)	.
Very severe	38 (3.4%)	50 (2.3%)	.	20 (5.7%)	.
Unknown	223 (16.6%)	380 (14.7%)	.	40 (10.2%)	.
COPD severity assessed by spirometry (imputed)			0.1192		-0.1215
Mild	(19.1%)	(19.4%)	.	(12.9%)	.
Moderate	(52.0%)	(59.0%)	.	(56.7%)	.
Severe	(25.6%)	(19.4%)	.	(24.6%)	.
Very severe	(3.4%)	(2.2%)	.	(5.9%)	.

THIN	QVA N(%)	Free LABA+ICS N(%)	Std Dif	Fixed LABA ICS N(%)	Std Dif
Total	1,346 (100.0%)	583 (100.0%)	.	21315 (100.0%)	.
COPD severity assessed by spirometry			0.1394		-0.0499
Mild	215 (19.2%)	135 (29.4%)	.	3,475 (20.9%)	.
Moderate	582 (51.8%)	256 (55.8%)	.	8,899 (53.4%)	.
Severe	288 (25.7%)	63 (13.7%)	.	3,829 (23.0%)	.
Very severe	38 (3.4%)	5 (1.1%)	.	457 (2.7%)	.
Unknown	223 (16.6%)	124 (21.3%)	.	4,655 (21.8%)	.
COPD severity assessed by spirometry (imputed)			0.3892		0.0805
Mild	(19.1%)	(30.3%)	.	(20.8%)	.
Moderate	(52.0%)	(55.3%)	.	(53.9%)	.
Severe	(25.6%)	(13.2%)	.	(22.6%)	.
Very severe	(3.4%)	(1.2%)	.	(2.7%)	.

THIN	QVA N(%)	Fixed LABA LAMA N(%)	Std Dif	LABA N(%)	Std Dif
Total	1,346 (100.0%)	4,921 (100.0%)	.	3,006 (100.0%)	.
COPD severity assessed by spirometry			0.0379		0.1842
Mild	215 (19.2%)	794 (19.6%)	.	628 (25.4%)	.
Moderate	582 (51.8%)	2,291 (56.6%)	.	1,486 (60.1%)	.
Severe	288 (25.7%)	871 (21.5%)	.	312 (12.6%)	.
Very severe	38 (3.4%)	91 (2.3%)	.	45 (1.8%)	.
Unknown	223 (16.6%)	874 (17.8%)	.	535 (17.8%)	.
COPD severity assessed by spirometry (imputed)			0.0909		0.3138
Mild	(19.1%)	(19.8%)	.	(26.0%)	.
Moderate	(52.0%)	(56.3%)	.	(59.2%)	.
Severe	(25.6%)	(21.6%)	.	(13.1%)	.
Very severe	(3.4%)	(2.3%)	.	(1.8%)	.

THIN	QVA N(%)	LAMA	Std Dif
Total	1,346 (100.0%)	18598 (100.0%)	.
COPD severity assessed by spirometry			-0.0131
Mild	215 (19.2%)	3,211 (22.7%)	.
Moderate	582 (51.8%)	8,199 (57.9%)	.
Severe	288 (25.7%)	2,485 (17.6%)	.
Very severe	38 (3.4%)	263 (1.9%)	.
Unknown	223 (16.6%)	4,440 (23.9%)	.
COPD severity assessed by spirometry (imputed)			0.1971
Mild	(19.1%)	(22.9%)	.
Moderate	(52.0%)	(57.6%)	.
Severe	(25.6%)	(17.7%)	.
Very severe	(3.4%)	(1.9%)	.

IPCI	QVA N(%)	Free LABA+LAMA without ICS N(%)	Std Dif	Free LABA+LAMA with ICS N(%)	Std Dif
Total	699 (100.0%)	1,148 (100.0%)	.	496 (100.0%)	.
COPD severity assessed by spirometry			0.2717		-0.1249
Mild	60 (17.1%)	153 (21.6%)	.	43 (20.9%)	.
Moderate	195 (55.6%)	416 (58.6%)	.	125 (60.7%)	.
Severe	90 (25.6%)	132 (18.6%)	.	36 (17.5%)	.
Very severe	6 (1.7%)	9 (1.3%)	.	2 (1.0%)	.
Unknown	348 (49.8%)	438 (38.2%)	.	290 (58.5%)	.
COPD severity assessed by spirometry (imputed)			0.1951		0.2095
Mild	(15.9%)	(21.3%)	.	(21.6%)	.
Moderate	(56.5%)	(58.5%)	.	(58.7%)	.
Severe	(26.0%)	(19.1%)	.	(18.6%)	.
Very severe	(1.5%)	(1.2%)	.	(1.1%)	.

IPCI	QVA N(%)	Free LABA+ICS N(%)	Std Dif	Fixed LABA ICS N(%)	Std Dif
Total	699 (100.0%)	597 (100.0%)	.	7,001 (100.0%)	.
COPD severity assessed by spirometry			0.1283		0.1193
Mild	60 (17.1%)	127 (43.6%)	.	1,202 (34.5%)	.
Moderate	195 (55.6%)	137 (47.1%)	.	1,888 (54.2%)	.
Severe	90 (25.6%)	23 (7.9%)	.	377 (10.8%)	.
Very severe	6 (1.7%)	4 (1.4%)	.	18 (0.5%)	.
Unknown	348 (49.8%)	306 (51.3%)	.	3,516 (50.2%)	.
COPD severity assessed by spirometry (imputed)			0.6727		0.527
Mild	(15.9%)	(42.1%)	.	(34.4%)	.
Moderate	(56.5%)	(47.9%)	.	(53.7%)	.
Severe	(26.0%)	(8.9%)	.	(11.4%)	.
Very severe	(1.5%)	(1.1%)	.	(0.5%)	.

IPCI	QVA N(%)	Fixed LABA LAMA N(%)	Std Dif	LABA N(%)	Std Dif
Total	699 (100.0%)	1,081 (100.0%)	.	1,526 (100.0%)	.
COPD severity assessed by spirometry			-0.0161		0.3621
Mild	60 (17.1%)	90 (17.0%)	.	317 (33.9%)	.
Moderate	195 (55.6%)	304 (57.4%)	.	515 (55.1%)	.
Severe	90 (25.6%)	128 (24.2%)	.	100 (10.7%)	.
Very severe	6 (1.7%)	8 (1.5%)	.	3 (0.3%)	.
Unknown	348 (49.8%)	551 (51.0%)	.	591 (38.7%)	.
COPD severity assessed by spirometry (imputed)			0.0577		0.5335
Mild	(15.9%)	(16.9%)	.	(33.7%)	.
Moderate	(56.5%)	(58.3%)	.	(55.3%)	.
Severe	(26.0%)	(23.2%)	.	(10.7%)	.
Very severe	(1.5%)	(1.7%)	.	(0.3%)	.

IPCI	QVA N(%)	LAMA	Std Dif
Total	699 (100.0%)	5,006 (100.0%)	.
COPD severity assessed by spirometry			0.274
Mild	60 (17.1%)	851 (29.5%)	.
Moderate	195 (55.6%)	1,737 (60.1%)	.
Severe	90 (25.6%)	287 (9.9%)	.
Very severe	6 (1.7%)	15 (0.5%)	.
Unknown	348 (49.8%)	2,116 (42.3%)	.
COPD severity assessed by spirometry (imputed)			0.4665
Mild	(15.9%)	(29.9%)	.
Moderate	(56.5%)	(58.6%)	.
Severe	(26.0%)	(11.0%)	.
Very severe	(1.5%)	(0.6%)	.

AARHUS	QVA N(%)	Free LABA+LAMA without ICS N(%)	Std Dif	Free LABA+LAMA with ICS N(%)	Std Dif
Total	1,807 (100.0%)	671 (100.0%)	.	242 (100.0%)	.
COPD severity assessed by spirometry			-0.0101		0.0373
Mild	60 (6.1%)	27 (7.7%)	.	9 (6.3%)	.
Moderate	444 (44.9%)	174 (49.6%)	.	53 (37.1%)	.
Severe	406 (41.1%)	124 (35.3%)	.	67 (46.9%)	.
Very severe	79 (8.0%)	26 (7.4%)	.	14 (9.8%)	.
Unknown	818 (45.3%)	320 (47.7%)	.	99 (40.9%)	.
COPD severity assessed by spirometry (imputed)			0.1332		-0.1133
Mild	(6.3%)	(8.7%)	.	(6.2%)	.
Moderate	(45.6%)	(49.5%)	.	(39.8%)	.
Severe	(40.5%)	(35.0%)	.	(44.1%)	.
Very severe	(7.7%)	(6.9%)	.	(9.8%)	.

AARHUS	QVA N(%)	Free LABA+ICS N(%)	Std Dif	Fixed LABA ICS N(%)	Std Dif
Total	1,807 (100.0%)	273 (100.0%)	.	3,481 (100.0%)	.
COPD severity assessed by spirometry			-0.2406		-0.1509
Mild	60 (6.1%)	7 (6.7%)	.	157 (9.9%)	.
Moderate	444 (44.9%)	64 (61.5%)	.	697 (44.0%)	.
Severe	406 (41.1%)	29 (27.9%)	.	620 (39.1%)	.
Very severe	79 (8.0%)	4 (3.9%)	.	110 (6.9%)	.
Unknown	818 (45.3%)	169 (61.9%)	.	1,897 (54.5%)	.
COPD severity assessed by spirometry (imputed)			0.2457		0.1347
Mild	(6.3%)	(8.0%)	.	(9.6%)	.
Moderate	(45.6%)	(55.6%)	.	(47.7%)	.
Severe	(40.5%)	(32.2%)	.	(36.4%)	.
Very severe	(7.7%)	(4.3%)	.	(6.3%)	.

AARHUS	QVA N(%)	Fixed LABA LAMA N(%)	Std Dif	LABA N(%)	Std Dif
Total	1,807 (100.0%)	1,758 (100.0%)	.	1,078 (100.0%)	.
COPD severity assessed by spirometry			0.2966		-0.091
Mild	60 (6.1%)	66 (5.3%)	.	66 (14.2%)	.
Moderate	444 (44.9%)	586 (47.3%)	.	285 (61.2%)	.
Severe	406 (41.1%)	487 (39.3%)	.	104 (22.3%)	.
Very severe	79 (8.0%)	100 (8.1%)	.	11 (2.4%)	.
Unknown	818 (45.3%)	519 (29.5%)	.	612 (56.8%)	.
COPD severity assessed by spirometry (imputed)			0.0131		0.569
Mild	(6.3%)	(5.8%)	.	(16.0%)	.
Moderate	(45.6%)	(47.1%)	.	(60.2%)	.
Severe	(40.5%)	(39.3%)	.	(21.5%)	.
Very severe	(7.7%)	(7.8%)	.	(2.4%)	.

AARHUS	QVA N(%)	LAMA	Std Dif
Total	1,807 (100.0%)	2,095 (100.0%)	.
COPD severity assessed by spirometry			-0.0415
Mild	60 (6.1%)	118 (11.8%)	.
Moderate	444 (44.9%)	554 (55.5%)	.
Severe	406 (41.1%)	281 (28.2%)	.
Very severe	79 (8.0%)	45 (4.5%)	.
Unknown	818 (45.3%)	1,097 (52.4%)	.
COPD severity assessed by spirometry (imputed)			0.324
Mild	(6.3%)	(11.6%)	.
Moderate	(45.6%)	(54.9%)	.
Severe	(40.5%)	(29.0%)	.
Very severe	(7.7%)	(4.6%)	.

HSD	QVA N(%)	Free LABA+LAMA without ICS N(%)	Std Dif	Free LABA+LAMA with ICS N(%)	Std Dif
Total	385 (100.0%)	995 (100.0%)	.	335 (100.0%)	.
COPD severity assessed by spirometry			-0.1117		-0.093
Mild	38 (25.5%)	65 (19.1%)	.	22 (18.5%)	.
Moderate	92 (61.7%)	223 (65.6%)	.	75 (63.0%)	.
Severe	19 (12.8%)	49 (14.4%)	.	22 (18.5%)	.
Very severe		3 (0.9%)	.		.
Unknown	236 (61.3%)	655 (65.8%)	.	216 (64.5%)	.
COPD severity assessed by spirometry (imputed)			-0.1949		-0.3236
Mild	(25.8%)	(18.7%)	.	(15.0%)	.
Moderate	(63.4%)	(66.2%)	.	(66.1%)	.
Severe	(10.5%)	(14.4%)	.	(18.6%)	.
Very severe	(0.3%)	(0.7%)	.	(0.3%)	.

HSD	QVA N(%)	Free LABA+ICS N(%)	Std Dif	Fixed LABA ICS N(%)	Std Dif
Total	385 (100.0%)	437 (100.0%)	.	5,897 (100.0%)	.
COPD severity assessed by spirometry			-0.0646		-0.3339
Mild	38 (25.5%)	47 (31.5%)	.	425 (31.7%)	.
Moderate	92 (61.7%)	94 (63.1%)	.	809 (60.4%)	.
Severe	19 (12.8%)	8 (5.4%)	.	100 (7.5%)	.
Very severe			.	6 (0.5%)	.
Unknown	236 (61.3%)	288 (65.9%)	.	4,557 (77.3%)	.
COPD severity assessed by spirometry (imputed)			0.1598		0.1852
Mild	(25.8%)	(31.3%)	.	(33.0%)	.
Moderate	(63.4%)	(61.8%)	.	(59.8%)	.
Severe	(10.5%)	(6.7%)	.	(6.8%)	.
Very severe	(0.3%)	(0.2%)	.	(0.3%)	.

HSD	QVA N(%)	Fixed LABA LAMA N(%)	Std Dif	LABA N(%)	Std Dif
Total	385 (100.0%)	426 (100.0%)	.	875 (100.0%)	.
COPD severity assessed by spirometry			-0.0469		-0.1304
Mild	38 (25.5%)	30 (18.6%)	.	89 (32.8%)	.
Moderate	92 (61.7%)	103 (64.0%)	.	168 (62.0%)	.
Severe	19 (12.8%)	23 (14.3%)	.	14 (5.2%)	.
Very severe		5 (3.1%)	.		.
Unknown	236 (61.3%)	265 (62.2%)	.	604 (69.0%)	.
COPD severity assessed by spirometry (imputed)			-0.2171		0.2634
Mild	(25.8%)	(17.8%)	.	(36.7%)	.
Moderate	(63.4%)	(66.9%)	.	(57.1%)	.
Severe	(10.5%)	(13.6%)	.	(6.1%)	.
Very severe	(0.3%)	(1.7%)	.	(0.2%)	.

HSD	QVA N(%)	LAMA	Std Dif
Total	385 (100.0%)	3,595 (100.0%)	.
COPD severity assessed by spirometry			-0.2557
Mild	38 (25.5%)	316 (34.4%)	.
Moderate	92 (61.7%)	558 (60.8%)	.
Severe	19 (12.8%)	43 (4.7%)	.
Very severe		1 (0.1%)	.
Unknown	236 (61.3%)	2,677 (74.5%)	.
COPD severity assessed by spirometry (imputed)			0.2231
Mild	(25.8%)	(34.3%)	.
Moderate	(63.4%)	(59.7%)	.
Severe	(10.5%)	(5.9%)	.
Very severe	(0.3%)	(0.2%)	.

SIDIAP	QVA N(%)	Free LABA+LAMA without ICS N(%)	Std Dif	Free LABA+LAMA with ICS N(%)	Std Dif
Total	5,561 (100.0%)	4,219 (100.0%)	.	1,725 (100.0%)	.
COPD severity assessed by spirometry			0.1358		0.059
Mild	357 (9.4%)	287 (9.3%)	.	108 (8.5%)	.
Moderate	2,057 (54.0%)	1,839 (59.4%)	.	649 (50.8%)	.
Severe	1,242 (32.6%)	885 (28.6%)	.	452 (35.4%)	.
Very severe	151 (4.0%)	87 (2.8%)	.	68 (5.3%)	.
Unknown	1,754 (31.5%)	1,121 (26.6%)	.	448 (26.0%)	.
COPD severity assessed by spirometry (imputed)			0.0843		-0.1076
Mild	(9.8%)	(9.8%)	.	(8.6%)	.
Moderate	(53.9%)	(58.4%)	.	(50.0%)	.
Severe	(32.5%)	(29.0%)	.	(36.1%)	.
Very severe	(3.9%)	(2.8%)	.	(5.3%)	.

SIDIAP	QVA N(%)	Free LABA+ICS N(%)	Std Dif	Fixed LABA ICS N(%)	Std Dif
Total	5,561 (100.0%)	2,738 (100.0%)	.	20638 (100.0%)	.
COPD severity assessed by spirometry			0.0922		-0.0495
Mild	357 (9.4%)	353 (19.8%)	.	2,460 (20.4%)	.
Moderate	2,057 (54.0%)	1,015 (56.9%)	.	6,684 (55.4%)	.
Severe	1,242 (32.6%)	386 (21.6%)	.	2,673 (22.1%)	.
Very severe	151 (4.0%)	31 (1.7%)	.	259 (2.1%)	.
Unknown	1,754 (31.5%)	953 (34.8%)	.	8,562 (41.5%)	.
COPD severity assessed by spirometry (imputed)			0.3569		0.3641
Mild	(9.8%)	(19.4%)	.	(20.2%)	.
Moderate	(53.9%)	(57.4%)	.	(56.6%)	.
Severe	(32.5%)	(21.5%)	.	(21.3%)	.
Very severe	(3.9%)	(1.7%)	.	(2.0%)	.

SIDIAP	QVA N(%)	Fixed LABA LAMA N(%)	Std Dif	LABA N(%)	Std Dif
Total	5,561 (100.0%)	964 (100.0%)	.	5,879 (100.0%)	.
COPD severity assessed by spirometry			0.0462		0.1412
Mild	357 (9.4%)	54 (7.8%)	.	808 (21.2%)	.
Moderate	2,057 (54.0%)	382 (55.2%)	.	2,358 (61.8%)	.
Severe	1,242 (32.6%)	223 (32.2%)	.	596 (15.6%)	.
Very severe	151 (4.0%)	33 (4.8%)	.	51 (1.3%)	.
Unknown	1,754 (31.5%)	272 (28.2%)	.	2,066 (35.1%)	.
COPD severity assessed by spirometry (imputed)			-0.0436		0.5008
Mild	(9.8%)	(8.2%)	.	(21.8%)	.
Moderate	(53.9%)	(54.4%)	.	(60.8%)	.
Severe	(32.5%)	(32.8%)	.	(15.9%)	.
Very severe	(3.9%)	(4.6%)	.	(1.4%)	.

SIDIAP	QVA N(%)	LAMA	Std Dif
Total	5,561 (100.0%)	13678 (100.0%)	.
COPD severity assessed by spirometry			0.0805
Mild	357 (9.4%)	1,630 (18.9%)	.
Moderate	2,057 (54.0%)	5,382 (62.5%)	.
Severe	1,242 (32.6%)	1,496 (17.4%)	.
Very severe	151 (4.0%)	107 (1.2%)	.
Unknown	1,754 (31.5%)	5,063 (37.0%)	.
COPD severity assessed by spirometry (imputed)			0.4424
Mild	(9.8%)	(19.8%)	.
Moderate	(53.9%)	(61.1%)	.
Severe	(32.5%)	(17.7%)	.
Very severe	(3.9%)	(1.3%)	.

Table 15-4 COPD characteristics – COPD severity (2) (pooled and by database)

POOLED	QVA N(%)	Free LABA+LAMA without ICS N(%)	Std Dif	Free LABA+LAMA with ICS N(%)	Std Dif
COPD severity assessed by proxy			-0.0701		-0.3578
Mild	1,498 (15.3%)	864 (9.0%)	.	58 (1.8%)	.
Moderate	6,907 (70.5%)	7,664 (79.7%)	.	2,553 (80.0%)	.
Severe	1,297 (13.2%)	957 (10.0%)	.	510 (16.0%)	.
Very severe	96 (1.0%)	134 (1.4%)	.	71 (2.2%)	.
Number of hospitalizations for COPD exacerbation			0.1563		0.0412
None	8,776 (89.6%)	9,024 (93.8%)	.	2,899 (90.8%)	.
1	781 (8.0%)	507 (5.3%)	.	219 (6.9%)	.
2	169 (1.7%)	66 (0.7%)	.	41 (1.3%)	.
3 or more	72 (0.7%)	22 (0.2%)	.	33 (1.0%)	.
Number of systemic steroids episodes			-0.0234		-0.1877
None	8,736 (89.2%)	8,513 (88.5%)	.	2,646 (82.9%)	.
1	902 (9.2%)	873 (9.1%)	.	394 (12.3%)	.
2	129 (1.3%)	172 (1.8%)	.	86 (2.7%)	.
3 or more	31 (0.3%)	61 (0.6%)	.	66 (2.1%)	.
Number of Antibiotic courses			0.0017		-0.108
None	7,830 (79.9%)	7,698 (80.0%)	.	2,424 (75.9%)	.
1	1,314 (13.4%)	1,270 (13.2%)	.	431 (13.5%)	.
2	445 (4.5%)	415 (4.3%)	.	207 (6.5%)	.
3 or more	209 (2.1%)	236 (2.5%)	.	130 (4.1%)	.

POOLED	QVA N(%)	Free LABA+ICS N(%)	Std Dif	Fixed LABA ICS N(%)	Std Dif
COPD severity assessed by proxy			-0.0542		0.172
Mild	1,498 (15.3%)	382 (8.3%)	.	12219 (21.0%)	.
Moderate	6,907 (70.5%)	3,795 (82.0%)	.	40030 (68.6%)	.
Severe	1,297 (13.2%)	402 (8.7%)	.	5,405 (9.3%)	.
Very severe	96 (1.0%)	49 (1.1%)	.	678 (1.2%)	.
Number of hospitalizations for COPD exacerbation			0.1841		0.1674
None	8,776 (89.6%)	4,375 (94.5%)	.	54894 (94.1%)	.
1	781 (8.0%)	194 (4.2%)	.	2,860 (4.9%)	.
2	169 (1.7%)	35 (0.8%)	.	411 (0.7%)	.
3 or more	72 (0.7%)	24 (0.5%)	.	167 (0.3%)	.
Number of systemic steroids episodes			0.0007		-0.0407
None	8,736 (89.2%)	4,130 (89.2%)	.	51269 (87.9%)	.
1	902 (9.2%)	400 (8.6%)	.	5,854 (10.0%)	.
2	129 (1.3%)	73 (1.6%)	.	927 (1.6%)	.
3 or more	31 (0.3%)	25 (0.5%)	.	282 (0.5%)	.
Number of Antibiotic courses			-0.0375		-0.0191
None	7,830 (79.9%)	3,629 (78.4%)	.	46139 (79.1%)	.
1	1,314 (13.4%)	660 (14.3%)	.	8,261 (14.2%)	.
2	445 (4.5%)	229 (5.0%)	.	2,679 (4.6%)	.
3 or more	209 (2.1%)	110 (2.4%)	.	1,253 (2.2%)	.

POOLED	QVA N(%)	Fixed LABA LAMA N(%)	Std Dif	LABA N(%)	Std Dif
COPD severity assessed by proxy			-0.0146		0.4076
Mild	1,498 (15.3%)	1,427 (15.6%)	.	3,681 (29.8%)	.
Moderate	6,907 (70.5%)	6,330 (69.2%)	.	7,899 (63.9%)	.
Severe	1,297 (13.2%)	1,239 (13.5%)	.	713 (5.8%)	.
Very severe	96 (1.0%)	154 (1.7%)	.	71 (0.6%)	.
Number of hospitalizations for COPD exacerbation			0.06		0.2779
None	8,776 (89.6%)	8,357 (91.3%)	.	11937 (96.6%)	.
1	781 (8.0%)	609 (6.7%)	.	356 (2.9%)	.
2	169 (1.7%)	119 (1.3%)	.	44 (0.4%)	.
3 or more	72 (0.7%)	65 (0.7%)	.	27 (0.2%)	.
Number of systemic steroids episodes			-0.149		0.0939
None	8,736 (89.2%)	7,706 (84.2%)	.	11364 (91.9%)	.
1	902 (9.2%)	1,134 (12.4%)	.	847 (6.9%)	.
2	129 (1.3%)	221 (2.4%)	.	118 (1.0%)	.
3 or more	31 (0.3%)	89 (1.0%)	.	35 (0.3%)	.
Number of Antibiotic courses			-0.0672		0.0729
None	7,830 (79.9%)	7,078 (77.4%)	.	10212 (82.6%)	.
1	1,314 (13.4%)	1,312 (14.3%)	.	1,541 (12.5%)	.
2	445 (4.5%)	440 (4.8%)	.	432 (3.5%)	.
3 or more	209 (2.1%)	320 (3.5%)	.	179 (1.5%)	.

POOLED	QVA N(%)	LAMA	Std Dif
COPD severity assessed by proxy			0.4865
Mild	1,498 (15.3%)	15320 (35.7%)	.
Moderate	6,907 (70.5%)	24394 (56.8%)	.
Severe	1,297 (13.2%)	2,833 (6.6%)	.
Very severe	96 (1.0%)	425 (1.0%)	.
Number of hospitalizations for COPD exacerbation			0.2487
None	8,776 (89.6%)	41227 (95.9%)	.
1	781 (8.0%)	1,504 (3.5%)	.
2	169 (1.7%)	171 (0.4%)	.
3 or more	72 (0.7%)	70 (0.2%)	.
Number of systemic steroids episodes			0.0644
None	8,736 (89.2%)	39142 (91.1%)	.
1	902 (9.2%)	3,241 (7.5%)	.
2	129 (1.3%)	443 (1.0%)	.
3 or more	31 (0.3%)	146 (0.3%)	.
Number of Antibiotic courses			0.0754
None	7,830 (79.9%)	35537 (82.7%)	.
1	1,314 (13.4%)	5,334 (12.4%)	.
2	445 (4.5%)	1,456 (3.4%)	.
3 or more	209 (2.1%)	645 (1.5%)	.

THIN	QVA N(%)	Free LABA+LAMA without ICS N(%)	Std Dif	Free LABA+LAMA with ICS N(%)	Std Dif
COPD severity assessed by proxy			0.038		-0.1543
Mild	111 (8.3%)	128 (5.0%)	.	2 (0.5%)	.
Moderate	971 (72.1%)	2,067 (79.9%)	.	313 (79.4%)	.
Severe	224 (16.6%)	355 (13.7%)	.	69 (17.5%)	.
Very severe	40 (3.0%)	36 (1.4%)	.	10 (2.5%)	.
Number of hospitalizations for COPD exacerbation			0.1363		0.1656
None	1,178 (87.5%)	2,370 (91.7%)	.	364 (92.4%)	.
1	147 (10.9%)	195 (7.5%)	.	29 (7.4%)	.
2	18 (1.3%)	19 (0.7%)	.	1 (0.3%)	.
3 or more	3 (0.2%)	2 (0.1%)	.		.
Number of systemic steroids episodes			0.0207		-0.1942
None	1,124 (83.5%)	2,181 (84.3%)	.	299 (75.9%)	.
1	181 (13.5%)	319 (12.3%)	.	73 (18.5%)	.
2	33 (2.5%)	71 (2.8%)	.	14 (3.6%)	.
3 or more	8 (0.6%)	15 (0.6%)	.	8 (2.0%)	.
Number of Antibiotic courses			-0.0142		-0.1567
None	1,066 (79.2%)	2,035 (78.7%)	.	288 (73.1%)	.
1	187 (13.9%)	358 (13.8%)	.	60 (15.2%)	.
2	58 (4.3%)	121 (4.7%)	.	23 (5.8%)	.
3 or more	35 (2.6%)	72 (2.8%)	.	23 (5.8%)	.

THIN	QVA N(%)	Free LABA+ICS N(%)	Std Dif	Fixed LABA ICS N(%)	Std Dif
COPD severity assessed by proxy			0.1497		0.2682
Mild	111 (8.3%)	25 (4.3%)	.	3,178 (14.9%)	.
Moderate	971 (72.1%)	501 (85.9%)	.	15490 (72.7%)	.
Severe	224 (16.6%)	54 (9.3%)	.	2,314 (10.9%)	.
Very severe	40 (3.0%)	3 (0.5%)	.	333 (1.6%)	.
Number of hospitalizations for COPD exacerbation			0.291		0.2035
None	1,178 (87.5%)	557 (95.5%)	.	19919 (93.5%)	.
1	147 (10.9%)	23 (4.0%)	.	1,248 (5.9%)	.
2	18 (1.3%)	2 (0.3%)	.	118 (0.6%)	.
3 or more	3 (0.2%)	1 (0.2%)	.	30 (0.1%)	.
Number of systemic steroids episodes			0.0739		0.0259
None	1,124 (83.5%)	503 (86.3%)	.	17995 (84.4%)	.
1	181 (13.5%)	61 (10.5%)	.	2,754 (12.9%)	.
2	33 (2.5%)	16 (2.7%)	.	454 (2.1%)	.
3 or more	8 (0.6%)	3 (0.5%)	.	112 (0.5%)	.
Number of Antibiotic courses			0.0455		0.0355
None	1,066 (79.2%)	471 (80.8%)	.	17188 (80.6%)	.
1	187 (13.9%)	82 (14.1%)	.	2,737 (12.8%)	.
2	58 (4.3%)	17 (2.9%)	.	890 (4.2%)	.
3 or more	35 (2.6%)	13 (2.2%)	.	500 (2.4%)	.

THIN	QVA N(%)	Fixed LABA LAMA N(%)	Std Dif	LABA N(%)	Std Dif
COPD severity assessed by proxy			0.2769		0.4784
Mild	111 (8.3%)	723 (14.7%)	.	678 (22.6%)	.
Moderate	971 (72.1%)	3,619 (73.5%)	.	2,064 (68.7%)	.
Severe	224 (16.6%)	484 (9.8%)	.	240 (8.0%)	.
Very severe	40 (3.0%)	95 (1.9%)	.	24 (0.8%)	.
Number of hospitalizations for COPD exacerbation			0.1997		0.2837
None	1,178 (87.5%)	4,594 (93.4%)	.	2,867 (95.4%)	.
1	147 (10.9%)	292 (5.9%)	.	123 (4.1%)	.
2	18 (1.3%)	28 (0.6%)	.	11 (0.4%)	.
3 or more	3 (0.2%)	7 (0.1%)	.	5 (0.2%)	.
Number of systemic steroids episodes			0.1279		0.1628
None	1,124 (83.5%)	4,328 (88.0%)	.	2,678 (89.1%)	.
1	181 (13.5%)	495 (10.1%)	.	269 (9.0%)	.
2	33 (2.5%)	70 (1.4%)	.	47 (1.6%)	.
3 or more	8 (0.6%)	28 (0.6%)	.	12 (0.4%)	.
Number of Antibiotic courses			0.1214		0.1702
None	1,066 (79.2%)	4,128 (83.9%)	.	2,574 (85.6%)	.
1	187 (13.9%)	533 (10.8%)	.	296 (9.9%)	.
2	58 (4.3%)	177 (3.6%)	.	86 (2.9%)	.
3 or more	35 (2.6%)	83 (1.7%)	.	50 (1.7%)	.

THIN	QVA N(%)	LAMA	Std Dif
COPD severity assessed by proxy			0.6788
Mild	111 (8.3%)	6,249 (33.6%)	.
Moderate	971 (72.1%)	10797 (58.1%)	.
Severe	224 (16.6%)	1,371 (7.4%)	.
Very severe	40 (3.0%)	181 (1.0%)	.
Number of hospitalizations for COPD exacerbation			0.2749
None	1,178 (87.5%)	17699 (95.2%)	.
1	147 (10.9%)	822 (4.4%)	.
2	18 (1.3%)	63 (0.3%)	.
3 or more	3 (0.2%)	14 (0.1%)	.
Number of systemic steroids episodes			0.1879
None	1,124 (83.5%)	16703 (89.8%)	.
1	181 (13.5%)	1,635 (8.8%)	.
2	33 (2.5%)	203 (1.1%)	.
3 or more	8 (0.6%)	57 (0.3%)	.
Number of Antibiotic courses			0.1873
None	1,066 (79.2%)	16013 (86.1%)	.
1	187 (13.9%)	1,905 (10.2%)	.
2	58 (4.3%)	477 (2.6%)	.
3 or more	35 (2.6%)	203 (1.1%)	.

IPCI	QVA N(%)	Free LABA+LAMA without ICS N(%)	Std Dif	Free LABA+LAMA with ICS N(%)	Std Dif
COPD severity assessed by proxy			-0.2361		-0.6174
Mild	148 (21.2%)	83 (7.2%)	.	7 (1.4%)	.
Moderate	424 (60.7%)	858 (74.7%)	.	318 (64.1%)	.
Severe	120 (17.2%)	195 (17.0%)	.	159 (32.1%)	.
Very severe	7 (1.0%)	12 (1.1%)	.	12 (2.4%)	.
Number of hospitalizations for COPD exacerbation			0.1149		-0.0579
None	644 (92.1%)	1,090 (95.0%)	.	449 (90.5%)	.
1	46 (6.6%)	49 (4.3%)	.	38 (7.7%)	.
2	4 (0.6%)	8 (0.7%)	.	3 (0.6%)	.
3 or more	5 (0.7%)	1 (0.1%)	.	6 (1.2%)	.
Number of systemic steroids episodes			-0.0515		-0.4443
None	516 (73.8%)	822 (71.6%)	.	267 (53.8%)	.
1	120 (17.2%)	212 (18.5%)	.	129 (26.0%)	.
2	45 (6.4%)	73 (6.4%)	.	54 (10.9%)	.
3 or more	18 (2.6%)	41 (3.6%)	.	46 (9.3%)	.
Number of Antibiotic courses			-0.0732		-0.2508
None	469 (67.1%)	734 (63.9%)	.	281 (56.7%)	.
1	133 (19.0%)	233 (20.3%)	.	98 (19.8%)	.
2	68 (9.7%)	109 (9.5%)	.	70 (14.1%)	.
3 or more	29 (4.2%)	72 (6.3%)	.	47 (9.5%)	.

IPCI	QVA N(%)	Free LABA+ICS N(%)	Std Dif	Fixed LABA ICS N(%)	Std Dif
COPD severity assessed by proxy			-0.3724		0.0603
Mild	148 (21.2%)	34 (5.7%)	.	1,444 (20.6%)	.
Moderate	424 (60.7%)	418 (70.0%)	.	4,595 (65.6%)	.
Severe	120 (17.2%)	127 (21.3%)	.	902 (12.9%)	.
Very severe	7 (1.0%)	18 (3.0%)	.	60 (0.9%)	.
Number of hospitalizations for COPD exacerbation			-0.0321		0.182
None	644 (92.1%)	545 (91.3%)	.	6,745 (96.3%)	.
1	46 (6.6%)	40 (6.7%)	.	231 (3.3%)	.
2	4 (0.6%)	6 (1.0%)	.	17 (0.2%)	.
3 or more	5 (0.7%)	6 (1.0%)	.	8 (0.1%)	.
Number of systemic steroids episodes			-0.0757		0.0842
None	516 (73.8%)	422 (70.7%)	.	5,410 (77.3%)	.
1	120 (17.2%)	109 (18.3%)	.	1,102 (15.7%)	.
2	45 (6.4%)	44 (7.4%)	.	336 (4.8%)	.
3 or more	18 (2.6%)	22 (3.7%)	.	153 (2.2%)	.
Number of Antibiotic courses			-0.0469		0.0291
None	469 (67.1%)	395 (66.2%)	.	4,776 (68.2%)	.
1	133 (19.0%)	98 (16.4%)	.	1,368 (19.5%)	.
2	68 (9.7%)	60 (10.1%)	.	544 (7.8%)	.
3 or more	29 (4.2%)	44 (7.4%)	.	313 (4.5%)	.

IPCI	QVA N(%)	Fixed LABA LAMA N(%)	Std Dif	LABA N(%)	Std Dif
COPD severity assessed by proxy			-0.1489		0.189
Mild	148 (21.2%)	181 (16.7%)	.	379 (24.8%)	.
Moderate	424 (60.7%)	650 (60.1%)	.	994 (65.1%)	.
Severe	120 (17.2%)	238 (22.0%)	.	143 (9.4%)	.
Very severe	7 (1.0%)	12 (1.1%)	.	10 (0.7%)	.
Number of hospitalizations for COPD exacerbation			0.0627		0.2215
None	644 (92.1%)	1,013 (93.7%)	.	1,482 (97.1%)	.
1	46 (6.6%)	61 (5.6%)	.	33 (2.2%)	.
2	4 (0.6%)	5 (0.5%)	.	6 (0.4%)	.
3 or more	5 (0.7%)	2 (0.2%)	.	5 (0.3%)	.
Number of systemic steroids episodes			-0.1226		0.192
None	516 (73.8%)	743 (68.7%)	.	1,243 (81.5%)	.
1	120 (17.2%)	204 (18.9%)	.	209 (13.7%)	.
2	45 (6.4%)	84 (7.8%)	.	54 (3.5%)	.
3 or more	18 (2.6%)	50 (4.6%)	.	20 (1.3%)	.
Number of Antibiotic courses			-0.1643		0.1089
None	469 (67.1%)	651 (60.2%)	.	1,091 (71.5%)	.
1	133 (19.0%)	228 (21.1%)	.	288 (18.9%)	.
2	68 (9.7%)	97 (9.0%)	.	96 (6.3%)	.
3 or more	29 (4.2%)	105 (9.7%)	.	51 (3.3%)	.

IPCI	QVA N(%)	LAMA	Std Dif
COPD severity assessed by proxy			0.3445
Mild	148 (21.2%)	1,754 (35.0%)	.
Moderate	424 (60.7%)	2,725 (54.4%)	.
Severe	120 (17.2%)	489 (9.8%)	.
Very severe	7 (1.0%)	38 (0.8%)	.
Number of hospitalizations for COPD exacerbation			0.2339
None	644 (92.1%)	4,872 (97.3%)	.
1	46 (6.6%)	114 (2.3%)	.
2	4 (0.6%)	14 (0.3%)	.
3 or more	5 (0.7%)	6 (0.1%)	.
Number of systemic steroids episodes			0.183
None	516 (73.8%)	4,066 (81.2%)	.
1	120 (17.2%)	673 (13.4%)	.
2	45 (6.4%)	186 (3.7%)	.
3 or more	18 (2.6%)	81 (1.6%)	.
Number of Antibiotic courses			0.0972
None	469 (67.1%)	3,556 (71.0%)	.
1	133 (19.0%)	953 (19.0%)	.
2	68 (9.7%)	312 (6.2%)	.
3 or more	29 (4.2%)	185 (3.7%)	.

AARHUS	QVA N(%)	Free LABA+LAMA without ICS N(%)	Std Dif	Free LABA+LAMA with ICS N(%)	Std Dif
COPD severity assessed by proxy			-0.1377		-0.3666
Mild	346 (19.2%)	34 (5.1%)	.	2 (0.8%)	.
Moderate	1,067 (59.1%)	530 (79.0%)	.	181 (74.8%)	.
Severe	394 (21.8%)	107 (16.0%)	.	59 (24.4%)	.
Number of hospitalizations for COPD exacerbation			0.1671		0.0446
None	1,490 (82.5%)	593 (88.4%)	.	205 (84.7%)	.
1	217 (12.0%)	54 (8.1%)	.	18 (7.4%)	.
2	62 (3.4%)	11 (1.6%)	.	10 (4.1%)	.
3 or more	38 (2.1%)	13 (1.9%)	.	9 (3.7%)	.
Number of systemic steroids episodes			0.0395		-0.1329
None	1,467 (81.2%)	555 (82.7%)	.	185 (76.5%)	.
1	302 (16.7%)	103 (15.4%)	.	41 (16.9%)	.
2	34 (1.9%)	10 (1.5%)	.	10 (4.1%)	.
3 or more	4 (0.2%)	3 (0.5%)	.	6 (2.5%)	.
Number of Antibiotic courses			0.0892		-0.0869
None	1,281 (70.9%)	505 (75.3%)	.	165 (68.2%)	.
1	359 (19.9%)	105 (15.7%)	.	41 (16.9%)	.
2	111 (6.1%)	41 (6.1%)	.	23 (9.5%)	.
3 or more	56 (3.1%)	20 (3.0%)	.	13 (5.4%)	.

AARHUS	QVA N(%)	Free LABA+ICS N(%)	Std Dif	Fixed LABA ICS N(%)	Std Dif
COPD severity assessed by proxy			-0.108		0.1084
Mild	346 (19.2%)	20 (7.3%)	.	882 (25.3%)	.
Moderate	1,067 (59.1%)	208 (76.2%)	.	1,871 (53.8%)	.
Severe	394 (21.8%)	45 (16.5%)	.	728 (20.9%)	.
Number of hospitalizations for COPD exacerbation			0.1485		0.0097
None	1,490 (82.5%)	239 (87.6%)	.	2,883 (82.8%)	.
1	217 (12.0%)	26 (9.5%)	.	406 (11.7%)	.
2	62 (3.4%)	6 (2.2%)	.	132 (3.8%)	.
3 or more	38 (2.1%)	2 (0.7%)	.	60 (1.7%)	.
Number of systemic steroids episodes			0.0439		-0.0155
None	1,467 (81.2%)	226 (82.8%)	.	2,803 (80.5%)	.
1	302 (16.7%)	43 (15.8%)	.	611 (17.6%)	.
2	34 (1.9%)	4 (1.5%)	.	61 (1.8%)	.
3 or more	4 (0.2%)		.	6 (0.2%)	.
Number of Antibiotic courses			0.2246		0.0079
None	1,281 (70.9%)	221 (81.0%)	.	2,477 (71.2%)	.
1	359 (19.9%)	32 (11.7%)	.	696 (20.0%)	.
2	111 (6.1%)	14 (5.1%)	.	207 (6.0%)	.
3 or more	56 (3.1%)	6 (2.2%)	.	101 (2.9%)	.

AARHUS	QVA N(%)	Fixed LABA LAMA N(%)	Std Dif	LABA N(%)	Std Dif
COPD severity assessed by proxy			0.0022		0.4693
Mild	346 (19.2%)	344 (19.6%)	.	404 (37.5%)	.
Moderate	1,067 (59.1%)	1,026 (58.4%)	.	563 (52.2%)	.
Severe	394 (21.8%)	388 (22.1%)	.	111 (10.3%)	.
Number of hospitalizations for COPD exacerbation			0.0312		0.3006
None	1,490 (82.5%)	1,474 (83.9%)	.	995 (92.3%)	.
1	217 (12.0%)	175 (10.0%)	.	60 (5.6%)	.
2	62 (3.4%)	61 (3.5%)	.	14 (1.3%)	.
3 or more	38 (2.1%)	48 (2.7%)	.	9 (0.8%)	.
Number of systemic steroids episodes			-0.1195		0.2412
None	1,467 (81.2%)	1,346 (76.6%)	.	966 (89.6%)	.
1	302 (16.7%)	341 (19.4%)	.	102 (9.5%)	.
2	34 (1.9%)	63 (3.6%)	.	8 (0.7%)	.
3 or more	4 (0.2%)	8 (0.5%)	.	2 (0.2%)	.
Number of Antibiotic courses			-0.1333		0.3157
None	1,281 (70.9%)	1,146 (65.2%)	.	905 (84.0%)	.
1	359 (19.9%)	392 (22.3%)	.	120 (11.1%)	.
2	111 (6.1%)	111 (6.3%)	.	39 (3.6%)	.
3 or more	56 (3.1%)	109 (6.2%)	.	14 (1.3%)	.

AARHUS	QVA N(%)	LAMA	Std Dif
COPD severity assessed by proxy			0.437
Mild	346 (19.2%)	832 (39.7%)	.
Moderate	1,067 (59.1%)	968 (46.2%)	.
Severe	394 (21.8%)	295 (14.1%)	.
Number of hospitalizations for COPD exacerbation			0.2109
None	1,490 (82.5%)	1,878 (89.6%)	.
1	217 (12.0%)	160 (7.6%)	.
2	62 (3.4%)	38 (1.8%)	.
3 or more	38 (2.1%)	19 (0.9%)	.
Number of systemic steroids episodes			0.1311
None	1,467 (81.2%)	1,800 (85.9%)	.
1	302 (16.7%)	276 (13.2%)	.
2	34 (1.9%)	16 (0.8%)	.
3 or more	4 (0.2%)	3 (0.1%)	.
Number of Antibiotic courses			0.1318
None	1,281 (70.9%)	1,609 (76.8%)	.
1	359 (19.9%)	328 (15.7%)	.
2	111 (6.1%)	101 (4.8%)	.
3 or more	56 (3.1%)	57 (2.7%)	.

HSD	QVA N(%)	Free LABA+LAMA without ICS N(%)	Std Dif	Free LABA+LAMA with ICS N(%)	Std Dif
COPD severity assessed by proxy			0.0938		-0.2289
Mild	43 (11.2%)	98 (9.9%)	.	5 (1.5%)	.
Moderate	277 (72.0%)	788 (79.2%)	.	267 (79.7%)	.
Severe	16 (4.2%)	23 (2.3%)	.	14 (4.2%)	.
Very severe	49 (12.7%)	86 (8.6%)	.	49 (14.6%)	.
Number of hospitalizations for COPD exacerbation			0.0753		0.1021
None	383 (99.5%)	994 (99.9%)	.	335 (100.0%)	.
1	2 (0.5%)	1 (0.1%)	.		.
2			.		.
Number of systemic steroids episodes			-0.0673		-0.1354
None	366 (95.1%)	930 (93.5%)	.	307 (91.6%)	.
1	15 (3.9%)	57 (5.7%)	.	26 (7.8%)	.
2	3 (0.8%)	7 (0.7%)	.		.
3 or more	1 (0.3%)	1 (0.1%)	.	2 (0.6%)	.
Number of Antibiotic courses			-0.0003		-0.0556
None	325 (84.4%)	840 (84.4%)	.	277 (82.7%)	.
1	43 (11.2%)	106 (10.7%)	.	34 (10.2%)	.
2	6 (1.6%)	31 (3.1%)	.	9 (2.7%)	.
3 or more	11 (2.9%)	18 (1.8%)	.	15 (4.5%)	.

HSD	QVA N(%)	Free LABA+ICS N(%)	Std Dif	Fixed LABA ICS N(%)	Std Dif
COPD severity assessed by proxy			0.0579		0.4989
Mild	43 (11.2%)	22 (5.0%)	.	1,655 (28.1%)	.
Moderate	277 (72.0%)	378 (86.5%)	.	3,827 (64.9%)	.
Severe	16 (4.2%)	9 (2.1%)	.	130 (2.2%)	.
Very severe	49 (12.7%)	28 (6.4%)	.	285 (4.8%)	.
Number of hospitalizations for COPD exacerbation			0.1021		0.0561
None	383 (99.5%)	437 (100.0%)	.	5,886 (99.8%)	.
1	2 (0.5%)		.	11 (0.2%)	.
2			.		.
Number of systemic steroids episodes			-0.0707		-0.0447
None	366 (95.1%)	408 (93.4%)	.	5,544 (94.0%)	.
1	15 (3.9%)	27 (6.2%)	.	318 (5.4%)	.
2	3 (0.8%)	2 (0.5%)	.	27 (0.5%)	.
3 or more	1 (0.3%)		.	8 (0.1%)	.
Number of Antibiotic courses			-0.0687		0.0175
None	325 (84.4%)	357 (81.7%)	.	5,017 (85.1%)	.
1	43 (11.2%)	60 (13.7%)	.	593 (10.1%)	.
2	6 (1.6%)	11 (2.5%)	.	193 (3.3%)	.
3 or more	11 (2.9%)	9 (2.1%)	.	94 (1.6%)	.

HSD	QVA N(%)	Fixed LABA LAMA N(%)	Std Dif	LABA N(%)	Std Dif
COPD severity assessed by proxy			0.1474		0.4821
Mild	43 (11.2%)	64 (15.0%)	.	232 (26.5%)	.
Moderate	277 (72.0%)	308 (72.3%)	.	585 (66.9%)	.
Severe	16 (4.2%)	7 (1.6%)	.	21 (2.4%)	.
Very severe	49 (12.7%)	47 (11.0%)	.	37 (4.2%)	.
Number of hospitalizations for COPD exacerbation			0.1021		0.1021
None	383 (99.5%)	426 (100.0%)	.	875 (100.0%)	.
1	2 (0.5%)		.		.
2			.		.
Number of systemic steroids episodes			-0.0952		0.0289
None	366 (95.1%)	395 (92.7%)	.	837 (95.7%)	.
1	15 (3.9%)	30 (7.0%)	.	33 (3.8%)	.
2	3 (0.8%)		.	4 (0.5%)	.
3 or more	1 (0.3%)	1 (0.2%)	.	1 (0.1%)	.
Number of Antibiotic courses			0.0199		0.0968
None	325 (84.4%)	363 (85.2%)	.	768 (87.8%)	.
1	43 (11.2%)	42 (9.9%)	.	74 (8.5%)	.
2	6 (1.6%)	11 (2.6%)	.	21 (2.4%)	.
3 or more	11 (2.9%)	10 (2.4%)	.	12 (1.4%)	.

HSD	QVA N(%)	LAMA	Std Dif
COPD severity assessed by proxy			0.5406
Mild	43 (11.2%)	1,160 (32.3%)	.
Moderate	277 (72.0%)	2,126 (59.1%)	.
Severe	16 (4.2%)	103 (2.9%)	.
Very severe	49 (12.7%)	206 (5.7%)	.
Number of hospitalizations for COPD exacerbation			0.0382
None	383 (99.5%)	3,585 (99.7%)	.
1	2 (0.5%)	8 (0.2%)	.
2		2 (0.1%)	.
Number of systemic steroids episodes			-0.0185
None	366 (95.1%)	3,402 (94.6%)	.
1	15 (3.9%)	170 (4.7%)	.
2	3 (0.8%)	18 (0.5%)	.
3 or more	1 (0.3%)	5 (0.1%)	.
Number of Antibiotic courses			-0.0154
None	325 (84.4%)	3,017 (83.9%)	.
1	43 (11.2%)	383 (10.7%)	.
2	6 (1.6%)	123 (3.4%)	.
3 or more	11 (2.9%)	72 (2.0%)	.

SIDIAP	QVA N(%)	Free LABA+LAMA without ICS N(%)	Std Dif	Free LABA+LAMA with ICS N(%)	Std Dif
COPD severity assessed by proxy			0.0015		-0.3501
Mild	850 (15.3%)	521 (12.4%)	.	42 (2.4%)	.
Moderate	4,168 (75.0%)	3,421 (81.1%)	.	1,474 (85.5%)	.
Severe	543 (9.8%)	277 (6.6%)	.	209 (12.1%)	.
Number of hospitalizations for COPD exacerbation			0.1141		-0.0603
None	5,081 (91.4%)	3,977 (94.3%)	.	1,546 (89.6%)	.
1	369 (6.6%)	208 (4.9%)	.	134 (7.8%)	.
2	85 (1.5%)	28 (0.7%)	.	27 (1.6%)	.
3 or more	26 (0.5%)	6 (0.1%)	.	18 (1.0%)	.
Number of systemic steroids episodes			0.0348		-0.1044
None	5,263 (94.6%)	4,025 (95.4%)	.	1,588 (92.1%)	.
1	284 (5.1%)	182 (4.3%)	.	125 (7.3%)	.
2	14 (0.3%)	11 (0.3%)	.	8 (0.5%)	.
3 or more		1 (0.0%)	.	4 (0.2%)	.
Number of Antibiotic courses			0.021		-0.0673
None	4,689 (84.3%)	3,584 (85.0%)	.	1,413 (81.9%)	.
1	592 (10.7%)	468 (11.1%)	.	198 (11.5%)	.
2	202 (3.6%)	113 (2.7%)	.	82 (4.8%)	.
3 or more	78 (1.4%)	54 (1.3%)	.	32 (1.9%)	.

SIDIAP	QVA N(%)	Free LABA+ICS N(%)	Std Dif	Fixed LABA ICS N(%)	Std Dif
COPD severity assessed by proxy			-0.0353		0.2477
Mild	850 (15.3%)	281 (10.3%)	.	5,060 (24.5%)	.
Moderate	4,168 (75.0%)	2,290 (83.6%)	.	14247 (69.0%)	.
Severe	543 (9.8%)	167 (6.1%)	.	1,331 (6.5%)	.
Number of hospitalizations for COPD exacerbation			0.137		0.1145
None	5,081 (91.4%)	2,597 (94.9%)	.	19461 (94.3%)	.
1	369 (6.6%)	105 (3.8%)	.	964 (4.7%)	.
2	85 (1.5%)	21 (0.8%)	.	144 (0.7%)	.
3 or more	26 (0.5%)	15 (0.6%)	.	69 (0.3%)	.
Number of systemic steroids episodes			-0.0318		-0.0032
None	5,263 (94.6%)	2,571 (93.9%)	.	19517 (94.6%)	.
1	284 (5.1%)	160 (5.8%)	.	1,069 (5.2%)	.
2	14 (0.3%)	7 (0.3%)	.	49 (0.2%)	.
3 or more			.	3 (0.0%)	.
Number of Antibiotic courses			-0.1153		-0.0876
None	4,689 (84.3%)	2,185 (79.8%)	.	16681 (80.8%)	.
1	592 (10.7%)	388 (14.2%)	.	2,867 (13.9%)	.
2	202 (3.6%)	127 (4.6%)	.	845 (4.1%)	.
3 or more	78 (1.4%)	38 (1.4%)	.	245 (1.2%)	.

SIDIAP	QVA N(%)	Fixed LABA LAMA N(%)	Std Dif	LABA N(%)	Std Dif
COPD severity assessed by proxy			-0.1257		0.4864
Mild	850 (15.3%)	115 (11.9%)	.	1,988 (33.8%)	.
Moderate	4,168 (75.0%)	727 (75.4%)	.	3,693 (62.8%)	.
Severe	543 (9.8%)	122 (12.7%)	.	198 (3.4%)	.
Number of hospitalizations for COPD exacerbation			-0.1072		0.2575
None	5,081 (91.4%)	850 (88.2%)	.	5,718 (97.3%)	.
1	369 (6.6%)	81 (8.4%)	.	140 (2.4%)	.
2	85 (1.5%)	25 (2.6%)	.	13 (0.2%)	.
3 or more	26 (0.5%)	8 (0.8%)	.	8 (0.1%)	.
Number of systemic steroids episodes			-0.0789		0.0613
None	5,263 (94.6%)	894 (92.7%)	.	5,640 (95.9%)	.
1	284 (5.1%)	64 (6.6%)	.	234 (4.0%)	.
2	14 (0.3%)	4 (0.4%)	.	5 (0.1%)	.
3 or more		2 (0.2%)	.		.
Number of Antibiotic courses			-0.0631		-0.0319
None	4,689 (84.3%)	790 (82.0%)	.	4,874 (82.9%)	.
1	592 (10.7%)	117 (12.1%)	.	763 (13.0%)	.
2	202 (3.6%)	44 (4.6%)	.	190 (3.2%)	.
3 or more	78 (1.4%)	13 (1.4%)	.	52 (0.9%)	.

SIDIAP	QVA N(%)	LAMA	Std Dif
COPD severity assessed by proxy			0.565
Mild	850 (15.3%)	5,325 (38.9%)	.
Moderate	4,168 (75.0%)	7,778 (56.9%)	.
Severe	543 (9.8%)	575 (4.2%)	.
Number of hospitalizations for COPD exacerbation			0.2144
None	5,081 (91.4%)	13193 (96.5%)	.
1	369 (6.6%)	400 (2.9%)	.
2	85 (1.5%)	54 (0.4%)	.
3 or more	26 (0.5%)	31 (0.2%)	.
Number of systemic steroids episodes			0.0795
None	5,263 (94.6%)	13171 (96.3%)	.
1	284 (5.1%)	487 (3.6%)	.
2	14 (0.3%)	20 (0.2%)	.
3 or more			.
Number of Antibiotic courses			-0.0317
None	4,689 (84.3%)	11342 (82.9%)	.
1	592 (10.7%)	1,765 (12.9%)	.
2	202 (3.6%)	443 (3.2%)	.
3 or more	78 (1.4%)	128 (0.9%)	.

Table 15-5 Co-morbidities (assessed at and prior to index date) by exposure cohort (pooled and by database)

POOLED	QVA N(%)	Free LABA+LAMA without ICS N(%)	Std Dif	Free LABA+LAMA with ICS N(%)	Std Dif
Total	9,798 (100.0%)	9,619 (100.0%)	0	3,192 (100.0%)	0
Chronic kidney disease			0.1421		0.1039
No CKD	2,704 (27.6%)	2,225 (23.1%)	.	767 (24.0%)	.
Stage unknown	142 (1.5%)	127 (1.3%)	.	48 (1.5%)	.
Stage 1	24 (0.2%)	55 (0.6%)	.	20 (0.6%)	.
Stage 2	4,782 (48.8%)	4,647 (48.3%)	.	1,596 (50.0%)	.
Stage 3	1,928 (19.7%)	2,317 (24.1%)	.	680 (21.3%)	.
Stage 4	177 (1.8%)	205 (2.1%)	.	61 (1.9%)	.
Stage 5	41 (0.4%)	43 (0.5%)	.	20 (0.6%)	.
Cardiovascular comorbidities	6,047 (61.7%)	6,010 (62.5%)	-0.0157	2,081 (65.2%)	-0.0723
- Arterial hypertension	5,138 (52.4%)	5,143 (53.5%)	-0.0206	1,773 (55.6%)	-0.0623
- Unstable angina pectoris	225 (2.3%)	180 (1.9%)	0.0298	53 (1.7%)	0.0457
- Angina pectoris	988 (10.1%)	925 (9.6%)	0.0157	270 (8.5%)	0.056

POOLED	QVA N(%)	Free LABA+ICS N(%)	Std Dif	Fixed LABA ICS N(%)	Std Dif
Total	9,798 (100.0%)	4,628 (100.0%)	0	58332 (100.0%)	0
Chronic kidney disease			0.1082		0.1476
No CKD	2,704 (27.6%)	1,099 (23.8%)	.	13914 (23.9%)	.
Stage unknown	142 (1.5%)	69 (1.5%)	.	820 (1.4%)	.
Stage 1	24 (0.2%)	22 (0.5%)	.	390 (0.7%)	.
Stage 2	4,782 (48.8%)	2,276 (49.2%)	.	27369 (46.9%)	.
Stage 3	1,928 (19.7%)	1,043 (22.5%)	.	14065 (24.1%)	.
Stage 4	177 (1.8%)	97 (2.1%)	.	1,423 (2.4%)	.
Stage 5	41 (0.4%)	22 (0.5%)	.	351 (0.6%)	.
Cardiovascular comorbidities	6,047 (61.7%)	2,958 (63.9%)	-0.0455	34854 (59.8%)	0.0403
- Arterial hypertension	5,138 (52.4%)	2,627 (56.8%)	-0.0869	29844 (51.2%)	0.0256
- Unstable angina pectoris	225 (2.3%)	73 (1.6%)	0.0522	1,221 (2.1%)	0.0139
- Angina pectoris	988 (10.1%)	335 (7.2%)	0.1013	5,930 (10.2%)	-0.0027

POOLED	QVA N(%)	Fixed LABA LAMA N(%)	Std Dif	LABA N(%)	Std Dif
Total	9,798 (100.0%)	9,150 (100.0%)	0	12364 (100.0%)	0
Chronic kidney disease			0.2343		0.0732
No CKD	2,704 (27.6%)	1,806 (19.7%)	.	3,152 (25.5%)	.
Stage unknown	142 (1.5%)	101 (1.1%)	.	170 (1.4%)	.
Stage 1	24 (0.2%)	40 (0.4%)	.	61 (0.5%)	.
Stage 2	4,782 (48.8%)	4,451 (48.6%)	.	6,012 (48.6%)	.
Stage 3	1,928 (19.7%)	2,498 (27.3%)	.	2,677 (21.7%)	.
Stage 4	177 (1.8%)	211 (2.3%)	.	236 (1.9%)	.
Stage 5	41 (0.4%)	43 (0.5%)	.	56 (0.5%)	.
Cardiovascular comorbidities	6,047 (61.7%)	5,264 (57.5%)	0.0854	7,340 (59.4%)	0.0481
- Arterial hypertension	5,138 (52.4%)	4,164 (45.5%)	0.139	6,431 (52.0%)	0.0085
- Unstable angina pectoris	225 (2.3%)	271 (3.0%)	-0.0416	223 (1.8%)	0.0348
- Angina pectoris	988 (10.1%)	1,396 (15.3%)	-0.156	1,103 (8.9%)	0.0397

POOLED	QVA N(%)	LAMA	Std Dif
Total	9,798 (100.0%)	42972 (100.0%)	0
Chronic kidney disease			0.1764
No CKD	2,704 (27.6%)	9,574 (22.3%)	.
Stage unknown	142 (1.5%)	531 (1.2%)	.
Stage 1	24 (0.2%)	217 (0.5%)	.
Stage 2	4,782 (48.8%)	20431 (47.5%)	.
Stage 3	1,928 (19.7%)	10901 (25.4%)	.
Stage 4	177 (1.8%)	1,073 (2.5%)	.
Stage 5	41 (0.4%)	245 (0.6%)	.
Cardiovascular comorbidities	6,047 (61.7%)	25774 (60.0%)	0.0356
- Arterial hypertension	5,138 (52.4%)	21816 (50.8%)	0.0334
- Unstable angina pectoris	225 (2.3%)	917 (2.1%)	0.011
- Angina pectoris	988 (10.1%)	4,792 (11.2%)	-0.0347

POOLED	QVA N(%)	Free LABA+LAMA without ICS N(%)	Std Dif	Free LABA+LAMA with ICS N(%)	Std Dif
- Myocardial infarction	732 (7.5%)	689 (7.2%)	0.0118	214 (6.7%)	0.0299
- Heart failure	883 (9.0%)	810 (8.4%)	0.021	333 (10.4%)	-0.0479
- Atrial fibrillation/flutter	8,466 (86.4%)	8,558 (89.0%)	0.0781	2,802 (87.8%)	0.0411
Cardia arrhythmia	1,678 (17.1%)	1,410 (14.7%)	0.0675	543 (17.0%)	0.003
- Atrial fibrillation/flutter	8,466 (86.4%)	8,558 (89.0%)	0.0781	2,802 (87.8%)	0.0411
- Torsade de Pointes/Long QT	1 (0.0%)	5 (0.1%)	-0.0237	1 (0.0%)	-0.0147
- Ventricular fibrillation	14 (0.1%)	9 (0.1%)	0.0144	9 (0.3%)	-0.0302
- Ventricular tachycardia	23 (0.2%)	28 (0.3%)	-0.011	8 (0.3%)	-0.0032
- AV block	166 (1.7%)	166 (1.7%)	-0.0024	70 (2.2%)	-0.0361
- Sick Sinus	41 (0.4%)	28 (0.3%)	0.0214	7 (0.2%)	0.0353
- Supraventricular tachycardia	159 (1.6%)	111 (1.2%)	0.0401	53 (1.7%)	-0.003
- Premature depolarization	140 (1.4%)	164 (1.7%)	-0.0222	71 (2.2%)	-0.0594
Cerebrovascular comorbidities	890 (9.1%)	911 (9.5%)	-0.0134	292 (9.2%)	-0.0022
- Stroke	643 (6.6%)	648 (6.7%)	-0.007	185 (5.8%)	0.0318

POOLED	QVA N(%)	Free LABA+ICS N(%)	Std Dif	Fixed LABA ICS N(%)	Std Dif
- Myocardial infarction	732 (7.5%)	266 (5.8%)	0.0694	4,104 (7.0%)	0.0168
- Heart failure	883 (9.0%)	402 (8.7%)	0.0115	4,932 (8.5%)	0.0197
- Atrial fibrillation/flutter	8,466 (86.4%)	4,069 (87.9%)	0.0453	51987 (89.1%)	0.083
Cardia arrhythmia	1,678 (17.1%)	746 (16.1%)	0.027	8,210 (14.1%)	0.0842
- Atrial fibrillation/flutter	8,466 (86.4%)	4,069 (87.9%)	0.0453	51987 (89.1%)	0.083
- Torsade de Pointes/Long QT	1 (0.0%)	0 (0.0%)	0.0143	24 (0.0%)	-0.0193
- Ventricular fibrillation	14 (0.1%)	3 (0.1%)	0.0242	89 (0.2%)	-0.0025
- Ventricular tachycardia	23 (0.2%)	11 (0.2%)	-0.0006	135 (0.2%)	0.0007
- AV block	166 (1.7%)	84 (1.8%)	-0.0092	720 (1.2%)	0.0383
- Sick Sinus	41 (0.4%)	11 (0.2%)	0.0316	181 (0.3%)	0.018
- Supraventricular tachycardia	159 (1.6%)	59 (1.3%)	0.0291	768 (1.3%)	0.0254
- Premature depolarization	140 (1.4%)	96 (2.1%)	-0.0492	843 (1.5%)	-0.0014
Cerebrovascular comorbidities	890 (9.1%)	414 (9.0%)	0.0048	5,554 (9.5%)	-0.0151
- Stroke	643 (6.6%)	286 (6.2%)	0.0157	4,097 (7.0%)	-0.0183

POOLED	QVA N(%)	Fixed LABA LAMA N(%)	Std Dif	LABA N(%)	Std Dif
- Myocardial infarction	732 (7.5%)	768 (8.4%)	-0.0341	774 (6.3%)	0.0479
- Heart failure	883 (9.0%)	891 (9.7%)	-0.0249	834 (6.8%)	0.0842
- Atrial fibrillation/flutter	8,466 (86.4%)	8,048 (88.0%)	0.0464	11109 (89.9%)	0.1066
Cardia arrhythmia	1,678 (17.1%)	1,371 (15.0%)	0.0584	1,659 (13.4%)	0.1032
- Atrial fibrillation/flutter	8,466 (86.4%)	8,048 (88.0%)	0.0464	11109 (89.9%)	0.1066
- Torsade de Pointes/Long QT	1 (0.0%)	2 (0.0%)	-0.0092	5 (0.0%)	-0.019
- Ventricular fibrillation	14 (0.1%)	14 (0.2%)	-0.0026	19 (0.2%)	-0.0028
- Ventricular tachycardia	23 (0.2%)	30 (0.3%)	-0.0176	24 (0.2%)	0.0088
- AV block	166 (1.7%)	94 (1.0%)	0.0576	191 (1.5%)	0.0118
- Sick Sinus	41 (0.4%)	37 (0.4%)	0.0022	34 (0.3%)	0.0244
- Supraventricular tachycardia	159 (1.6%)	163 (1.8%)	-0.0123	144 (1.2%)	0.0391
- Premature depolarization	140 (1.4%)	112 (1.2%)	0.0179	174 (1.4%)	0.0018
Cerebrovascular comorbidities	890 (9.1%)	913 (10.0%)	-0.0305	1,116 (9.0%)	0.002
- Stroke	643 (6.6%)	653 (7.1%)	-0.0227	768 (6.2%)	0.0144

POOLED	QVA N(%)	LAMA	Std Dif
- Myocardial infarction	732 (7.5%)	3,355 (7.8%)	-0.0127
- Heart failure	883 (9.0%)	3,482 (8.1%)	0.0325
- Atrial fibrillation/flutter	8,466 (86.4%)	38207 (88.9%)	0.0762
Cardia arrhythmia	1,678 (17.1%)	6,210 (14.5%)	0.0734
- Atrial fibrillation/flutter	8,466 (86.4%)	38207 (88.9%)	0.0762
- Torsade de Pointes/Long QT	1 (0.0%)	12 (0.0%)	-0.0128
- Ventricular fibrillation	14 (0.1%)	66 (0.2%)	-0.0028
- Ventricular tachycardia	23 (0.2%)	117 (0.3%)	-0.0075
- AV block	166 (1.7%)	536 (1.3%)	0.0371
- Sick Sinus	41 (0.4%)	112 (0.3%)	0.0271
- Supraventricular tachycardia	159 (1.6%)	548 (1.3%)	0.0291
- Premature depolarization	140 (1.4%)	719 (1.7%)	-0.0198
Cerebrovascular comorbidities	890 (9.1%)	4,047 (9.4%)	-0.0115
- Stroke	643 (6.6%)	3,010 (7.0%)	-0.0176

POOLED	QVA N(%)	Free LABA+LAMA without ICS N(%)	Std Dif	Free LABA+LAMA with ICS N(%)	Std Dif
- TIA	344 (3.5%)	404 (4.2%)	-0.0358	129 (4.0%)	-0.0278
Diabetes Mellitus (validated)	1,914 (19.5%)	1,822 (18.9%)	0.015	642 (20.1%)	-0.0145
Hyperlipidemia	2,035 (20.8%)	2,143 (22.3%)	-0.0367	706 (22.1%)	-0.0329
Hepatic injury	200 (2.0%)	293 (3.1%)	-0.0638	64 (2.0%)	0.0026
Lung cancer	295 (3.0%)	215 (2.2%)	0.0485	85 (2.7%)	0.021
Cancer (excluding lung cancer)	1,627 (16.6%)	1,539 (16.0%)	0.0164	512 (16.0%)	0.0153
Asthma	1,167 (11.9%)	1,373 (14.3%)	-0.0701	756 (23.7%)	-0.3115
BPH	1,808 (18.5%)	1,662 (17.3%)	0.0307	652 (20.4%)	-0.0499
Bladder obstruction/urinary retention	228 (2.3%)	250 (2.6%)	-0.0175	91 (2.9%)	-0.033

POOLED	QVA N(%)	Free LABA+ICS N(%)	Std Dif	Fixed LABA ICS N(%)	Std Dif
- TIA	344 (3.5%)	166 (3.6%)	-0.0041	2,388 (4.1%)	-0.0305
Diabetes Mellitus (validated)	1,914 (19.5%)	990 (21.4%)	-0.046	10431 (17.9%)	0.0424
Hyperlipidemia	2,035 (20.8%)	1,009 (21.8%)	-0.0252	13153 (22.6%)	-0.0432
Hepatic injury	200 (2.0%)	102 (2.2%)	-0.0113	1,945 (3.3%)	-0.08
Lung cancer	295 (3.0%)	72 (1.6%)	0.0975	956 (1.6%)	0.0911
Cancer (excluding lung cancer)	1,627 (16.6%)	729 (15.8%)	0.0232	7,873 (13.5%)	0.087
Asthma	1,167 (11.9%)	1,226 (26.5%)	-0.3766	14517 (24.9%)	-0.3397
BPH	1,808 (18.5%)	883 (19.1%)	-0.0161	7,328 (12.6%)	0.1633
Bladder obstruction/urinary retention	228 (2.3%)	108 (2.3%)	-0.0004	1,376 (2.4%)	-0.0021

POOLED	QVA N(%)	Fixed LABA LAMA N(%)	Std Dif	LABA N(%)	Std Dif
- TIA	344 (3.5%)	410 (4.5%)	-0.0495	503 (4.1%)	-0.0292
Diabetes Mellitus (validated)	1,914 (19.5%)	1,508 (16.5%)	0.0795	2,255 (18.2%)	0.0331
Hyperlipidemia	2,035 (20.8%)	2,032 (22.2%)	-0.035	2,585 (20.9%)	-0.0034
Hepatic injury	200 (2.0%)	357 (3.9%)	-0.1097	336 (2.7%)	-0.0444
Lung cancer	295 (3.0%)	262 (2.9%)	0.0087	172 (1.4%)	0.1106
Cancer (excluding lung cancer)	1,627 (16.6%)	1,319 (14.4%)	0.0605	1,742 (14.1%)	0.0698
Asthma	1,167 (11.9%)	1,880 (20.6%)	-0.2358	1,655 (13.4%)	-0.0444
BPH	1,808 (18.5%)	921 (10.1%)	0.2416	1,822 (14.7%)	0.1
Bladder obstruction/urinary retention	228 (2.3%)	261 (2.9%)	-0.0331	280 (2.3%)	0.0042

POOLED	QVA N(%)	LAMA	Std Dif
- TIA	344 (3.5%)	1,794 (4.2%)	-0.0345
Diabetes Mellitus (validated)	1,914 (19.5%)	7,469 (17.4%)	0.0555
Hyperlipidemia	2,035 (20.8%)	9,942 (23.1%)	-0.0572
Hepatic injury	200 (2.0%)	1,516 (3.5%)	-0.0904
Lung cancer	295 (3.0%)	625 (1.5%)	0.1055
Cancer (excluding lung cancer)	1,627 (16.6%)	5,801 (13.5%)	0.0869
Asthma	1,167 (11.9%)	7,540 (17.6%)	-0.1595
BPH	1,808 (18.5%)	5,550 (12.9%)	0.1527
Bladder obstruction/urinary retention	228 (2.3%)	1,029 (2.4%)	-0.0045

THIN	QVA N(%)	Free LABA+LAMA without ICS N(%)	Std Dif	Free LABA+LAMA with ICS N(%)	Std Dif
Total	1,346 (100.0%)	2,586 (100.0%)	0	394 (100.0%)	0
Chronic kidney disease			0.1206		0.127
No CKD	184 (13.7%)	332 (12.8%)	.	50 (12.7%)	.
Stage unknown	8 (0.6%)	20 (0.8%)	.	4 (1.0%)	.
Stage 1	2 (0.2%)		.		.
Stage 2	665 (49.4%)	1,276 (49.3%)	.	208 (52.8%)	.
Stage 3	438 (32.5%)	897 (34.7%)	.	123 (31.2%)	.
Stage 4	42 (3.1%)	59 (2.3%)	.	7 (1.8%)	.
Stage 5	7 (0.5%)	2 (0.1%)	.	2 (0.5%)	.
Cardiovascular comorbidities	793 (58.9%)	1,454 (56.2%)	0.0544	220 (55.8%)	0.0622
- Arterial hypertension	641 (47.6%)	1,192 (46.1%)	0.0306	178 (45.2%)	0.049
- Unstable angina pectoris	49 (3.6%)	67 (2.6%)	0.0604	9 (2.3%)	0.08
- Angina pectoris	251 (18.7%)	417 (16.1%)	0.0666	53 (13.5%)	0.1418

THIN	QVA N(%)	Free LABA+ICS N(%)	Std Dif	Fixed LABA ICS N(%)	Std Dif
Total	1,346 (100.0%)	583 (100.0%)	0	21315 (100.0%)	0
Chronic kidney disease			0.17		0.0739
No CKD	184 (13.7%)	75 (12.9%)	.	3,003 (14.1%)	.
Stage unknown	8 (0.6%)	6 (1.0%)	.	219 (1.0%)	.
Stage 1	2 (0.2%)	1 (0.2%)	.	7 (0.0%)	.
Stage 2	665 (49.4%)	293 (50.3%)	.	10469 (49.1%)	.
Stage 3	438 (32.5%)	201 (34.5%)	.	6,980 (32.8%)	.
Stage 4	42 (3.1%)	6 (1.0%)	.	564 (2.7%)	.
Stage 5	7 (0.5%)	1 (0.2%)	.	73 (0.3%)	.
Cardiovascular comorbidities	793 (58.9%)	322 (55.2%)	0.0744	11776 (55.3%)	0.0741
- Arterial hypertension	641 (47.6%)	274 (47.0%)	0.0125	9,740 (45.7%)	0.0386
- Unstable angina pectoris	49 (3.6%)	13 (2.2%)	0.0836	568 (2.7%)	0.0558
- Angina pectoris	251 (18.7%)	75 (12.9%)	0.1591	3,324 (15.6%)	0.0811

THIN	QVA N(%)	Fixed LABA LAMA N(%)	Std Dif	LABA N(%)	Std Dif
Total	1,346 (100.0%)	4,921 (100.0%)	0	3,006 (100.0%)	0
Chronic kidney disease			0.0885		0.0898
No CKD	184 (13.7%)	635 (12.9%)	.	382 (12.7%)	.
Stage unknown	8 (0.6%)	54 (1.1%)	.	29 (1.0%)	.
Stage 1	2 (0.2%)	2 (0.0%)	.		.
Stage 2	665 (49.4%)	2,401 (48.8%)	.	1,482 (49.3%)	.
Stage 3	438 (32.5%)	1,679 (34.1%)	.	1,024 (34.1%)	.
Stage 4	42 (3.1%)	138 (2.8%)	.	80 (2.7%)	.
Stage 5	7 (0.5%)	12 (0.2%)	.	9 (0.3%)	.
Cardiovascular comorbidities	793 (58.9%)	2,732 (55.5%)	0.0687	1,617 (53.8%)	0.1034
- Arterial hypertension	641 (47.6%)	2,229 (45.3%)	0.0467	1,340 (44.6%)	0.0611
- Unstable angina pectoris	49 (3.6%)	138 (2.8%)	0.0473	76 (2.5%)	0.0643
- Angina pectoris	251 (18.7%)	800 (16.3%)	0.063	466 (15.5%)	0.0836

THIN	QVA N(%)	LAMA	Std Dif
Total	1,346 (100.0%)	18598 (100.0%)	0
Chronic kidney disease			0.0759
No CKD	184 (13.7%)	2,642 (14.2%)	.
Stage unknown	8 (0.6%)	149 (0.8%)	.
Stage 1	2 (0.2%)	1 (0.0%)	.
Stage 2	665 (49.4%)	9,023 (48.5%)	.
Stage 3	438 (32.5%)	6,208 (33.4%)	.
Stage 4	42 (3.1%)	525 (2.8%)	.
Stage 5	7 (0.5%)	50 (0.3%)	.
Cardiovascular comorbidities	793 (58.9%)	10368 (55.8%)	0.0641
- Arterial hypertension	641 (47.6%)	8,514 (45.8%)	0.0369
- Unstable angina pectoris	49 (3.6%)	476 (2.6%)	0.0624
- Angina pectoris	251 (18.7%)	2,936 (15.8%)	0.0758

THIN	QVA N(%)	Free LABA+LAMA without ICS N(%)	Std Dif	Free LABA+LAMA with ICS N(%)	Std Dif
- Myocardial infarction	114 (8.5%)	217 (8.4%)	0.0028	26 (6.6%)	0.0709
- Heart failure	131 (9.7%)	189 (7.3%)	0.0869	24 (6.1%)	0.1351
- Atrial fibrillation/flutter	1,194 (88.7%)	2,366 (91.5%)	0.0933	368 (93.4%)	0.1649
Cardia arrhythmia	175 (13.0%)	264 (10.2%)	0.0873	32 (8.1%)	0.1592
- Atrial fibrillation/flutter	1,194 (88.7%)	2,366 (91.5%)	0.0933	368 (93.4%)	0.1649
- Torsade de Pointes/Long QT	0 (0.0%)	2 (0.1%)	-0.0393	0 (0.0%)	.
- Ventricular fibrillation	1 (0.1%)	1 (0.0%)	0.015	0 (0.0%)	0.0385
- Ventricular tachycardia	0 (0.0%)	3 (0.1%)	-0.0482	0 (0.0%)	.
- AV block	2 (0.2%)	10 (0.4%)	-0.0461	0 (0.0%)	0.0545
- Sick Sinus	0 (0.0%)	2 (0.1%)	-0.0393	0 (0.0%)	.
- Supraventricular tachycardia	19 (1.4%)	27 (1.0%)	0.0334	9 (2.3%)	-0.0648
- Premature depolarization	12 (0.9%)	16 (0.6%)	0.0315	2 (0.5%)	0.046
Cerebrovascular comorbidities	141 (10.5%)	306 (11.8%)	-0.0431	34 (8.6%)	0.0628
- Stroke	110 (8.2%)	248 (9.6%)	-0.0498	20 (5.1%)	0.1246

THIN	QVA N(%)	Free LABA+ICS N(%)	Std Dif	Fixed LABA ICS N(%)	Std Dif
- Myocardial infarction	114 (8.5%)	33 (5.7%)	0.1097	1,737 (8.2%)	0.0116
- Heart failure	131 (9.7%)	31 (5.3%)	0.1679	1,598 (7.5%)	0.0797
- Atrial fibrillation/flutter	1,194 (88.7%)	540 (92.6%)	0.1349	19349 (90.8%)	0.0682
Cardia arrhythmia	175 (13.0%)	54 (9.3%)	0.119	2,301 (10.8%)	0.0682
- Atrial fibrillation/flutter	1,194 (88.7%)	540 (92.6%)	0.1349	19349 (90.8%)	0.0682
- Torsade de Pointes/Long QT	0 (0.0%)	0 (0.0%)	.	17 (0.1%)	-0.04
- Ventricular fibrillation	1 (0.1%)	1 (0.2%)	-0.0277	22 (0.1%)	-0.0097
- Ventricular tachycardia	0 (0.0%)	1 (0.2%)	-0.0586	45 (0.2%)	-0.065
- AV block	2 (0.2%)	1 (0.2%)	-0.0057	30 (0.1%)	0.0021
- Sick Sinus	0 (0.0%)	0 (0.0%)	.	24 (0.1%)	-0.0475
- Supraventricular tachycardia	19 (1.4%)	11 (1.9%)	-0.0373	232 (1.1%)	0.0291
- Premature depolarization	12 (0.9%)	3 (0.5%)	0.0451	140 (0.7%)	0.0268
Cerebrovascular comorbidities	141 (10.5%)	48 (8.2%)	0.077	2,267 (10.6%)	-0.0052
- Stroke	110 (8.2%)	39 (6.7%)	0.0565	1,841 (8.6%)	-0.0167

THIN	QVA N(%)	Fixed LABA LAMA N(%)	Std Dif	LABA N(%)	Std Dif
- Myocardial infarction	114 (8.5%)	414 (8.4%)	0.002	258 (8.6%)	-0.0041
- Heart failure	131 (9.7%)	394 (8.0%)	0.0607	212 (7.1%)	0.0967
- Atrial fibrillation/flutter	1,194 (88.7%)	4,452 (90.5%)	0.0577	2,743 (91.3%)	0.0848
Cardia arrhythmia	175 (13.0%)	550 (11.2%)	0.056	307 (10.2%)	0.0871
- Atrial fibrillation/flutter	1,194 (88.7%)	4,452 (90.5%)	0.0577	2,743 (91.3%)	0.0848
- Torsade de Pointes/Long QT	0 (0.0%)	1 (0.0%)	-0.0202	2 (0.1%)	-0.0365
- Ventricular fibrillation	1 (0.1%)	2 (0.0%)	0.014	5 (0.2%)	-0.0265
- Ventricular tachycardia	0 (0.0%)	12 (0.2%)	-0.0699	4 (0.1%)	-0.0516
- AV block	2 (0.2%)	11 (0.2%)	-0.0174	4 (0.1%)	0.0041
- Sick Sinus	0 (0.0%)	3 (0.1%)	-0.0349	3 (0.1%)	-0.0447
- Supraventricular tachycardia	19 (1.4%)	50 (1.0%)	0.0361	26 (0.9%)	0.0515
- Premature depolarization	12 (0.9%)	27 (0.6%)	0.0405	18 (0.6%)	0.034
Cerebrovascular comorbidities	141 (10.5%)	483 (9.8%)	0.0219	297 (9.9%)	0.0197
- Stroke	110 (8.2%)	380 (7.7%)	0.0166	225 (7.5%)	0.0256

THIN	QVA N(%)	LAMA	Std Dif
- Myocardial infarction	114 (8.5%)	1,587 (8.5%)	-0.0023
- Heart failure	131 (9.7%)	1,370 (7.4%)	0.0847
- Atrial fibrillation/flutter	1,194 (88.7%)	16842 (90.6%)	0.0607
Cardia arrhythmia	175 (13.0%)	2,074 (11.2%)	0.0568
- Atrial fibrillation/flutter	1,194 (88.7%)	16842 (90.6%)	0.0607
- Torsade de Pointes/Long QT	0 (0.0%)	6 (0.0%)	-0.0254
- Ventricular fibrillation	1 (0.1%)	21 (0.1%)	-0.0126
- Ventricular tachycardia	0 (0.0%)	42 (0.2%)	-0.0673
- AV block	2 (0.2%)	36 (0.2%)	-0.0109
- Sick Sinus	0 (0.0%)	10 (0.1%)	-0.0328
- Supraventricular tachycardia	19 (1.4%)	202 (1.1%)	0.0293
- Premature depolarization	12 (0.9%)	132 (0.7%)	0.0204
Cerebrovascular comorbidities	141 (10.5%)	1,867 (10.0%)	0.0144
- Stroke	110 (8.2%)	1,542 (8.3%)	-0.0043

THIN	QVA N(%)	Free LABA+LAMA without ICS N(%)	Std Dif	Free LABA+LAMA with ICS N(%)	Std Dif
- TIA	78 (5.8%)	155 (6.0%)	-0.0084	23 (5.8%)	-0.0018
Diabetes Mellitus (validated)	221 (16.4%)	337 (13.0%)	0.0957	41 (10.4%)	0.177
Hyperlipidemia	290 (21.6%)	588 (22.7%)	-0.0287	87 (22.1%)	-0.013
Hepatic injury	62 (4.6%)	137 (5.3%)	-0.0319	19 (4.8%)	-0.0102
Lung cancer	29 (2.2%)	49 (1.9%)	0.0184	7 (1.8%)	0.0272
Cancer (excluding lung cancer)	165 (12.3%)	331 (12.8%)	-0.0163	41 (10.4%)	0.0584
Asthma	385 (28.6%)	709 (27.4%)	0.0264	242 (61.4%)	-0.6982
BPH	117 (8.7%)	196 (7.6%)	0.0407	34 (8.6%)	0.0022
Bladder obstruction/urinary retention	46 (3.4%)	81 (3.1%)	0.016	16 (4.1%)	-0.0339

THIN	QVA N(%)	Free LABA+ICS N(%)	Std Dif	Fixed LABA ICS N(%)	Std Dif
- TIA	78 (5.8%)	21 (3.6%)	0.1037	1,111 (5.2%)	0.0255
Diabetes Mellitus (validated)	221 (16.4%)	89 (15.3%)	0.0316	3,026 (14.2%)	0.0617
Hyperlipidemia	290 (21.6%)	147 (25.2%)	-0.0867	4,700 (22.1%)	-0.0122
Hepatic injury	62 (4.6%)	20 (3.4%)	0.0599	1,014 (4.8%)	-0.0071
Lung cancer	29 (2.2%)	3 (0.5%)	0.1432	291 (1.4%)	0.06
Cancer (excluding lung cancer)	165 (12.3%)	67 (11.5%)	0.0237	2,623 (12.3%)	-0.0014
Asthma	385 (28.6%)	371 (63.6%)	-0.7502	7,973 (37.4%)	-0.188
BPH	117 (8.7%)	52 (8.9%)	-0.008	1,490 (7.0%)	0.0633
Bladder obstruction/urinary retention	46 (3.4%)	27 (4.6%)	-0.0617	616 (2.9%)	0.0302

THIN	QVA N(%)	Fixed LABA LAMA N(%)	Std Dif	LABA N(%)	Std Dif
- TIA	78 (5.8%)	220 (4.5%)	0.06	163 (5.4%)	0.0162
Diabetes Mellitus (validated)	221 (16.4%)	743 (15.1%)	0.0362	397 (13.2%)	0.0905
Hyperlipidemia	290 (21.6%)	1,137 (23.1%)	-0.0375	605 (20.1%)	0.0349
Hepatic injury	62 (4.6%)	264 (5.4%)	-0.0348	140 (4.7%)	-0.0024
Lung cancer	29 (2.2%)	98 (2.0%)	0.0114	30 (1.0%)	0.0929
Cancer (excluding lung cancer)	165 (12.3%)	631 (12.8%)	-0.017	362 (12.0%)	0.0066
Asthma	385 (28.6%)	1,332 (27.1%)	0.0343	702 (23.4%)	0.1199
BPH	117 (8.7%)	392 (8.0%)	0.0263	237 (7.9%)	0.0293
Bladder obstruction/urinary retention	46 (3.4%)	143 (2.9%)	0.0292	99 (3.3%)	0.0069

THIN	QVA N(%)	LAMA	Std Dif
- TIA	78 (5.8%)	908 (4.9%)	0.0406
Diabetes Mellitus (validated)	221 (16.4%)	2,583 (13.9%)	0.0706
Hyperlipidemia	290 (21.6%)	4,076 (21.9%)	-0.009
Hepatic injury	62 (4.6%)	913 (4.9%)	-0.0142
Lung cancer	29 (2.2%)	230 (1.2%)	0.0711
Cancer (excluding lung cancer)	165 (12.3%)	2,268 (12.2%)	0.0019
Asthma	385 (28.6%)	4,731 (25.4%)	0.0713
BPH	117 (8.7%)	1,377 (7.4%)	0.0474
Bladder obstruction/urinary retention	46 (3.4%)	544 (2.9%)	0.0281

IPCI	QVA N(%)	Free LABA+LAMA without ICS N(%)	Std Dif	Free LABA+LAMA with ICS N(%)	Std Dif
Total	699 (100.0%)	1,148 (100.0%)	0	496 (100.0%)	0
Chronic kidney disease			0.135		0.1387
No CKD	251 (35.9%)	366 (31.9%)	.	152 (30.7%)	.
Stage unknown	17 (2.4%)	22 (1.9%)	.	12 (2.4%)	.
Stage 2	335 (47.9%)	558 (48.6%)	.	267 (53.8%)	.
Stage 3	92 (13.2%)	190 (16.6%)	.	60 (12.1%)	.
Stage 4	3 (0.4%)	11 (1.0%)	.	3 (0.6%)	.
Stage 5	1 (0.1%)	1 (0.1%)	.	2 (0.4%)	.
Cardiovascular comorbidities	411 (58.8%)	713 (62.1%)	-0.0677	296 (59.7%)	-0.0179
- Arterial hypertension	301 (43.1%)	555 (48.3%)	-0.1061	220 (44.4%)	-0.0261
- Unstable angina pectoris	24 (3.4%)	37 (3.2%)	0.0117	14 (2.8%)	0.0351
- Angina pectoris	93 (13.3%)	195 (17.0%)	-0.1028	86 (17.3%)	-0.1121
- Myocardial infarction	76 (10.9%)	123 (10.7%)	0.0051	46 (9.3%)	0.0531

IPCI	QVA N(%)	Free LABA+ICS N(%)	Std Dif	Fixed LABA ICS N(%)	Std Dif
Total	699 (100.0%)	597 (100.0%)	0	7,001 (100.0%)	0
Chronic kidney disease			0.1997		0.1045
No CKD	251 (35.9%)	175 (29.3%)	.	2,641 (37.7%)	.
Stage unknown	17 (2.4%)	6 (1.0%)	.	113 (1.6%)	.
Stage 2	335 (47.9%)	320 (53.6%)	.	3,275 (46.8%)	.
Stage 3	92 (13.2%)	88 (14.7%)	.	887 (12.7%)	.
Stage 4	3 (0.4%)	6 (1.0%)	.	78 (1.1%)	.
Stage 5	1 (0.1%)	2 (0.3%)	.	7 (0.1%)	.
Cardiovascular comorbidities	411 (58.8%)	383 (64.2%)	-0.1101	4,061 (58.0%)	0.0161
- Arterial hypertension	301 (43.1%)	297 (49.8%)	-0.1343	3,109 (44.4%)	-0.0271
- Unstable angina pectoris	24 (3.4%)	17 (2.9%)	0.0336	227 (3.2%)	0.0106
- Angina pectoris	93 (13.3%)	93 (15.6%)	-0.0647	1,006 (14.4%)	-0.0308
- Myocardial infarction	76 (10.9%)	66 (11.1%)	-0.0058	674 (9.6%)	0.0411

IPCI	QVA N(%)	Fixed LABA LAMA N(%)	Std Dif	LABA N(%)	Std Dif
Total	699 (100.0%)	1,081 (100.0%)	0	1,526 (100.0%)	0
Chronic kidney disease			0.1551		0.0706
No CKD	251 (35.9%)	345 (31.9%)	.	527 (34.5%)	.
Stage unknown	17 (2.4%)	22 (2.0%)	.	32 (2.1%)	.
Stage 2	335 (47.9%)	518 (47.9%)	.	732 (48.0%)	.
Stage 3	92 (13.2%)	180 (16.7%)	.	220 (14.4%)	.
Stage 4	3 (0.4%)	15 (1.4%)	.	13 (0.9%)	.
Stage 5	1 (0.1%)	1 (0.1%)	.	2 (0.1%)	.
Cardiovascular comorbidities	411 (58.8%)	657 (60.8%)	-0.0403	866 (56.8%)	0.0415
- Arterial hypertension	301 (43.1%)	479 (44.3%)	-0.0252	696 (45.6%)	-0.0513
- Unstable angina pectoris	24 (3.4%)	36 (3.3%)	0.0057	40 (2.6%)	0.0474
- Angina pectoris	93 (13.3%)	150 (13.9%)	-0.0167	196 (12.8%)	0.0137
- Myocardial infarction	76 (10.9%)	112 (10.4%)	0.0166	137 (9.0%)	0.0634

IPCI	QVA N(%)	LAMA	Std Dif
Total	699 (100.0%)	5,006 (100.0%)	0
Chronic kidney disease			0.0856
No CKD	251 (35.9%)	1,776 (35.5%)	.
Stage unknown	17 (2.4%)	82 (1.6%)	.
Stage 2	335 (47.9%)	2,386 (47.7%)	.
Stage 3	92 (13.2%)	715 (14.3%)	.
Stage 4	3 (0.4%)	43 (0.9%)	.
Stage 5	1 (0.1%)	4 (0.1%)	.
Cardiovascular comorbidities	411 (58.8%)	2,968 (59.3%)	-0.01
- Arterial hypertension	301 (43.1%)	2,256 (45.1%)	-0.0404
- Unstable angina pectoris	24 (3.4%)	148 (3.0%)	0.0271
- Angina pectoris	93 (13.3%)	753 (15.0%)	-0.0498
- Myocardial infarction	76 (10.9%)	526 (10.5%)	0.0118

IPCI	QVA N(%)	Free LABA+LAMA without ICS N(%)	Std Dif	Free LABA+LAMA with ICS N(%)	Std Dif
- Heart failure	80 (11.4%)	126 (11.0%)	0.0149	68 (13.7%)	-0.0683
- Atrial fibrillation/flutter	594 (85.0%)	1,005 (87.5%)	0.0745	439 (88.5%)	0.1041
Cardia arrhythmia	129 (18.5%)	196 (17.1%)	0.0361	89 (17.9%)	0.0132
- Atrial fibrillation/flutter	594 (85.0%)	1,005 (87.5%)	0.0745	439 (88.5%)	0.1041
- Torsade de Pointes/Long QT	0 (0.0%)	1 (0.1%)	-0.0417	1 (0.2%)	-0.0635
- Ventricular fibrillation	3 (0.4%)	3 (0.3%)	0.0286	6 (1.2%)	-0.0866
- Ventricular tachycardia	2 (0.3%)	8 (0.7%)	-0.0587	5 (1.0%)	-0.09
- AV block	7 (1.0%)	18 (1.6%)	-0.0503	4 (0.8%)	0.0206
- Sick Sinus	3 (0.4%)	4 (0.4%)	0.013	0 (0.0%)	0.0928
- Supraventricular tachycardia	8 (1.1%)	20 (1.7%)	-0.0501	15 (3.0%)	-0.1317
- Premature depolarization	16 (2.3%)	34 (3.0%)	-0.0421	22 (4.4%)	-0.1192
Cerebrovascular comorbidities	85 (12.2%)	131 (11.4%)	0.0232	61 (12.3%)	-0.0042
- Stroke	52 (7.4%)	77 (6.7%)	0.0285	33 (6.7%)	0.0307
- TIA	49 (7.0%)	73 (6.4%)	0.0261	33 (6.7%)	0.0141

IPCI	QVA N(%)	Free LABA+ICS N(%)	Std Dif	Fixed LABA ICS N(%)	Std Dif
- Heart failure	80 (11.4%)	92 (15.4%)	-0.1164	767 (11.0%)	0.0155
- Atrial fibrillation/flutter	594 (85.0%)	510 (85.4%)	0.0126	6,185 (88.3%)	0.0991
Cardia arrhythmia	129 (18.5%)	119 (19.9%)	-0.0375	1,129 (16.1%)	0.0616
- Atrial fibrillation/flutter	594 (85.0%)	510 (85.4%)	0.0126	6,185 (88.3%)	0.0991
- Torsade de Pointes/Long QT	0 (0.0%)	0 (0.0%)	.	4 (0.1%)	-0.0338
- Ventricular fibrillation	3 (0.4%)	2 (0.3%)	0.0153	46 (0.7%)	-0.031
- Ventricular tachycardia	2 (0.3%)	7 (1.2%)	-0.1042	39 (0.6%)	-0.0418
- AV block	7 (1.0%)	9 (1.5%)	-0.0454	74 (1.1%)	-0.0055
- Sick Sinus	3 (0.4%)	5 (0.8%)	-0.0514	22 (0.3%)	0.0189
- Supraventricular tachycardia	8 (1.1%)	16 (2.7%)	-0.1122	161 (2.3%)	-0.0889
- Premature depolarization	16 (2.3%)	16 (2.7%)	-0.0251	178 (2.5%)	-0.0165
Cerebrovascular comorbidities	85 (12.2%)	67 (11.2%)	0.0292	781 (11.2%)	0.0313
- Stroke	52 (7.4%)	37 (6.2%)	0.0492	455 (6.5%)	0.0369
- TIA	49 (7.0%)	38 (6.4%)	0.0258	425 (6.1%)	0.038

IPCI	QVA N(%)	Fixed LABA LAMA N(%)	Std Dif	LABA N(%)	Std Dif
- Heart failure	80 (11.4%)	136 (12.6%)	-0.0349	146 (9.6%)	0.0612
- Atrial fibrillation/flutter	594 (85.0%)	925 (85.6%)	0.0167	1,329 (87.1%)	0.0609
Cardia arrhythmia	129 (18.5%)	192 (17.8%)	0.018	263 (17.2%)	0.0319
- Atrial fibrillation/flutter	594 (85.0%)	925 (85.6%)	0.0167	1,329 (87.1%)	0.0609
- Torsade de Pointes/Long QT	0 (0.0%)	1 (0.1%)	-0.043	2 (0.1%)	-0.0512
- Ventricular fibrillation	3 (0.4%)	8 (0.7%)	-0.0408	11 (0.7%)	-0.0386
- Ventricular tachycardia	2 (0.3%)	4 (0.4%)	-0.0147	7 (0.5%)	-0.0283
- AV block	7 (1.0%)	12 (1.1%)	-0.0106	23 (1.5%)	-0.0454
- Sick Sinus	3 (0.4%)	3 (0.3%)	0.0255	2 (0.1%)	0.0564
- Supraventricular tachycardia	8 (1.1%)	20 (1.9%)	-0.0581	26 (1.7%)	-0.0472
- Premature depolarization	16 (2.3%)	22 (2.0%)	0.0174	39 (2.6%)	-0.0173
Cerebrovascular comorbidities	85 (12.2%)	135 (12.5%)	-0.01	190 (12.5%)	-0.0088
- Stroke	52 (7.4%)	76 (7.0%)	0.0158	106 (7.0%)	0.0191
- TIA	49 (7.0%)	71 (6.6%)	0.0176	106 (7.0%)	0.0025

IPCI	QVA N(%)	LAMA	Std Dif
- Heart failure	80 (11.4%)	550 (11.0%)	0.0145
- Atrial fibrillation/flutter	594 (85.0%)	4,342 (86.7%)	0.0504
Cardia arrhythmia	129 (18.5%)	929 (18.6%)	-0.0026
- Atrial fibrillation/flutter	594 (85.0%)	4,342 (86.7%)	0.0504
- Torsade de Pointes/Long QT	0 (0.0%)	4 (0.1%)	-0.04
- Ventricular fibrillation	3 (0.4%)	34 (0.7%)	-0.0337
- Ventricular tachycardia	2 (0.3%)	32 (0.6%)	-0.052
- AV block	7 (1.0%)	82 (1.6%)	-0.0558
- Sick Sinus	3 (0.4%)	17 (0.3%)	0.0145
- Supraventricular tachycardia	8 (1.1%)	102 (2.0%)	-0.0714
- Premature depolarization	16 (2.3%)	171 (3.4%)	-0.0677
Cerebrovascular comorbidities	85 (12.2%)	586 (11.7%)	0.014
- Stroke	52 (7.4%)	348 (7.0%)	0.0189
- TIA	49 (7.0%)	321 (6.4%)	0.0239

IPCI	QVA N(%)	Free LABA+LAMA without ICS N(%)	Std Dif	Free LABA+LAMA with ICS N(%)	Std Dif
Diabetes Mellitus (validated)	107 (15.3%)	208 (18.1%)	-0.0754	84 (16.9%)	-0.0442
Hyperlipidemia	129 (18.5%)	276 (24.0%)	-0.1368	101 (20.4%)	-0.0482
Hepatic injury	23 (3.3%)	34 (3.0%)	0.0189	10 (2.0%)	0.0793
Lung cancer	38 (5.4%)	51 (4.4%)	0.0458	22 (4.4%)	0.0462
Cancer (excluding lung cancer)	100 (14.3%)	165 (14.4%)	-0.0019	68 (13.7%)	0.0172
Asthma	119 (17.0%)	227 (19.8%)	-0.071	190 (38.3%)	-0.4894
BPH	70 (10.0%)	123 (10.7%)	-0.023	56 (11.3%)	-0.0413
Bladder obstruction/urinary retention	32 (4.6%)	54 (4.7%)	-0.006	34 (6.9%)	-0.0981

IPCI	QVA N(%)	Free LABA+ICS N(%)	Std Dif	Fixed LABA ICS N(%)	Std Dif
Diabetes Mellitus (validated)	107 (15.3%)	120 (20.1%)	-0.1257	1,259 (18.0%)	-0.0718
Hyperlipidemia	129 (18.5%)	125 (20.9%)	-0.0624	1,495 (21.4%)	-0.0726
Hepatic injury	23 (3.3%)	19 (3.2%)	0.0061	226 (3.2%)	0.0035
Lung cancer	38 (5.4%)	27 (4.5%)	0.042	241 (3.4%)	0.0969
Cancer (excluding lung cancer)	100 (14.3%)	79 (13.2%)	0.0311	921 (13.2%)	0.0334
Asthma	119 (17.0%)	297 (49.8%)	-0.7393	2,439 (34.8%)	-0.415
BPH	70 (10.0%)	59 (9.9%)	0.0044	590 (8.4%)	0.0548
Bladder obstruction/urinary retention	32 (4.6%)	28 (4.7%)	-0.0053	290 (4.1%)	0.0213

IPCI	QVA N(%)	Fixed LABA LAMA N(%)	Std Dif	LABA N(%)	Std Dif
Diabetes Mellitus (validated)	107 (15.3%)	204 (18.9%)	-0.0947	247 (16.2%)	-0.0241
Hyperlipidemia	129 (18.5%)	236 (21.8%)	-0.0842	330 (21.6%)	-0.0792
Hepatic injury	23 (3.3%)	21 (1.9%)	0.0845	49 (3.2%)	0.0045
Lung cancer	38 (5.4%)	50 (4.6%)	0.0371	39 (2.6%)	0.1474
Cancer (excluding lung cancer)	100 (14.3%)	181 (16.7%)	-0.0673	205 (13.4%)	0.0252
Asthma	119 (17.0%)	180 (16.7%)	0.01	373 (24.4%)	-0.1837
BPH	70 (10.0%)	107 (9.9%)	0.0039	140 (9.2%)	0.0285
Bladder obstruction/urinary retention	32 (4.6%)	60 (5.6%)	-0.0443	71 (4.7%)	-0.0036

IPCI	QVA N(%)	LAMA	Std Dif
Diabetes Mellitus (validated)	107 (15.3%)	819 (16.4%)	-0.0288
Hyperlipidemia	129 (18.5%)	1,135 (22.7%)	-0.1045
Hepatic injury	23 (3.3%)	148 (3.0%)	0.0192
Lung cancer	38 (5.4%)	146 (2.9%)	0.1261
Cancer (excluding lung cancer)	100 (14.3%)	704 (14.1%)	0.007
Asthma	119 (17.0%)	1,098 (21.9%)	-0.1242
BPH	70 (10.0%)	472 (9.4%)	0.0198
Bladder obstruction/urinary retention	32 (4.6%)	201 (4.0%)	0.0277

Aarhus	QVA N(%)	Free LABA+LAMA without ICS N(%)	Std Dif	Free LABA+LAMA with ICS N(%)	Std Dif
Total	1,807 (100.0%)	671 (100.0%)	0	242 (100.0%)	0
Chronic kidney disease			0.0933		0.2484
No CKD	512 (28.3%)	168 (25.0%)	.	86 (35.5%)	.
Stage unknown	10 (0.6%)	3 (0.5%)	.	1 (0.4%)	.
Stage 2	858 (47.5%)	344 (51.3%)	.	115 (47.5%)	.
Stage 3	382 (21.1%)	143 (21.3%)	.	39 (16.1%)	.
Stage 4	37 (2.1%)	11 (1.6%)	.	1 (0.4%)	.
Stage 5	8 (0.4%)	2 (0.3%)	.		.
Cardiovascular comorbidities	989 (54.7%)	362 (54.0%)	0.0157	128 (52.9%)	0.0369
- Arterial hypertension	640 (35.4%)	237 (35.3%)	0.002	78 (32.2%)	0.0673
- Unstable angina pectoris	89 (4.9%)	33 (4.9%)	0.0003	11 (4.6%)	0.0179
- Angina pectoris	435 (24.1%)	158 (23.6%)	0.0123	52 (21.5%)	0.0616
- Myocardial infarction	187 (10.4%)	63 (9.4%)	0.0322	28 (11.6%)	-0.0391

Aarhus	QVA N(%)	Free LABA+ICS N(%)	Std Dif	Fixed LABA ICS N(%)	Std Dif
Total	1,807 (100.0%)	273 (100.0%)	0	3,481 (100.0%)	0
Chronic kidney disease			0.1536		0.0973
No CKD	512 (28.3%)	79 (28.9%)	.	1,100 (31.6%)	.
Stage unknown	10 (0.6%)		.	12 (0.3%)	.
Stage 2	858 (47.5%)	136 (49.8%)	.	1,521 (43.7%)	.
Stage 3	382 (21.1%)	52 (19.1%)	.	739 (21.2%)	.
Stage 4	37 (2.1%)	6 (2.2%)	.	85 (2.4%)	.
Stage 5	8 (0.4%)		.	24 (0.7%)	.
Cardiovascular comorbidities	989 (54.7%)	146 (53.5%)	0.0251	1,896 (54.5%)	0.0053
- Arterial hypertension	640 (35.4%)	106 (38.8%)	-0.0705	1,303 (37.4%)	-0.0419
- Unstable angina pectoris	89 (4.9%)	16 (5.9%)	-0.0414	199 (5.7%)	-0.0353
- Angina pectoris	435 (24.1%)	70 (25.6%)	-0.0362	805 (23.1%)	0.0223
- Myocardial infarction	187 (10.4%)	27 (9.9%)	0.0152	350 (10.1%)	0.0097

Aarhus	QVA N(%)	Fixed LABA LAMA N(%)	Std Dif	LABA N(%)	Std Dif
Total	1,807 (100.0%)	1,758 (100.0%)	0	1,078 (100.0%)	0
Chronic kidney disease			0.0793		0.098
No CKD	512 (28.3%)	488 (27.8%)	.	286 (26.5%)	.
Stage unknown	10 (0.6%)	8 (0.5%)	.	5 (0.5%)	.
Stage 2	858 (47.5%)	885 (50.3%)	.	523 (48.5%)	.
Stage 3	382 (21.1%)	338 (19.2%)	.	249 (23.1%)	.
Stage 4	37 (2.1%)	27 (1.5%)	.	12 (1.1%)	.
Stage 5	8 (0.4%)	12 (0.7%)	.	3 (0.3%)	.
Cardiovascular comorbidities	989 (54.7%)	959 (54.6%)	0.0036	580 (53.8%)	0.0186
- Arterial hypertension	640 (35.4%)	640 (36.4%)	-0.0206	401 (37.2%)	-0.037
- Unstable angina pectoris	89 (4.9%)	89 (5.1%)	-0.0063	59 (5.5%)	-0.0247
- Angina pectoris	435 (24.1%)	407 (23.2%)	0.0217	279 (25.9%)	-0.0418
- Myocardial infarction	187 (10.4%)	152 (8.7%)	0.0581	102 (9.5%)	0.0297

Aarhus	QVA N(%)	LAMA	Std Dif
Total	1,807 (100.0%)	2,095 (100.0%)	0
Chronic kidney disease			0.06
No CKD	512 (28.3%)	557 (26.6%)	.
Stage unknown	10 (0.6%)	10 (0.5%)	.
Stage 2	858 (47.5%)	985 (47.0%)	.
Stage 3	382 (21.1%)	483 (23.1%)	.
Stage 4	37 (2.1%)	51 (2.4%)	.
Stage 5	8 (0.4%)	9 (0.4%)	.
Cardiovascular comorbidities	989 (54.7%)	1,138 (54.3%)	0.0083
- Arterial hypertension	640 (35.4%)	779 (37.2%)	-0.0367
- Unstable angina pectoris	89 (4.9%)	141 (6.7%)	-0.0771
- Angina pectoris	435 (24.1%)	538 (25.7%)	-0.0372
- Myocardial infarction	187 (10.4%)	203 (9.7%)	0.0219

Aarhus	QVA N(%)	Free LABA+LAMA without ICS N(%)	Std Dif	Free LABA+LAMA with ICS N(%)	Std Dif
- Heart failure	257 (14.2%)	84 (12.5%)	0.0501	28 (11.6%)	0.0791
- Atrial fibrillation/flutter	1,431 (79.2%)	556 (82.9%)	0.0936	205 (84.7%)	0.1437
Cardia arrhythmia	441 (24.4%)	142 (21.2%)	0.0773	53 (21.9%)	0.0593
- Atrial fibrillation/flutter	1,431 (79.2%)	556 (82.9%)	0.0936	205 (84.7%)	0.1437
- Torsade de Pointes/Long QT	0 (0.0%)	0 (0.0%)	.	0 (0.0%)	.
- Ventricular fibrillation	2 (0.1%)	1 (0.2%)	-0.0106	2 (0.8%)	-0.1048
- Ventricular tachycardia	10 (0.6%)	2 (0.3%)	0.0392	1 (0.4%)	0.0202
- AV block	34 (1.9%)	9 (1.3%)	0.0429	9 (3.7%)	-0.1114
- Sick Sinus	31 (1.7%)	12 (1.8%)	-0.0055	3 (1.2%)	0.0394
- Supraventricular tachycardia	90 (5.0%)	43 (6.4%)	-0.0616	14 (5.8%)	-0.0356
- Premature depolarization	26 (1.4%)	9 (1.3%)	0.0083	4 (1.7%)	-0.0173
Cerebrovascular comorbidities	191 (10.6%)	76 (11.3%)	-0.0242	18 (7.4%)	0.1095
- Stroke	140 (7.8%)	55 (8.2%)	-0.0166	14 (5.8%)	0.0781
- TIA	66 (3.7%)	29 (4.3%)	-0.0342	5 (2.1%)	0.0952

Aarhus	QVA N(%)	Free LABA+ICS N(%)	Std Dif	Fixed LABA ICS N(%)	Std Dif
- Heart failure	257 (14.2%)	29 (10.6%)	0.1092	516 (14.8%)	-0.0171
- Atrial fibrillation/flutter	1,431 (79.2%)	226 (82.8%)	0.0915	2,825 (81.2%)	0.0492
Cardia arrhythmia	441 (24.4%)	65 (23.8%)	0.0139	813 (23.4%)	0.0246
- Atrial fibrillation/flutter	1,431 (79.2%)	226 (82.8%)	0.0915	2,825 (81.2%)	0.0492
- Torsade de Pointes/Long QT	0 (0.0%)	0 (0.0%)	.	0 (0.0%)	.
- Ventricular fibrillation	2 (0.1%)	0 (0.0%)	0.0471	8 (0.2%)	-0.0289
- Ventricular tachycardia	10 (0.6%)	1 (0.4%)	0.0276	21 (0.6%)	-0.0066
- AV block	34 (1.9%)	10 (3.7%)	-0.1085	93 (2.7%)	-0.053
- Sick Sinus	31 (1.7%)	2 (0.7%)	0.0894	68 (2.0%)	-0.0177
- Supraventricular tachycardia	90 (5.0%)	11 (4.0%)	0.0458	177 (5.1%)	-0.0048
- Premature depolarization	26 (1.4%)	15 (5.5%)	-0.2227	45 (1.3%)	0.0126
Cerebrovascular comorbidities	191 (10.6%)	31 (11.4%)	-0.0251	413 (11.9%)	-0.041
- Stroke	140 (7.8%)	21 (7.7%)	0.0021	325 (9.3%)	-0.0569
- TIA	66 (3.7%)	11 (4.0%)	-0.0196	126 (3.6%)	0.0018

Aarhus	QVA N(%)	Fixed LABA LAMA N(%)	Std Dif	LABA N(%)	Std Dif
- Heart failure	257 (14.2%)	258 (14.7%)	-0.0129	136 (12.6%)	0.0471
- Atrial fibrillation/flutter	1,431 (79.2%)	1,439 (81.9%)	0.0672	883 (81.9%)	0.0687
Cardia arrhythmia	441 (24.4%)	393 (22.4%)	0.0484	246 (22.8%)	0.0373
- Atrial fibrillation/flutter	1,431 (79.2%)	1,439 (81.9%)	0.0672	883 (81.9%)	0.0687
- Torsade de Pointes/Long QT	0 (0.0%)	0 (0.0%)	.	0 (0.0%)	.
- Ventricular fibrillation	2 (0.1%)	4 (0.2%)	-0.0284	1 (0.1%)	0.0056
- Ventricular tachycardia	10 (0.6%)	11 (0.6%)	-0.0094	4 (0.4%)	0.0269
- AV block	34 (1.9%)	38 (2.2%)	-0.0199	23 (2.1%)	-0.018
- Sick Sinus	31 (1.7%)	22 (1.3%)	0.0384	23 (2.1%)	-0.0304
- Supraventricular tachycardia	90 (5.0%)	82 (4.7%)	0.0148	47 (4.4%)	0.0294
- Premature depolarization	26 (1.4%)	28 (1.6%)	-0.0126	23 (2.1%)	-0.0524
Cerebrovascular comorbidities	191 (10.6%)	174 (9.9%)	0.0222	129 (12.0%)	-0.0442
- Stroke	140 (7.8%)	122 (6.9%)	0.031	97 (9.0%)	-0.0451
- TIA	66 (3.7%)	64 (3.6%)	0.0006	47 (4.4%)	-0.0361

Aarhus	QVA N(%)	LAMA	Std Dif
- Heart failure	257 (14.2%)	305 (14.6%)	-0.0096
- Atrial fibrillation/flutter	1,431 (79.2%)	1,714 (81.8%)	0.0662
Cardia arrhythmia	441 (24.4%)	485 (23.2%)	0.0295
- Atrial fibrillation/flutter	1,431 (79.2%)	1,714 (81.8%)	0.0662
- Torsade de Pointes/Long QT	0 (0.0%)	0 (0.0%)	.
- Ventricular fibrillation	2 (0.1%)	5 (0.2%)	-0.0306
- Ventricular tachycardia	10 (0.6%)	15 (0.7%)	-0.0205
- AV block	34 (1.9%)	52 (2.5%)	-0.0411
- Sick Sinus	31 (1.7%)	37 (1.8%)	-0.0039
- Supraventricular tachycardia	90 (5.0%)	103 (4.9%)	0.003
- Premature depolarization	26 (1.4%)	35 (1.7%)	-0.0187
Cerebrovascular comorbidities	191 (10.6%)	230 (11.0%)	-0.0132
- Stroke	140 (7.8%)	175 (8.4%)	-0.0223
- TIA	66 (3.7%)	71 (3.4%)	0.0143

Aarhus	QVA N(%)	Free LABA+LAMA without ICS N(%)	Std Dif	Free LABA+LAMA with ICS N(%)	Std Dif
Diabetes Mellitus (validated)	204 (11.3%)	61 (9.1%)	0.0727	26 (10.7%)	0.0174
Hyperlipidemia	266 (14.7%)	106 (15.8%)	-0.0299	29 (12.0%)	0.0804
Hepatic injury	21 (1.2%)	10 (1.5%)	-0.0287	2 (0.8%)	0.0338
Lung cancer	81 (4.5%)	25 (3.7%)	0.0381	8 (3.3%)	0.0608
Cancer (excluding lung cancer)	243 (13.5%)	96 (14.3%)	-0.0248	25 (10.3%)	0.0963
Asthma	211 (11.7%)	89 (13.3%)	-0.048	59 (24.4%)	-0.3346
BPH	122 (6.8%)	38 (5.7%)	0.0451	15 (6.2%)	0.0225
Bladder obstruction/urinary retention	31 (1.7%)	11 (1.6%)	0.0059	4 (1.7%)	0.0049

Aarhus	QVA N(%)	Free LABA+ICS N(%)	Std Dif	Fixed LABA ICS N(%)	Std Dif
Diabetes Mellitus (validated)	204 (11.3%)	33 (12.1%)	-0.0248	470 (13.5%)	-0.0672
Hyperlipidemia	266 (14.7%)	34 (12.5%)	0.0661	583 (16.8%)	-0.0557
Hepatic injury	21 (1.2%)	3 (1.1%)	0.006	67 (1.9%)	-0.0619
Lung cancer	81 (4.5%)	8 (2.9%)	0.0822	97 (2.8%)	0.0907
Cancer (excluding lung cancer)	243 (13.5%)	39 (14.3%)	-0.0242	465 (13.4%)	0.0026
Asthma	211 (11.7%)	80 (29.3%)	-0.4469	718 (20.6%)	-0.245
BPH	122 (6.8%)	21 (7.7%)	-0.0363	207 (6.0%)	0.033
Bladder obstruction/urinary retention	31 (1.7%)	5 (1.8%)	-0.0088	69 (2.0%)	-0.0198

Aarhus	QVA N(%)	Fixed LABA LAMA N(%)	Std Dif	LABA N(%)	Std Dif
Diabetes Mellitus (validated)	204 (11.3%)	217 (12.3%)	-0.0327	154 (14.3%)	-0.0898
Hyperlipidemia	266 (14.7%)	305 (17.4%)	-0.0717	186 (17.3%)	-0.0691
Hepatic injury	21 (1.2%)	30 (1.7%)	-0.0458	14 (1.3%)	-0.0124
Lung cancer	81 (4.5%)	72 (4.1%)	0.0191	38 (3.5%)	0.0488
Cancer (excluding lung cancer)	243 (13.5%)	289 (16.4%)	-0.084	159 (14.8%)	-0.0374
Asthma	211 (11.7%)	227 (12.9%)	-0.0376	131 (12.2%)	-0.0147
BPH	122 (6.8%)	106 (6.0%)	0.0295	66 (6.1%)	0.0256
Bladder obstruction/urinary retention	31 (1.7%)	37 (2.1%)	-0.0284	19 (1.8%)	-0.0036

Aarhus	QVA N(%)	LAMA	Std Dif
Diabetes Mellitus (validated)	204 (11.3%)	248 (11.8%)	-0.0171
Hyperlipidemia	266 (14.7%)	383 (18.3%)	-0.096
Hepatic injury	21 (1.2%)	42 (2.0%)	-0.0675
Lung cancer	81 (4.5%)	67 (3.2%)	0.0669
Cancer (excluding lung cancer)	243 (13.5%)	308 (14.7%)	-0.0361
Asthma	211 (11.7%)	295 (14.1%)	-0.0718
BPH	122 (6.8%)	122 (5.8%)	0.0382
Bladder obstruction/urinary retention	31 (1.7%)	36 (1.7%)	-0.0002

HSD	QVA N(%)	Free LABA+LAMA without ICS N(%)	Std Dif	Free LABA+LAMA with ICS N(%)	Std Dif
Total	385 (100.0%)	995 (100.0%)	0	335 (100.0%)	0
Chronic kidney disease			0.1501		0.1347
No CKD	50 (13.0%)	106 (10.7%)	.	37 (11.0%)	.
Stage unknown		2 (0.2%)	.		.
Stage 1	22 (5.7%)	55 (5.5%)	.	20 (6.0%)	.
Stage 2	155 (40.3%)	383 (38.5%)	.	123 (36.7%)	.
Stage 3	131 (34.0%)	357 (35.9%)	.	124 (37.0%)	.
Stage 4	14 (3.6%)	60 (6.0%)	.	19 (5.7%)	.
Stage 5	13 (3.4%)	32 (3.2%)	.	12 (3.6%)	.
Cardiovascular comorbidities	270 (70.1%)	685 (68.8%)	0.0279	233 (69.6%)	0.0126
- Arterial hypertension	244 (63.4%)	608 (61.1%)	0.0468	205 (61.2%)	0.045
- Unstable angina pectoris	0 (0.0%)	5 (0.5%)	-0.1005	2 (0.6%)	-0.1094
- Angina pectoris	10 (2.6%)	30 (3.0%)	-0.0253	14 (4.2%)	-0.0874

HSD	QVA N(%)	Free LABA+ICS N(%)	Std Dif	Fixed LABA ICS N(%)	Std Dif
Total	385 (100.0%)	437 (100.0%)	0	5,897 (100.0%)	0
Chronic kidney disease			0.1954		0.1423
No CKD	50 (13.0%)	42 (9.6%)	.	854 (14.5%)	.
Stage unknown		3 (0.7%)	.	11 (0.2%)	.
Stage 1	22 (5.7%)	21 (4.8%)	.	383 (6.5%)	.
Stage 2	155 (40.3%)	163 (37.3%)	.	2,139 (36.3%)	.
Stage 3	131 (34.0%)	175 (40.1%)	.	1,968 (33.4%)	.
Stage 4	14 (3.6%)	17 (3.9%)	.	339 (5.8%)	.
Stage 5	13 (3.4%)	16 (3.7%)	.	203 (3.4%)	.
Cardiovascular comorbidities	270 (70.1%)	290 (66.4%)	0.0809	3,892 (66.0%)	0.0886
- Arterial hypertension	244 (63.4%)	257 (58.8%)	0.0937	3,459 (58.7%)	0.0968
- Unstable angina pectoris	0 (0.0%)	1 (0.2%)	-0.0677	33 (0.6%)	-0.1061
- Angina pectoris	10 (2.6%)	10 (2.3%)	0.02	170 (2.9%)	-0.0175

HSD	QVA N(%)	Fixed LABA LAMA N(%)	Std Dif	LABA N(%)	Std Dif
Total	385 (100.0%)	426 (100.0%)	0	875 (100.0%)	0
Chronic kidney disease			0.1627		0.1437
No CKD	50 (13.0%)	41 (9.6%)	.	104 (11.9%)	.
Stage unknown			.	3 (0.3%)	.
Stage 1	22 (5.7%)	38 (8.9%)	.	61 (7.0%)	.
Stage 2	155 (40.3%)	179 (42.0%)	.	353 (40.3%)	.
Stage 3	131 (34.0%)	140 (32.9%)	.	283 (32.3%)	.
Stage 4	14 (3.6%)	13 (3.1%)	.	48 (5.5%)	.
Stage 5	13 (3.4%)	15 (3.5%)	.	23 (2.6%)	.
Cardiovascular comorbidities	270 (70.1%)	288 (67.6%)	0.0545	587 (67.1%)	0.0656
- Arterial hypertension	244 (63.4%)	252 (59.2%)	0.0866	535 (61.1%)	0.0461
- Unstable angina pectoris	0 (0.0%)	4 (0.9%)	-0.1375	4 (0.5%)	-0.0958
- Angina pectoris	10 (2.6%)	13 (3.1%)	-0.0274	19 (2.2%)	0.0279

HSD	QVA N(%)	LAMA	Std Dif
Total	385 (100.0%)	3,595 (100.0%)	0
Chronic kidney disease			0.1882
No CKD	50 (13.0%)	421 (11.7%)	.
Stage unknown		6 (0.2%)	.
Stage 1	22 (5.7%)	216 (6.0%)	.
Stage 2	155 (40.3%)	1,255 (34.9%)	.
Stage 3	131 (34.0%)	1,303 (36.2%)	.
Stage 4	14 (3.6%)	247 (6.9%)	.
Stage 5	13 (3.4%)	147 (4.1%)	.
Cardiovascular comorbidities	270 (70.1%)	2,528 (70.3%)	-0.0042
- Arterial hypertension	244 (63.4%)	2,197 (61.1%)	0.0467
- Unstable angina pectoris	0 (0.0%)	30 (0.8%)	-0.1297
- Angina pectoris	10 (2.6%)	126 (3.5%)	-0.0527

HSD	QVA N(%)	Free LABA+LAMA without ICS N(%)	Std Dif	Free LABA+LAMA with ICS N(%)	Std Dif
- Myocardial infarction	24 (6.2%)	51 (5.1%)	0.0478	18 (5.4%)	0.0368
- Heart failure	39 (10.1%)	92 (9.3%)	0.0298	31 (9.3%)	0.0296
- Atrial fibrillation/flutter	330 (85.7%)	871 (87.5%)	0.0535	288 (86.0%)	0.0073
Cardia arrhythmia	87 (22.6%)	194 (19.5%)	0.076	68 (20.3%)	0.056
- Atrial fibrillation/flutter	330 (85.7%)	871 (87.5%)	0.0535	288 (86.0%)	0.0073
- Torsade de Pointes/Long QT	0 (0.0%)	1 (0.1%)	-0.0448	0 (0.0%)	.
- Ventricular fibrillation	1 (0.3%)	1 (0.1%)	0.0375	0 (0.0%)	0.0721
- Ventricular tachycardia	2 (0.5%)	3 (0.3%)	0.0341	1 (0.3%)	0.0346
- AV block	5 (1.3%)	15 (1.5%)	-0.0177	5 (1.5%)	-0.0165
- Sick Sinus	7 (1.8%)	10 (1.0%)	0.0689	4 (1.2%)	0.0512
- Supraventricular tachycardia	1 (0.3%)	7 (0.7%)	-0.0641	3 (0.9%)	-0.0838
- Premature depolarization	27 (7.0%)	59 (5.9%)	0.044	17 (5.1%)	0.0813
Cerebrovascular comorbidities	18 (4.7%)	58 (5.8%)	-0.0517	22 (6.6%)	-0.0821
- Stroke	11 (2.9%)	22 (2.2%)	0.0411	14 (4.2%)	-0.0717

HSD	QVA N(%)	Free LABA+ICS N(%)	Std Dif	Fixed LABA ICS N(%)	Std Dif
- Myocardial infarction	24 (6.2%)	25 (5.7%)	0.0216	286 (4.9%)	0.0605
- Heart failure	39 (10.1%)	28 (6.4%)	0.1353	484 (8.2%)	0.0666
- Atrial fibrillation/flutter	330 (85.7%)	388 (88.8%)	0.0921	5,276 (89.5%)	0.114
Cardia arrhythmia	87 (22.6%)	78 (17.9%)	0.1183	968 (16.4%)	0.1564
- Atrial fibrillation/flutter	330 (85.7%)	388 (88.8%)	0.0921	5,276 (89.5%)	0.114
- Torsade de Pointes/Long QT	0 (0.0%)	0 (0.0%)	.	2 (0.0%)	-0.026
- Ventricular fibrillation	1 (0.3%)	0 (0.0%)	0.0721	0 (0.0%)	0.0721
- Ventricular tachycardia	2 (0.5%)	0 (0.0%)	0.1021	3 (0.1%)	0.0879
- AV block	5 (1.3%)	2 (0.5%)	0.0901	78 (1.3%)	-0.0021
- Sick Sinus	7 (1.8%)	3 (0.7%)	0.1018	64 (1.1%)	0.0612
- Supraventricular tachycardia	1 (0.3%)	4 (0.9%)	-0.0858	29 (0.5%)	-0.0379
- Premature depolarization	27 (7.0%)	27 (6.2%)	0.0336	260 (4.4%)	0.1123
Cerebrovascular comorbidities	18 (4.7%)	22 (5.0%)	-0.0167	340 (5.8%)	-0.049
- Stroke	11 (2.9%)	6 (1.4%)	0.1032	147 (2.5%)	0.0226

HSD	QVA N(%)	Fixed LABA LAMA N(%)	Std Dif	LABA N(%)	Std Dif
- Myocardial infarction	24 (6.2%)	26 (6.1%)	0.0054	30 (3.4%)	0.131
- Heart failure	39 (10.1%)	42 (9.9%)	0.009	60 (6.9%)	0.1175
- Atrial fibrillation/flutter	330 (85.7%)	381 (89.4%)	0.1129	790 (90.3%)	0.1409
Cardia arrhythmia	87 (22.6%)	86 (20.2%)	0.0587	134 (15.3%)	0.1864
- Atrial fibrillation/flutter	330 (85.7%)	381 (89.4%)	0.1129	790 (90.3%)	0.1409
- Torsade de Pointes/Long QT	0 (0.0%)	0 (0.0%)	.	0 (0.0%)	.
- Ventricular fibrillation	1 (0.3%)	0 (0.0%)	0.0721	0 (0.0%)	0.0721
- Ventricular tachycardia	2 (0.5%)	1 (0.2%)	0.0464	0 (0.0%)	0.1021
- AV block	5 (1.3%)	8 (1.9%)	-0.0463	11 (1.3%)	0.0037
- Sick Sinus	7 (1.8%)	9 (2.1%)	-0.0212	6 (0.7%)	0.1019
- Supraventricular tachycardia	1 (0.3%)	5 (1.2%)	-0.1084	7 (0.8%)	-0.0744
- Premature depolarization	27 (7.0%)	25 (5.9%)	0.0466	41 (4.7%)	0.0992
Cerebrovascular comorbidities	18 (4.7%)	30 (7.0%)	-0.1008	54 (6.2%)	-0.066
- Stroke	11 (2.9%)	15 (3.5%)	-0.0377	26 (3.0%)	-0.0068

HSD	QVA N(%)	LAMA	Std Dif
- Myocardial infarction	24 (6.2%)	233 (6.5%)	-0.0101
- Heart failure	39 (10.1%)	395 (11.0%)	-0.0279
- Atrial fibrillation/flutter	330 (85.7%)	3,095 (86.1%)	0.0108
Cardia arrhythmia	87 (22.6%)	756 (21.0%)	0.038
- Atrial fibrillation/flutter	330 (85.7%)	3,095 (86.1%)	0.0108
- Torsade de Pointes/Long QT	0 (0.0%)	1 (0.0%)	-0.0236
- Ventricular fibrillation	1 (0.3%)	2 (0.1%)	0.0514
- Ventricular tachycardia	2 (0.5%)	5 (0.1%)	0.0664
- AV block	5 (1.3%)	63 (1.8%)	-0.037
- Sick Sinus	7 (1.8%)	47 (1.3%)	0.0412
- Supraventricular tachycardia	1 (0.3%)	24 (0.7%)	-0.06
- Premature depolarization	27 (7.0%)	208 (5.8%)	0.0501
Cerebrovascular comorbidities	18 (4.7%)	261 (7.3%)	-0.1092
- Stroke	11 (2.9%)	114 (3.2%)	-0.0183

HSD	QVA N(%)	Free LABA+LAMA without ICS N(%)	Std Dif	Free LABA+LAMA with ICS N(%)	Std Dif
- TIA	8 (2.1%)	37 (3.7%)	-0.0978	8 (2.4%)	-0.021
Diabetes Mellitus (validated)	81 (21.0%)	194 (19.5%)	0.0383	65 (19.4%)	0.0407
Hyperlipidemia	131 (34.0%)	330 (33.2%)	0.0182	96 (28.7%)	0.1158
Hepatic injury	31 (8.1%)	72 (7.2%)	0.0307	23 (6.9%)	0.0451
Lung cancer	6 (1.6%)	13 (1.3%)	0.0212	9 (2.7%)	-0.0782
Cancer (excluding lung cancer)	35 (9.1%)	87 (8.7%)	0.0122	29 (8.7%)	0.0152
Asthma	73 (19.0%)	142 (14.3%)	0.1261	63 (18.8%)	0.004
BPH	88 (22.9%)	179 (18.0%)	0.1208	52 (15.5%)	0.1868
Bladder obstruction/urinary retention	10 (2.6%)	15 (1.5%)	0.0768	0 (0.0%)	0.2306

HSD	QVA N(%)	Free LABA+ICS N(%)	Std Dif	Fixed LABA ICS N(%)	Std Dif
- TIA	8 (2.1%)	17 (3.9%)	-0.1065	210 (3.6%)	-0.0896
Diabetes Mellitus (validated)	81 (21.0%)	81 (18.5%)	0.0628	1,074 (18.2%)	0.0712
Hyperlipidemia	131 (34.0%)	134 (30.7%)	0.0718	1,879 (31.9%)	0.046
Hepatic injury	31 (8.1%)	28 (6.4%)	0.0635	404 (6.9%)	0.0457
Lung cancer	6 (1.6%)	10 (2.3%)	-0.0531	69 (1.2%)	0.0335
Cancer (excluding lung cancer)	35 (9.1%)	35 (8.0%)	0.0386	393 (6.7%)	0.0901
Asthma	73 (19.0%)	64 (14.7%)	0.1155	1,077 (18.3%)	0.0179
BPH	88 (22.9%)	70 (16.0%)	0.1733	799 (13.6%)	0.2428
Bladder obstruction/urinary retention	10 (2.6%)	4 (0.9%)	0.1282	55 (0.9%)	0.1266

HSD	QVA N(%)	Fixed LABA LAMA N(%)	Std Dif	LABA N(%)	Std Dif
- TIA	8 (2.1%)	18 (4.2%)	-0.123	30 (3.4%)	-0.0825
Diabetes Mellitus (validated)	81 (21.0%)	103 (24.2%)	-0.075	169 (19.3%)	0.0429
Hyperlipidemia	131 (34.0%)	154 (36.2%)	-0.0445	292 (33.4%)	0.0138
Hepatic injury	31 (8.1%)	33 (7.8%)	0.0113	65 (7.4%)	0.0233
Lung cancer	6 (1.6%)	12 (2.8%)	-0.086	10 (1.1%)	0.036
Cancer (excluding lung cancer)	35 (9.1%)	32 (7.5%)	0.0572	58 (6.6%)	0.0915
Asthma	73 (19.0%)	78 (18.3%)	0.0167	128 (14.6%)	0.116
BPH	88 (22.9%)	72 (16.9%)	0.1495	143 (16.3%)	0.1645
Bladder obstruction/urinary retention	10 (2.6%)	5 (1.2%)	0.1047	9 (1.0%)	0.1177

HSD	QVA N(%)	LAMA	Std Dif
- TIA	8 (2.1%)	162 (4.5%)	-0.1363
Diabetes Mellitus (validated)	81 (21.0%)	728 (20.3%)	0.0195
Hyperlipidemia	131 (34.0%)	1,213 (33.7%)	0.006
Hepatic injury	31 (8.1%)	271 (7.5%)	0.0191
Lung cancer	6 (1.6%)	35 (1.0%)	0.0523
Cancer (excluding lung cancer)	35 (9.1%)	249 (6.9%)	0.0798
Asthma	73 (19.0%)	557 (15.5%)	0.0918
BPH	88 (22.9%)	526 (14.6%)	0.2118
Bladder obstruction/urinary retention	10 (2.6%)	45 (1.3%)	0.098

SIDIAP	QVA N(%)	Free LABA+LAMA without ICS N(%)	Std Dif	Free LABA+LAMA with ICS N(%)	Std Dif
Total	5,561 (100.0%)	4,219 (100.0%)	0	1,725 (100.0%)	0
Chronic kidney disease			0.043		0.1309
No CKD	1,707 (30.7%)	1,253 (29.7%)	.	442 (25.6%)	.
Stage unknown	107 (1.9%)	80 (1.9%)	.	31 (1.8%)	.
Stage 2	2,769 (49.8%)	2,086 (49.4%)	.	883 (51.2%)	.
Stage 3	885 (15.9%)	730 (17.3%)	.	334 (19.4%)	.
Stage 4	81 (1.5%)	64 (1.5%)	.	31 (1.8%)	.
Stage 5	12 (0.2%)	6 (0.1%)	.	4 (0.2%)	.
Cardiovascular comorbidities	3,584 (64.5%)	2,796 (66.3%)	-0.0383	1,204 (69.8%)	-0.114
- Arterial hypertension	3,312 (59.6%)	2,551 (60.5%)	-0.0185	1,092 (63.3%)	-0.077
- Unstable angina pectoris	63 (1.1%)	38 (0.9%)	0.0231	17 (1.0%)	0.0144
- Angina pectoris	199 (3.6%)	125 (3.0%)	0.0346	65 (3.8%)	-0.0101
- Myocardial infarction	331 (6.0%)	235 (5.6%)	0.0164	96 (5.6%)	0.0166

SIDIAP	QVA N(%)	Free LABA+ICS N(%)	Std Dif	Fixed LABA ICS N(%)	Std Dif
Total	5,561 (100.0%)	2,738 (100.0%)	0	20638 (100.0%)	0
Chronic kidney disease			0.1284		0.0454
No CKD	1,707 (30.7%)	728 (26.6%)	.	6,316 (30.6%)	.
Stage unknown	107 (1.9%)	54 (2.0%)	.	465 (2.3%)	.
Stage 2	2,769 (49.8%)	1,364 (49.8%)	.	9,965 (48.3%)	.
Stage 3	885 (15.9%)	527 (19.3%)	.	3,491 (16.9%)	.
Stage 4	81 (1.5%)	62 (2.3%)	.	357 (1.7%)	.
Stage 5	12 (0.2%)	3 (0.1%)	.	44 (0.2%)	.
Cardiovascular comorbidities	3,584 (64.5%)	1,817 (66.4%)	-0.0402	13229 (64.1%)	0.0073
- Arterial hypertension	3,312 (59.6%)	1,693 (61.8%)	-0.0466	12233 (59.3%)	0.0058
- Unstable angina pectoris	63 (1.1%)	26 (1.0%)	0.0181	194 (0.9%)	0.019
- Angina pectoris	199 (3.6%)	87 (3.2%)	0.0222	625 (3.0%)	0.0308
- Myocardial infarction	331 (6.0%)	115 (4.2%)	0.0799	1,057 (5.1%)	0.0363

SIDIAP	QVA N(%)	Fixed LABA LAMA N(%)	Std Dif	LABA N(%)	Std Dif
Total	5,561 (100.0%)	964 (100.0%)	0	5,879 (100.0%)	0
Chronic kidney disease			0.0469		0.0334
No CKD	1,707 (30.7%)	297 (30.8%)	.	1,853 (31.5%)	.
Stage unknown	107 (1.9%)	17 (1.8%)	.	101 (1.7%)	.
Stage 2	2,769 (49.8%)	468 (48.6%)	.	2,922 (49.7%)	.
Stage 3	885 (15.9%)	161 (16.7%)	.	901 (15.3%)	.
Stage 4	81 (1.5%)	18 (1.9%)	.	83 (1.4%)	.
Stage 5	12 (0.2%)	3 (0.3%)	.	19 (0.3%)	.
Cardiovascular comorbidities	3,584 (64.5%)	628 (65.2%)	-0.0146	3,690 (62.8%)	0.035
- Arterial hypertension	3,312 (59.6%)	564 (58.5%)	0.0214	3,459 (58.8%)	0.0147
- Unstable angina pectoris	63 (1.1%)	4 (0.4%)	0.082	44 (0.8%)	0.0398
- Angina pectoris	199 (3.6%)	26 (2.7%)	0.0506	143 (2.4%)	0.0672
- Myocardial infarction	331 (6.0%)	64 (6.6%)	-0.0283	247 (4.2%)	0.0798

SIDIAP	QVA N(%)	LAMA	Std Dif
Total	5,561 (100.0%)	13678 (100.0%)	0
Chronic kidney disease			0.0152
No CKD	1,707 (30.7%)	4,178 (30.6%)	.
Stage unknown	107 (1.9%)	284 (2.1%)	.
Stage 2	2,769 (49.8%)	6,782 (49.6%)	.
Stage 3	885 (15.9%)	2,192 (16.0%)	.
Stage 4	81 (1.5%)	207 (1.5%)	.
Stage 5	12 (0.2%)	35 (0.3%)	.
Cardiovascular comorbidities	3,584 (64.5%)	8,772 (64.1%)	0.0066
- Arterial hypertension	3,312 (59.6%)	8,070 (59.0%)	0.0114
- Unstable angina pectoris	63 (1.1%)	122 (0.9%)	0.0241
- Angina pectoris	199 (3.6%)	439 (3.2%)	0.0204
- Myocardial infarction	331 (6.0%)	806 (5.9%)	0.0025

SIDIAP	QVA N(%)	Free LABA+LAMA without ICS N(%)	Std Dif	Free LABA+LAMA with ICS N(%)	Std Dif
- Heart failure	376 (6.8%)	319 (7.6%)	-0.031	182 (10.6%)	-0.135
- Atrial fibrillation/flutter	4,917 (88.4%)	3,760 (89.1%)	0.0222	1,502 (87.1%)	-0.0411
Cardia arrhythmia	846 (15.2%)	614 (14.6%)	0.0185	301 (17.5%)	-0.0605
- Atrial fibrillation/flutter	4,917 (88.4%)	3,760 (89.1%)	0.0222	1,502 (87.1%)	-0.0411
- Torsade de Pointes/Long QT	1 (0.0%)	1 (0.0%)	-0.004	0 (0.0%)	0.019
- Ventricular fibrillation	7 (0.1%)	3 (0.1%)	0.0175	1 (0.1%)	0.0224
- Ventricular tachycardia	9 (0.2%)	12 (0.3%)	-0.026	1 (0.1%)	0.0313
- AV block	118 (2.1%)	114 (2.7%)	-0.0378	52 (3.0%)	-0.0564
- Sick Sinus	0 (0.0%)	0 (0.0%)	.	0 (0.0%)	.
- Supraventricular tachycardia	41 (0.7%)	14 (0.3%)	0.0556	12 (0.7%)	0.0049
- Premature depolarization	59 (1.1%)	46 (1.1%)	-0.0028	26 (1.5%)	-0.0396
Cerebrovascular comorbidities	455 (8.2%)	340 (8.1%)	0.0045	157 (9.1%)	-0.0327
- Stroke	330 (5.9%)	246 (5.8%)	0.0044	104 (6.0%)	-0.004
- TIA	143 (2.6%)	110 (2.6%)	-0.0023	60 (3.5%)	-0.053

SIDIAP	QVA N(%)	Free LABA+ICS N(%)	Std Dif	Fixed LABA ICS N(%)	Std Dif
- Heart failure	376 (6.8%)	222 (8.1%)	-0.0513	1,567 (7.6%)	-0.0322
- Atrial fibrillation/flutter	4,917 (88.4%)	2,405 (87.8%)	-0.018	18352 (88.9%)	0.0159
Cardia arrhythmia	846 (15.2%)	430 (15.7%)	-0.0136	2,999 (14.5%)	0.0192
- Atrial fibrillation/flutter	4,917 (88.4%)	2,405 (87.8%)	-0.018	18352 (88.9%)	0.0159
- Torsade de Pointes/Long QT	1 (0.0%)	0 (0.0%)	0.019	1 (0.0%)	0.0123
- Ventricular fibrillation	7 (0.1%)	0 (0.0%)	0.0502	13 (0.1%)	0.0205
- Ventricular tachycardia	9 (0.2%)	2 (0.1%)	0.0259	27 (0.1%)	0.0081
- AV block	118 (2.1%)	62 (2.3%)	-0.0097	445 (2.2%)	-0.0024
- Sick Sinus	0 (0.0%)	1 (0.0%)	-0.027	3 (0.0%)	-0.0171
- Supraventricular tachycardia	41 (0.7%)	17 (0.6%)	0.0142	169 (0.8%)	-0.0093
- Premature depolarization	59 (1.1%)	35 (1.3%)	-0.0202	220 (1.1%)	-0.0005
Cerebrovascular comorbidities	455 (8.2%)	246 (9.0%)	-0.0287	1,753 (8.5%)	-0.0113
- Stroke	330 (5.9%)	183 (6.7%)	-0.0308	1,329 (6.4%)	-0.021
- TIA	143 (2.6%)	79 (2.9%)	-0.0193	516 (2.5%)	0.0045

SIDIAP	QVA N(%)	Fixed LABA LAMA N(%)	Std Dif	LABA N(%)	Std Dif
- Heart failure	376 (6.8%)	61 (6.3%)	0.0175	280 (4.8%)	0.0858
- Atrial fibrillation/flutter	4,917 (88.4%)	851 (88.3%)	-0.0044	5,364 (91.2%)	0.0934
Cardia arrhythmia	846 (15.2%)	150 (15.6%)	-0.0096	709 (12.1%)	0.092
- Atrial fibrillation/flutter	4,917 (88.4%)	851 (88.3%)	-0.0044	5,364 (91.2%)	0.0934
- Torsade de Pointes/Long QT	1 (0.0%)	0 (0.0%)	0.019	1 (0.0%)	0.0007
- Ventricular fibrillation	7 (0.1%)	0 (0.0%)	0.0502	2 (0.0%)	0.0325
- Ventricular tachycardia	9 (0.2%)	2 (0.2%)	-0.0106	9 (0.2%)	0.0022
- AV block	118 (2.1%)	25 (2.6%)	-0.0311	130 (2.2%)	-0.0061
- Sick Sinus	0 (0.0%)	0 (0.0%)	.	0 (0.0%)	.
- Supraventricular tachycardia	41 (0.7%)	6 (0.6%)	0.014	38 (0.7%)	0.011
- Premature depolarization	59 (1.1%)	10 (1.0%)	0.0023	53 (0.9%)	0.0162
Cerebrovascular comorbidities	455 (8.2%)	91 (9.4%)	-0.0444	446 (7.6%)	0.0221
- Stroke	330 (5.9%)	60 (6.2%)	-0.0121	314 (5.3%)	0.0257
- TIA	143 (2.6%)	37 (3.8%)	-0.0719	157 (2.7%)	-0.0062

SIDIAP	QVA N(%)	LAMA	Std Dif
- Heart failure	376 (6.8%)	862 (6.3%)	0.0186
- Atrial fibrillation/flutter	4,917 (88.4%)	12214 (89.3%)	0.0279
Cardia arrhythmia	846 (15.2%)	1,966 (14.4%)	0.0236
- Atrial fibrillation/flutter	4,917 (88.4%)	12214 (89.3%)	0.0279
- Torsade de Pointes/Long QT	1 (0.0%)	1 (0.0%)	0.0095
- Ventricular fibrillation	7 (0.1%)	4 (0.0%)	0.0347
- Ventricular tachycardia	9 (0.2%)	23 (0.2%)	-0.0016
- AV block	118 (2.1%)	303 (2.2%)	-0.0064
- Sick Sinus	0 (0.0%)	1 (0.0%)	-0.0121
- Supraventricular tachycardia	41 (0.7%)	117 (0.9%)	-0.0133
- Premature depolarization	59 (1.1%)	173 (1.3%)	-0.019
Cerebrovascular comorbidities	455 (8.2%)	1,103 (8.1%)	0.0043
- Stroke	330 (5.9%)	831 (6.1%)	-0.0059
- TIA	143 (2.6%)	332 (2.4%)	0.0092

SIDIAP	QVA N(%)	Free LABA+LAMA without ICS N(%)	Std Dif	Free LABA+LAMA with ICS N(%)	Std Dif
Diabetes Mellitus (validated)	1,301 (23.4%)	1,022 (24.2%)	-0.0195	426 (24.7%)	-0.0304
Hyperlipidemia	1,219 (21.9%)	843 (20.0%)	0.0477	393 (22.8%)	-0.0207
Hepatic injury	63 (1.1%)	40 (1.0%)	0.0182	10 (0.6%)	0.0601
Lung cancer	141 (2.5%)	77 (1.8%)	0.0487	39 (2.3%)	0.0179
Cancer (excluding lung cancer)	1,084 (19.5%)	860 (20.4%)	-0.0223	349 (20.2%)	-0.0185
Asthma	379 (6.8%)	206 (4.9%)	0.0824	202 (11.7%)	-0.1694
BPH	1,411 (25.4%)	1,126 (26.7%)	-0.03	495 (28.7%)	-0.0748
Bladder obstruction/urinary retention	109 (2.0%)	89 (2.1%)	-0.0106	37 (2.1%)	-0.013

SIDIAP	QVA N(%)	Free LABA+ICS N(%)	Std Dif	Fixed LABA ICS N(%)	Std Dif
Diabetes Mellitus (validated)	1,301 (23.4%)	667 (24.4%)	-0.0227	4,602 (22.3%)	0.0261
Hyperlipidemia	1,219 (21.9%)	569 (20.8%)	0.0278	4,496 (21.8%)	0.0033
Hepatic injury	63 (1.1%)	32 (1.2%)	-0.0034	234 (1.1%)	-0.0001
Lung cancer	141 (2.5%)	24 (0.9%)	0.1284	258 (1.3%)	0.0944
Cancer (excluding lung cancer)	1,084 (19.5%)	509 (18.6%)	0.023	3,471 (16.8%)	0.0694
Asthma	379 (6.8%)	414 (15.1%)	-0.2681	2,310 (11.2%)	-0.1534
BPH	1,411 (25.4%)	681 (24.9%)	0.0115	4,242 (20.6%)	0.1148
Bladder obstruction/urinary retention	109 (2.0%)	44 (1.6%)	0.0267	346 (1.7%)	0.0212

SIDIAP	QVA N(%)	Fixed LABA LAMA N(%)	Std Dif	LABA N(%)	Std Dif
Diabetes Mellitus (validated)	1,301 (23.4%)	241 (25.0%)	-0.0375	1,288 (21.9%)	0.0355
Hyperlipidemia	1,219 (21.9%)	200 (20.8%)	0.0286	1,172 (19.9%)	0.0488
Hepatic injury	63 (1.1%)	9 (0.9%)	0.0197	68 (1.2%)	-0.0022
Lung cancer	141 (2.5%)	30 (3.1%)	-0.0348	55 (0.9%)	0.1227
Cancer (excluding lung cancer)	1,084 (19.5%)	186 (19.3%)	0.005	958 (16.3%)	0.0835
Asthma	379 (6.8%)	63 (6.5%)	0.0112	321 (5.5%)	0.0565
BPH	1,411 (25.4%)	244 (25.3%)	0.0014	1,236 (21.0%)	0.1032
Bladder obstruction/urinary retention	109 (2.0%)	16 (1.7%)	0.0225	82 (1.4%)	0.044

SIDIAP	QVA N(%)	LAMA	Std Dif
Diabetes Mellitus (validated)	1,301 (23.4%)	3,091 (22.6%)	0.0189
Hyperlipidemia	1,219 (21.9%)	3,135 (22.9%)	-0.024
Hepatic injury	63 (1.1%)	142 (1.0%)	0.0091
Lung cancer	141 (2.5%)	147 (1.1%)	0.1099
Cancer (excluding lung cancer)	1,084 (19.5%)	2,272 (16.6%)	0.075
Asthma	379 (6.8%)	859 (6.3%)	0.0216
BPH	1,411 (25.4%)	3,053 (22.3%)	0.0717
Bladder obstruction/urinary retention	109 (2.0%)	203 (1.5%)	0.0366

Cardiac arrhythmia- combined consists of combined events of ventricular tachycardia, ventricular fibrillation, Torsade de Pointes/LongQTc, atrial flutter/fibrillation and AV block , CKD=Chronic kidney disease; CKD stage based on both disease codes and lab results. If CKD stage based on both disease codes and lab results were available, CKD stage closest and most severe to the index date is reported; ≈Stage 1 based on disease codes for CKD stage 1 only; ±Defined as no event of CKD available AND no serum creatinine measurement OR this measurement results in a GFR ≥90 mL/min/1.73m2; CI=Confidence interval, BPH= benign prostatic hyperplasia, denominator men only

Table 15-6 Use of other respiratory medications (assessed during the year prior to index date and including the index date), (pooled and by database)

POOLED	QVA N(%)	Free LABA+LAMA without ICS N(%)	Std Dif	Free LABA+LAMA with ICS N(%)	Std Dif
Total	9,798 (100.0%)	9,619 (100.0%)	.	3,192 (100.0%)	.
Single-ingredient short-acting muscarinic agents	2,024 (20.7%)	1,641 (17.1%)	0.0921	888 (27.8%)	-0.1677
Single-ingredient short-acting ß2 agonists	5,192 (53.0%)	5,223 (54.3%)	-0.0262	1,917 (60.1%)	-0.1429
LABA	2,756 (28.1%)	9,619 (100.0%)	-2.2605	3,192 (100.0%)	-2.2605
LAMA	5,113 (52.2%)	9,619 (100.0%)	-1.3537	3,192 (100.0%)	-1.3537
Inhaled corticosteroids (ICS)	2,542 (25.9%)	1,424 (14.8%)	0.2792	3,192 (100.0%)	-2.3892
Xanthines	214 (2.2%)	221 (2.3%)	-0.0077	140 (4.4%)	-0.1238
Fixed combination therapy LABA+ICS	3,282 (33.5%)	2,668 (27.7%)	0.1252	780 (24.4%)	0.2007
Fixed combination therapy LABA+LAMA	168 (1.7%)	63 (0.7%)	0.098	11 (0.3%)	0.136
QVA	9,798 (100.0%)	161 (1.7%)	10.8387	59 (1.9%)	10.3039
Fixed combination therapy other	0 (0.0%)	0 (0.0%)	.	0 (0.0%)	.
Fixed combination therapy SABA+SAMA	234 (2.4%)	212 (2.2%)	0.0123	184 (5.8%)	-0.1713
Oral ß2-agonists	45 (0.5%)	33 (0.3%)	0.0184	12 (0.4%)	0.0129
Leukotriene receptor antagonists (LTRA)	205 (2.1%)	127 (1.3%)	0.0596	145 (4.5%)	-0.1371
Systemic corticosteroids	3,601 (36.8%)	3,355 (34.9%)	0.0391	1,676 (52.5%)	-0.3209
Systemic corticosteroids with indication COPD	1,062 (10.8%)	1,106 (11.5%)	-0.0209	546 (17.1%)	-0.1815
Oral phosphodiesterase-4 (PDE-4) inhibitors	129 (1.3%)	39 (0.4%)	0.0987	52 (1.6%)	-0.0259

POOLED	QVA N(%)	Free LABA+ICS N(%)	Std Dif	Fixed LABA ICS N(%)	Std Dif
Total	9,798 (100.0%)	4,628 (100.0%)	.	58332 (100.0%)	.
Single-ingredient short-acting muscarinic agents	2,024 (20.7%)	1,711 (37.0%)	-0.3662	10269 (17.6%)	0.0777
Single-ingredient short-acting ß2 agonists	5,192 (53.0%)	2,517 (54.4%)	-0.028	33769 (57.9%)	-0.0987
LABA	2,756 (28.1%)	4,628 (100.0%)	-2.2605	7,549 (12.9%)	0.3828
LAMA	5,113 (52.2%)	845 (18.3%)	0.7597	24977 (42.8%)	0.1884
Inhaled corticosteroids (ICS)	2,542 (25.9%)	4,628 (100.0%)	-2.3892	15332 (26.3%)	-0.0077
Xanthines	214 (2.2%)	108 (2.3%)	-0.0101	1,030 (1.8%)	0.0301
Fixed combination therapy LABA+ICS	3,282 (33.5%)	890 (19.2%)	0.3281	58332 (100.0%)	-1.9926
Fixed combination therapy LABA+LAMA	168 (1.7%)	18 (0.4%)	0.1302	633 (1.1%)	0.0536
QVA	9,798 (100.0%)	50 (1.1%)	13.5307	686 (1.2%)	12.9638
Fixed combination therapy other	0 (0.0%)	0 (0.0%)	.	0 (0.0%)	.
Fixed combination therapy SABA+SAMA	234 (2.4%)	198 (4.3%)	-0.1054	1,410 (2.4%)	-0.0019
Oral ß2-agonists	45 (0.5%)	19 (0.4%)	0.0074	176 (0.3%)	0.0256
Leukotriene receptor antagonists (LTRA)	205 (2.1%)	177 (3.8%)	-0.1024	1,227 (2.1%)	-0.0008
Systemic corticosteroids	3,601 (36.8%)	1,941 (41.9%)	-0.1063	22672 (38.9%)	-0.0436
Systemic corticosteroids with indication COPD	1,062 (10.8%)	498 (10.8%)	0.0025	7,063 (12.1%)	-0.0398
Oral phosphodiesterase-4 (PDE-4) inhibitors	129 (1.3%)	22 (0.5%)	0.0894	88 (0.2%)	0.1369

POOLED	QVA N(%)	Fixed LABA LAMA N(%)	Std Dif	LABA N(%)	Std Dif
Total	9,798 (100.0%)	9,150 (100.0%)	.	12364 (100.0%)	.
Single-ingredient short-acting muscarinic agents	2,024 (20.7%)	757 (8.3%)	0.3576	2,726 (22.1%)	-0.0339
Single-ingredient short-acting ß2 agonists	5,192 (53.0%)	6,387 (69.8%)	-0.3506	6,010 (48.6%)	0.0877
LABA	2,756 (28.1%)	1,429 (15.6%)	0.3062	12364 (100.0%)	-2.2605
LAMA	5,113 (52.2%)	4,948 (54.1%)	-0.0379	2,676 (21.6%)	0.6671
Inhaled corticosteroids (ICS)	2,542 (25.9%)	1,578 (17.3%)	0.2126	1,548 (12.5%)	0.3456
Xanthines	214 (2.2%)	185 (2.0%)	0.0113	151 (1.2%)	0.0745
Fixed combination therapy LABA+ICS	3,282 (33.5%)	2,955 (32.3%)	0.0256	2,517 (20.4%)	0.2995
Fixed combination therapy LABA+LAMA	168 (1.7%)	9,150 (100.0%)	-10.7066	70 (0.6%)	0.1083
QVA	9,798 (100.0%)	497 (5.4%)	5.9006	121 (1.0%)	14.2249
Fixed combination therapy other	0 (0.0%)	0 (0.0%)	.	0 (0.0%)	.
Fixed combination therapy SABA+SAMA	234 (2.4%)	233 (2.6%)	-0.0102	178 (1.4%)	0.0693
Oral ß2-agonists	45 (0.5%)	31 (0.3%)	0.0191	38 (0.3%)	0.0246
Leukotriene receptor antagonists (LTRA)	205 (2.1%)	155 (1.7%)	0.0292	116 (0.9%)	0.0946
Systemic corticosteroids	3,601 (36.8%)	3,759 (41.1%)	-0.0889	3,394 (27.5%)	0.2002
Systemic corticosteroids with indication COPD	1,062 (10.8%)	1,444 (15.8%)	-0.1459	1,000 (8.1%)	0.0941
Oral phosphodiesterase-4 (PDE-4) inhibitors	129 (1.3%)	44 (0.5%)	0.0886	13 (0.1%)	0.1446

POOLED	QVA N(%)	LAMA	Std Dif
Total	9,798 (100.0%)	42972 (100.0%)	.
Single-ingredient short-acting muscarinic agents	2,024 (20.7%)	6,617 (15.4%)	0.1371
Single-ingredient short-acting ß2 agonists	5,192 (53.0%)	23395 (54.4%)	-0.0291
LABA	2,756 (28.1%)	2,298 (5.4%)	0.6408
LAMA	5,113 (52.2%)	42972 (100.0%)	-1.3537
Inhaled corticosteroids (ICS)	2,542 (25.9%)	7,183 (16.7%)	0.2267
Xanthines	214 (2.2%)	582 (1.4%)	0.063
Fixed combination therapy LABA+ICS	3,282 (33.5%)	9,106 (21.2%)	0.2788
Fixed combination therapy LABA+LAMA	168 (1.7%)	147 (0.3%)	0.1364
QVA	9,798 (100.0%)	250 (0.6%)	18.487
Fixed combination therapy other	0 (0.0%)	0 (0.0%)	.
Fixed combination therapy SABA+SAMA	234 (2.4%)	731 (1.7%)	0.0486
Oral ß2-agonists	45 (0.5%)	103 (0.2%)	0.0372
Leukotriene receptor antagonists (LTRA)	205 (2.1%)	634 (1.5%)	0.0466
Systemic corticosteroids	3,601 (36.8%)	12874 (30.0%)	0.1445
Systemic corticosteroids with indication COPD	1,062 (10.8%)	3,830 (8.9%)	0.0646
Oral phosphodiesterase-4 (PDE-4) inhibitors	129 (1.3%)	31 (0.1%)	0.1503

THIN	QVA N(%)	Free LABA+LAMA without ICS N(%)	Std Dif	Free LABA+LAMA with ICS N(%)	Std Dif
Total	1,346 (100.0%)	2,586 (100.0%)	.	394 (100.0%)	.
Single-ingredient short-acting muscarinic agents	43 (3.2%)	107 (4.1%)	-0.0502	55 (14.0%)	-0.3913
Single-ingredient short-acting ß2 agonists	1,230 (91.4%)	2,361 (91.3%)	0.0029	373 (94.7%)	-0.1293
LABA	263 (19.5%)	2,586 (100.0%)	-2.8687	394 (100.0%)	-2.8687
LAMA	910 (67.6%)	2,586 (100.0%)	-0.9785	394 (100.0%)	-0.9785
Inhaled corticosteroids (ICS)	135 (10.0%)	184 (7.1%)	0.1042	394 (100.0%)	-4.2341
Xanthines	52 (3.9%)	64 (2.5%)	0.0793	22 (5.6%)	-0.0811
Fixed combination therapy LABA+ICS	431 (32.0%)	585 (22.6%)	0.212	87 (22.1%)	0.225
Fixed combination therapy LABA+LAMA	91 (6.8%)	29 (1.1%)	0.2928	2 (0.5%)	0.3388
QVA	1,346 (100.0%)	8 (0.3%)	25.3821	0 (0.0%)	.
Fixed combination therapy other	0 (0.0%)	0 (0.0%)	.	0 (0.0%)	.
Fixed combination therapy SABA+SAMA	3 (0.2%)	2 (0.1%)	0.0376	2 (0.5%)	-0.0472
Oral ß2-agonists	0 (0.0%)	3 (0.1%)	-0.0482	3 (0.8%)	-0.1237
Leukotriene receptor antagonists (LTRA)	15 (1.1%)	24 (0.9%)	0.0185	26 (6.6%)	-0.2874
Systemic corticosteroids	624 (46.4%)	1,124 (43.5%)	0.0582	246 (62.4%)	-0.3268
Systemic corticosteroids with indication COPD	222 (16.5%)	405 (15.7%)	0.0226	95 (24.1%)	-0.1901
Oral phosphodiesterase-4 (PDE-4) inhibitors	0 (0.0%)	0 (0.0%)	.	0 (0.0%)	.

THIN	QVA N(%)	Free LABA+ICS N(%)	Std Dif	Fixed LABA ICS N(%)	Std Dif
Total	1,346 (100.0%)	583 (100.0%)	.	21315 (100.0%)	.
Single-ingredient short-acting muscarinic agents	43 (3.2%)	52 (8.9%)	-0.2416	1,166 (5.5%)	-0.1119
Single-ingredient short-acting ß2 agonists	1,230 (91.4%)	540 (92.6%)	-0.0458	18839 (88.4%)	0.0995
LABA	263 (19.5%)	583 (100.0%)	-2.8687	2,466 (11.6%)	0.2212
LAMA	910 (67.6%)	93 (16.0%)	1.2287	11019 (51.7%)	0.3286
Inhaled corticosteroids (ICS)	135 (10.0%)	583 (100.0%)	-4.2341	6,013 (28.2%)	-0.4751
Xanthines	52 (3.9%)	16 (2.7%)	0.0626	343 (1.6%)	0.1385
Fixed combination therapy LABA+ICS	431 (32.0%)	90 (15.4%)	0.3972	21315 (100.0%)	-2.0598
Fixed combination therapy LABA+LAMA	91 (6.8%)	4 (0.7%)	0.3249	473 (2.2%)	0.2206
QVA	1,346 (100.0%)	0 (0.0%)	.	119 (0.6%)	18.8738
Fixed combination therapy other	0 (0.0%)	0 (0.0%)	.	0 (0.0%)	.
Fixed combination therapy SABA+SAMA	3 (0.2%)	2 (0.3%)	-0.0226	60 (0.3%)	-0.0117
Oral ß2-agonists	0 (0.0%)	2 (0.3%)	-0.0829	35 (0.2%)	-0.0574
Leukotriene receptor antagonists (LTRA)	15 (1.1%)	21 (3.6%)	-0.1644	398 (1.9%)	-0.0621
Systemic corticosteroids	624 (46.4%)	320 (54.9%)	-0.1711	10142 (47.6%)	-0.0245
Systemic corticosteroids with indication COPD	222 (16.5%)	80 (13.7%)	0.0774	3,320 (15.6%)	0.025
Oral phosphodiesterase-4 (PDE-4) inhibitors	0 (0.0%)	1 (0.2%)	-0.0586	0 (0.0%)	.

THIN	QVA N(%)	Fixed LABA LAMA N(%)	Std Dif	LABA N(%)	Std Dif
Total	1,346 (100.0%)	4,921 (100.0%)	.	3,006 (100.0%)	.
Single-ingredient short-acting muscarinic agents	43 (3.2%)	201 (4.1%)	-0.0475	191 (6.4%)	-0.1485
Single-ingredient short-acting ß2 agonists	1,230 (91.4%)	4,285 (87.1%)	0.1392	2,641 (87.9%)	0.1157
LABA	263 (19.5%)	579 (11.8%)	0.2151	3,006 (100.0%)	-2.8687
LAMA	910 (67.6%)	2,771 (56.3%)	0.2343	845 (28.1%)	0.8606
Inhaled corticosteroids (ICS)	135 (10.0%)	443 (9.0%)	0.035	245 (8.2%)	0.0654
Xanthines	52 (3.9%)	99 (2.0%)	0.1098	34 (1.1%)	0.1757
Fixed combination therapy LABA+ICS	431 (32.0%)	1,372 (27.9%)	0.0905	477 (15.9%)	0.3854
Fixed combination therapy LABA+LAMA	91 (6.8%)	4,921 (100.0%)	-5.2499	35 (1.2%)	0.2898
QVA	1,346 (100.0%)	128 (2.6%)	8.6531	10 (0.3%)	24.4745
Fixed combination therapy other	0 (0.0%)	0 (0.0%)	.	0 (0.0%)	.
Fixed combination therapy SABA+SAMA	3 (0.2%)	10 (0.2%)	0.0043	3 (0.1%)	0.0307
Oral ß2-agonists	0 (0.0%)	6 (0.1%)	-0.0494	6 (0.2%)	-0.0632
Leukotriene receptor antagonists (LTRA)	15 (1.1%)	66 (1.3%)	-0.0206	17 (0.6%)	0.0602
Systemic corticosteroids	624 (46.4%)	1,988 (40.4%)	0.1205	1,044 (34.7%)	0.2385
Systemic corticosteroids with indication COPD	222 (16.5%)	593 (12.1%)	0.1272	328 (10.9%)	0.1628
Oral phosphodiesterase-4 (PDE-4) inhibitors	0 (0.0%)	0 (0.0%)	.	0 (0.0%)	.

THIN	QVA N(%)	LAMA	Std Dif
Total	1,346 (100.0%)	18598 (100.0%)	.
Single-ingredient short-acting muscarinic agents	43 (3.2%)	1,081 (5.8%)	-0.1265
Single-ingredient short-acting ß2 agonists	1,230 (91.4%)	15573 (83.7%)	0.2332
LABA	263 (19.5%)	602 (3.2%)	0.5308
LAMA	910 (67.6%)	18598 (100.0%)	-0.9785
Inhaled corticosteroids (ICS)	135 (10.0%)	2,446 (13.2%)	-0.0976
Xanthines	52 (3.9%)	196 (1.1%)	0.1821
Fixed combination therapy LABA+ICS	431 (32.0%)	3,340 (18.0%)	0.3291
Fixed combination therapy LABA+LAMA	91 (6.8%)	90 (0.5%)	0.3407
QVA	1,346 (100.0%)	11 (0.1%)	58.1315
Fixed combination therapy other	0 (0.0%)	0 (0.0%)	.
Fixed combination therapy SABA+SAMA	3 (0.2%)	34 (0.2%)	0.0089
Oral ß2-agonists	0 (0.0%)	22 (0.1%)	-0.0487
Leukotriene receptor antagonists (LTRA)	15 (1.1%)	263 (1.4%)	-0.0268
Systemic corticosteroids	624 (46.4%)	6,457 (34.7%)	0.2387
Systemic corticosteroids with indication COPD	222 (16.5%)	1,895 (10.2%)	0.1862
Oral phosphodiesterase-4 (PDE-4) inhibitors	0 (0.0%)	0 (0.0%)	.

IPCI	QVA N(%)	Free LABA+LAMA without ICS N(%)	Std Dif	Free LABA+LAMA with ICS N(%)	Std Dif
Total	699 (100.0%)	1,148 (100.0%)	.	496 (100.0%)	.
Single-ingredient short-acting muscarinic agents	89 (12.7%)	128 (11.2%)	0.0488	88 (17.7%)	-0.1396
Single-ingredient short-acting ß2 agonists	271 (38.8%)	457 (39.8%)	-0.0213	259 (52.2%)	-0.2723
LABA	142 (20.3%)	1,148 (100.0%)	-2.7989	496 (100.0%)	-2.7989
LAMA	298 (42.6%)	1,148 (100.0%)	-1.6393	496 (100.0%)	-1.6393
Inhaled corticosteroids (ICS)	111 (15.9%)	125 (10.9%)	0.1469	496 (100.0%)	-3.2526
Xanthines	5 (0.7%)	14 (1.2%)	-0.0515	15 (3.0%)	-0.1709
Fixed combination therapy LABA+ICS	179 (25.6%)	321 (28.0%)	-0.0531	118 (23.8%)	0.0421
Fixed combination therapy LABA+LAMA	15 (2.2%)	16 (1.4%)	0.057	4 (0.8%)	0.1112
QVA	699 (100.0%)	23 (2.0%)	9.8864	13 (2.6%)	8.6115
Fixed combination therapy other	0 (0.0%)	0 (0.0%)	.	0 (0.0%)	.
Fixed combination therapy SABA+SAMA	28 (4.0%)	27 (2.4%)	0.0943	32 (6.5%)	-0.1099
Oral ß2-agonists	0 (0.0%)	0 (0.0%)	.	0 (0.0%)	.
Leukotriene receptor antagonists (LTRA)	7 (1.0%)	23 (2.0%)	-0.0824	38 (7.7%)	-0.3313
Systemic corticosteroids	270 (38.6%)	434 (37.8%)	0.0169	308 (62.1%)	-0.4825
Systemic corticosteroids with indication COPD	183 (26.2%)	326 (28.4%)	-0.0498	229 (46.2%)	-0.4249
Oral phosphodiesterase-4 (PDE-4) inhibitors	0 (0.0%)	1 (0.1%)	-0.0417	1 (0.2%)	-0.0635

IPCI	QVA N(%)	Free LABA+ICS N(%)	Std Dif	Fixed LABA ICS N(%)	Std Dif
Total	699 (100.0%)	597 (100.0%)	.	7,001 (100.0%)	.
Single-ingredient short-acting muscarinic agents	89 (12.7%)	148 (24.8%)	-0.3124	861 (12.3%)	0.0131
Single-ingredient short-acting ß2 agonists	271 (38.8%)	252 (42.2%)	-0.0701	2,630 (37.6%)	0.0248
LABA	142 (20.3%)	597 (100.0%)	-2.7989	566 (8.1%)	0.3557
LAMA	298 (42.6%)	125 (20.9%)	0.4787	2,611 (37.3%)	0.1091
Inhaled corticosteroids (ICS)	111 (15.9%)	597 (100.0%)	-3.2526	1,092 (15.6%)	0.0077
Xanthines	5 (0.7%)	4 (0.7%)	0.0055	32 (0.5%)	0.0338
Fixed combination therapy LABA+ICS	179 (25.6%)	137 (23.0%)	0.062	7,001 (100.0%)	-2.4087
Fixed combination therapy LABA+LAMA	15 (2.2%)	3 (0.5%)	0.144	27 (0.4%)	0.1579
QVA	699 (100.0%)	4 (0.7%)	17.2047	49 (0.7%)	16.8438
Fixed combination therapy other	0 (0.0%)	0 (0.0%)	.	0 (0.0%)	.
Fixed combination therapy SABA+SAMA	28 (4.0%)	44 (7.4%)	-0.1455	231 (3.3%)	0.0376
Oral ß2-agonists	0 (0.0%)	0 (0.0%)	.	3 (0.0%)	-0.0293
Leukotriene receptor antagonists (LTRA)	7 (1.0%)	31 (5.2%)	-0.2435	142 (2.0%)	-0.0841
Systemic corticosteroids	270 (38.6%)	289 (48.4%)	-0.1981	2,518 (36.0%)	0.055
Systemic corticosteroids with indication COPD	183 (26.2%)	175 (29.3%)	-0.07	1,591 (22.7%)	0.0804
Oral phosphodiesterase-4 (PDE-4) inhibitors	0 (0.0%)	0 (0.0%)	.	0 (0.0%)	.

IPCI	QVA N(%)	Fixed LABA LAMA N(%)	Std Dif	LABA N(%)	Std Dif
Total	699 (100.0%)	1,081 (100.0%)	.	1,526 (100.0%)	.
Single-ingredient short-acting muscarinic agents	89 (12.7%)	144 (13.3%)	-0.0175	247 (16.2%)	-0.0983
Single-ingredient short-acting ß2 agonists	271 (38.8%)	487 (45.1%)	-0.1275	534 (35.0%)	0.0783
LABA	142 (20.3%)	253 (23.4%)	-0.0748	1,526 (100.0%)	-2.7989
LAMA	298 (42.6%)	536 (49.6%)	-0.1397	385 (25.2%)	0.3737
Inhaled corticosteroids (ICS)	111 (15.9%)	216 (20.0%)	-0.107	139 (9.1%)	0.2057
Xanthines	5 (0.7%)	9 (0.8%)	-0.0134	5 (0.3%)	0.0538
Fixed combination therapy LABA+ICS	179 (25.6%)	318 (29.4%)	-0.0853	392 (25.7%)	-0.0018
Fixed combination therapy LABA+LAMA	15 (2.2%)	1,081 (100.0%)	-9.543	14 (0.9%)	0.1001
QVA	699 (100.0%)	49 (4.5%)	6.4872	17 (1.1%)	13.3196
Fixed combination therapy other	0 (0.0%)	0 (0.0%)	.	0 (0.0%)	.
Fixed combination therapy SABA+SAMA	28 (4.0%)	58 (5.4%)	-0.0643	31 (2.0%)	0.1155
Oral ß2-agonists	0 (0.0%)	1 (0.1%)	-0.043	0 (0.0%)	.
Leukotriene receptor antagonists (LTRA)	7 (1.0%)	18 (1.7%)	-0.0579	17 (1.1%)	-0.011
Systemic corticosteroids	270 (38.6%)	484 (44.8%)	-0.1248	459 (30.1%)	0.1806
Systemic corticosteroids with indication COPD	183 (26.2%)	338 (31.3%)	-0.1125	283 (18.6%)	0.1839
Oral phosphodiesterase-4 (PDE-4) inhibitors	0 (0.0%)	1 (0.1%)	-0.043	0 (0.0%)	.

IPCI	QVA N(%)	LAMA	Std Dif
Total	699 (100.0%)	5,006 (100.0%)	.
Single-ingredient short-acting muscarinic agents	89 (12.7%)	633 (12.6%)	0.0026
Single-ingredient short-acting ß2 agonists	271 (38.8%)	1,520 (30.4%)	0.1774
LABA	142 (20.3%)	241 (4.8%)	0.4807
LAMA	298 (42.6%)	5,006 (100.0%)	-1.6393
Inhaled corticosteroids (ICS)	111 (15.9%)	657 (13.1%)	0.0783
Xanthines	5 (0.7%)	15 (0.3%)	0.0585
Fixed combination therapy LABA+ICS	179 (25.6%)	1,072 (21.4%)	0.099
Fixed combination therapy LABA+LAMA	15 (2.2%)	20 (0.4%)	0.1562
QVA	699 (100.0%)	35 (0.7%)	16.8523
Fixed combination therapy other	0 (0.0%)	0 (0.0%)	.
Fixed combination therapy SABA+SAMA	28 (4.0%)	102 (2.0%)	0.1151
Oral ß2-agonists	0 (0.0%)	2 (0.0%)	-0.0283
Leukotriene receptor antagonists (LTRA)	7 (1.0%)	60 (1.2%)	-0.0189
Systemic corticosteroids	270 (38.6%)	1,520 (30.4%)	0.1744
Systemic corticosteroids with indication COPD	183 (26.2%)	940 (18.8%)	0.178
Oral phosphodiesterase-4 (PDE-4) inhibitors	0 (0.0%)	0 (0.0%)	.

Aarhus	QVA N(%)	Free LABA+LAMA without ICS N(%)	Std Dif	Free LABA+LAMA with ICS N(%)	Std Dif
Total	1,807 (100.0%)	671 (100.0%)	.	242 (100.0%)	.
Single-ingredient short-acting muscarinic agents	18 (1.0%)	8 (1.2%)	-0.0188	1 (0.4%)	0.0697
Single-ingredient short-acting ß2 agonists	1,135 (62.8%)	417 (62.2%)	0.0137	166 (68.6%)	-0.1219
LABA	540 (29.9%)	671 (100.0%)	-2.1656	242 (100.0%)	-2.1656
LAMA	862 (47.7%)	671 (100.0%)	-1.4803	242 (100.0%)	-1.4803
Inhaled corticosteroids (ICS)	391 (21.6%)	77 (11.5%)	0.2759	242 (100.0%)	-2.6905
Xanthines	10 (0.6%)	2 (0.3%)	0.0392	5 (2.1%)	-0.1331
Fixed combination therapy LABA+ICS	609 (33.7%)	226 (33.7%)	0.0004	75 (31.0%)	0.0579
Fixed combination therapy LABA+LAMA	41 (2.3%)	8 (1.2%)	0.0826	3 (1.2%)	0.0784
QVA	1,807 (100.0%)	32 (4.8%)	6.3149	16 (6.6%)	5.3041
Fixed combination therapy other	0 (0.0%)	0 (0.0%)	.	0 (0.0%)	.
Fixed combination therapy SABA+SAMA	113 (6.3%)	30 (4.5%)	0.0792	20 (8.3%)	-0.0775
Oral ß2-agonists	14 (0.8%)	8 (1.2%)	-0.0423	4 (1.7%)	-0.0801
Leukotriene receptor antagonists (LTRA)	41 (2.3%)	9 (1.3%)	0.0697	11 (4.6%)	-0.1256
Systemic corticosteroids	754 (41.7%)	266 (39.6%)	0.0424	143 (59.1%)	-0.3522
Systemic corticosteroids with indication COPD	340 (18.8%)	116 (17.3%)	0.0397	57 (23.6%)	-0.116
Oral phosphodiesterase-4 (PDE-4) inhibitors	4 (0.2%)	1 (0.2%)	0.0168	1 (0.4%)	-0.0341

Aarhus	QVA N(%)	Free LABA+ICS N(%)	Std Dif	Fixed LABA ICS N(%)	Std Dif
Total	1,807 (100.0%)	273 (100.0%)	.	3,481 (100.0%)	.
Single-ingredient short-acting muscarinic agents	18 (1.0%)	0 (0.0%)	0.1418	19 (0.6%)	0.0515
Single-ingredient short-acting ß2 agonists	1,135 (62.8%)	178 (65.2%)	-0.0498	2,182 (62.7%)	0.0027
LABA	540 (29.9%)	273 (100.0%)	-2.1656	573 (16.5%)	0.3222
LAMA	862 (47.7%)	77 (28.2%)	0.4098	1,707 (49.0%)	-0.0267
Inhaled corticosteroids (ICS)	391 (21.6%)	273 (100.0%)	-2.6905	770 (22.1%)	-0.0117
Xanthines	10 (0.6%)	2 (0.7%)	-0.0224	23 (0.7%)	-0.0138
Fixed combination therapy LABA+ICS	609 (33.7%)	47 (17.2%)	0.3851	3,481 (100.0%)	-1.983
Fixed combination therapy LABA+LAMA	41 (2.3%)	8 (2.9%)	-0.0415	85 (2.4%)	-0.0114
QVA	1,807 (100.0%)	15 (5.5%)	5.8544	125 (3.6%)	7.3267
Fixed combination therapy other	0 (0.0%)	0 (0.0%)	.	0 (0.0%)	.
Fixed combination therapy SABA+SAMA	113 (6.3%)	16 (5.9%)	0.0164	272 (7.8%)	-0.061
Oral ß2-agonists	14 (0.8%)	2 (0.7%)	0.0049	33 (1.0%)	-0.0187
Leukotriene receptor antagonists (LTRA)	41 (2.3%)	17 (6.2%)	-0.1969	75 (2.2%)	0.0078
Systemic corticosteroids	754 (41.7%)	129 (47.3%)	-0.1113	1,421 (40.8%)	0.0184
Systemic corticosteroids with indication COPD	340 (18.8%)	47 (17.2%)	0.0416	678 (19.5%)	-0.0168
Oral phosphodiesterase-4 (PDE-4) inhibitors	4 (0.2%)	1 (0.4%)	-0.0267	6 (0.2%)	0.0111

Aarhus	QVA N(%)	Fixed LABA LAMA N(%)	Std Dif	LABA N(%)	Std Dif
Total	1,807 (100.0%)	1,758 (100.0%)	.	1,078 (100.0%)	.
Single-ingredient short-acting muscarinic agents	18 (1.0%)	16 (0.9%)	0.0088	7 (0.7%)	0.0384
Single-ingredient short-acting ß2 agonists	1,135 (62.8%)	1,081 (61.5%)	0.0272	518 (48.1%)	0.3002
LABA	540 (29.9%)	336 (19.1%)	0.2524	1,078 (100.0%)	-2.1656
LAMA	862 (47.7%)	902 (51.3%)	-0.0721	231 (21.4%)	0.5746
Inhaled corticosteroids (ICS)	391 (21.6%)	456 (25.9%)	-0.1011	86 (8.0%)	0.3918
Xanthines	10 (0.6%)	10 (0.6%)	-0.0021	6 (0.6%)	-0.0004
Fixed combination therapy LABA+ICS	609 (33.7%)	648 (36.9%)	-0.0661	227 (21.1%)	0.2864
Fixed combination therapy LABA+LAMA	41 (2.3%)	1,758 (100.0%)	-9.2789	16 (1.5%)	0.0578
QVA	1,807 (100.0%)	201 (11.4%)	3.9349	35 (3.3%)	7.7165
Fixed combination therapy other	0 (0.0%)	0 (0.0%)	.	0 (0.0%)	.
Fixed combination therapy SABA+SAMA	113 (6.3%)	113 (6.4%)	-0.0072	37 (3.4%)	0.1317
Oral ß2-agonists	14 (0.8%)	19 (1.1%)	-0.0319	7 (0.7%)	0.0149
Leukotriene receptor antagonists (LTRA)	41 (2.3%)	38 (2.2%)	0.0073	15 (1.4%)	0.0655
Systemic corticosteroids	754 (41.7%)	751 (42.7%)	-0.0201	308 (28.6%)	0.2781
Systemic corticosteroids with indication COPD	340 (18.8%)	412 (23.4%)	-0.1133	112 (10.4%)	0.2402
Oral phosphodiesterase-4 (PDE-4) inhibitors	4 (0.2%)	20 (1.1%)	-0.1117	2 (0.2%)	0.0079

Aarhus	QVA N(%)	LAMA	Std Dif
Total	1,807 (100.0%)	2,095 (100.0%)	.
Single-ingredient short-acting muscarinic agents	18 (1.0%)	12 (0.6%)	0.048
Single-ingredient short-acting ß2 agonists	1,135 (62.8%)	1,046 (49.9%)	0.2619
LABA	540 (29.9%)	176 (8.4%)	0.5675
LAMA	862 (47.7%)	2,095 (100.0%)	-1.4803
Inhaled corticosteroids (ICS)	391 (21.6%)	227 (10.8%)	0.296
Xanthines	10 (0.6%)	7 (0.3%)	0.033
Fixed combination therapy LABA+ICS	609 (33.7%)	557 (26.6%)	0.1555
Fixed combination therapy LABA+LAMA	41 (2.3%)	19 (0.9%)	0.1091
QVA	1,807 (100.0%)	43 (2.1%)	9.7671
Fixed combination therapy other	0 (0.0%)	0 (0.0%)	.
Fixed combination therapy SABA+SAMA	113 (6.3%)	90 (4.3%)	0.0876
Oral ß2-agonists	14 (0.8%)	17 (0.8%)	-0.0041
Leukotriene receptor antagonists (LTRA)	41 (2.3%)	34 (1.6%)	0.0468
Systemic corticosteroids	754 (41.7%)	685 (32.7%)	0.1876
Systemic corticosteroids with indication COPD	340 (18.8%)	295 (14.1%)	0.1279
Oral phosphodiesterase-4 (PDE-4) inhibitors	4 (0.2%)	1 (0.1%)	0.0474

HSD	QVA N(%)	Free LABA+LAMA without ICS N(%)	Std Dif	Free LABA+LAMA with ICS N(%)	Std Dif
Total	385 (100.0%)	995 (100.0%)	.	335 (100.0%)	.
Single-ingredient short-acting muscarinic agents	28 (7.3%)	51 (5.1%)	0.089	46 (13.7%)	-0.2115
Single-ingredient short-acting ß2 agonists	68 (17.7%)	172 (17.3%)	0.0099	99 (29.6%)	-0.2824
LABA	125 (32.5%)	995 (100.0%)	-2.037	335 (100.0%)	-2.037
LAMA	228 (59.2%)	995 (100.0%)	-1.172	335 (100.0%)	-1.172
Inhaled corticosteroids (ICS)	133 (34.6%)	306 (30.8%)	0.0809	335 (100.0%)	-1.9441
Xanthines	40 (10.4%)	104 (10.5%)	-0.002	53 (15.8%)	-0.1612
Fixed combination therapy LABA+ICS	165 (42.9%)	373 (37.5%)	0.1096	95 (28.4%)	0.3059
Fixed combination therapy LABA+LAMA	6 (1.6%)	2 (0.2%)	0.1456	0 (0.0%)	0.1777
QVA	385 (100.0%)	15 (1.5%)	11.4252	2 (0.6%)	18.221
Fixed combination therapy other	0 (0.0%)	0 (0.0%)	.	0 (0.0%)	.
Fixed combination therapy SABA+SAMA	57 (14.8%)	138 (13.9%)	0.0267	107 (31.9%)	-0.4129
Oral ß2-agonists	0 (0.0%)	0 (0.0%)	.	0 (0.0%)	.
Leukotriene receptor antagonists (LTRA)	7 (1.8%)	20 (2.0%)	-0.014	9 (2.7%)	-0.0585
Systemic corticosteroids	163 (42.3%)	406 (40.8%)	0.0311	170 (50.8%)	-0.1689
Systemic corticosteroids with indication COPD	19 (4.9%)	65 (6.5%)	-0.0687	28 (8.4%)	-0.1376
Oral phosphodiesterase-4 (PDE-4) inhibitors	1 (0.3%)	0 (0.0%)	0.0721	5 (1.5%)	-0.1324

HSD	QVA N(%)	Free LABA+ICS N(%)	Std Dif	Fixed LABA ICS N(%)	Std Dif
Total	385 (100.0%)	437 (100.0%)	.	5,897 (100.0%)	.
Single-ingredient short-acting muscarinic agents	28 (7.3%)	46 (10.5%)	-0.1143	270 (4.6%)	0.1142
Single-ingredient short-acting ß2 agonists	68 (17.7%)	99 (22.7%)	-0.1245	769 (13.0%)	0.1284
LABA	125 (32.5%)	437 (100.0%)	-2.037	654 (11.1%)	0.5357
LAMA	228 (59.2%)	103 (23.6%)	0.7755	2,113 (35.8%)	0.4814
Inhaled corticosteroids (ICS)	133 (34.6%)	437 (100.0%)	-1.9441	1,899 (32.2%)	0.0497
Xanthines	40 (10.4%)	60 (13.7%)	-0.1026	483 (8.2%)	0.0757
Fixed combination therapy LABA+ICS	165 (42.9%)	90 (20.6%)	0.492	5,897 (100.0%)	-1.6309
Fixed combination therapy LABA+LAMA	6 (1.6%)	0 (0.0%)	0.1777	15 (0.3%)	0.1378
QVA	385 (100.0%)	4 (0.9%)	14.6971	29 (0.5%)	20.1152
Fixed combination therapy other	0 (0.0%)	0 (0.0%)	.	0 (0.0%)	.
Fixed combination therapy SABA+SAMA	57 (14.8%)	116 (26.5%)	-0.2926	737 (12.5%)	0.0672
Oral ß2-agonists	0 (0.0%)	1 (0.2%)	-0.0677	6 (0.1%)	-0.0451
Leukotriene receptor antagonists (LTRA)	7 (1.8%)	23 (5.3%)	-0.187	124 (2.1%)	-0.0205
Systemic corticosteroids	163 (42.3%)	182 (41.7%)	0.014	2,253 (38.2%)	0.0843
Systemic corticosteroids with indication COPD	19 (4.9%)	29 (6.6%)	-0.0728	353 (6.0%)	-0.0462
Oral phosphodiesterase-4 (PDE-4) inhibitors	1 (0.3%)	1 (0.2%)	0.0063	0 (0.0%)	0.0721

HSD	QVA N(%)	Fixed LABA LAMA N(%)	Std Dif	LABA N(%)	Std Dif
Total	385 (100.0%)	426 (100.0%)	.	875 (100.0%)	.
Single-ingredient short-acting muscarinic agents	28 (7.3%)	38 (8.9%)	-0.0603	38 (4.3%)	0.1254
Single-ingredient short-acting ß2 agonists	68 (17.7%)	73 (17.1%)	0.0139	100 (11.4%)	0.1773
LABA	125 (32.5%)	67 (15.7%)	0.3986	875 (100.0%)	-2.037
LAMA	228 (59.2%)	245 (57.5%)	0.0346	230 (26.3%)	0.7053
Inhaled corticosteroids (ICS)	133 (34.6%)	160 (37.6%)	-0.0627	204 (23.3%)	0.2494
Xanthines	40 (10.4%)	47 (11.0%)	-0.0208	73 (8.3%)	0.0702
Fixed combination therapy LABA+ICS	165 (42.9%)	226 (53.1%)	-0.2049	261 (29.8%)	0.2731
Fixed combination therapy LABA+LAMA	6 (1.6%)	426 (100.0%)	-11.2252	2 (0.2%)	0.1415
QVA	385 (100.0%)	17 (4.0%)	6.9285	4 (0.5%)	20.8567
Fixed combination therapy other	0 (0.0%)	0 (0.0%)	.	0 (0.0%)	.
Fixed combination therapy SABA+SAMA	57 (14.8%)	45 (10.6%)	0.1276	92 (10.5%)	0.1292
Oral ß2-agonists	0 (0.0%)	0 (0.0%)	.	0 (0.0%)	.
Leukotriene receptor antagonists (LTRA)	7 (1.8%)	6 (1.4%)	0.0325	17 (1.9%)	-0.0092
Systemic corticosteroids	163 (42.3%)	177 (41.6%)	0.016	317 (36.2%)	0.1252
Systemic corticosteroids with indication COPD	19 (4.9%)	31 (7.3%)	-0.0978	38 (4.3%)	0.0281
Oral phosphodiesterase-4 (PDE-4) inhibitors	1 (0.3%)	1 (0.2%)	0.005	0 (0.0%)	0.0721

HSD	QVA N(%)	LAMA	Std Dif
Total	385 (100.0%)	3,595 (100.0%)	.
Single-ingredient short-acting muscarinic agents	28 (7.3%)	194 (5.4%)	0.077
Single-ingredient short-acting ß2 agonists	68 (17.7%)	393 (10.9%)	0.193
LABA	125 (32.5%)	219 (6.1%)	0.7087
LAMA	228 (59.2%)	3,595 (100.0%)	-1.172
Inhaled corticosteroids (ICS)	133 (34.6%)	1,231 (34.2%)	0.0064
Xanthines	40 (10.4%)	290 (8.1%)	0.0803
Fixed combination therapy LABA+ICS	165 (42.9%)	1,053 (29.3%)	0.2852
Fixed combination therapy LABA+LAMA	6 (1.6%)	9 (0.3%)	0.1383
QVA	385 (100.0%)	15 (0.4%)	21.8449
Fixed combination therapy other	0 (0.0%)	0 (0.0%)	.
Fixed combination therapy SABA+SAMA	57 (14.8%)	472 (13.1%)	0.0483
Oral ß2-agonists	0 (0.0%)	0 (0.0%)	.
Leukotriene receptor antagonists (LTRA)	7 (1.8%)	87 (2.4%)	-0.0418
Systemic corticosteroids	163 (42.3%)	1,249 (34.7%)	0.1564
Systemic corticosteroids with indication COPD	19 (4.9%)	193 (5.4%)	-0.0196
Oral phosphodiesterase-4 (PDE-4) inhibitors	1 (0.3%)	0 (0.0%)	0.0721

SIDIAP	QVA N(%)	Free LABA+LAMA without ICS N(%)	Std Dif	Free LABA+LAMA with ICS N(%)	Std Dif
Total	5,561 (100.0%)	4,219 (100.0%)	.	1,725 (100.0%)	.
Single-ingredient short-acting muscarinic agents	1,846 (33.2%)	1,347 (31.9%)	0.0271	698 (40.5%)	-0.1511
Single-ingredient short-acting ß2 agonists	2,488 (44.7%)	1,816 (43.0%)	0.0342	1,020 (59.1%)	-0.291
LABA	1,686 (30.3%)	4,219 (100.0%)	-2.1438	1,725 (100.0%)	-2.1438
LAMA	2,815 (50.6%)	4,219 (100.0%)	-1.3966	1,725 (100.0%)	-1.3966
Inhaled corticosteroids (ICS)	1,772 (31.9%)	732 (17.4%)	0.3418	1,725 (100.0%)	-2.0678
Xanthines	107 (1.9%)	37 (0.9%)	0.0892	45 (2.6%)	-0.046
Fixed combination therapy LABA+ICS	1,898 (34.1%)	1,163 (27.6%)	0.1425	405 (23.5%)	0.2368
Fixed combination therapy LABA+LAMA	15 (0.3%)	8 (0.2%)	0.0167	2 (0.1%)	0.0351
QVA	5,561 (100.0%)	83 (2.0%)	9.9819	28 (1.6%)	11.0065
Fixed combination therapy other	0 (0.0%)	0 (0.0%)	.	0 (0.0%)	.
Fixed combination therapy SABA+SAMA	33 (0.6%)	15 (0.4%)	0.0346	23 (1.3%)	-0.0758
Oral ß2-agonists	31 (0.6%)	22 (0.5%)	0.0049	5 (0.3%)	0.0412
Leukotriene receptor antagonists (LTRA)	135 (2.4%)	51 (1.2%)	0.0913	61 (3.5%)	-0.0652
Systemic corticosteroids	1,790 (32.2%)	1,125 (26.7%)	0.1214	809 (46.9%)	-0.3043
Systemic corticosteroids with indication COPD	298 (5.4%)	194 (4.6%)	0.035	137 (7.9%)	-0.1038
Oral phosphodiesterase-4 (PDE-4) inhibitors	124 (2.2%)	37 (0.9%)	0.1095	45 (2.6%)	-0.0247

SIDIAP	QVA N(%)	Free LABA+ICS N(%)	Std Dif	Fixed LABA ICS N(%)	Std Dif
Total	5,561 (100.0%)	2,738 (100.0%)	.	20638 (100.0%)	.
Single-ingredient short-acting muscarinic agents	1,846 (33.2%)	1,465 (53.5%)	-0.4187	7,953 (38.5%)	-0.1115
Single-ingredient short-acting ß2 agonists	2,488 (44.7%)	1,448 (52.9%)	-0.1635	9,349 (45.3%)	-0.0113
LABA	1,686 (30.3%)	2,738 (100.0%)	-2.1438	3,290 (15.9%)	0.346
LAMA	2,815 (50.6%)	447 (16.3%)	0.78	7,527 (36.5%)	0.2883
Inhaled corticosteroids (ICS)	1,772 (31.9%)	2,738 (100.0%)	-2.0678	5,558 (26.9%)	0.1085
Xanthines	107 (1.9%)	26 (1.0%)	0.0819	149 (0.7%)	0.1053
Fixed combination therapy LABA+ICS	1,898 (34.1%)	526 (19.2%)	0.3422	20638 (100.0%)	-1.9645
Fixed combination therapy LABA+LAMA	15 (0.3%)	3 (0.1%)	0.0368	33 (0.2%)	0.0237
QVA	5,561 (100.0%)	27 (1.0%)	14.1683	364 (1.8%)	10.5542
Fixed combination therapy other	0 (0.0%)	0 (0.0%)	.	0 (0.0%)	.
Fixed combination therapy SABA+SAMA	33 (0.6%)	20 (0.7%)	-0.0169	110 (0.5%)	0.0081
Oral ß2-agonists	31 (0.6%)	14 (0.5%)	0.0063	99 (0.5%)	0.0108
Leukotriene receptor antagonists (LTRA)	135 (2.4%)	85 (3.1%)	-0.0413	488 (2.4%)	0.0041
Systemic corticosteroids	1,790 (32.2%)	1,021 (37.3%)	-0.1073	6,338 (30.7%)	0.0318
Systemic corticosteroids with indication COPD	298 (5.4%)	167 (6.1%)	-0.0319	1,121 (5.4%)	-0.0032
Oral phosphodiesterase-4 (PDE-4) inhibitors	124 (2.2%)	19 (0.7%)	0.1282	82 (0.4%)	0.1615

SIDIAP	QVA N(%)	Fixed LABA LAMA N(%)	Std Dif	LABA N(%)	Std Dif
Total	5,561 (100.0%)	964 (100.0%)	.	5,879 (100.0%)	.
Single-ingredient short-acting muscarinic agents	1,846 (33.2%)	358 (37.1%)	-0.0826	2,243 (38.2%)	-0.1036
Single-ingredient short-acting ß2 agonists	2,488 (44.7%)	461 (47.8%)	-0.0618	2,217 (37.7%)	0.1432
LABA	1,686 (30.3%)	194 (20.1%)	0.2363	5,879 (100.0%)	-2.1438
LAMA	2,815 (50.6%)	494 (51.2%)	-0.0125	985 (16.8%)	0.7674
Inhaled corticosteroids (ICS)	1,772 (31.9%)	303 (31.4%)	0.0093	874 (14.9%)	0.41
Xanthines	107 (1.9%)	20 (2.1%)	-0.0108	33 (0.6%)	0.1232
Fixed combination therapy LABA+ICS	1,898 (34.1%)	391 (40.6%)	-0.1332	1,160 (19.7%)	0.3289
Fixed combination therapy LABA+LAMA	15 (0.3%)	964 (100.0%)	-27.1907	3 (0.1%)	0.0547
QVA	5,561 (100.0%)	102 (10.6%)	4.1091	55 (0.9%)	14.5515
Fixed combination therapy other	0 (0.0%)	0 (0.0%)	.	0 (0.0%)	.
Fixed combination therapy SABA+SAMA	33 (0.6%)	7 (0.7%)	-0.0164	15 (0.3%)	0.0521
Oral ß2-agonists	31 (0.6%)	5 (0.5%)	0.0053	25 (0.4%)	0.0189
Leukotriene receptor antagonists (LTRA)	135 (2.4%)	27 (2.8%)	-0.0234	50 (0.9%)	0.1244
Systemic corticosteroids	1,790 (32.2%)	359 (37.2%)	-0.1062	1,266 (21.5%)	0.2421
Systemic corticosteroids with indication COPD	298 (5.4%)	70 (7.3%)	-0.0783	239 (4.1%)	0.0611
Oral phosphodiesterase-4 (PDE-4) inhibitors	124 (2.2%)	22 (2.3%)	-0.0035	11 (0.2%)	0.1878

SIDIAP	QVA N(%)	LAMA	Std Dif
Total	5,561 (100.0%)	13678 (100.0%)	.
Single-ingredient short-acting muscarinic agents	1,846 (33.2%)	4,697 (34.3%)	-0.0242
Single-ingredient short-acting ß2 agonists	2,488 (44.7%)	4,863 (35.6%)	0.1882
LABA	1,686 (30.3%)	1,060 (7.8%)	0.6002
LAMA	2,815 (50.6%)	13678 (100.0%)	-1.3966
Inhaled corticosteroids (ICS)	1,772 (31.9%)	2,622 (19.2%)	0.2943
Xanthines	107 (1.9%)	74 (0.5%)	0.1256
Fixed combination therapy LABA+ICS	1,898 (34.1%)	3,084 (22.6%)	0.2592
Fixed combination therapy LABA+LAMA	15 (0.3%)	9 (0.1%)	0.0498
QVA	5,561 (100.0%)	146 (1.1%)	13.6146
Fixed combination therapy other	0 (0.0%)	0 (0.0%)	.
Fixed combination therapy SABA+SAMA	33 (0.6%)	33 (0.2%)	0.0546
Oral ß2-agonists	31 (0.6%)	62 (0.5%)	0.0147
Leukotriene receptor antagonists (LTRA)	135 (2.4%)	190 (1.4%)	0.076
Systemic corticosteroids	1,790 (32.2%)	2,963 (21.7%)	0.239
Systemic corticosteroids with indication COPD	298 (5.4%)	507 (3.7%)	0.0795
Oral phosphodiesterase-4 (PDE-4) inhibitors	124 (2.2%)	30 (0.2%)	0.1836

LAMA/LABA*= free combination of LAMA and LABA, LABA/ICS^= free combination of LABA and ICS, LAMA/LABA/ICS$= free combination of LAMA, LABA and ICS, LABA+LAMA# = fixed combination of LABA and LAMA other than QVA149

Table 15-7 Use of concomitant medications (assessed during the year prior to index date and on index date) by exposure cohort (pooled and by database)

	QVA N(%)	Free LABA+LAMA without ICS N(%)		Free LABA+LAMA with ICS N(%)	
POOLED	9,798	9,619	Std Dif	3,192	Std Dif
CNS drugs					
Opioids	2,185 (22.3%)	2,413 (25.1%)	-0.0655	737 (23.1%)	-0.0188
Hypnotics and sedatives	847 (8.6%)	873 (9.1%)	-0.0152	307 (9.6%)	-0.0338
Anxiolytics	1,816 (18.5%)	1,636 (17.0%)	0.0399	675 (21.2%)	-0.0655
Anti-epileptic drugs	1,016 (10.4%)	951 (9.9%)	0.016	346 (10.8%)	-0.0153
SSRI	1,435 (14.7%)	1,332 (13.9%)	0.0228	486 (15.2%)	-0.0163
Anticholinergic drugs					
Antipsychotic drugs	550 (5.6%)	526 (5.5%)	0.0063	167 (5.2%)	0.0168
Antidepressant agents	1,171 (12.0%)	1,175 (12.2%)	-0.0081	347 (10.9%)	0.034
Disopyramide	0 (0.0%)	3 (0.0%)	-0.025	1 (0.0%)	-0.025
Antispasmodics	73 (0.8%)	128 (1.3%)	-0.0578	31 (1.0%)	-0.0245
Antiparkinson drugs	24 (0.2%)	17 (0.2%)	0.0149	8 (0.3%)	-0.0011
Cholinesterase inhibitors	7 (0.1%)	5 (0.1%)	0.0078	3 (0.1%)	-0.0078
Atropine	1 (0.0%)	0 (0.0%)	0.0143	0 (0.0%)	0.0143
H1 antihistaminics	1,359 (13.9%)	1,275 (13.3%)	0.018	579 (18.1%)	-0.1166
Anticholinergics for treatment overactive bladder	308 (3.1%)	311 (3.2%)	-0.0051	106 (3.3%)	-0.01

POOLED	QVA N(%) 9,798	Free LABA+ICS N(%) 4,628	Std Dif	Fixed LABA ICS N(%) 58,332	Std Dif
CNS drugs	9,798 (100.0%)	4,628 (100.0%)	.	58332 (100.0%)	.
Opioids	2,185 (22.3%)	1,072 (23.2%)	-0.0206	15552 (26.7%)	-0.1015
Hypnotics and sedatives	847 (8.6%)	473 (10.2%)	-0.0539	5,608 (9.6%)	-0.0337
Anxiolytics	1,816 (18.5%)	1,043 (22.5%)	-0.0992	9,845 (16.9%)	0.0434
Anti-epileptic drugs	1,016 (10.4%)	504 (10.9%)	-0.0169	6,099 (10.5%)	-0.0028
SSRI	1,435 (14.7%)	699 (15.1%)	-0.0129	8,949 (15.3%)	-0.0195
Anticholinergic drugs					
Antipsychotic drugs	550 (5.6%)	287 (6.2%)	-0.0249	3,769 (6.5%)	-0.0356
Antidepressant agents (tricyclic and tetracyclic)	1,171 (12.0%)	530 (11.5%)	0.0155	7,934 (13.6%)	-0.0494
Disopyramide	0 (0.0%)	0 (0.0%)	.	6 (0.0%)	-0.0143
Antispasmodics	73 (0.8%)	45 (1.0%)	-0.0246	902 (1.6%)	-0.0753
Antiparkinson drugs	24 (0.2%)	12 (0.3%)	-0.0029	184 (0.3%)	-0.0133
Cholinesterase inhibitors	7 (0.1%)	3 (0.1%)	0.0025	40 (0.1%)	0.0011
Atropine	1 (0.0%)	0 (0.0%)	0.0143	2 (0.0%)	0.0082
H1 antihistaminics	1,359 (13.9%)	860 (18.6%)	-0.1281	8,882 (15.2%)	-0.0385
Anticholinergics for treatment overactive bladder	308 (3.1%)	0 (0.0%)	0.2548	1,968 (3.4%)	-0.013

	Fixed LABA				
	QVA	LAMA		LABA	
	N(%)	N(%)		N(%)	
POOLED	9,798	9,150	Std Dif	12,364	Std Dif
CNS drugs					
Opioids	2,185 (22.3%)	3,089 (33.8%)	-0.2572	2,808 (22.7%)	-0.0098
Hypnotics and sedatives	847 (8.6%)	808 (8.8%)	-0.0066	1,030 (8.3%)	0.0113
Anxiolytics	1,816 (18.5%)	979 (10.7%)	0.2231	2,105 (17.0%)	0.0395
Anti-epileptic drugs	1,016 (10.4%)	1,068 (11.7%)	-0.0416	1,182 (9.6%)	0.027
SSRI	1,435 (14.7%)	1,428 (15.6%)	-0.0268	1,690 (13.7%)	0.028
Anticholinergic drugs					
Antipsychotic drugs	550 (5.6%)	577 (6.3%)	-0.0293	668 (5.4%)	0.0092
Antidepressant agents (tricyclic and tetracyclic)	1,171 (12.0%)	1,523 (16.6%)	-0.1344	1,439 (11.6%)	0.0097
Disopyramide	0 (0.0%)	1 (0.0%)	-0.0148	1 (0.0%)	-0.0127
Antispasmodics	73 (0.8%)	176 (1.9%)	-0.1028	145 (1.2%)	-0.0439
Antiparkinson drugs	24 (0.2%)	31 (0.3%)	-0.0174	33 (0.3%)	-0.0043
Cholinesterase inhibitors	7 (0.1%)	11 (0.1%)	-0.0158	13 (0.1%)	-0.0113
Atropine	1 (0.0%)	0 (0.0%)	0.0143	0 (0.0%)	0.0143
H1 antihistaminics	1,359 (13.9%)	1,108 (12.1%)	0.0524	1,732 (14.0%)	-0.004
Anticholinergics for treatment overactive bladder	308 (3.1%)	0 (0.0%)	0.2548	386 (3.1%)	0.0012

POOLED	QVA N(%) 9,798	LAMA 42,972	Std Dif
CNS drugs	9,798 (100.0%)	42972 (100.0%)	.
Opioids	2,185 (22.3%)	11587 (27.0%)	-0.1084
Hypnotics and sedatives	847 (8.6%)	3,839 (8.9%)	-0.0102
Anxiolytics	1,816 (18.5%)	6,531 (15.2%)	0.0892
Anti-epileptic drugs	1,016 (10.4%)	4,226 (9.8%)	0.0178
SSRI	1,435 (14.7%)	6,094 (14.2%)	0.0132
Anticholinergic drugs			
Antipsychotic drugs	550 (5.6%)	2,521 (5.9%)	-0.0109
Antidepressant agents (tricyclic and tetracyclic)	1,171 (12.0%)	5,667 (13.2%)	-0.0373
Disopyramide	0 (0.0%)	9 (0.0%)	-0.0205
Antispasmodics	73 (0.8%)	733 (1.7%)	-0.0874
Antiparkinson drugs	24 (0.2%)	148 (0.3%)	-0.0183
Cholinesterase inhibitors	7 (0.1%)	30 (0.1%)	0.0006
Atropine	1 (0.0%)	0 (0.0%)	0.0143
H1 antihistaminics	1,359 (13.9%)	5,765 (13.4%)	0.0132
Anticholinergics for treatment overactive bladder	308 (3.1%)	1,502 (3.5%)	-0.0196

POOLED	QVA N(%)	Free LABA+LAMA without ICS N(%)	Std Dif	Free LABA+LAMA with ICS N(%)	Std Dif
Drugs affecting cerebrovascular and cardiovascular disease					
NSAIDs	2,631 (26.9%)	2,630 (27.3%)	-0.011	935 (29.3%)	-0.0543
Antithrombotic agents	4,286 (43.7%)	4,243 (44.1%)	-0.0074	1,434 (44.9%)	-0.0238
Lipid lowering drugs	4,510 (46.0%)	4,495 (46.7%)	-0.014	1,417 (44.4%)	0.0329
Platelet Aggregation Inhibitor	3,279 (33.5%)	3,401 (35.4%)	-0.0398	1,084 (34.0%)	-0.0104
Nitrates	1,017 (10.4%)	987 (10.3%)	0.0039	322 (10.1%)	0.0096
Anti-arrhythmics	282 (2.9%)	225 (2.3%)	0.0338	107 (3.4%)	-0.0273
Cardiac glycosides	422 (4.3%)	356 (3.7%)	0.0309	155 (4.9%)	-0.0263
Anti-diabetic drugs	1,885 (19.2%)	1,733 (18.0%)	0.0314	606 (19.0%)	0.0065
Anti-hypertensive drugs	6,597 (67.3%)	6,328 (65.8%)	0.0327	2,228 (69.8%)	-0.0532

POOLED	QVA N(%)	Free LABA+ICS N(%)	Std Dif	Fixed LABA ICS N(%)	Std Dif
Drugs affecting cerebrovascular and cardiovascular disease					
NSAIDs	2,631 (26.9%)	1,460 (31.6%)	-0.1034	15402 (26.4%)	0.0101
Antithrombotic agents	4,286 (43.7%)	1,845 (39.9%)	0.0787	23391 (40.1%)	0.0739
Lipid lowering drugs	4,510 (46.0%)	1,968 (42.5%)	0.0706	25332 (43.4%)	0.0524
Platelet Aggregation Inhibitor	3,279 (33.5%)	1,421 (30.7%)	0.0592	18416 (31.6%)	0.0405
Nitrates	1,017 (10.4%)	409 (8.8%)	0.0523	5,661 (9.7%)	0.0225
Anti-arrhythmics	282 (2.9%)	129 (2.8%)	0.0055	1,299 (2.2%)	0.0413
Cardiac glycosides	422 (4.3%)	164 (3.5%)	0.0393	1,959 (3.4%)	0.0494
Anti-diabetic drugs	1,885 (19.2%)	939 (20.3%)	-0.0264	9,684 (16.6%)	0.0688
Anti-hypertensive drugs	6,597 (67.3%)	3,098 (66.9%)	0.0083	36497 (62.6%)	0.0999

POOLED	QVA N(%)	Fixed LABA LAMA N(%)	Std Dif	LABA N(%)	Std Dif
Drugs affecting cerebrovascular and cardiovascular disease					
NSAIDs	2,631 (26.9%)	1,824 (19.9%)	0.164	3,549 (28.7%)	-0.0414
Antithrombotic agents	4,286 (43.7%)	3,994 (43.7%)	0.0019	4,643 (37.6%)	0.1263
Lipid lowering drugs	4,510 (46.0%)	4,353 (47.6%)	-0.0309	5,355 (43.3%)	0.0547
Platelet Aggregation Inhibitor	3,279 (33.5%)	3,087 (33.7%)	-0.0058	3,706 (30.0%)	0.0751
Nitrates	1,017 (10.4%)	1,064 (11.6%)	-0.0399	1,010 (8.2%)	0.0763
Anti-arrhythmics	282 (2.9%)	150 (1.6%)	0.0834	239 (1.9%)	0.0617
Cardiac glycosides	422 (4.3%)	322 (3.5%)	0.0406	337 (2.7%)	0.0859
Anti-diabetic drugs	1,885 (19.2%)	1,330 (14.5%)	0.1258	2,072 (16.8%)	0.0646
Anti-hypertensive drugs	6,597 (67.3%)	5,713 (62.4%)	0.1026	7,657 (61.9%)	0.1131

POOLED	QVA N(%)	LAMA	Std Dif
Drugs affecting cerebrovascular and cardiovascular disease			
NSAIDs	2,631 (26.9%)	10703 (24.9%)	0.0444
Antithrombotic agents	4,286 (43.7%)	17701 (41.2%)	0.0516
Lipid lowering drugs	4,510 (46.0%)	19622 (45.7%)	0.0074
Platelet Aggregation Inhibitor	3,279 (33.5%)	14000 (32.6%)	0.0189
Nitrates	1,017 (10.4%)	4,436 (10.3%)	0.0019
Anti-arrhythmics	282 (2.9%)	972 (2.3%)	0.0389
Cardiac glycosides	422 (4.3%)	1,389 (3.2%)	0.0564
Anti-diabetic drugs	1,885 (19.2%)	6,810 (15.9%)	0.0892
Anti-hypertensive drugs	6,597 (67.3%)	26833 (62.4%)	0.1025

THIN	QVA N(%) 1,346	Free LABA+LAMA without ICS N(%) 2,586	Std Dif	Free LABA+LAMA with ICS N(%) 394	Std Dif
CNS drugs					
Opioids	585 (43.5%)	1,101 (42.6%)	0.0179	168 (42.6%)	0.0166
Hypnotics and sedatives	141 (10.5%)	261 (10.1%)	0.0126	32 (8.1%)	0.081
Anxiolytics	137 (10.2%)	224 (8.7%)	0.0519	46 (11.7%)	-0.048
Anti-epileptic drugs	180 (13.4%)	279 (10.8%)	0.0793	44 (11.2%)	0.0672
SSRI	258 (19.2%)	467 (18.1%)	0.0285	71 (18.0%)	0.0295
Anticholinergic drugs					
Antipsychotic drugs	100 (7.4%)	193 (7.5%)	-0.0013	29 (7.4%)	0.0026
Antidepressant agents (tricyclic and tetracyclic)	293 (21.8%)	509 (19.7%)	0.0514	79 (20.1%)	0.0422
Disopyramide	0 (0.0%)	1 (0.0%)	-0.0278	0 (0.0%)	.
Antispasmodics	40 (3.0%)	88 (3.4%)	-0.0245	14 (3.6%)	-0.0327
Antiparkinson drugs	3 (0.2%)	7 (0.3%)	-0.0096	0 (0.0%)	0.0668
Cholinesterase inhibitors	0 (0.0%)	1 (0.0%)	-0.0278	1 (0.3%)	-0.0712
Atropine	0 (0.0%)	0 (0.0%)	.	0 (0.0%)	.
H1 antihistaminics	193 (14.3%)	350 (13.5%)	0.0232	89 (22.6%)	-0.2136
Anticholinergics for treatment overactive bladder	62 (4.6%)	110 (4.3%)	0.0171	14 (3.6%)	0.0532

THIN	QVA N(%) 1,346	Free LABA+ICS N(%) 583	Std Dif	Fixed LABA ICS N(%) 21315	Std Dif
CNS drugs					
Opioids	585 (43.5%)	251 (43.1%)	0.0082	8,445 (39.6%)	0.078
Hypnotics and sedatives	141 (10.5%)	57 (9.8%)	0.0231	2,146 (10.1%)	0.0134
Anxiolytics	137 (10.2%)	46 (7.9%)	0.0798	2,038 (9.6%)	0.0207
Anti-epileptic drugs	180 (13.4%)	73 (12.5%)	0.0254	2,493 (11.7%)	0.0507
SSRI	258 (19.2%)	107 (18.4%)	0.0209	3,851 (18.1%)	0.0283
Anticholinergic drugs					
Antipsychotic drugs	100 (7.4%)	47 (8.1%)	-0.0236	1,691 (7.9%)	-0.0189
Antidepressant agents (tricyclic and tetracyclic)	293 (21.8%)	112 (19.2%)	0.0633	4,154 (19.5%)	0.0563
Disopyramide	0 (0.0%)	0 (0.0%)	.	4 (0.0%)	-0.0194
Antispasmodics	40 (3.0%)	22 (3.8%)	-0.0444	673 (3.2%)	-0.0108
Antiparkinson drugs	3 (0.2%)	0 (0.0%)	0.0668	73 (0.3%)	-0.0225
Cholinesterase inhibitors	0 (0.0%)	0 (0.0%)	.	12 (0.1%)	-0.0336
Atropine	0 (0.0%)	0 (0.0%)	.	1 (0.0%)	-0.0097
H1 antihistaminics	193 (14.3%)	106 (18.2%)	-0.1042	3,128 (14.7%)	-0.0095
Anticholinergics for treatment overactive bladder	62 (4.6%)	0 (0.0%)	0.3106	1,011 (4.7%)	-0.0065

THIN	QVA N(%) 1,346	Fixed LABA LAMA N(%) 4,921	Std Dif	LABA N(%) 3,006	Std Dif
CNS drugs					
Opioids	585 (43.5%)	2,101 (42.7%)	0.0155	1,128 (37.5%)	0.1211
Hypnotics and sedatives	141 (10.5%)	507 (10.3%)	0.0057	244 (8.1%)	0.0813
Anxiolytics	137 (10.2%)	477 (9.7%)	0.0162	246 (8.2%)	0.0691
Anti-epileptic drugs	180 (13.4%)	689 (14.0%)	-0.0183	338 (11.2%)	0.0648
SSRI	258 (19.2%)	869 (17.7%)	0.0389	489 (16.3%)	0.076
Anticholinergic drugs					
Antipsychotic drugs	100 (7.4%)	375 (7.6%)	-0.0072	200 (6.7%)	0.0303
Antidepressant agents (tricyclic and tetracyclic)	293 (21.8%)	1,043 (21.2%)	0.014	523 (17.4%)	0.1102
Disopyramide	0 (0.0%)	1 (0.0%)	-0.0202	0 (0.0%)	.
Antispasmodics	40 (3.0%)	152 (3.1%)	-0.0068	95 (3.2%)	-0.0109
Antiparkinson drugs	3 (0.2%)	17 (0.4%)	-0.023	13 (0.4%)	-0.0367
Cholinesterase inhibitors	0 (0.0%)	7 (0.1%)	-0.0534	7 (0.2%)	-0.0683
Atropine	0 (0.0%)	0 (0.0%)	.	0 (0.0%)	.
H1 antihistaminics	193 (14.3%)	689 (14.0%)	0.0097	384 (12.8%)	0.0457
Anticholinergics for treatment overactive bladder	62 (4.6%)	0 (0.0%)	0.3106	150 (5.0%)	-0.018

THIN	QVA N(%) 1,346	LAMA 18,598	Std Dif
CNS drugs			
Opioids	585 (43.5%)	7,375 (39.7%)	0.0773
Hypnotics and sedatives	141 (10.5%)	1,755 (9.4%)	0.0347
Anxiolytics	137 (10.2%)	1,667 (9.0%)	0.0413
Anti-epileptic drugs	180 (13.4%)	2,084 (11.2%)	0.066
SSRI	258 (19.2%)	3,068 (16.5%)	0.0698
Anticholinergic drugs			
Antipsychotic drugs	100 (7.4%)	1,338 (7.2%)	0.009
Antidepressant agents (tricyclic and tetracyclic)	293 (21.8%)	3,432 (18.5%)	0.0827
Disopyramide	0 (0.0%)	3 (0.0%)	-0.018
Antispasmodics	40 (3.0%)	564 (3.0%)	-0.0036
Antiparkinson drugs	3 (0.2%)	69 (0.4%)	-0.0272
Cholinesterase inhibitors	0 (0.0%)	14 (0.1%)	-0.0388
Atropine	0 (0.0%)	0 (0.0%)	.
H1 antihistaminics	193 (14.3%)	2,388 (12.8%)	0.0437
Anticholinergics for treatment overactive bladder	62 (4.6%)	867 (4.7%)	-0.0026

THIN	QVA N(%)	Free LABA+LAMA without ICS N(%)	Std Dif	Free LABA+LAMA with ICS N(%)	Std Dif
Drugs affecting cerebrovascular and cardiovascular disease					
NSAIDs	187 (13.9%)	453 (17.5%)	-0.0997	68 (17.3%)	-0.0928
Antithrombotic agents	555 (41.2%)	1,046 (40.5%)	0.016	133 (33.8%)	0.1548
Lipid lowering drugs	680 (50.5%)	1,282 (49.6%)	0.0189	163 (41.4%)	0.1842
Platelet Aggregation Inhibitor	421 (31.3%)	859 (33.2%)	-0.0415	109 (27.7%)	0.0792
Nitrates	187 (13.9%)	348 (13.5%)	0.0127	45 (11.4%)	0.0743
Anti-arrhythmics	17 (1.3%)	19 (0.7%)	0.0531	1 (0.3%)	0.1165
Cardiac glycosides	40 (3.0%)	68 (2.6%)	0.0207	8 (2.0%)	0.0603
Anti-diabetic drugs	163 (12.1%)	262 (10.1%)	0.0629	25 (6.4%)	0.2
Anti-hypertensive drugs	839 (62.3%)	1,523 (58.9%)	0.0704	237 (60.2%)	0.0447

THIN	QVA N(%)	Free LABA+ICS N(%)	Std Dif	Fixed LABA ICS N(%)	Std Dif
Drugs affecting cerebrovascular and cardiovascular disease					
NSAIDs	187 (13.9%)	101 (17.3%)	-0.0946	3,480 (16.3%)	-0.068
Antithrombotic agents	555 (41.2%)	189 (32.4%)	0.1834	8,048 (37.8%)	0.0711
Lipid lowering drugs	680 (50.5%)	255 (43.7%)	0.1361	9,869 (46.3%)	0.0845
Platelet Aggregation Inhibitor	421 (31.3%)	157 (26.9%)	0.0958	6,550 (30.7%)	0.0119
Nitrates	187 (13.9%)	53 (9.1%)	0.1509	2,540 (11.9%)	0.059
Anti-arrhythmics	17 (1.3%)	5 (0.9%)	0.0396	198 (0.9%)	0.0321
Cardiac glycosides	40 (3.0%)	14 (2.4%)	0.0353	585 (2.7%)	0.0136
Anti-diabetic drugs	163 (12.1%)	75 (12.9%)	-0.0228	2,443 (11.5%)	0.0201
Anti-hypertensive drugs	839 (62.3%)	329 (56.4%)	0.1203	12216 (57.3%)	0.1025

THIN	QVA N(%)	Fixed LABA LAMA N(%)	Std Dif	LABA N(%)	Std Dif
Drugs affecting cerebrovascular and cardiovascular disease					
NSAIDs	187 (13.9%)	805 (16.4%)	-0.0688	474 (15.8%)	-0.0528
Antithrombotic agents	555 (41.2%)	1,970 (40.0%)	0.0244	1,071 (35.6%)	0.1154
Lipid lowering drugs	680 (50.5%)	2,443 (49.6%)	0.0175	1,354 (45.0%)	0.1098
Platelet Aggregation Inhibitor	421 (31.3%)	1,559 (31.7%)	-0.0087	864 (28.7%)	0.0553
Nitrates	187 (13.9%)	648 (13.2%)	0.0212	350 (11.6%)	0.0674
Anti-arrhythmics	17 (1.3%)	33 (0.7%)	0.0606	28 (0.9%)	0.0318
Cardiac glycosides	40 (3.0%)	135 (2.7%)	0.0137	74 (2.5%)	0.0314
Anti-diabetic drugs	163 (12.1%)	583 (11.9%)	0.0081	302 (10.1%)	0.0658
Anti-hypertensive drugs	839 (62.3%)	2,843 (57.8%)	0.0932	1,667 (55.5%)	0.1401

THIN	QVA N(%)	LAMA	Std Dif
Drugs affecting cerebrovascular and cardiovascular disease			
NSAIDs	187 (13.9%)	3,149 (16.9%)	-0.0842
Antithrombotic agents	555 (41.2%)	7,087 (38.1%)	0.0639
Lipid lowering drugs	680 (50.5%)	8,794 (47.3%)	0.0647
Platelet Aggregation Inhibitor	421 (31.3%)	5,740 (30.9%)	0.009
Nitrates	187 (13.9%)	2,216 (11.9%)	0.059
Anti-arrhythmics	17 (1.3%)	166 (0.9%)	0.0359
Cardiac glycosides	40 (3.0%)	481 (2.6%)	0.0234
Anti-diabetic drugs	163 (12.1%)	2,044 (11.0%)	0.035
Anti-hypertensive drugs	839 (62.3%)	10711 (57.6%)	0.0968

IPCI	QVA N(%) 699	Free LABA+LAMA without ICS N(%) 1,148	Std Dif	Free LABA+LAMA with ICS N(%) 496	Std Dif
CNS drugs					
Opioids	122 (17.5%)	226 (19.7%)	-0.0574	109 (22.0%)	-0.1138
Hypnotics and sedatives	93 (13.3%)	179 (15.6%)	-0.0651	81 (16.3%)	-0.0852
Anxiolytics	127 (18.2%)	183 (15.9%)	0.0592	96 (19.4%)	-0.0304
Anti-epileptic drugs	39 (5.6%)	63 (5.5%)	0.004	36 (7.3%)	-0.0685
SSRI	56 (8.0%)	89 (7.8%)	0.0096	54 (10.9%)	-0.0983
Anticholinergic drugs					
Antipsychotic drugs	33 (4.7%)	45 (3.9%)	0.0394	22 (4.4%)	0.0137
Antidepressant agents (tricyclic and tetracyclic)	83 (11.9%)	118 (10.3%)	0.0508	45 (9.1%)	0.0915
Disopyramide	0 (0.0%)	0 (0.0%)	.	0 (0.0%)	.
Antispasmodics	12 (1.7%)	19 (1.7%)	0.0048	9 (1.8%)	-0.0074
Antiparkinson drugs	1 (0.1%)	2 (0.2%)	-0.0078	1 (0.2%)	-0.0141
Cholinesterase inhibitors	1 (0.1%)	1 (0.1%)	0.0165	0 (0.0%)	0.0535
Atropine	1 (0.1%)	0 (0.0%)	0.0535	0 (0.0%)	0.0535
H1 antihistaminics	80 (11.4%)	107 (9.3%)	0.0696	85 (17.1%)	-0.163
Anticholinergics for treatment overactive bladder	16 (2.3%)	28 (2.4%)	-0.0099	10 (2.0%)	0.0188

IPCI	QVA N(%) 699	Free LABA+ICS N(%) 597	Std Dif	Fixed LABA ICS N(%) 7,001	Std Dif
CNS drugs					
Opioids	122 (17.5%)	131 (21.9%)	-0.113	1,405 (20.1%)	-0.067
Hypnotics and sedatives	93 (13.3%)	88 (14.7%)	-0.0413	951 (13.6%)	-0.0082
Anxiolytics	127 (18.2%)	117 (19.6%)	-0.0365	1,187 (17.0%)	0.0319
Anti-epileptic drugs	39 (5.6%)	38 (6.4%)	-0.0331	414 (5.9%)	-0.0143
SSRI	56 (8.0%)	53 (8.9%)	-0.0311	533 (7.6%)	0.0148
Anticholinergic drugs					
Antipsychotic drugs	33 (4.7%)	17 (2.9%)	0.0982	252 (3.6%)	0.0562
Antidepressant agents (tricyclic and tetracyclic)	83 (11.9%)	47 (7.9%)	0.1343	636 (9.1%)	0.0911
Disopyramide	0 (0.0%)	0 (0.0%)	.	2 (0.0%)	-0.0239
Antispasmodics	12 (1.7%)	14 (2.4%)	-0.0445	127 (1.8%)	-0.0074
Antiparkinson drugs	1 (0.1%)	0 (0.0%)	0.0535	21 (0.3%)	-0.0334
Cholinesterase inhibitors	1 (0.1%)	0 (0.0%)	0.0535	7 (0.1%)	0.0124
Atropine	1 (0.1%)	0 (0.0%)	0.0535	1 (0.0%)	0.0459
H1 antihistaminics	80 (11.4%)	109 (18.3%)	-0.1923	851 (12.2%)	-0.022
Anticholinergics for treatment overactive bladder	16 (2.3%)	0 (0.0%)	0.2163	172 (2.5%)	-0.011

IPCI	QVA N(%) 699	Fixed LABA LAMA N(%) 1,081	Std Dif	LABA N(%) 1,526	Std Dif
CNS drugs					
Opioids	122 (17.5%)	228 (21.1%)	-0.0923	298 (19.5%)	-0.0534
Hypnotics and sedatives	93 (13.3%)	169 (15.6%)	-0.0662	212 (13.9%)	-0.0171
Anxiolytics	127 (18.2%)	187 (17.3%)	0.0228	215 (14.1%)	0.111
Anti-epileptic drugs	39 (5.6%)	86 (8.0%)	-0.0947	87 (5.7%)	-0.0053
SSRI	56 (8.0%)	92 (8.5%)	-0.0181	122 (8.0%)	0.0006
Anticholinergic drugs					
Antipsychotic drugs	33 (4.7%)	38 (3.5%)	0.0607	49 (3.2%)	0.0774
Antidepressant agents (tricyclic and tetracyclic)	83 (11.9%)	109 (10.1%)	0.0573	132 (8.7%)	0.1063
Disopyramide	0 (0.0%)	0 (0.0%)	.	1 (0.1%)	-0.0362
Antispasmodics	12 (1.7%)	22 (2.0%)	-0.0235	31 (2.0%)	-0.0232
Antiparkinson drugs	1 (0.1%)	4 (0.4%)	-0.0449	3 (0.2%)	-0.013
Cholinesterase inhibitors	1 (0.1%)	3 (0.3%)	-0.0293	3 (0.2%)	-0.013
Atropine	1 (0.1%)	0 (0.0%)	0.0535	0 (0.0%)	0.0535
H1 antihistaminics	80 (11.4%)	118 (10.9%)	0.0168	151 (9.9%)	0.0502
Anticholinergics for treatment overactive bladder	16 (2.3%)	0 (0.0%)	0.2163	39 (2.6%)	-0.0173

IPCI	QVA N(%) 699	LAMA 5,006	Std Dif
CNS drugs	699 (100.0%)	5,006 (100.0%)	.
Opioids	122 (17.5%)	849 (17.0%)	0.0131
Hypnotics and sedatives	93 (13.3%)	659 (13.2%)	0.0041
Anxiolytics	127 (18.2%)	768 (15.3%)	0.0757
Anti-epileptic drugs	39 (5.6%)	265 (5.3%)	0.0126
SSRI	56 (8.0%)	365 (7.3%)	0.0271
Anticholinergic drugs			
Antipsychotic drugs	33 (4.7%)	196 (3.9%)	0.0396
Antidepressant agents (tricyclic and tetracyclic)	83 (11.9%)	420 (8.4%)	0.1156
Disopyramide	0 (0.0%)	5 (0.1%)	-0.0447
Antispasmodics	12 (1.7%)	102 (2.0%)	-0.0236
Antiparkinson drugs	1 (0.1%)	13 (0.3%)	-0.026
Cholinesterase inhibitors	1 (0.1%)	4 (0.1%)	0.0189
Atropine	1 (0.1%)	0 (0.0%)	0.0535
H1 antihistaminics	80 (11.4%)	503 (10.1%)	0.0451
Anticholinergics for treatment overactive bladder	16 (2.3%)	118 (2.4%)	-0.0045

IPCI	QVA N(%)	Free LABA+LAMA without ICS N(%)	Std Dif	Free LABA+LAMA with ICS N(%)	Std Dif
Drugs affecting cerebrovascular and cardiovascular disease					
NSAIDs	120 (17.2%)	231 (20.1%)	-0.0759	113 (22.8%)	-0.1407
Antithrombotic agents	303 (43.4%)	521 (45.4%)	-0.041	228 (46.0%)	-0.0527
Lipid lowering drugs	284 (40.6%)	532 (46.3%)	-0.1153	216 (43.6%)	-0.0591
Platelet Aggregation Inhibitor	237 (33.9%)	405 (35.3%)	-0.0289	157 (31.7%)	0.048
Nitrates	61 (8.7%)	115 (10.0%)	-0.0443	49 (9.9%)	-0.0396
Anti-arrhythmics	10 (1.4%)	18 (1.6%)	-0.0113	13 (2.6%)	-0.0845
Cardiac glycosides	21 (3.0%)	37 (3.2%)	-0.0126	19 (3.8%)	-0.0455
Anti-diabetic drugs	97 (13.9%)	182 (15.9%)	-0.0556	66 (13.3%)	0.0166
Anti-hypertensive drugs	394 (56.4%)	696 (60.6%)	-0.0865	310 (62.5%)	-0.1251

IPCI	QVA N(%)	Free LABA+ICS N(%)	Std Dif	Fixed LABA ICS N(%)	Std Dif
Drugs affecting cerebrovascular and cardiovascular disease					
NSAIDs	120 (17.2%)	137 (23.0%)	-0.1446	1,638 (23.4%)	-0.1553
Antithrombotic agents	303 (43.4%)	231 (38.7%)	0.0947	2,658 (38.0%)	0.1097
Lipid lowering drugs	284 (40.6%)	238 (39.9%)	0.0156	2,657 (38.0%)	0.0548
Platelet Aggregation Inhibitor	237 (33.9%)	162 (27.1%)	0.1473	1,916 (27.4%)	0.1421
Nitrates	61 (8.7%)	60 (10.1%)	-0.0454	567 (8.1%)	0.0226
Anti-arrhythmics	10 (1.4%)	20 (3.4%)	-0.1258	143 (2.0%)	-0.0468
Cardiac glycosides	21 (3.0%)	17 (2.9%)	0.0093	194 (2.8%)	0.0139
Anti-diabetic drugs	97 (13.9%)	102 (17.1%)	-0.0887	1,083 (15.5%)	-0.045
Anti-hypertensive drugs	394 (56.4%)	364 (61.0%)	-0.0936	3,840 (54.9%)	0.0305

IPCI	QVA N(%)	Fixed LABA LAMA N(%)	Std Dif	LABA N(%)	Std Dif
Drugs affecting cerebrovascular and cardiovascular disease					
NSAIDs	120 (17.2%)	221 (20.4%)	-0.0839	361 (23.7%)	-0.1614
Antithrombotic agents	303 (43.4%)	492 (45.5%)	-0.0436	564 (37.0%)	0.1305
Lipid lowering drugs	284 (40.6%)	476 (44.0%)	-0.0689	597 (39.1%)	0.0308
Platelet Aggregation Inhibitor	237 (33.9%)	359 (33.2%)	0.0147	411 (26.9%)	0.1519
Nitrates	61 (8.7%)	102 (9.4%)	-0.0247	110 (7.2%)	0.0561
Anti-arrhythmics	10 (1.4%)	20 (1.9%)	-0.033	24 (1.6%)	-0.0117
Cardiac glycosides	21 (3.0%)	32 (3.0%)	0.0026	34 (2.2%)	0.0486
Anti-diabetic drugs	97 (13.9%)	170 (15.7%)	-0.0521	204 (13.4%)	0.0148
Anti-hypertensive drugs	394 (56.4%)	643 (59.5%)	-0.0631	837 (54.9%)	0.0305

IPCI	QVA N(%)	LAMA	Std Dif
Drugs affecting cerebrovascular and cardiovascular disease			
NSAIDs	120 (17.2%)	1,081 (21.6%)	-0.1121
Antithrombotic agents	303 (43.4%)	2,042 (40.8%)	0.0518
Lipid lowering drugs	284 (40.6%)	2,003 (40.0%)	0.0126
Platelet Aggregation Inhibitor	237 (33.9%)	1,512 (30.2%)	0.0794
Nitrates	61 (8.7%)	432 (8.6%)	0.0034
Anti-arrhythmics	10 (1.4%)	100 (2.0%)	-0.0437
Cardiac glycosides	21 (3.0%)	145 (2.9%)	0.0064
Anti-diabetic drugs	97 (13.9%)	697 (13.9%)	-0.0013
Anti-hypertensive drugs	394 (56.4%)	2,838 (56.7%)	-0.0066

	QVA N(%)		Free LABA+LAMA without ICS N(%)		Free LABA+LAMA with ICS N(%)	
Aarhus	1,807		671	Std Dif	242	Std Dif
CNS drugs						
Opioids	518	(28.7%)	189 (28.2%)	0.0111	63 (26.0%)	0.059
Hypnotics and sedatives	7	(0.4%)	3 (0.5%)	-0.0093	3 (1.2%)	-0.0948
Anxiolytics	11	(0.6%)	4 (0.6%)	0.0016	1 (0.4%)	0.0274
Anti-epileptic drugs	158	(8.7%)	54 (8.1%)	0.0251	15 (6.2%)	0.0968
SSRI	275	(15.2%)	124 (18.5%)	-0.0872	51 (21.1%)	-0.1522
Anticholinergic drugs						
Antipsychotic drugs	118	(6.5%)	42 (6.3%)	0.0111	18 (7.4%)	-0.0356
Antidepressant agents (tricyclic and tetracyclic)	252	(14.0%)	104 (15.5%)	-0.0438	39 (16.1%)	-0.0607
Disopyramide	0	(0.0%)	0 (0.0%)	.	0 (0.0%)	.
Antispasmodics	0	(0.0%)	0 (0.0%)	.	0 (0.0%)	.
Antiparkinson drugs	3	(0.2%)	1 (0.2%)	0.0043	2 (0.8%)	-0.0939
Cholinesterase inhibitors	1	(0.1%)	0 (0.0%)	0.0333	0 (0.0%)	0.0333
Atropine	0	(0.0%)	0 (0.0%)	.	0 (0.0%)	.
H1 antihistaminics	109	(6.0%)	39 (5.8%)	0.0093	29 (12.0%)	-0.2087
Anticholinergics for treatment overactive bladder	44	(2.4%)	18 (2.7%)	-0.0157	4 (1.7%)	0.0552

Aarhus	QVA N(%) 1,807	Free LABA+ICS N(%) 273	Std Dif	Fixed LABA ICS N(%) 3,481	Std Dif
CNS drugs					
Opioids	518 (28.7%)	90 (33.0%)	-0.0931	1,109 (31.9%)	-0.0695
Hypnotics and sedatives	7 (0.4%)	2 (0.7%)	-0.0462	20 (0.6%)	-0.0271
Anxiolytics	11 (0.6%)	1 (0.4%)	0.0348	11 (0.3%)	0.0432
Anti-epileptic drugs	158 (8.7%)	19 (7.0%)	0.0663	332 (9.5%)	-0.0275
SSRI	275 (15.2%)	55 (20.2%)	-0.1293	649 (18.6%)	-0.0914
Anticholinergic drugs					
Antipsychotic drugs	118 (6.5%)	22 (8.1%)	-0.0587	280 (8.0%)	-0.0582
Antidepressant agents (tricyclic and tetracyclic)	252 (14.0%)	39 (14.3%)	-0.0098	630 (18.1%)	-0.1134
Disopyramide	0 (0.0%)	0 (0.0%)	.	0 (0.0%)	.
Antispasmodics	0 (0.0%)	0 (0.0%)	.	0 (0.0%)	.
Antiparkinson drugs	3 (0.2%)	0 (0.0%)	0.0577	21 (0.6%)	-0.0707
Cholinesterase inhibitors	1 (0.1%)	0 (0.0%)	0.0333	2 (0.1%)	-0.0009
Atropine	0 (0.0%)	0 (0.0%)	.	0 (0.0%)	.
H1 antihistaminics	109 (6.0%)	33 (12.1%)	-0.2119	218 (6.3%)	-0.0096
Anticholinergics for treatment overactive bladder	44 (2.4%)	0 (0.0%)	0.2234	101 (2.9%)	-0.0289

Aarhus	QVA N(%) 1,807	Fixed LABA LAMA N(%) 1,758	Std Dif	LABA N(%) 1,078	Std Dif
CNS drugs					
Opioids	518 (28.7%)	499 (28.4%)	0.0062	308 (28.6%)	0.0021
Hypnotics and sedatives	7 (0.4%)	8 (0.5%)	-0.0104	8 (0.7%)	-0.0473
Anxiolytics	11 (0.6%)	9 (0.5%)	0.013	4 (0.4%)	0.034
Anti-epileptic drugs	158 (8.7%)	128 (7.3%)	0.0539	78 (7.2%)	0.0556
SSRI	275 (15.2%)	289 (16.4%)	-0.0334	188 (17.4%)	-0.0601
Anticholinergic drugs					
Antipsychotic drugs	118 (6.5%)	96 (5.5%)	0.045	79 (7.3%)	-0.0314
Antidepressant agents (tricyclic and tetracyclic)	252 (14.0%)	267 (15.2%)	-0.0352	169 (15.7%)	-0.0487
Disopyramide	0 (0.0%)	0 (0.0%)	.	0 (0.0%)	.
Antispasmodics	0 (0.0%)	0 (0.0%)	.	0 (0.0%)	.
Antiparkinson drugs	3 (0.2%)	6 (0.3%)	-0.0348	6 (0.6%)	-0.0651
Cholinesterase inhibitors	1 (0.1%)	0 (0.0%)	0.0333	1 (0.1%)	-0.0138
Atropine	0 (0.0%)	0 (0.0%)	.	0 (0.0%)	.
H1 antihistaminics	109 (6.0%)	93 (5.3%)	0.0321	59 (5.5%)	0.024
Anticholinergics for treatment overactive bladder	44 (2.4%)	0 (0.0%)	0.2234	25 (2.3%)	0.0076

Aarhus	QVA N(%) 1,807	LAMA 2,095	Std Dif
CNS drugs			
Opioids	518 (28.7%)	613 (29.3%)	-0.0131
Hypnotics and sedatives	7 (0.4%)	7 (0.3%)	0.0089
Anxiolytics	11 (0.6%)	12 (0.6%)	0.0047
Anti-epileptic drugs	158 (8.7%)	201 (9.6%)	-0.0295
SSRI	275 (15.2%)	368 (17.6%)	-0.0634
Anticholinergic drugs			
Antipsychotic drugs	118 (6.5%)	164 (7.8%)	-0.0503
Antidepressant agents (tricyclic and tetracyclic)	252 (14.0%)	352 (16.8%)	-0.0792
Disopyramide	0 (0.0%)	0 (0.0%)	.
Antispasmodics	0 (0.0%)	2 (0.1%)	-0.0437
Antiparkinson drugs	3 (0.2%)	8 (0.4%)	-0.0413
Cholinesterase inhibitors	1 (0.1%)	1 (0.1%)	0.0034
Atropine	0 (0.0%)	0 (0.0%)	.
H1 antihistaminics	109 (6.0%)	132 (6.3%)	-0.0112
Anticholinergics for treatment overactive bladder	44 (2.4%)	61 (2.9%)	-0.0295

Aarhus	QVA N(%)	Free LABA+LAMA without ICS N(%)	Std Dif	Free LABA+LAMA with ICS N(%)	Std Dif
Drugs affecting cerebrovascular and cardiovascular disease					
NSAIDs	392 (21.7%)	120 (17.9%)	0.0957	41 (16.9%)	0.1204
Antithrombotic agents	891 (49.3%)	337 (50.2%)	-0.0183	107 (44.2%)	0.1021
Lipid lowering drugs	806 (44.6%)	306 (45.6%)	-0.0201	101 (41.7%)	0.0579
Platelet Aggregation Inhibitor	652 (36.1%)	280 (41.7%)	-0.116	89 (36.8%)	-0.0144
Nitrates	200 (11.1%)	68 (10.1%)	0.0303	24 (9.9%)	0.0375
Anti-arrhythmics	53 (2.9%)	15 (2.2%)	0.044	3 (1.2%)	0.1186
Cardiac glycosides	128 (7.1%)	41 (6.1%)	0.0392	17 (7.0%)	0.0023
Anti-diabetic drugs	261 (14.4%)	75 (11.2%)	0.0978	28 (11.6%)	0.0854
Anti-hypertensive drugs	1,293 (71.6%)	478 (71.2%)	0.007	176 (72.7%)	-0.0261

Aarhus	QVA N(%)	Free LABA+ICS N(%)	Std Dif	Fixed LABA ICS N(%)	Std Dif
Drugs affecting cerebrovascular and cardiovascular disease					
NSAIDs	392 (21.7%)	71 (26.0%)	-0.1012	744 (21.4%)	0.0078
Antithrombotic agents	891 (49.3%)	111 (40.7%)	0.1743	1,691 (48.6%)	0.0146
Lipid lowering drugs	806 (44.6%)	113 (41.4%)	0.0649	1,507 (43.3%)	0.0264
Platelet Aggregation Inhibitor	652 (36.1%)	86 (31.5%)	0.0968	1,326 (38.1%)	-0.0416
Nitrates	200 (11.1%)	19 (7.0%)	0.1437	388 (11.2%)	-0.0025
Anti-arrhythmics	53 (2.9%)	3 (1.1%)	0.1307	70 (2.0%)	0.0594
Cardiac glycosides	128 (7.1%)	21 (7.7%)	-0.0232	222 (6.4%)	0.0282
Anti-diabetic drugs	261 (14.4%)	37 (13.6%)	0.0256	529 (15.2%)	-0.0212
Anti-hypertensive drugs	1,293 (71.6%)	183 (67.0%)	0.098	2,410 (69.2%)	0.0509

Aarhus	QVA N(%)	Fixed LABA LAMA N(%)	Std Dif	LABA N(%)	Std Dif
Drugs affecting cerebrovascular and cardiovascular disease					
NSAIDs	392 (21.7%)	326 (18.5%)	0.0786	233 (21.6%)	0.0019
Antithrombotic agents	891 (49.3%)	876 (49.8%)	-0.0104	543 (50.4%)	-0.0212
Lipid lowering drugs	806 (44.6%)	799 (45.5%)	-0.017	526 (48.8%)	-0.084
Platelet Aggregation Inhibitor	652 (36.1%)	645 (36.7%)	-0.0126	428 (39.7%)	-0.0747
Nitrates	200 (11.1%)	186 (10.6%)	0.0157	123 (11.4%)	-0.0108
Anti-arrhythmics	53 (2.9%)	42 (2.4%)	0.0338	21 (2.0%)	0.0638
Cardiac glycosides	128 (7.1%)	107 (6.1%)	0.0402	67 (6.2%)	0.0348
Anti-diabetic drugs	261 (14.4%)	231 (13.1%)	0.0378	178 (16.5%)	-0.0572
Anti-hypertensive drugs	1,293 (71.6%)	1,220 (69.4%)	0.0473	751 (69.7%)	0.0415

Aarhus	QVA N(%)	LAMA	Std Dif
Drugs affecting cerebrovascular and cardiovascular disease			
NSAIDs	392 (21.7%)	435 (20.8%)	0.0227
Antithrombotic agents	891 (49.3%)	1,049 (50.1%)	-0.0153
Lipid lowering drugs	806 (44.6%)	938 (44.8%)	-0.0034
Platelet Aggregation Inhibitor	652 (36.1%)	806 (38.5%)	-0.0494
Nitrates	200 (11.1%)	235 (11.2%)	-0.0047
Anti-arrhythmics	53 (2.9%)	55 (2.6%)	0.0187
Cardiac glycosides	128 (7.1%)	128 (6.1%)	0.0392
Anti-diabetic drugs	261 (14.4%)	277 (13.2%)	0.0354
Anti-hypertensive drugs	1,293 (71.6%)	1,457 (69.6%)	0.0441

HSD	QVA N(%) 385	Free LABA+LAMA without ICS N(%) 995	Std Dif	Free LABA+LAMA with ICS N(%) 335	Std Dif
CNS drugs					
Opioids	55 (14.3%)	190 (19.1%)	-0.1291	57 (17.0%)	-0.0751
Hypnotics and sedatives	19 (4.9%)	55 (5.5%)	-0.0266	13 (3.9%)	0.0513
Anxiolytics	54 (14.0%)	139 (14.0%)	0.0016	45 (13.4%)	0.0172
Anti-epileptic drugs	26 (6.8%)	77 (7.7%)	-0.038	31 (9.3%)	-0.0921
SSRI	47 (12.2%)	106 (10.7%)	0.0488	48 (14.3%)	-0.0625
Anticholinergic drugs					
Antipsychotic drugs	16 (4.2%)	37 (3.7%)	0.0225	14 (4.2%)	-0.0012
Antidepressant agents (tricyclic and tetracyclic)	21 (5.5%)	65 (6.5%)	-0.0454	20 (6.0%)	-0.0222
Disopyramide	0 (0.0%)	0 (0.0%)	.	0 (0.0%)	.
Antispasmodics	6 (1.6%)	11 (1.1%)	0.0395	4 (1.2%)	0.0312
Antiparkinson drugs	1 (0.3%)	1 (0.1%)	0.0375	0 (0.0%)	0.0721
Cholinesterase inhibitors	0 (0.0%)	0 (0.0%)	.	0 (0.0%)	.
Atropine	0 (0.0%)	0 (0.0%)	.	0 (0.0%)	.
H1 antihistaminics	50 (13.0%)	87 (8.7%)	0.1365	45 (13.4%)	-0.0131
Anticholinergics for treatment overactive bladder	1 (0.3%)	6 (0.6%)	-0.0524	3 (0.9%)	-0.0838

HSD	QVA N(%) 385	Free LABA+ICS N(%) 437	Std Dif	Fixed LABA ICS N(%) 5,897	Std Dif
CNS drugs					
Opioids	55 (14.3%)	90 (20.6%)	-0.1666	1,080 (18.3%)	-0.1092
Hypnotics and sedatives	19 (4.9%)	29 (6.6%)	-0.0728	329 (5.6%)	-0.0288
Anxiolytics	54 (14.0%)	52 (11.9%)	0.0633	714 (12.1%)	0.0569
Anti-epileptic drugs	26 (6.8%)	31 (7.1%)	-0.0134	478 (8.1%)	-0.0516
SSRI	47 (12.2%)	42 (9.6%)	0.0833	671 (11.4%)	0.0257
Anticholinergic drugs					
Antipsychotic drugs	16 (4.2%)	12 (2.8%)	0.0772	249 (4.2%)	-0.0033
Antidepressant agents (tricyclic and tetracyclic)	21 (5.5%)	27 (6.2%)	-0.0309	404 (6.9%)	-0.0581
Disopyramide	0 (0.0%)	0 (0.0%)	.	0 (0.0%)	.
Antispasmodics	6 (1.6%)	3 (0.7%)	0.0827	54 (0.9%)	0.0581
Antiparkinson drugs	1 (0.3%)	1 (0.2%)	0.0063	14 (0.2%)	0.0045
Cholinesterase inhibitors	0 (0.0%)	0 (0.0%)	.	4 (0.1%)	-0.0368
Atropine	0 (0.0%)	0 (0.0%)	.	0 (0.0%)	.
H1 antihistaminics	50 (13.0%)	55 (12.6%)	0.012	705 (12.0%)	0.0312
Anticholinergics for treatment overactive bladder	1 (0.3%)	0 (0.0%)	0.0721	20 (0.3%)	-0.0145

	QVA N(%)	Fixed LABA LAMA N(%)		LABA N(%)	
HSD	385	426	Std Dif	875	Std Dif
CNS drugs					
Opioids	55 (14.3%)	77 (18.1%)	-0.1029	172 (19.7%)	-0.1433
Hypnotics and sedatives	19 (4.9%)	24 (5.6%)	-0.0312	36 (4.1%)	0.0395
Anxiolytics	54 (14.0%)	54 (12.7%)	0.0396	110 (12.6%)	0.0428
Anti-epileptic drugs	26 (6.8%)	34 (8.0%)	-0.047	73 (8.3%)	-0.0601
SSRI	47 (12.2%)	52 (12.2%)	0	84 (9.6%)	0.0837
Anticholinergic drugs					
Antipsychotic drugs	16 (4.2%)	22 (5.2%)	-0.0478	32 (3.7%)	0.0257
Antidepressant agents (tricyclic and tetracyclic)	21 (5.5%)	26 (6.1%)	-0.0278	79 (9.0%)	-0.1381
Disopyramide	0 (0.0%)	0 (0.0%)	.	0 (0.0%)	.
Antispasmodics	6 (1.6%)	1 (0.2%)	0.1406	8 (0.9%)	0.0583
Antiparkinson drugs	1 (0.3%)	2 (0.5%)	-0.0348	2 (0.2%)	0.0063
Cholinesterase inhibitors	0 (0.0%)	0 (0.0%)	.	0 (0.0%)	.
Atropine	0 (0.0%)	0 (0.0%)	.	0 (0.0%)	.
H1 antihistaminics	50 (13.0%)	42 (9.9%)	0.0983	96 (11.0%)	0.062
Anticholinergics for treatment overactive bladder	1 (0.3%)	0 (0.0%)	0.0721	3 (0.3%)	-0.0152

HSD	QVA N(%) 385	LAMA 3,595	Std Dif
CNS drugs			
Opioids	55 (14.3%)	633 (17.6%)	-0.0908
Hypnotics and sedatives	19 (4.9%)	207 (5.8%)	-0.0366
Anxiolytics	54 (14.0%)	442 (12.3%)	0.0512
Anti-epileptic drugs	26 (6.8%)	322 (9.0%)	-0.0819
SSRI	47 (12.2%)	418 (11.6%)	0.0179
Anticholinergic drugs			
Antipsychotic drugs	16 (4.2%)	147 (4.1%)	0.0034
Antidepressant agents (tricyclic and tetracyclic)	21 (5.5%)	259 (7.2%)	-0.0719
Disopyramide	0 (0.0%)	0 (0.0%)	.
Antispasmodics	6 (1.6%)	34 (1.0%)	0.0551
Antiparkinson drugs	1 (0.3%)	11 (0.3%)	-0.0087
Cholinesterase inhibitors	0 (0.0%)	4 (0.1%)	-0.0472
Atropine	0 (0.0%)	0 (0.0%)	.
H1 antihistaminics	50 (13.0%)	378 (10.5%)	0.0768
Anticholinergics for treatment overactive bladder	1 (0.3%)	27 (0.8%)	-0.0693

HSD	QVA N(%)	Free LABA+LAMA without ICS N(%)	Std Dif	Free LABA+LAMA with ICS N(%)	Std Dif
Drugs affecting cerebrovascular and cardiovascular disease					
NSAIDs	159 (41.3%)	443 (44.5%)	-0.0651	157 (46.9%)	-0.1121
Antithrombotic agents	216 (56.1%)	539 (54.2%)	0.0388	182 (54.3%)	0.0357
Lipid lowering drugs	161 (41.8%)	411 (41.3%)	0.0104	131 (39.1%)	0.0552
Platelet Aggregation Inhibitor	184 (47.8%)	459 (46.1%)	0.0333	154 (46.0%)	0.0365
Nitrates	34 (8.8%)	87 (8.7%)	0.0031	31 (9.3%)	-0.0147
Anti-arrhythmics	23 (6.0%)	53 (5.3%)	0.028	23 (6.9%)	-0.0363
Cardiac glycosides	20 (5.2%)	69 (6.9%)	-0.0729	29 (8.7%)	-0.1365
Anti-diabetic drugs	92 (23.9%)	223 (22.4%)	0.0352	74 (22.1%)	0.0429
Anti-hypertensive drugs	288 (74.8%)	768 (77.2%)	-0.0557	261 (77.9%)	-0.073

HSD	QVA N(%)	Free LABA+ICS N(%)	Std Dif	Fixed LABA ICS N(%)	Std Dif
Drugs affecting cerebrovascular and cardiovascular disease					
NSAIDs	159 (41.3%)	209 (47.8%)	-0.1314	2,600 (44.1%)	-0.0564
Antithrombotic agents	216 (56.1%)	234 (53.6%)	0.0513	2,903 (49.2%)	0.1379
Lipid lowering drugs	161 (41.8%)	165 (37.8%)	0.0829	2,194 (37.2%)	0.0944
Platelet Aggregation Inhibitor	184 (47.8%)	203 (46.5%)	0.0268	2,475 (42.0%)	0.1172
Nitrates	34 (8.8%)	36 (8.2%)	0.0212	505 (8.6%)	0.0095
Anti-arrhythmics	23 (6.0%)	26 (6.0%)	0.001	278 (4.7%)	0.056
Cardiac glycosides	20 (5.2%)	9 (2.1%)	0.1681	264 (4.5%)	0.0334
Anti-diabetic drugs	92 (23.9%)	87 (19.9%)	0.0964	1,173 (19.9%)	0.0969
Anti-hypertensive drugs	288 (74.8%)	333 (76.2%)	-0.0324	4,370 (74.1%)	0.016

HSD	QVA N(%)	Fixed LABA LAMA N(%)	Std Dif	LABA N(%)	Std Dif
Drugs affecting cerebrovascular and cardiovascular disease					
NSAIDs	159 (41.3%)	184 (43.2%)	-0.0383	409 (46.7%)	-0.1097
Antithrombotic agents	216 (56.1%)	228 (53.5%)	0.0518	399 (45.6%)	0.2111
Lipid lowering drugs	161 (41.8%)	182 (42.7%)	-0.0183	326 (37.3%)	0.0933
Platelet Aggregation Inhibitor	184 (47.8%)	199 (46.7%)	0.0216	356 (40.7%)	0.1433
Nitrates	34 (8.8%)	34 (8.0%)	0.0306	62 (7.1%)	0.0645
Anti-arrhythmics	23 (6.0%)	26 (6.1%)	-0.0054	37 (4.2%)	0.0793
Cardiac glycosides	20 (5.2%)	13 (3.1%)	0.1078	29 (3.3%)	0.0932
Anti-diabetic drugs	92 (23.9%)	112 (26.3%)	-0.0552	182 (20.8%)	0.0743
Anti-hypertensive drugs	288 (74.8%)	339 (79.6%)	-0.1138	635 (72.6%)	0.0507

HSD	QVA N(%)	LAMA	Std Dif
Drugs affecting cerebrovascular and cardiovascular disease			
NSAIDs	159 (41.3%)	1,581 (44.0%)	-0.0542
Antithrombotic agents	216 (56.1%)	2,036 (56.6%)	-0.0107
Lipid lowering drugs	161 (41.8%)	1,476 (41.1%)	0.0154
Platelet Aggregation Inhibitor	184 (47.8%)	1,679 (46.7%)	0.0218
Nitrates	34 (8.8%)	386 (10.7%)	-0.0641
Anti-arrhythmics	23 (6.0%)	238 (6.6%)	-0.0266
Cardiac glycosides	20 (5.2%)	212 (5.9%)	-0.0307
Anti-diabetic drugs	92 (23.9%)	818 (22.8%)	0.027
Anti-hypertensive drugs	288 (74.8%)	2,835 (78.9%)	-0.0961

SIDIAP	QVA N(%) 5,561		Free LABA+LAMA without ICS N(%) 4,219	Std Dif	Free LABA+LAMA with ICS N(%) 1,725	Std Dif
CNS drugs						
Opioids	905	(16.3%)	707 (16.8%)	-0.013	340 (19.7%)	-0.0895
Hypnotics and sedatives	587	(10.6%)	375 (8.9%)	0.0563	178 (10.3%)	0.0077
Anxiolytics	1,487	(26.7%)	1,086 (25.7%)	0.0227	487 (28.2%)	-0.0334
Anti-epileptic drugs	613	(11.0%)	478 (11.3%)	-0.0097	220 (12.8%)	-0.0535
SSRI	799	(14.4%)	546 (12.9%)	0.0415	262 (15.2%)	-0.0231
Anticholinergic drugs						
Antipsychotic drugs	283	(5.1%)	209 (5.0%)	0.0062	84 (4.9%)	0.0101
Antidepressant agents (tricyclic and tetracyclic)	522	(9.4%)	379 (9.0%)	0.014	164 (9.5%)	-0.0041
Disopyramide	0	(0.0%)	2 (0.1%)	-0.0308	1 (0.1%)	-0.0341
Antispasmodics	15	(0.3%)	10 (0.2%)	0.0065	4 (0.2%)	0.0076
Antiparkinson drugs	16	(0.3%)	6 (0.1%)	0.0314	5 (0.3%)	-0.0004
Cholinesterase inhibitors	5	(0.1%)	3 (0.1%)	0.0066	2 (0.1%)	-0.0081
Atropine	0	(0.0%)	0 (0.0%)	.	0 (0.0%)	.
H1 antihistaminics	927	(16.7%)	692 (16.4%)	0.0072	331 (19.2%)	-0.0657
Anticholinergics for treatment overactive bladder	185	(3.3%)	149 (3.5%)	-0.0113	75 (4.4%)	-0.0532

SIDIAP	QVA N(%) 5,561	Free LABA+ICS N(%) 2,738	Std Dif	Fixed LABA ICS N(%) 20,638	Std Dif
CNS drugs					
Opioids	905 (16.3%)	510 (18.6%)	-0.062	3,513 (17.0%)	-0.0201
Hypnotics and sedatives	587 (10.6%)	297 (10.9%)	-0.0094	2,162 (10.5%)	0.0026
Anxiolytics	1,487 (26.7%)	827 (30.2%)	-0.0768	5,895 (28.6%)	-0.0408
Anti-epileptic drugs	613 (11.0%)	343 (12.5%)	-0.0467	2,382 (11.5%)	-0.0164
SSRI	799 (14.4%)	442 (16.1%)	-0.0494	3,245 (15.7%)	-0.0379
Anticholinergic drugs					
Antipsychotic drugs	283 (5.1%)	189 (6.9%)	-0.0764	1,297 (6.3%)	-0.0516
Antidepressant agents (tricyclic and tetracyclic)	522 (9.4%)	305 (11.1%)	-0.0578	2,110 (10.2%)	-0.0281
Disopyramide	0 (0.0%)	0 (0.0%)	.	0 (0.0%)	.
Antispasmodics	15 (0.3%)	6 (0.2%)	0.0102	48 (0.2%)	0.0074
Antiparkinson drugs	16 (0.3%)	11 (0.4%)	-0.0195	55 (0.3%)	0.004
Cholinesterase inhibitors	5 (0.1%)	3 (0.1%)	-0.0062	15 (0.1%)	0.006
Atropine	0 (0.0%)	0 (0.0%)	.	0 (0.0%)	.
H1 antihistaminics	927 (16.7%)	557 (20.3%)	-0.0947	3,980 (19.3%)	-0.0681
Anticholinergics for treatment overactive bladder	185 (3.3%)	0 (0.0%)	0.2623	664 (3.2%)	0.0061

SIDIAP	QVA N(%) 5,561	Fixed LABA LAMA N(%) 964	Std Dif	LABA N(%) 5,879	Std Dif
CNS drugs					
Opioids	905 (16.3%)	184 (19.1%)	-0.0738	902 (15.3%)	0.0255
Hypnotics and sedatives	587 (10.6%)	100 (10.4%)	0.006	530 (9.0%)	0.0519
Anxiolytics	1,487 (26.7%)	252 (26.1%)	0.0136	1,530 (26.0%)	0.0162
Anti-epileptic drugs	613 (11.0%)	131 (13.6%)	-0.0781	606 (10.3%)	0.0232
SSRI	799 (14.4%)	126 (13.1%)	0.0377	807 (13.7%)	0.0184
Anticholinergic drugs					
Antipsychotic drugs	283 (5.1%)	46 (4.8%)	0.0146	308 (5.2%)	-0.0068
Antidepressant agents (tricyclic and tetracyclic)	522 (9.4%)	78 (8.1%)	0.0459	536 (9.1%)	0.0093
Disopyramide	0 (0.0%)	0 (0.0%)	.	0 (0.0%)	.
Antispasmodics	15 (0.3%)	1 (0.1%)	0.0384	11 (0.2%)	0.0173
Antiparkinson drugs	16 (0.3%)	2 (0.2%)	0.0161	9 (0.2%)	0.0287
Cholinesterase inhibitors	5 (0.1%)	1 (0.1%)	-0.0044	2 (0.0%)	0.0225
Atropine	0 (0.0%)	0 (0.0%)	.	0 (0.0%)	.
H1 antihistaminics	927 (16.7%)	166 (17.2%)	-0.0147	1,042 (17.7%)	-0.0279
Anticholinergics for treatment overactive bladder	185 (3.3%)	0 (0.0%)	0.2623	169 (2.9%)	0.0261

SIDIAP	QVA N(%) 5,561	LAMA 13,678	Std Dif
CNS drugs			
Opioids	905 (16.3%)	2,117 (15.5%)	0.0218
Hypnotics and sedatives	587 (10.6%)	1,211 (8.9%)	0.0575
Anxiolytics	1,487 (26.7%)	3,642 (26.6%)	0.0026
Anti-epileptic drugs	613 (11.0%)	1,354 (9.9%)	0.0367
SSRI	799 (14.4%)	1,875 (13.7%)	0.019
Anticholinergic drugs			
Antipsychotic drugs	283 (5.1%)	676 (4.9%)	0.0067
Antidepressant agents (tricyclic and tetracyclic)	522 (9.4%)	1,204 (8.8%)	0.0203
Disopyramide	0 (0.0%)	1 (0.0%)	-0.0121
Antispasmodics	15 (0.3%)	31 (0.2%)	0.0087
Antiparkinson drugs	16 (0.3%)	47 (0.3%)	-0.01
Cholinesterase inhibitors	5 (0.1%)	7 (0.1%)	0.0146
Atropine	0 (0.0%)	0 (0.0%)	.
H1 antihistaminics	927 (16.7%)	2,364 (17.3%)	-0.0163
Anticholinergics for treatment overactive bladder	185 (3.3%)	429 (3.1%)	0.0108

SIDIAP	QVA N(%)	Free LABA+LAMA without ICS N(%)	Std Dif	Free LABA+LAMA with ICS N(%)	Std Dif
Drugs affecting cerebrovascular and cardiovascular disease					
NSAIDs	1,773 (31.9%)	1,383 (32.8%)	-0.0192	556 (32.2%)	-0.0075
Antithrombotic agents	2,321 (41.7%)	1,800 (42.7%)	-0.0188	784 (45.5%)	-0.0749
Lipid lowering drugs	2,579 (46.4%)	1,964 (46.6%)	-0.0035	806 (46.7%)	-0.007
Platelet Aggregation Inhibitor	1,785 (32.1%)	1,398 (33.1%)	-0.0221	575 (33.3%)	-0.0263
Nitrates	535 (9.6%)	369 (8.8%)	0.0303	173 (10.0%)	-0.0137
Anti-arrhythmics	179 (3.2%)	120 (2.8%)	0.0218	67 (3.9%)	-0.0359
Cardiac glycosides	213 (3.8%)	141 (3.3%)	0.0263	82 (4.8%)	-0.0456
Anti-diabetic drugs	1,272 (22.9%)	991 (23.5%)	-0.0146	413 (23.9%)	-0.0252
Anti-hypertensive drugs	3,783 (68.0%)	2,863 (67.9%)	0.0036	1,244 (72.1%)	-0.0894

SIDIAP	QVA N(%)	Free LABA+ICS N(%)	Std Dif	Fixed LABA ICS N(%)	Std Dif
Drugs affecting cerebrovascular and cardiovascular disease					
NSAIDs	1,773 (31.9%)	942 (34.4%)	-0.0536	6,940 (33.6%)	-0.0372
Antithrombotic agents	2,321 (41.7%)	1,080 (39.4%)	0.0467	8,091 (39.2%)	0.0516
Lipid lowering drugs	2,579 (46.4%)	1,197 (43.7%)	0.0534	9,105 (44.1%)	0.0454
Platelet Aggregation Inhibitor	1,785 (32.1%)	813 (29.7%)	0.0521	6,149 (29.8%)	0.0499
Nitrates	535 (9.6%)	241 (8.8%)	0.0283	1,661 (8.1%)	0.0554
Anti-arrhythmics	179 (3.2%)	75 (2.7%)	0.0282	610 (3.0%)	0.0152
Cardiac glycosides	213 (3.8%)	103 (3.8%)	0.0036	694 (3.4%)	0.0251
Anti-diabetic drugs	1,272 (22.9%)	638 (23.3%)	-0.0102	4,456 (21.6%)	0.0308
Anti-hypertensive drugs	3,783 (68.0%)	1,889 (69.0%)	-0.0208	13661 (66.2%)	0.039

SIDIAP	QVA N(%)	Fixed LABA LAMA N(%)	Std Dif	LABA N(%)	Std Dif
Drugs affecting cerebrovascular and cardiovascular disease					
NSAIDs	1,773 (31.9%)	288 (29.9%)	0.0434	2,072 (35.2%)	-0.0712
Antithrombotic agents	2,321 (41.7%)	428 (44.4%)	-0.0537	2,066 (35.1%)	0.1359
Lipid lowering drugs	2,579 (46.4%)	453 (47.0%)	-0.0123	2,552 (43.4%)	0.0597
Platelet Aggregation Inhibitor	1,785 (32.1%)	325 (33.7%)	-0.0344	1,647 (28.0%)	0.0891
Nitrates	535 (9.6%)	94 (9.8%)	-0.0044	365 (6.2%)	0.1266
Anti-arrhythmics	179 (3.2%)	29 (3.0%)	0.0121	129 (2.2%)	0.0632
Cardiac glycosides	213 (3.8%)	35 (3.6%)	0.0105	133 (2.3%)	0.0913
Anti-diabetic drugs	1,272 (22.9%)	234 (24.3%)	-0.033	1,206 (20.5%)	0.0573
Anti-hypertensive drugs	3,783 (68.0%)	668 (69.3%)	-0.0273	3,767 (64.1%)	0.0835

SIDIAP	QVA N(%)	LAMA	Std Dif
Drugs affecting cerebrovascular and cardiovascular disease			
NSAIDs	1,773 (31.9%)	4,457 (32.6%)	-0.015
Antithrombotic agents	2,321 (41.7%)	5,487 (40.1%)	0.033
Lipid lowering drugs	2,579 (46.4%)	6,411 (46.9%)	-0.0099
Platelet Aggregation Inhibitor	1,785 (32.1%)	4,263 (31.2%)	0.02
Nitrates	535 (9.6%)	1,167 (8.5%)	0.0379
Anti-arrhythmics	179 (3.2%)	413 (3.0%)	0.0115
Cardiac glycosides	213 (3.8%)	423 (3.1%)	0.0404
Anti-diabetic drugs	1,272 (22.9%)	2,974 (21.7%)	0.0272
Anti-hypertensive drugs	3,783 (68.0%)	8,992 (65.7%)	0.0486

Table 15-8 Details on validation by database (IPCI, HSD and SIDIAP)

IPCI	Total cases to be validated	Definite Case	Probable Case	Possible Case	Non- Case	New date§	PPV
AFIFLUT	149	141	6	0	2	34	98.7%
AP	71	24	7	7	33	17	53.5%
AVBLOCK	31	16	3	1	11	3	64.5%
BPH	47	34	10	1	1	7	95.7%
BRONCHOSPASM	259	25	0	0	234	15	9.7%
COPD	1,000	872	121	0	6	388	99.3%
DEATH	NAP						
HOSPHF	198	183	9	4	2	20	99.0%
HOSPACS	115	73	2	9	31	32	73.0%
LONGQT	2	0	1	0	1	0	50.0%
MI	76	55	1	13	7	24	90.8%
NARGLAUC	2	1	0	0	0	0	50.0%
OTHGLAUC	15	7	3	2	3	4	80.0%
PREMATDEP	26	14	1	0	11	2	57.7%
SICKSINUS	1	0	0	0	1	0	0.0%
STROKE	87	53	16	9	9	23	89.7%
SVT	26	21	4	0	1	2	96.2%
TIA	74	45	17	0	12	19	83.8%
TORSPOINT	0	0	0	0	0	0	Nap
UNSTABLEAP	36	16	2	3	15	4	58.3%
URINRETENTION	119	98	7	1	13	24	89.1%
VENTFIBR	8	6	2	0	0	0	100.0%

IPCI	Total cases to be validated	Definite Case	Probable Case	Possible Case	Non- Case	New date§	PPV
VENTTACH	9	8	1	0	0	2	100.0%

HSD	Total cases to be validated	Definite Case	Probable Case	Possible Case	Non- Case	New date§	PPV
AFIFLUT	131	54		43	34	5	74.0%
AP	13	3		9	1	1	92.3%
AVBLOCK	10	4		3	3		70.0%
BPH	62	9	13	11	29		53.2%
BRONCHOSPASM	165			12	153		7.3%
COPD	1,000	790			210		79.0%
DEATH	77	77					100.0%
HF	142	9			133	3	6.3%
LONGQT	1	1					100.0%
MI	19	15			4		78.9%
OTHGLAUC	33	8	17		8	1	75.8%
PREMATDEP	23	11		8	4		82.6%
SICKSINUS	9	5			4		55.6%
STROKE	72	19			53	1	26.4%
SVT	4	3			1		75.0%
TIA	11	9			2		81.8%
TORSPOINT	1	1					100.0%
UNSTABLEAP	5	5					100.0%
URINRETENTION	15	12		3			100.0%
VENTTACH	2	1		1			100.0%

SIDIAP	Total cases to be validated	Definite Case	Probable Case	Possible Case	Non- Case	PPV
AFIFLUT	522	351	18	94	59	88.7%
AP	86	63	0	14	9	89.5%
AVBLOCK	118	76	0	27	15	87.3%
BPH	468	144	13	231	21	82.9%
BRONCHOSPASM	259	2	0	71	186	28.2%
COPD	1,000	881			119	88.1%
LONGQT	3	2	0	1	0	100.0%
MI	115	88	0	17	10	91.3%
OTHGLAUC	156	8	0	15	3	14.7%
PREMATDEP	79	58	0	16	5	93.7%
SICKSINUS	1	0	0	1	0	100.0%
STROKE	144	78	9	22	35	75.7%
SVT	23	12	1	6	4	82.6%
TIA	72	37	1	25	9	87.5%
UNSTABLEAP	38	18	4	9	7	81.6%
URINRETENTION	174	126	1	22	25	85.6%
VENTFIBR	1	1	0	0	0	100.0%
VENTTACH	11	7	1	1	2	81.8%

Table 15-9 Number of endpoint events, pooled, by exposure cohort

Pooled Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
MACE	Total FU	528	512	188	238	2746	312	534	1932
	Cohort Time	292	126	44	61	1125	206	151	644
	CT 1 yr	272	119	42	59	1024	197	146	593
	CT ext 60	287	121	45	65	1164	209	162	648
	Unr drugs	284	125	44	65	1037	205	184	709
Ischemic heart disease	Total FU	143	179	71	67	976	110	204	817
	Cohort Time	76	46	14	16	345	56	41	240
	CT 1 yr	67	40	13	14	301	50	41	210
	CT ext 60	72	40	13	14	344	54	49	231
	Unr drugs	69	44	13	16	307	56	53	256

MACE= Major adverse cardiovascular event

Pooled Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Cardiac arrhythmia	Total FU	203	281	106	136	1462	145	291	1060
	Cohort Time	91	57	23	29	554	88	58	334
	CT 1 yr	80	54	21	28	490	79	56	300
	CT ext 60	87	58	21	33	555	84	70	341
	Unr drugs	93	60	21	31	492	89	71	354
Cerebrovascular disorders	Total FU	142	192	62	85	1072	101	235	857
	Cohort Time	60	27	14	17	334	58	54	228
	CT 1 yr	53	25	14	17	269	51	48	199
	CT ext 60	61	26	15	19	329	54	58	219
	Unr drugs	54	26	16	17	273	52	55	239

Pooled Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Glaucoma	Total FU	50	68	22	33	358	18	77	260
	Cohort Time	19	15	6	1	92	10	17	74
	CT 1 yr	15	15	6	1	77	9	17	67
	CT ext 60	18	16	7	1	90	10	18	78
	Unr drugs	15	16	6	1	77	11	18	79
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	Total FU	215	284	92	132	1211	73	308	944
	Cohort Time	94	58	17	15	381	44	76	267
	CT 1 yr	80	51	16	15	344	39	73	244
	CT ext 60	91	54	16	15	391	40	80	273
	Unr drugs	84	53	17	18	347	42	87	299

Pooled Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Diabetes mellitus	Total FU	152	198	67	82	1128	94	212	764
	Cohort Time	82	58	12	14	443	65	58	256
	CT 1 yr	76	52	12	13	386	59	54	234
	CT ext 60	79	54	12	16	429	61	59	252
	Unr drugs	81	56	14	15	389	60	62	270
Bronchospasm	Total FU	23	26	24	39	308	10	41	133
	Cohort Time	6	3	2	6	52	4	6	15
	CT 1 yr	6	3	2	6	51	4	6	14
	CT ext 60	8	3	2	6	63	6	6	18
	Unr drugs	7	4	2	7	51	5	9	22

Pooled Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Mortality	Total FU	840	864	331	402	5140	484	861	3238
	Cohort Time	312	96	20	46	1588	232	159	687
	CT 1 yr	251	88	18	46	1330	209	149	612
	CT ext 60	301	95	20	60	1644	243	178	745
	Unr drugs	265	96	19	49	1349	229	197	805
Atrial fibrillation/flutter	Total FU	196	278	102	135	1420	140	285	1023
	Cohort Time	86	57	19	29	537	84	58	318
	CT 1 yr	75	54	17	28	475	75	56	284
	CT ext 60	82	58	17	33	536	79	70	324
	Unr drugs	88	60	17	31	477	85	70	333

Pooled Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Angina pectoris	Total FU	65	76	33	29	423	46	85	346
	Cohort Time	32	16	4	5	150	21	19	104
	CT 1 yr	29	13	3	4	134	19	19	90
	CT ext 60	33	13	3	4	154	21	23	95
	Unr drugs	30	15	3	4	137	22	24	113
AV block	Total FU	41	43	14	18	173	15	35	132
	Cohort Time	18	8	0	4	52	8	7	30
	CT 1 yr	15	7	0	4	49	8	7	28
	CT ext 60	15	7	0	4	56	8	9	33
	Unr drugs	17	7	0	4	51	8	8	39

Pooled Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Incident benign prostatic hyperplasia	Total FU	147	194	52	95	771	43	209	592
	Cohort Time	59	33	9	12	230	25	54	162
	CT 1 yr	50	29	9	12	212	22	52	153
	CT ext 60	57	32	9	12	245	22	58	171
	Unr drugs	52	31	9	13	214	23	59	177
Hospitalization for acute coronary syndrome	Total FU	97	106	36	43	493	55	88	359
	Cohort Time	49	27	11	14	172	27	21	109
	CT 1 yr	43	25	11	12	154	22	21	100
	CT ext 60	44	25	11	12	174	25	22	105
	Unr drugs	44	27	11	14	158	27	28	124

Pooled Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Hospitalization for heart failure	Total FU	349	247	111	142	1392	184	255	836
	Cohort Time	203	71	26	36	664	137	92	345
	CT 1 yr	190	69	24	36	640	133	89	336
	CT ext 60	198	70	26	40	711	142	95	362
	Unr drugs	199	73	26	40	649	137	114	398
Myocardial infarction	Total FU	73	107	39	38	508	57	107	401
	Cohort Time	39	25	9	9	178	27	17	114
	CT 1 yr	33	23	9	8	152	23	17	99
	CT ext 60	33	23	9	8	171	26	21	112
	Unr drugs	35	26	9	9	155	27	25	118

Pooled Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Long QT	Total FU	2	1	1	1	9	3	7	10
	Cohort Time	2	1	0	0	1	1	0	1
	CT 1 yr	2	1	0	0	1	1	0	1
	CT ext 60	2	1	0	0	2	1	0	1
	Unr drugs	2	1	0	0	1	1	0	3
Narrow angle glaucoma	Total FU	1	0	0	0	2	1	2	4
	Cohort Time	0	0	0	0	1	1	0	1
	CT 1 yr	0	0	0	0	0	0	0	1
	CT ext 60	0	0	0	0	0	0	0	1
	Unr drugs	0	0	0	0	0	0	0	1

Pooled Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Other glaucoma	Total FU	49	68	22	33	356	17	75	256
	Cohort Time	19	15	6	1	91	9	17	73
	CT 1 yr	15	15	6	1	77	9	17	66
	CT ext 60	18	16	7	1	90	10	18	77
	Unr drugs	15	16	6	1	77	11	18	78
Premature depolarization	Total FU	25	27	17	21	198	8	37	116
	Cohort Time	9	4	2	3	54	5	10	30
	CT 1 yr	8	4	2	3	48	5	9	28
	CT ext 60	10	4	2	3	58	5	9	29
	Unr drugs	8	5	2	5	50	5	11	35

Pooled Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Sick sinus	Total FU	8	4	0	0	27	1	8	13
	Cohort Time	4	0	0	0	9	0	5	4
	CT 1 yr	4	0	0	0	8	0	5	3
	CT ext 60	4	0	0	0	8	0	5	3
	Unr drugs	4	0	0	0	8	0	5	3
Stroke	Total FU	95	140	37	58	791	77	171	633
	Cohort Time	37	20	6	12	247	45	32	151
	CT 1 yr	34	18	6	12	196	42	29	130
	CT ext 60	40	19	7	14	244	44	37	144
	Unr drugs	35	18	6	12	197	43	34	159

Pooled Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Supraventricular tachycardia	Total FU	15	23	3	4	109	9	23	67
	Cohort Time	10	6	0	1	42	5	7	16
	CT 1 yr	10	4	0	1	36	5	7	13
	CT ext 60	10	4	0	2	37	5	8	16
	Unr drugs	10	5	0	1	37	5	7	18
TIA	Total FU	52	60	27	31	332	27	83	279
	Cohort Time	25	8	9	7	100	15	26	88
	CT 1 yr	20	8	9	7	83	11	23	77
	CT ext 60	22	8	9	7	97	12	27	83
	Unr drugs	20	9	11	7	86	11	25	88

Pooled Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Torsades de Pointes	Total FU	0	0	0	0	2	0	2	2
	Cohort Time	0	0	0	0	0	0	0	1
	CT 1 yr	0	0	0	0	0	0	0	1
	CT ext 60	0	0	0	0	0	0	0	1
	Unr drugs	0	0	0	0	0	0	0	1
Unstable angina pectoris	Total FU	26	30	9	13	173	20	34	151
	Cohort Time	16	9	2	5	54	14	11	36
	CT 1 yr	13	8	2	3	50	13	11	35
	CT ext 60	14	8	2	3	60	13	11	40
	Unr drugs	13	10	2	4	51	13	12	45

Pooled Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Urinary retention	Total FU	77	100	46	45	490	32	107	396
	Cohort Time	38	26	9	3	166	21	22	114
	CT 1 yr	32	23	8	3	145	19	21	98
	CT ext 60	36	23	8	3	162	20	22	110
	Unr drugs	34	23	9	5	146	21	28	132
Ventricular tachycardia	Total FU	5	2	4	2	40	5	5	26
	Cohort Time	4	0	3	0	15	2	0	9
	CT 1 yr	4	0	3	0	13	2	0	9
	CT ext 60	4	0	3	0	15	4	0	10
	Unr drugs	4	0	3	0	13	2	1	11

Pooled Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Ventricular fibrillation	Total FU	3	1	1	0	12	2	1	17
	Cohort Time	1	0	1	0	4	2	0	6
	CT 1 yr	1	0	1	0	4	2	0	6
	CT ext 60	1	0	1	0	7	2	0	6
	Unr drugs	1	0	1	0	4	2	0	9
Cardiovascular death	Total FU	34	27	5	5	135	6	33	88
	Cohort Time	21	9	0	1	57	4	7	28
	CT 1 yr	21	9	0	1	56	4	7	26
	CT ext 60	22	9	0	1	66	4	9	32
	Unr drugs	22	9	0	1	57	4	11	30

Pooled Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Respiratory death	Total FU	74	56	25	29	299	23	61	162
	Cohort Time	38	14	4	8	134	10	18	54
	CT 1 yr	32	14	3	8	124	9	17	53
	CT ext 60	35	14	3	8	143	9	20	57
	Unr drugs	32	16	4	10	126	10	28	80
Cardiovascular and respiratory death	Total FU	3	12	7	5	31	2	2	25
	Cohort Time	2	3	2	0	14	1	0	10
	CT 1 yr	1	3	2	0	14	1	0	8
	CT ext 60	1	3	2	0	14	1	1	8
	Unr drugs	1	4	2	0	14	1	0	13

Pooled Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Cerebrovascular death	Total FU	6	5	2	1	27	3	8	30
	Cohort Time	0	0	0	1	8	3	2	8
	CT 1 yr	0	0	0	1	7	3	2	8
	CT ext 60	0	0	0	1	11	3	2	9
	Unr drugs	1	0	0	1	8	3	2	10
Cancer death (excluding lungcancer)	Total FU	18	23	6	9	97	4	26	76
	Cohort Time	10	3	1	2	42	2	7	30
	CT 1 yr	9	3	1	2	37	2	7	26
	CT ext 60	10	3	1	2	41	3	7	28
	Unr drugs	9	3	1	2	37	2	9	31

Pooled Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Death due to other causes	Total FU	45	27	11	10	177	17	38	95
	Cohort Time	28	7	2	1	70	8	10	23
	CT 1 yr	24	7	1	1	67	8	8	23
	CT ext 60	25	7	1	2	85	9	9	26
	Unr drugs	25	7	1	1	67	9	13	34
Death with cause unknown	Total FU	614	428	220	288	2917	302	491	1435
	Cohort Time	215	60	11	33	1265	205	115	536
	CT 1 yr	166	52	11	33	1027	183	108	470
	CT ext 60	206	57	13	44	1177	203	123	530
	Unr drugs	173	54	11	34	1033	189	120	507

THIN Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
MACE	Total FU	38	117	13	18	757	88	130	684
	Cohort Time	19	27	3	5	307	41	27	199
	CT 1 yr	19	24	3	4	243	38	25	161
	CT ext 60	20	24	4	4	272	39	30	179
	Unr drugs	20	25	3	5	243	41	35	205
Ischemic heart disease	Total FU	26	70	10	9	451	64	72	440
	Cohort Time	15	19	2	1	185	27	18	128
	CT 1 yr	15	14	2	0	153	25	18	103
	CT ext 60	15	14	2	0	169	27	20	112
	Unr drugs	16	14	2	1	153	29	24	134

MACE=Major Adverse Cardiovascular Event

THIN Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Cardiac arrhythmia	Total FU	15	58	18	16	490	59	74	434
	Cohort Time	7	11	0	3	232	32	16	129
	CT 1 yr	6	10	0	2	188	27	15	107
	CT ext 60	6	11	0	2	205	31	19	121
	Unr drugs	9	10	0	2	189	32	19	129
Cerebrovascular disorders	Total FU	19	71	10	12	486	58	83	446
	Cohort Time	8	10	1	2	190	33	20	133
	CT 1 yr	7	9	1	2	135	27	15	110
	CT ext 60	9	9	2	2	154	28	19	120
	Unr drugs	7	9	2	2	136	27	16	131

THIN Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Glaucoma	Total FU	3	5	5	3	86	6	10	83
	Cohort Time	3	1	2	0	33	4	5	24
	CT 1 yr	2	1	2	0	26	4	5	20
	CT ext 60	2	1	2	0	27	4	5	24
	Unr drugs	2	2	2	0	26	4	5	25
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	Total FU	10	42	5	8	272	35	44	240
	Cohort Time	7	14	1	0	121	18	12	77
	CT 1 yr	6	9	1	0	95	14	10	67
	CT ext 60	7	9	1	0	103	15	10	71
	Unr drugs	6	10	1	0	96	16	10	90

THIN Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Diabetes mellitus	Total FU	12	73	11	12	444	54	70	345
	Cohort Time	9	20	2	3	186	33	19	120
	CT 1 yr	8	19	2	2	139	28	16	104
	CT ext 60	8	20	2	2	150	30	17	109
	Unr drugs	8	19	4	2	139	29	19	128
Bronchospasm	Total FU	0	0	0	0	0	0	0	0
	Cohort Time	0	0	0	0	0	0	0	0
	CT 1 yr	0	0	0	0	0	0	0	0
	CT ext 60	0	0	0	0	0	0	0	0
	Unr drugs	0	0	0	0	0	0	0	0

THIN Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Mortality	Total FU	120	281	46	50	2165	253	238	1600
	Cohort Time	71	34	4	8	817	117	53	356
	CT 1 yr	61	27	4	8	626	102	48	297
	CT ext 60	65	29	4	10	720	115	54	348
	Unr drugs	64	29	4	8	634	114	64	398
Atrial fibrillation/flutter	Total FU	14	57	17	16	477	56	73	426
	Cohort Time	7	11	0	3	224	30	16	125
	CT 1 yr	6	10	0	2	181	25	15	103
	CT ext 60	6	11	0	2	198	28	19	117
	Unr drugs	9	10	0	2	182	30	18	125

THIN Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Angina pectoris	Total FU	10	29	5	4	196	33	28	194
	Cohort Time	5	7	0	1	84	14	9	67
	CT 1 yr	5	4	0	0	70	12	9	55
	CT ext 60	5	4	0	0	77	14	10	57
	Unr drugs	5	4	0	0	70	15	10	70
AV block	Total FU	1	0	0	0	10	1	1	10
	Cohort Time	1	0	0	0	3	0	0	0
	CT 1 yr	1	0	0	0	1	0	0	0
	CT ext 60	1	0	0	0	1	0	0	1
	Unr drugs	1	0	0	0	1	0	0	3

THIN Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Incident benign prostatic hyperplasia	Total FU	2	19	3	5	122	17	20	101
	Cohort Time	1	6	1	0	58	9	5	33
	CT 1 yr	1	4	1	0	45	7	4	28
	CT ext 60	1	4	1	0	51	7	4	31
	Unr drugs	1	5	1	0	46	8	4	36
Hospitalization for acute coronary syndrome	Total FU	8	23	2	5	129	20	20	117
	Cohort Time	4	7	0	1	52	5	4	32
	CT 1 yr	4	6	0	0	46	4	4	28
	CT ext 60	4	6	0	0	51	4	4	29
	Unr drugs	4	6	0	1	46	6	7	39

THIN Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Hospitalization for heart failure	Total FU	5	17	1	6	138	17	26	117
	Cohort Time	3	5	1	2	63	11	7	37
	CT 1 yr	3	5	1	2	58	11	7	33
	CT ext 60	3	5	1	2	60	11	7	37
	Unr drugs	3	6	1	2	58	12	11	46
Myocardial infarction	Total FU	15	42	5	5	227	29	38	209
	Cohort Time	9	9	1	0	91	10	7	56
	CT 1 yr	9	8	1	0	75	9	7	43
	CT ext 60	9	8	1	0	82	9	8	49
	Unr drugs	10	8	1	1	75	11	12	54

THIN Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Long QT	Total FU	0	0	0	0	6	3	1	5
	Cohort Time	0	0	0	0	0	1	0	0
	CT 1 yr	0	0	0	0	0	1	0	0
	CT ext 60	0	0	0	0	0	1	0	0
	Unr drugs	0	0	0	0	0	1	0	1
Narrow angle glaucoma	Total FU	0	0	0	0	1	0	0	1
	Cohort Time	0	0	0	0	1	0	0	0
	CT 1 yr	0	0	0	0	0	0	0	0
	CT ext 60	0	0	0	0	0	0	0	0
	Unr drugs	0	0	0	0	0	0	0	0

THIN Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Other glaucoma	Total FU	3	5	5	3	85	6	10	82
	Cohort Time	3	1	2	0	32	4	5	24
	CT 1 yr	2	1	2	0	26	4	5	20
	CT ext 60	2	1	2	0	27	4	5	24
	Unr drugs	2	2	2	0	26	4	5	25
Premature depolarization	Total FU	2	1	2	0	26	3	2	15
	Cohort Time	1	0	0	0	9	0	1	3
	CT 1 yr	1	0	0	0	7	0	1	3
	CT ext 60	1	0	0	0	7	0	1	4
	Unr drugs	1	0	0	0	7	0	1	4

THIN Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Sick sinus	Total FU	0	1	0	0	2	1	1	1
	Cohort Time	0	0	0	0	1	0	0	1
	CT 1 yr	0	0	0	0	1	0	0	0
	CT ext 60	0	0	0	0	1	0	0	0
	Unr drugs	0	0	0	0	1	0	0	0
Stroke	Total FU	14	58	7	7	379	42	65	339
	Cohort Time	4	9	1	2	144	21	12	95
	CT 1 yr	4	8	1	2	100	19	10	76
	CT ext 60	5	8	2	2	117	20	14	83
	Unr drugs	4	8	1	2	100	19	10	91

THIN Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Supraventricular tachycardia	Total FU	1	5	1	2	40	4	3	18
	Cohort Time	1	0	0	1	17	1	0	4
	CT 1 yr	1	0	0	1	13	1	0	3
	CT ext 60	1	0	0	1	13	1	0	3
	Unr drugs	1	1	0	1	13	1	0	3
TIA	Total FU	8	18	4	7	141	18	29	145
	Cohort Time	4	1	1	2	57	14	10	47
	CT 1 yr	3	1	1	2	43	10	7	40
	CT ext 60	4	1	1	2	46	10	7	43
	Unr drugs	3	1	2	2	44	10	8	46

THIN Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Torsades de Pointes	Total FU	0	0	0	0	0	0	0	0
	Cohort Time	0	0	0	0	0	0	0	0
	CT 1 yr	0	0	0	0	0	0	0	0
	CT ext 60	0	0	0	0	0	0	0	0
	Unr drugs	0	0	0	0	0	0	0	0
Unstable angina pectoris	Total FU	3	10	3	2	79	10	12	75
	Cohort Time	2	3	1	1	28	7	4	14
	CT 1 yr	2	2	1	0	25	7	4	14
	CT ext 60	2	2	1	0	29	7	4	15
	Unr drugs	2	2	1	0	25	7	4	22

THIN Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Urinary retention	Total FU	8	25	2	5	158	18	25	149
	Cohort Time	6	9	0	0	66	9	7	48
	CT 1 yr	5	6	0	0	52	7	6	41
	CT ext 60	6	6	0	0	54	8	6	43
	Unr drugs	5	6	0	0	52	8	6	57
Ventricular tachycardia	Total FU	0	1	1	0	14	3	2	7
	Cohort Time	0	0	0	0	7	1	0	4
	CT 1 yr	0	0	0	0	6	1	0	4
	CT ext 60	0	0	0	0	6	3	0	4
	Unr drugs	0	0	0	0	6	1	1	4

THIN Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Ventricular fibrillation	Total FU	1	0	0	0	3	1	0	2
	Cohort Time	0	0	0	0	1	1	0	0
	CT 1 yr	0	0	0	0	1	1	0	0
	CT ext 60	0	0	0	0	1	1	0	0
	Unr drugs	0	0	0	0	1	1	0	0
Cardiovascular death	Total FU	3	4	0	0	12	3	4	10
	Cohort Time	2	1	0	0	7	1	1	5
	CT 1 yr	2	1	0	0	6	1	1	4
	CT ext 60	2	1	0	0	7	1	1	4
	Unr drugs	2	1	0	0	6	1	2	5

THIN Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Respiratory death	Total FU	2	7	0	0	17	7	4	26
	Cohort Time	0	0	0	0	7	1	1	6
	CT 1 yr	0	0	0	0	5	0	1	6
	CT ext 60	0	0	0	0	6	0	1	6
	Unr drugs	0	0	0	0	5	0	3	9
Cardiovascular and respiratory death	Total FU	0	0	0	0	1	0	0	0
	Cohort Time	0	0	0	0	1	0	0	0
	CT 1 yr	0	0	0	0	1	0	0	0
	CT ext 60	0	0	0	0	1	0	0	0
	Unr drugs	0	0	0	0	1	0	0	0

THIN Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Cerebrovascular death	Total FU	0	0	0	0	0	0	1	2
	Cohort Time	0	0	0	0	0	0	0	0
	CT 1 yr	0	0	0	0	0	0	0	0
	CT ext 60	0	0	0	0	0	0	0	0
	Unr drugs	0	0	0	0	0	0	0	0
Cancer death (excluding lungcancer)	Total FU	0	0	0	0	8	0	0	6
	Cohort Time	0	0	0	0	4	0	0	4
	CT 1 yr	0	0	0	0	3	0	0	2
	CT ext 60	0	0	0	0	3	0	0	2
	Unr drugs	0	0	0	0	3	0	0	2

THIN Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Death due to other causes	Total FU	1	0	0	0	12	0	2	8
	Cohort Time	1	0	0	0	1	0	1	1
	CT 1 yr	1	0	0	0	1	0	1	1
	CT ext 60	1	0	0	0	2	0	1	1
	Unr drugs	1	0	0	0	1	0	1	1
Death with cause unknown	Total FU	68	33	4	8	802	116	51	349
	Cohort Time	68	33	4	8	798	115	50	341
	CT 1 yr	58	26	4	8	611	101	45	285
	CT ext 60	58	26	4	8	611	102	45	285
	Unr drugs	58	26	4	8	611	101	45	286

IPCI Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
MACE	Total FU	35	72	34	38	360	29	68	267
	Cohort Time	16	17	6	11	142	20	18	90
	CT 1 yr	13	16	6	11	128	19	18	85
	CT ext 60	14	16	6	13	143	21	20	88
	Unr drugs	13	18	7	13	133	19	23	108
Ischemic heart disease	Total FU	14	34	19	15	156	9	25	142
	Cohort Time	5	7	4	4	41	6	3	43
	CT 1 yr	4	7	4	4	34	5	3	41
	CT ext 60	6	7	4	4	40	5	3	43
	Unr drugs	4	10	4	5	36	5	6	50

MACE=Major Adverse Cardiovascular Event

IPCI Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Cardiac arrhythmia	Total FU	23	31	12	16	166	10	34	131
	Cohort Time	9	7	7	6	57	7	4	50
	CT 1 yr	8	7	6	6	50	6	4	46
	CT ext 60	9	8	6	7	58	6	8	49
	Unr drugs	9	8	6	7	50	6	7	53
Cerebrovascular disorders	Total FU	23	30	16	19	146	8	45	135
	Cohort Time	13	6	4	5	53	4	12	41
	CT 1 yr	11	5	4	5	47	4	12	35
	CT ext 60	11	5	4	6	57	5	13	36
	Unr drugs	11	6	5	5	49	4	14	43

IPCI Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Glaucoma	Total FU	2	5	1	0	26	1	4	20
	Cohort Time	1	0	1	0	5	0	0	5
	CT 1 yr	1	0	1	0	5	0	0	3
	CT ext 60	1	0	1	0	7	0	0	6
	Unr drugs	1	0	1	0	5	0	0	4
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	Total FU	27	34	20	22	166	13	37	146
	Cohort Time	11	5	4	4	51	9	6	44
	CT 1 yr	9	5	3	4	46	9	6	39
	CT ext 60	10	5	3	4	53	9	6	44
	Unr drugs	9	5	4	7	47	9	8	47

IPCI Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Diabetes mellitus	Total FU	12	9	8	2	75	6	11	54
	Cohort Time	6	5	1	2	26	5	1	16
	CT 1 yr	5	3	1	2	25	4	1	16
	CT ext 60	5	3	1	2	27	4	2	16
	Unr drugs	6	4	1	2	26	4	1	19
Bronchospasm	Total FU	1	0	1	0	4	1	0	4
	Cohort Time	1	0	0	0	0	1	0	2
	CT 1 yr	1	0	0	0	0	1	0	2
	CT ext 60	1	0	0	0	0	1	0	2
	Unr drugs	1	0	0	0	0	1	0	3

IPCI Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Mortality	Total FU	50	103	45	55	474	31	91	307
	Cohort Time	20	23	8	13	179	19	32	85
	CT 1 yr	15	23	6	13	161	19	32	77
	CT ext 60	15	24	6	15	189	21	35	90
	Unr drugs	15	26	7	14	163	21	39	101
Atrial fibrillation/flutter	Total FU	21	29	10	15	148	9	31	116
	Cohort Time	8	7	5	6	53	6	4	43
	CT 1 yr	7	7	4	6	47	5	4	39
	CT ext 60	8	8	4	7	53	5	8	42
	Unr drugs	8	8	4	7	47	5	7	44

IPCI Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Angina pectoris	Total FU	5	14	7	5	55	2	12	48
	Cohort Time	1	2	1	0	10	1	1	9
	CT 1 yr	1	2	1	0	9	1	1	8
	CT ext 60	2	2	1	0	13	1	1	9
	Unr drugs	1	3	1	0	10	1	3	12
AV block	Total FU	1	5	1	1	26	2	4	23
	Cohort Time	0	1	0	1	10	2	0	5
	CT 1 yr	0	1	0	1	9	2	0	4
	CT ext 60	0	1	0	1	10	2	0	5
	Unr drugs	0	1	0	1	9	2	0	4

IPCI Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Incident benign prostatic hyperplasia	Total FU	10	10	2	9	59	7	18	53
	Cohort Time	2	0	0	2	14	3	3	16
	CT 1 yr	2	0	0	2	13	3	3	14
	CT ext 60	2	0	0	2	16	3	3	15
	Unr drugs	2	0	0	3	13	3	3	15
Hospitalization for acute coronary syndrome	Total FU	10	28	12	14	110	7	17	88
	Cohort Time	4	7	3	4	30	5	2	29
	CT 1 yr	3	7	3	4	24	4	2	27
	CT ext 60	4	7	3	4	28	4	2	27
	Unr drugs	3	9	3	5	25	4	5	35

IPCI Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Hospitalization for heart failure	Total FU	12	33	17	18	185	19	24	115
	Cohort Time	4	8	3	5	79	13	8	44
	CT 1 yr	3	8	3	5	75	13	8	43
	CT ext 60	3	8	3	6	82	15	9	46
	Unr drugs	3	8	4	6	78	13	10	53
Myocardial infarction	Total FU	7	22	12	8	81	4	12	66
	Cohort Time	3	4	3	2	23	3	2	22
	CT 1 yr	2	4	3	2	18	3	2	22
	CT ext 60	2	4	3	2	21	3	2	22
	Unr drugs	2	7	3	2	19	3	3	27

IPCI Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Long QT	Total FU	0	1	0	0	1	0	2	2
	Cohort Time	0	1	0	0	0	0	0	0
	CT 1 yr	0	1	0	0	0	0	0	0
	CT ext 60	0	1	0	0	1	0	0	0
	Unr drugs	0	1	0	0	0	0	0	0
Narrow angle glaucoma	Total FU	0	0	0	0	1	0	1	2
	Cohort Time	0	0	0	0	0	0	0	1
	CT 1 yr	0	0	0	0	0	0	0	1
	CT ext 60	0	0	0	0	0	0	0	1
	Unr drugs	0	0	0	0	0	0	0	1

IPCI Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Other glaucoma	Total FU	2	5	1	0	25	1	3	18
	Cohort Time	1	0	1	0	5	0	0	4
	CT 1 yr	1	0	1	0	5	0	0	2
	CT ext 60	1	0	1	0	7	0	0	5
	Unr drugs	1	0	1	0	5	0	0	3
Premature depolarization	Total FU	2	5	3	4	28	0	5	15
	Cohort Time	0	1	1	0	6	0	1	4
	CT 1 yr	0	1	1	0	5	0	1	2
	CT ext 60	0	1	1	0	8	0	1	2
	Unr drugs	0	1	1	1	5	0	1	3

IPCI Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Sick sinus	Total FU	0	0	0	0	2	0	0	0
	Cohort Time	0	0	0	0	0	0	0	0
	CT 1 yr	0	0	0	0	0	0	0	0
	CT ext 60	0	0	0	0	0	0	0	0
	Unr drugs	0	0	0	0	0	0	0	0
Stroke	Total FU	15	18	7	11	84	5	32	82
	Cohort Time	8	4	0	3	36	4	8	19
	CT 1 yr	7	3	0	3	32	4	8	17
	CT ext 60	7	3	0	4	38	4	9	18
	Unr drugs	7	3	0	3	33	4	9	22

IPCI Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Supraventricular tachycardia	Total FU	1	7	0	0	31	0	6	22
	Cohort Time	1	3	0	0	13	0	2	6
	CT 1 yr	1	2	0	0	11	0	2	5
	CT ext 60	1	2	0	0	12	0	2	6
	Unr drugs	1	2	0	0	11	0	2	7
TIA	Total FU	9	15	10	10	70	3	18	64
	Cohort Time	6	3	4	2	18	0	5	24
	CT 1 yr	5	3	4	2	16	0	5	20
	CT ext 60	5	3	4	2	21	1	6	20
	Unr drugs	5	4	5	2	17	0	6	23

IPCI Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Torsades de Pointes	Total FU	0	0	0	0	1	0	1	1
	Cohort Time	0	0	0	0	0	0	0	0
	CT 1 yr	0	0	0	0	0	0	0	0
	CT ext 60	0	0	0	0	0	0	0	0
	Unr drugs	0	0	0	0	0	0	0	0
Unstable angina pectoris	Total FU	3	5	1	6	31	4	5	35
	Cohort Time	1	1	0	2	9	3	0	12
	CT 1 yr	1	1	0	2	8	2	0	11
	CT ext 60	2	1	0	2	8	2	0	13
	Unr drugs	1	3	0	3	8	2	0	12

IPCI Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Urinary retention	Total FU	19	29	19	15	125	8	22	108
	Cohort Time	10	5	4	2	39	8	3	31
	CT 1 yr	8	5	3	2	35	8	3	28
	CT ext 60	9	5	3	2	40	8	3	32
	Unr drugs	8	5	4	4	36	8	5	37
Ventricular tachycardia	Total FU	1	1	1	1	14	1	2	6
	Cohort Time	1	0	1	0	3	1	0	3
	CT 1 yr	1	0	1	0	2	1	0	3
	CT ext 60	1	0	1	0	3	1	0	3
	Unr drugs	1	0	1	0	2	1	0	3

IPCI Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Ventricular fibrillation	Total FU	1	1	1	0	8	0	1	12
	Cohort Time	0	0	1	0	3	0	0	4
	CT 1 yr	0	0	1	0	3	0	0	4
	CT ext 60	0	0	1	0	5	0	0	4
	Unr drugs	0	0	1	0	3	0	0	6
Cardiovascular death	Total FU	2	9	3	3	52	1	8	38
	Cohort Time	1	6	0	1	20	1	4	9
	CT 1 yr	1	6	0	1	20	1	4	8
	CT ext 60	1	6	0	1	23	1	4	12
	Unr drugs	1	6	0	1	20	1	4	10

IPCI Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Respiratory death	Total FU	15	26	11	22	148	10	28	77
	Cohort Time	7	6	2	6	65	7	10	28
	CT 1 yr	5	6	1	6	61	7	10	27
	CT ext 60	5	6	1	6	69	7	11	29
	Unr drugs	5	7	2	7	63	8	15	39
Cardiovascular and respiratory death	Total FU	3	12	7	5	30	2	2	25
	Cohort Time	2	3	2	0	13	1	0	10
	CT 1 yr	1	3	2	0	13	1	0	8
	CT ext 60	1	3	2	0	13	1	1	8
	Unr drugs	1	4	2	0	13	1	0	13

IPCI Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Cerebrovascular death	Total FU	4	3	2	1	12	1	4	16
	Cohort Time	0	0	0	1	4	1	1	2
	CT 1 yr	0	0	0	1	3	1	1	2
	CT ext 60	0	0	0	1	5	1	1	3
	Unr drugs	0	0	0	1	3	1	1	3
Cancer death (excluding lungcancer)	Total FU	5	11	4	6	53	2	15	41
	Cohort Time	3	2	1	1	19	0	4	16
	CT 1 yr	2	2	1	1	16	0	4	14
	CT ext 60	2	2	1	1	19	1	4	16
	Unr drugs	2	2	1	1	16	0	5	16

IPCI Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Death due to other causes	Total FU	5	6	5	2	29	7	8	28
	Cohort Time	1	3	2	0	11	4	3	7
	CT 1 yr	1	3	1	0	10	4	3	7
	CT ext 60	1	3	1	0	13	5	3	7
	Unr drugs	1	3	1	0	10	4	3	7
Death with cause unknown	Total FU	16	36	13	16	150	8	26	82
	Cohort Time	6	3	1	4	47	5	10	13
	CT 1 yr	5	3	1	4	38	5	10	11
	CT ext 60	5	4	1	6	47	5	11	15
	Unr drugs	5	4	1	4	38	6	11	13

Aarhus Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
MACE	Total FU	217	79	30	33	445	157	102	262
	Cohort Time	139	30	14	13	234	121	43	133
	CT 1 yr	126	30	14	12	223	116	41	130
	CT ext 60	129	30	14	12	247	123	45	136
	Unr drugs	132	32	14	12	229	118	53	152
Ischemic heart disease	Total FU	64	17	12	16	113	27	32	55
	Cohort Time	39	4	2	5	42	16	11	15
	CT 1 yr	33	4	2	4	40	13	11	15
	CT ext 60	35	4	2	4	48	15	12	16
	Unr drugs	34	4	2	4	44	14	12	18

MACE=Major Adverse Cardiovascular Event

Aarhus Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Cardiac arrhythmia	Total FU	69	32	7	11	138	55	37	80
	Cohort Time	32	6	2	2	52	35	10	32
	CT 1 yr	24	6	2	2	48	33	9	28
	CT ext 60	26	7	2	3	54	34	9	32
	Unr drugs	30	7	2	2	48	36	11	33
Cerebrovascular disorders	Total FU	39	17	4	5	83	28	27	52
	Cohort Time	20	2	2	2	22	19	5	13
	CT 1 yr	18	2	2	2	21	18	4	13
	CT ext 60	18	2	2	2	25	18	5	15
	Unr drugs	18	2	2	2	22	18	6	19

Aarhus Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Glaucoma	Total FU	2	3	2	0	9	6	1	7
	Cohort Time	0	1	0	0	2	4	0	3
	CT 1 yr	0	1	0	0	1	3	0	3
	CT ext 60	1	1	0	0	1	3	0	3
	Unr drugs	0	1	0	0	1	4	0	3
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	Total FU	19	10	1	1	38	12	10	26
	Cohort Time	9	2	0	1	11	7	1	7
	CT 1 yr	7	2	0	1	11	7	1	6
	CT ext 60	8	2	0	1	12	7	1	6
	Unr drugs	9	2	0	1	11	8	2	7

Aarhus Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Diabetes mellitus	Total FU	13	7	1	2	47	12	9	27
	Cohort Time	7	0	0	0	16	10	1	7
	CT 1 yr	7	0	0	0	15	10	1	7
	CT ext 60	7	0	0	0	17	10	1	7
	Unr drugs	7	0	0	0	17	10	2	8
Bronchospasm	Total FU	0	0	0	0	0	0	0	0
	Cohort Time	0	0	0	0	0	0	0	0
	CT 1 yr	0	0	0	0	0	0	0	0
	CT ext 60	0	0	0	0	0	0	0	0
	Unr drugs	0	0	0	0	0	0	0	0

Aarhus Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Mortality	Total FU	296	122	40	30	670	161	165	341
	Cohort Time	138	16	2	5	236	82	28	86
	CT 1 yr	103	16	2	5	216	75	25	86
	CT ext 60	109	16	2	6	257	86	31	95
	Unr drugs	107	18	2	6	220	81	40	120
Atrial fibrillation/flutter	Total FU	67	32	7	11	136	54	37	76
	Cohort Time	30	6	2	2	52	34	10	30
	CT 1 yr	22	6	2	2	48	32	9	26
	CT ext 60	24	7	2	3	53	33	9	30
	Unr drugs	28	7	2	2	48	35	11	30

Aarhus Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Angina pectoris	Total FU	35	7	5	9	63	9	18	26
	Cohort Time	19	2	0	1	28	5	6	6
	CT 1 yr	16	2	0	1	27	5	6	6
	CT ext 60	18	2	0	1	30	5	7	6
	Unr drugs	17	2	0	1	29	5	7	7
AV block	Total FU	14	5	0	0	11	7	3	13
	Cohort Time	5	1	0	0	3	2	1	3
	CT 1 yr	3	1	0	0	3	2	1	3
	CT ext 60	3	1	0	0	3	2	1	3
	Unr drugs	5	1	0	0	4	2	2	5

Aarhus Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Incident benign prostatic hyperplasia	Total FU	11	7	0	1	24	8	8	18
	Cohort Time	5	1	0	1	7	4	1	3
	CT 1 yr	5	1	0	1	7	4	1	3
	CT ext 60	5	1	0	1	7	4	1	3
	Unr drugs	7	1	0	1	7	4	2	4
Hospitalization for acute coronary syndrome	Total FU	50	14	10	11	89	22	19	49
	Cohort Time	30	3	3	5	34	14	9	14
	CT 1 yr	25	3	3	4	31	11	9	14
	CT ext 60	25	3	3	4	37	13	9	15
	Unr drugs	26	3	3	4	34	12	10	17

Aarhus Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Hospitalization for heart failure	Total FU	166	58	17	24	327	126	75	189
	Cohort Time	108	26	9	8	192	97	34	113
	CT 1 yr	97	26	9	8	184	93	32	110
	CT ext 60	100	26	9	8	200	100	36	114
	Unr drugs	102	28	9	8	188	95	42	128
Myocardial infarction	Total FU	28	9	8	9	53	17	9	23
	Cohort Time	18	2	2	4	16	9	2	6
	CT 1 yr	15	2	2	3	14	6	2	6
	CT ext 60	15	2	2	3	17	9	2	6
	Unr drugs	16	2	2	3	16	7	3	9

Aarhus Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Long QT	Total FU	0	0	0	0	0	0	0	0
	Cohort Time	0	0	0	0	0	0	0	0
	CT 1 yr	0	0	0	0	0	0	0	0
	CT ext 60	0	0	0	0	0	0	0	0
	Unr drugs	0	0	0	0	0	0	0	0
Narrow angle glaucoma	Total FU	1	0	0	0	0	1	0	1
	Cohort Time	0	0	0	0	0	1	0	0
	CT 1 yr	0	0	0	0	0	0	0	0
	CT ext 60	0	0	0	0	0	0	0	0
	Unr drugs	0	0	0	0	0	0	0	0

Aarhus Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Other glaucoma	Total FU	1	3	2	0	9	5	1	6
	Cohort Time	0	1	0	0	2	3	0	3
	CT 1 yr	0	1	0	0	1	3	0	3
	CT ext 60	1	1	0	0	1	3	0	3
	Unr drugs	0	1	0	0	1	4	0	3
Premature depolarization	Total FU	3	2	1	1	9	1	4	4
	Cohort Time	1	0	0	0	6	1	3	2
	CT 1 yr	1	0	0	0	5	1	3	2
	CT ext 60	1	0	0	0	5	1	3	2
	Unr drugs	1	0	0	0	5	1	3	3

Aarhus Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Sick sinus	Total FU	7	3	0	0	9	0	4	5
	Cohort Time	3	0	0	0	5	0	4	2
	CT 1 yr	3	0	0	0	4	0	4	2
	CT ext 60	3	0	0	0	4	0	4	2
	Unr drugs	3	0	0	0	4	0	4	2
Stroke	Total FU	28	14	4	5	66	23	18	40
	Cohort Time	14	2	2	2	19	18	3	10
	CT 1 yr	13	2	2	2	18	17	2	10
	CT ext 60	13	2	2	2	20	17	2	11
	Unr drugs	13	2	2	2	18	17	4	15

Aarhus Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Supraventricular tachycardia	Total FU	9	3	0	1	9	4	3	13
	Cohort Time	6	1	0	0	3	3	2	3
	CT 1 yr	6	1	0	0	3	3	2	2
	CT ext 60	6	1	0	0	3	3	3	3
	Unr drugs	6	1	0	0	3	3	2	5
TIA	Total FU	11	3	0	0	20	6	9	12
	Cohort Time	6	0	0	0	4	1	2	3
	CT 1 yr	5	0	0	0	4	1	2	3
	CT ext 60	5	0	0	0	6	1	3	4
	Unr drugs	5	0	0	0	5	1	2	4

Aarhus Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Torsades de Pointes	Total FU	0	0	0	0	0	0	0	0
	Cohort Time	0	0	0	0	0	0	0	0
	CT 1 yr	0	0	0	0	0	0	0	0
	CT ext 60	0	0	0	0	0	0	0	0
	Unr drugs	0	0	0	0	0	0	0	0
Unstable angina pectoris	Total FU	13	3	0	3	21	4	9	14
	Cohort Time	9	0	0	1	6	3	5	4
	CT 1 yr	6	0	0	0	6	3	5	4
	CT ext 60	6	0	0	0	9	3	5	5
	Unr drugs	6	0	0	0	7	3	5	4

Aarhus Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Urinary retention	Total FU	8	3	1	0	14	4	2	9
	Cohort Time	4	1	0	0	4	3	0	5
	CT 1 yr	2	1	0	0	4	3	0	4
	CT ext 60	3	1	0	0	5	3	0	4
	Unr drugs	2	1	0	0	4	4	0	4
Ventricular tachycardia	Total FU	2	0	0	0	2	1	0	3
	Cohort Time	1	0	0	0	0	0	0	1
	CT 1 yr	1	0	0	0	0	0	0	1
	CT ext 60	1	0	0	0	0	0	0	1
	Unr drugs	1	0	0	0	0	0	0	1

Aarhus Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Ventricular fibrillation	Total FU	1	0	0	0	1	1	0	2
	Cohort Time	1	0	0	0	0	1	0	1
	CT 1 yr	1	0	0	0	0	1	0	1
	CT ext 60	1	0	0	0	1	1	0	1
	Unr drugs	1	0	0	0	0	1	0	2
Cardiovascular death	Total FU	29	14	2	2	71	2	21	40
	Cohort Time	18	2	0	0	30	2	2	14
	CT 1 yr	18	2	0	0	30	2	2	14
	CT ext 60	19	2	0	0	36	2	4	16
	Unr drugs	19	2	0	0	31	2	5	15

Aarhus Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Respiratory death	Total FU	57	23	14	7	134	6	29	59
	Cohort Time	31	8	2	2	62	2	7	20
	CT 1 yr	27	8	2	2	58	2	6	20
	CT ext 60	30	8	2	2	68	2	8	22
	Unr drugs	27	9	2	3	58	2	10	32
Cardiovascular and respiratory death	Total FU	0	0	0	0	0	0	0	0
	Cohort Time	0	0	0	0	0	0	0	0
	CT 1 yr	0	0	0	0	0	0	0	0
	CT ext 60	0	0	0	0	0	0	0	0
	Unr drugs	0	0	0	0	0	0	0	0

Aarhus Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Cerebrovascular death	Total FU	2	2	0	0	15	2	3	12
	Cohort Time	0	0	0	0	4	2	1	6
	CT 1 yr	0	0	0	0	4	2	1	6
	CT ext 60	0	0	0	0	6	2	1	6
	Unr drugs	1	0	0	0	5	2	1	7
Cancer death (excluding lungcancer)	Total FU	13	12	2	3	36	2	11	29
	Cohort Time	7	1	0	1	19	2	3	10
	CT 1 yr	7	1	0	1	18	2	3	10
	CT ext 60	8	1	0	1	19	2	3	10
	Unr drugs	7	1	0	1	18	2	4	13

Aarhus Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Death due to other causes	Total FU	39	21	6	8	136	10	28	59
	Cohort Time	26	4	0	1	58	4	6	15
	CT 1 yr	22	4	0	1	56	4	4	15
	CT ext 60	23	4	0	2	70	4	5	18
	Unr drugs	23	4	0	1	56	5	9	26
Death with cause unknown	Total FU	158	50	16	10	284	140	74	143
	Cohort Time	58	1	0	1	64	71	9	22
	CT 1 yr	31	1	0	1	51	64	9	22
	CT ext 60	31	1	0	1	60	75	10	24
	Unr drugs	32	2	0	1	53	69	12	28

HSD Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
MACE	Total FU	3	15	7	4	91	5	10	67
	Cohort Time	2	3	1	0	15	2	2	15
	CT 1 yr	2	3	1	0	15	2	2	14
	CT ext 60	2	3	1	0	23	2	2	18
	Unr drugs	2	3	1	0	15	3	2	16
Ischemic heart disease	Total FU	3	9	8	2	61	3	9	41
	Cohort Time	1	2	1	0	13	1	1	7
	CT 1 yr	1	2	1	0	13	1	1	6
	CT ext 60	1	2	1	0	16	1	1	9
	Unr drugs	1	2	1	0	13	2	1	6

MACE=Major Adverse Cardiovascular Event

HSD Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Cardiac arrhythmia	Total FU	6	40	11	13	162	12	30	111
	Cohort Time	3	10	0	1	44	9	3	26
	CT 1 yr	3	10	0	1	41	9	3	23
	CT ext 60	3	10	0	1	45	9	4	27
	Unr drugs	5	11	0	1	41	9	4	29
Cerebrovascular disorders	Total FU	4	20	7	5	79	1	9	53
	Cohort Time	3	4	1	0	8	0	4	8
	CT 1 yr	3	4	1	0	8	0	4	8
	CT ext 60	3	4	1	0	15	0	4	9
	Unr drugs	3	4	1	0	8	0	4	10

HSD Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Glaucoma	Total FU	3	16	5	3	65	2	6	35
	Cohort Time	1	4	1	0	10	1	0	8
	CT 1 yr	0	4	1	0	8	1	0	7
	CT ext 60	0	4	1	0	11	2	0	7
	Unr drugs	0	4	1	0	8	1	0	8
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	Total FU	4	23	6	6	114	2	16	78
	Cohort Time	3	4	1	0	21	1	4	14
	CT 1 yr	1	4	1	0	20	1	4	12
	CT ext 60	1	4	1	0	26	1	4	15
	Unr drugs	1	4	1	0	20	1	4	14

HSD Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Diabetes mellitus	Total FU	8	20	9	10	121	8	18	76
	Cohort Time	6	6	2	0	34	4	2	15
	CT 1 yr	5	4	2	0	34	4	2	13
	CT ext 60	5	4	2	0	39	4	2	14
	Unr drugs	5	5	2	1	34	4	3	16
Bronchospasm	Total FU	1	8	5	6	134	4	10	45
	Cohort Time	0	0	0	0	13	1	0	4
	CT 1 yr	0	0	0	0	12	1	0	3
	CT ext 60	0	0	0	0	14	3	0	5
	Unr drugs	0	1	0	0	12	1	0	6

HSD Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Mortality	Total FU	5	52	14	15	206	3	33	168
	Cohort Time	3	3	1	2	56	2	6	39
	CT 1 yr	3	3	1	2	54	2	6	37
	CT ext 60	3	3	1	2	73	2	7	43
	Unr drugs	4	4	1	2	55	2	8	43
Atrial fibrillation/flutter	Total FU	6	40	11	13	160	12	29	109
	Cohort Time	3	10	0	1	43	9	3	25
	CT 1 yr	3	10	0	1	40	9	3	22
	CT ext 60	3	10	0	1	44	9	4	26
	Unr drugs	5	11	0	1	40	9	4	27

HSD Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Angina pectoris	Total FU	2	4	3	0	27	0	2	17
	Cohort Time	1	2	0	0	7	0	0	2
	CT 1 yr	1	2	0	0	7	0	0	2
	CT ext 60	1	2	0	0	8	0	0	2
	Unr drugs	1	2	0	0	7	0	0	2
AV block	Total FU	1	2	1	1	9	1	4	13
	Cohort Time	1	1	0	0	3	0	0	1
	CT 1 yr	1	1	0	0	3	0	0	1
	CT ext 60	1	1	0	0	4	0	1	2
	Unr drugs	1	1	0	0	3	0	0	2

HSD Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Incident benign prostatic hyperplasia	Total FU	3	20	6	6	92	2	14	58
	Cohort Time	3	4	1	0	15	1	3	6
	CT 1 yr	1	4	1	0	15	1	3	6
	CT ext 60	1	4	1	0	20	1	3	8
	Unr drugs	1	4	1	0	15	1	3	7
Hospitalization for acute coronary syndrome	Total FU	0	1	1	0	6	2	1	6
	Cohort Time	0	0	1	0	6	1	1	5
	CT 1 yr	0	0	1	0	6	1	1	4
	CT ext 60	0	0	1	0	6	1	1	4
	Unr drugs	0	0	1	0	6	2	1	4

HSD Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Hospitalization for heart failure	Total FU	0	1	0	0	2	1	0	4
	Cohort Time	0	0	0	0	2	1	0	4
	CT 1 yr	0	0	0	0	2	1	0	4
	CT ext 60	0	0	0	0	2	1	0	4
	Unr drugs	0	0	0	0	2	1	0	4
Myocardial infarction	Total FU	1	5	5	2	34	3	7	25
	Cohort Time	0	0	1	0	6	1	1	5
	CT 1 yr	0	0	1	0	6	1	1	4
	CT ext 60	0	0	1	0	8	1	1	7
	Unr drugs	0	0	1	0	6	2	1	4

HSD Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Long QT	Total FU	0	0	0	0	1	0	1	1
	Cohort Time	0	0	0	0	0	0	0	1
	CT 1 yr	0	0	0	0	0	0	0	1
	CT ext 60	0	0	0	0	0	0	0	1
	Unr drugs	0	0	0	0	0	0	0	1
Narrow angle glaucoma	Total FU	0	0	0	0	0	0	0	0
	Cohort Time	0	0	0	0	0	0	0	0
	CT 1 yr	0	0	0	0	0	0	0	0
	CT ext 60	0	0	0	0	0	0	0	0
	Unr drugs	0	0	0	0	0	0	0	0

HSD Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Other glaucoma	Total FU	3	16	5	3	65	2	6	35
	Cohort Time	1	4	1	0	10	1	0	8
	CT 1 yr	0	4	1	0	8	1	0	7
	CT ext 60	0	4	1	0	11	2	0	7
	Unr drugs	0	4	1	0	8	1	0	8
Premature depolarization	Total FU	2	6	2	3	42	3	8	33
	Cohort Time	1	0	0	0	8	3	2	5
	CT 1 yr	0	0	0	0	7	3	1	5
	CT ext 60	0	0	0	0	9	3	1	5
	Unr drugs	0	0	0	0	7	3	2	8

HSD Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Sick sinus	Total FU	1	0	0	0	14	0	3	6
	Cohort Time	1	0	0	0	3	0	1	0
	CT 1 yr	1	0	0	0	3	0	1	0
	CT ext 60	1	0	0	0	3	0	1	0
	Unr drugs	1	0	0	0	3	0	1	0
Stroke	Total FU	2	9	2	2	56	1	3	38
	Cohort Time	2	3	0	0	7	0	1	6
	CT 1 yr	2	3	0	0	7	0	1	6
	CT ext 60	2	3	0	0	14	0	1	7
	Unr drugs	2	3	0	0	7	0	1	8

HSD Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Supraventricular tachycardia	Total FU	0	0	0	0	8	0	2	3
	Cohort Time	0	0	0	0	2	0	0	1
	CT 1 yr	0	0	0	0	2	0	0	1
	CT ext 60	0	0	0	0	2	0	0	1
	Unr drugs	0	0	0	0	2	0	0	1
TIA	Total FU	2	11	5	3	25	0	6	17
	Cohort Time	1	1	1	0	1	0	3	2
	CT 1 yr	1	1	1	0	1	0	3	2
	CT ext 60	1	1	1	0	1	0	3	2
	Unr drugs	1	1	1	0	1	0	3	2

HSD Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Torsades de Pointes	Total FU	0	0	0	0	1	0	1	1
	Cohort Time	0	0	0	0	0	0	0	1
	CT 1 yr	0	0	0	0	0	0	0	1
	CT ext 60	0	0	0	0	0	0	0	1
	Unr drugs	0	0	0	0	0	0	0	1
Unstable angina pectoris	Total FU	0	3	0	0	9	0	1	6
	Cohort Time	0	2	0	0	2	0	0	1
	CT 1 yr	0	2	0	0	2	0	0	1
	CT ext 60	0	2	0	0	2	0	0	1
	Unr drugs	0	2	0	0	2	0	0	1

HSD Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Urinary retention	Total FU	1	3	0	0	23	0	3	22
	Cohort Time	0	0	0	0	6	0	1	8
	CT 1 yr	0	0	0	0	5	0	1	6
	CT ext 60	0	0	0	0	7	0	1	7
	Unr drugs	0	0	0	0	5	0	1	7
Ventricular tachycardia	Total FU	0	0	0	0	1	0	0	1
	Cohort Time	0	0	0	0	1	0	0	0
	CT 1 yr	0	0	0	0	1	0	0	0
	CT ext 60	0	0	0	0	1	0	0	0
	Unr drugs	0	0	0	0	1	0	0	1

HSD Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Ventricular fibrillation	Total FU	0	0	0	0	0	0	0	0
	Cohort Time	0	0	0	0	0	0	0	0
	CT 1 yr	0	0	0	0	0	0	0	0
	CT ext 60	0	0	0	0	0	0	0	0
	Unr drugs	0	0	0	0	0	0	0	0
Cardiovascular death	Total FU	0	0	0	0	0	0	0	0
	Cohort Time	0	0	0	0	0	0	0	0
	CT 1 yr	0	0	0	0	0	0	0	0
	CT ext 60	0	0	0	0	0	0	0	0
	Unr drugs	0	0	0	0	0	0	0	0

HSD Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Respiratory death	Total FU	0	0	0	0	0	0	0	0
	Cohort Time	0	0	0	0	0	0	0	0
	CT 1 yr	0	0	0	0	0	0	0	0
	CT ext 60	0	0	0	0	0	0	0	0
	Unr drugs	0	0	0	0	0	0	0	0
Cardiovascular and respiratory death	Total FU	0	0	0	0	0	0	0	0
	Cohort Time	0	0	0	0	0	0	0	0
	CT 1 yr	0	0	0	0	0	0	0	0
	CT ext 60	0	0	0	0	0	0	0	0
	Unr drugs	0	0	0	0	0	0	0	0

HSD Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Cerebrovascular death	Total FU	0	0	0	0	0	0	0	0
	Cohort Time	0	0	0	0	0	0	0	0
	CT 1 yr	0	0	0	0	0	0	0	0
	CT ext 60	0	0	0	0	0	0	0	0
	Unr drugs	0	0	0	0	0	0	0	0
Cancer death (excluding lungcancer)	Total FU	0	0	0	0	0	0	0	0
	Cohort Time	0	0	0	0	0	0	0	0
	CT 1 yr	0	0	0	0	0	0	0	0
	CT ext 60	0	0	0	0	0	0	0	0
	Unr drugs	0	0	0	0	0	0	0	0

HSD Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Death due to other causes	Total FU	0	0	0	0	0	0	0	0
	Cohort Time	0	0	0	0	0	0	0	0
	CT 1 yr	0	0	0	0	0	0	0	0
	CT ext 60	0	0	0	0	0	0	0	0
	Unr drugs	0	0	0	0	0	0	0	0
Death with cause unknown	Total FU	3	3	1	2	56	2	6	39
	Cohort Time	3	3	1	2	56	2	6	39
	CT 1 yr	3	3	1	2	54	2	6	37
	CT ext 60	3	3	1	2	54	2	6	37
	Unr drugs	3	3	1	2	54	2	6	37

SIDIAP Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
MACE	Total FU	235	229	104	145	1093	33	224	652
	Cohort Time	116	49	20	32	427	22	61	207
	CT 1 yr	112	46	18	32	415	22	60	203
	CT ext 60	122	48	20	36	479	24	65	227
	Unr drugs	117	47	19	35	417	24	71	228
Ischemic heart disease	Total FU	36	49	22	25	195	7	66	139
	Cohort Time	16	14	5	6	64	6	8	47
	CT 1 yr	14	13	4	6	61	6	8	45
	CT ext 60	15	13	4	6	71	6	13	51
	Unr drugs	14	14	4	6	61	6	10	48

MACE=Major Adverse Cardiovascular Event

SIDIAP Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Cardiac arrhythmia	Total FU	90	120	58	80	506	9	116	304
	Cohort Time	40	23	14	17	169	5	25	97
	CT 1 yr	39	21	13	17	163	4	25	96
	CT ext 60	43	22	13	20	193	4	30	112
	Unr drugs	40	24	13	19	164	6	30	110
Cerebrovascular disorders	Total FU	57	54	25	44	278	6	71	171
	Cohort Time	16	5	6	8	61	2	13	33
	CT 1 yr	14	5	6	8	58	2	13	33
	CT ext 60	20	6	6	9	78	3	17	39
	Unr drugs	15	5	6	8	58	3	15	36

SIDIAP Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Glaucoma	Total FU	40	39	9	27	172	3	56	115
	Cohort Time	14	9	2	1	42	1	12	34
	CT 1 yr	12	9	2	1	37	1	12	34
	CT ext 60	14	10	3	1	44	1	13	38
	Unr drugs	12	9	2	1	37	2	13	39
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	Total FU	155	175	60	95	621	11	201	454
	Cohort Time	64	33	11	10	177	9	53	125
	CT 1 yr	57	31	11	10	172	8	52	120
	CT ext 60	65	34	11	10	197	8	59	137
	Unr drugs	59	32	11	10	173	8	63	141

SIDIAP Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Diabetes mellitus	Total FU	107	89	38	56	441	14	104	262
	Cohort Time	54	27	7	9	181	13	35	98
	CT 1 yr	51	26	7	9	173	13	34	94
	CT ext 60	54	27	7	12	196	13	37	106
	Unr drugs	55	28	7	10	173	13	37	99
Bronchospasm	Total FU	21	18	18	33	170	5	31	84
	Cohort Time	5	3	2	6	39	2	6	9
	CT 1 yr	5	3	2	6	39	2	6	9
	CT ext 60	7	3	2	6	49	2	6	11
	Unr drugs	6	3	2	7	39	3	9	13

SIDIAP Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Mortality	Total FU	369	306	186	252	1625	36	334	822
	Cohort Time	80	20	5	18	300	12	40	121
	CT 1 yr	69	19	5	18	273	11	38	115
	CT ext 60	109	23	7	27	405	19	51	169
	Unr drugs	75	19	5	19	277	11	46	143
Atrial fibrillation/flutter	Total FU	88	120	57	80	499	9	115	296
	Cohort Time	38	23	12	17	165	5	25	95
	CT 1 yr	37	21	11	17	159	4	25	94
	CT ext 60	41	22	11	20	188	4	30	109
	Unr drugs	38	24	11	19	160	6	30	107

SIDIAP Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Angina pectoris	Total FU	13	22	13	11	82	2	25	61
	Cohort Time	6	3	3	3	21	1	3	20
	CT 1 yr	6	3	2	3	21	1	3	19
	CT ext 60	7	3	2	3	26	1	5	21
	Unr drugs	6	4	2	3	21	1	4	22
AV block	Total FU	24	31	12	16	117	4	23	73
	Cohort Time	11	5	0	3	33	4	6	21
	CT 1 yr	10	4	0	3	33	4	6	20
	CT ext 60	10	4	0	3	38	4	7	22
	Unr drugs	10	4	0	3	34	4	6	25

SIDIAP Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Incident benign prostatic hyperplasia	Total FU	121	138	41	74	474	9	149	362
	Cohort Time	48	22	7	9	136	8	42	104
	CT 1 yr	41	20	7	9	132	7	41	102
	CT ext 60	48	23	7	9	151	7	47	114
	Unr drugs	41	21	7	9	133	7	47	115
Hospitalization for acute coronary syndrome	Total FU	29	40	11	13	159	4	31	99
	Cohort Time	11	10	4	4	50	2	5	29
	CT 1 yr	11	9	4	4	47	2	5	27
	CT ext 60	11	9	4	4	52	3	6	30
	Unr drugs	11	9	4	4	47	3	5	29

SIDIAP Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Hospitalization for heart failure	Total FU	166	138	76	94	740	21	130	411
	Cohort Time	88	32	13	21	328	15	43	147
	CT 1 yr	87	30	11	21	321	15	42	146
	CT ext 60	92	31	13	24	367	15	43	161
	Unr drugs	91	31	12	24	323	16	51	167
Myocardial infarction	Total FU	22	29	9	14	113	4	41	78
	Cohort Time	9	10	2	3	42	4	5	25
	CT 1 yr	7	9	2	3	39	4	5	24
	CT ext 60	7	9	2	3	43	4	8	28
	Unr drugs	7	9	2	3	39	4	6	24

SIDIAP Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Long QT	Total FU	2	0	1	1	1	0	3	2
	Cohort Time	2	0	0	0	1	0	0	0
	CT 1 yr	2	0	0	0	1	0	0	0
	CT ext 60	2	0	0	0	1	0	0	0
	Unr drugs	2	0	0	0	1	0	0	1
Narrow angle glaucoma	Total FU	0	0	0	0	0	0	1	0
	Cohort Time	0	0	0	0	0	0	0	0
	CT 1 yr	0	0	0	0	0	0	0	0
	CT ext 60	0	0	0	0	0	0	0	0
	Unr drugs	0	0	0	0	0	0	0	0

SIDIAP Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Other glaucoma	Total FU	40	39	9	27	172	3	55	115
	Cohort Time	14	9	2	1	42	1	12	34
	CT 1 yr	12	9	2	1	37	1	12	34
	CT ext 60	14	10	3	1	44	1	13	38
	Unr drugs	12	9	2	1	37	2	13	39
Premature depolarization	Total FU	16	13	9	13	93	1	18	49
	Cohort Time	6	3	1	3	25	1	3	16
	CT 1 yr	6	3	1	3	24	1	3	16
	CT ext 60	8	3	1	3	29	1	3	16
	Unr drugs	6	4	1	4	26	1	4	17

SIDIAP Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Sick sinus	Total FU	0	0	0	0	0	0	0	1
	Cohort Time	0	0	0	0	0	0	0	1
	CT 1 yr	0	0	0	0	0	0	0	1
	CT ext 60	0	0	0	0	0	0	0	1
	Unr drugs	0	0	0	0	0	0	0	1
Stroke	Total FU	36	41	17	33	206	6	53	134
	Cohort Time	9	2	3	5	41	2	8	21
	CT 1 yr	8	2	3	5	39	2	8	21
	CT ext 60	13	3	3	6	55	3	11	25
	Unr drugs	9	2	3	5	39	3	10	23

SIDIAP Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Supraventricular tachycardia	Total FU	4	8	2	1	21	1	9	11
	Cohort Time	2	2	0	0	7	1	3	2
	CT 1 yr	2	1	0	0	7	1	3	2
	CT ext 60	2	1	0	1	7	1	3	3
	Unr drugs	2	1	0	0	8	1	3	2
TIA	Total FU	22	13	8	11	76	0	21	41
	Cohort Time	8	3	3	3	20	0	6	12
	CT 1 yr	6	3	3	3	19	0	6	12
	CT ext 60	7	3	3	3	23	0	8	14
	Unr drugs	6	3	3	3	19	0	6	13

SIDIAP Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Torsades de Pointes	Total FU	0	0	0	0	0	0	0	0
	Cohort Time	0	0	0	0	0	0	0	0
	CT 1 yr	0	0	0	0	0	0	0	0
	CT ext 60	0	0	0	0	0	0	0	0
	Unr drugs	0	0	0	0	0	0	0	0
Unstable angina pectoris	Total FU	7	9	5	2	33	2	7	21
	Cohort Time	4	3	1	1	9	1	2	5
	CT 1 yr	4	3	1	1	9	1	2	5
	CT ext 60	4	3	1	1	12	1	2	6
	Unr drugs	4	3	1	1	9	1	3	6

SIDIAP Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Urinary retention	Total FU	41	40	24	25	170	2	55	108
	Cohort Time	18	11	5	1	51	1	11	22
	CT 1 yr	17	11	5	1	49	1	11	19
	CT ext 60	18	11	5	1	56	1	12	24
	Unr drugs	19	11	5	1	49	1	16	27
Ventricular tachycardia	Total FU	2	0	2	1	9	0	1	9
	Cohort Time	2	0	2	0	4	0	0	1
	CT 1 yr	2	0	2	0	4	0	0	1
	CT ext 60	2	0	2	0	5	0	0	2
	Unr drugs	2	0	2	0	4	0	0	2

SIDIAP Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Ventricular fibrillation	Total FU	0	0	0	0	0	0	0	1
	Cohort Time	0	0	0	0	0	0	0	1
	CT 1 yr	0	0	0	0	0	0	0	1
	CT ext 60	0	0	0	0	0	0	0	1
	Unr drugs	0	0	0	0	0	0	0	1
Cardiovascular death	Total FU	0	0	0	0	0	0	0	0
	Cohort Time	0	0	0	0	0	0	0	0
	CT 1 yr	0	0	0	0	0	0	0	0
	CT ext 60	0	0	0	0	0	0	0	0
	Unr drugs	0	0	0	0	0	0	0	0

SIDIAP Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Respiratory death	Total FU	0	0	0	0	0	0	0	0
	Cohort Time	0	0	0	0	0	0	0	0
	CT 1 yr	0	0	0	0	0	0	0	0
	CT ext 60	0	0	0	0	0	0	0	0
	Unr drugs	0	0	0	0	0	0	0	0
Cardiovascular and respiratory death	Total FU	0	0	0	0	0	0	0	0
	Cohort Time	0	0	0	0	0	0	0	0
	CT 1 yr	0	0	0	0	0	0	0	0
	CT ext 60	0	0	0	0	0	0	0	0
	Unr drugs	0	0	0	0	0	0	0	0

SIDIAP Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Cerebrovascular death	Total FU	0	0	0	0	0	0	0	0
	Cohort Time	0	0	0	0	0	0	0	0
	CT 1 yr	0	0	0	0	0	0	0	0
	CT ext 60	0	0	0	0	0	0	0	0
	Unr drugs	0	0	0	0	0	0	0	0
Cancer death (excluding lungcancer)	Total FU	0	0	0	0	0	0	0	0
	Cohort Time	0	0	0	0	0	0	0	0
	CT 1 yr	0	0	0	0	0	0	0	0
	CT ext 60	0	0	0	0	0	0	0	0
	Unr drugs	0	0	0	0	0	0	0	0

SIDIAP Endpoint	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA ICS	Fixed LABA LAMA	LABA	LAMA
Death due to other causes	Total FU	0	0	0	0	0	0	0	0
	Cohort Time	0	0	0	0	0	0	0	0
	CT 1 yr	0	0	0	0	0	0	0	0
	CT ext 60	0	0	0	0	0	0	0	0
	Unr drugs	0	0	0	0	0	0	0	0
Death with cause unknown	Total FU	369	306	186	252	1625	36	334	822
	Cohort Time	80	20	5	18	300	12	40	121
	CT 1 yr	69	19	5	18	273	11	38	115
	CT ext 60	109	23	7	27	405	19	51	169
	Unr drugs	75	19	5	19	277	11	46	143

CV= cardiovascular, MI= myocardial infarction, Hosp= hospitalization, HF= heart failure, ACS= acute coronary syndrome, AP= Angina Pectoris, Vent tach= Ventricular tachycardia, Vent fibr= Ventricular fibrillation, TDP= Torsade de Pointes, A Flut= atrial flutter, A Fibr= Atrial f brillation, AV block= atrioventricular block, SVT= Supraventricular tachycardia, Premat Dep= Premature Depolarisation, TIA= Transient Ischemic Attack, Blad obstr= Bladder obstruction, UR= urinary retention, BPH= incident Benign Prostatic Hyperplasia

Table 15-10 Cause-specific death (THIN, IPCI, Aarhus)

Mortality in THIN	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA+ICS	Fixed LABA+LAMA	LABA	LAMA
Mortality	CT 1 yr	61 (100%)	27 (100%)	4 (100%)	8 (100%)	626 (100%)	102 (100%)	48 (100%)	297 (100%)
Cardiovascular death[¤]	CT 1 yr	2 (66.7%)	1 (100%)	0 (0%)	0 (0%)	6 (37.5%)	1 (100%)	1 (33.3%)	4 (30.8%)
Respiratory death[¤]	CT 1 yr	0 (0%)	0 (0%)	0 (0%)	0 (0%)	5 (31.3%)	0 (0%)	1 (33.3%)	6 (46.2%)
Cardiovascular and respiratory death[¤]	CT 1 yr	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (6.3%)	0 (0%)	0 (0%)	0 (0%)
Cerebrovascular death[¤]	CT 1 yr	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Cancer death (excluding lungcancer)[¤]	CT 1 yr	0 (0%)	0 (0%)	0 (0%)	0 (0%)	3 (18.8%)	0 (0%)	0 (0%)	2 (15.4%)
Death due to other causes[¤]	CT 1 yr	1 (33.3%)	0 (0%)	0 (0%)	0 (0%)	1 (6.3%)	0 (0%)	1 (33.3%)	1 (7.7%)
Death with cause unknown[¥]	CT 1 yr	58 (95.1%)	26 (96.3%)	4 (100%)	8 (100%)	611 (97.6%)	101 (99%)	45 (93.8%)	285 (96%)

Mortality in IPCI	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA+ICS	Fixed LABA+LAMA	LABA	LAMA
Mortality	CT 1 yr	15 (100%)	23 (100%)	6 (100%)	13 (100%)	161 (100%)	19 (100%)	32 (100%)	77 (100%)
Cardiovascular death[x]	CT 1 yr	1 (10%)	6 (30%)	0 (0%)	1 (11.1%)	20 (16.3%)	1 (7.1%)	4 (18.2%)	8 (12.1%)
Respiratory death[x]	CT 1 yr	5 (50%)	6 (30%)	1 (20%)	6 (66.7%)	61 (49.6%)	7 (50%)	10 (45.5%)	27 (40.9%)
Cardiovascular and respiratory death[x]	CT 1 yr	1 (10%)	3 (15%)	2 (40%)	0 (0%)	13 (10.6%)	1 (7.1%)	0 (0%)	8 (12.1%)
Cerebrovascular death[x]	CT 1 yr	0 (0%)	0 (0%)	0 (0%)	1 (11.1%)	3 (2.4%)	1 (7.1%)	1 (4.5%)	2 (3%)
Cancer death (excluding lungcancer)[x]	CT 1 yr	2 (20%)	2 (10%)	1 (20%)	1 (11.1%)	16 (13%)	0 (0%)	4 (18.2%)	14 (21.2%)
Death due to other causes[x]	CT 1 yr	1 (10%)	3 (15%)	1 (20%)	0 (0%)	10 (8.1%)	4 (28.6%)	3 (13.6%)	7 (10.6%)
Death with cause unknown[¥]	CT 1 yr	5 (33.3%)	3 (13%)	1 (16.7%)	4 (30.8%)	38 (23.6%)	5 (26.3%)	10 (31.3%)	11 (14.3%)

Mortality in Aarhus	Time period	QVA149	Free LABA+LAMA without ICS	Free LABA+LAMA with ICS	Free LABA+ICS	Fixed LABA+ICS	Fixed LABA+LAMA	LABA	LAMA
Mortality	CT 1 yr	103 (100%)	16 (100%)	2 (100%)	5 (100%)	216 (100%)	75 (100%)	25 (100%)	86 (100%)
Cardiovascular death	CT 1 yr	18 (24.3%)	2 (13.3%)	0 (0%)	0 (0%)	30 (18.1%)	2 (16.7%)	2 (12.5%)	14 (21.5%)
Respiratory death	CT 1 yr	27 (36.5%)	8 (53.3%)	2 (100%)	2 (50%)	58 (34.9%)	2 (16.7%)	6 (12.5%)	20 (30.8%)
Cardiovascular and respiratory death	CT 1 yr	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (12.5%)	0 (0%)
Cerebrovascular death	CT 1 yr	0 (0%)	0 (0%)	0 (0%)	0 (0%)	4 (2.4%)	2 (16.7%)	1 (12.5%)	6 (9.2%)
Cancer death (excluding lungcancer)	CT 1 yr	7 (9.5%)	1 (6.7%)	0 (0%)	1 (25%)	18 (10.8%)	2 (16.7%)	3 (12.5%)	10 (15.4%)
Death due to other causes	CT 1 yr	22 (29.7%)	4 (26.7%)	0 (0%)	1 (25%)	56 (33.7%)	4 (33.3%)	4 (12.5%)	15 (23.1%)
Death with cause unknown	CT 1 yr	31 (30.1%)	1 (6.3%)	0 (0%)	1 (20%)	51 (23.6%)	64 (85.3%)	9 (36%)	22 (25.6%)

¥: percentage of total death. ¥ Percentage of death for which cause is known Respiratory death includes death due to lung cancer. Cancer death excludes death due to lung cancer.

Table 15-11 Crude hazard ratios for QVA versus comparators (Model 0), pooled analysis

Pooled dataset	QVA compared to Free LABA+LAMA without ICS			QVA compared to Free LABA+LAMA with ICS		
Endpoint	HR	95% CI	P	HR	95% CI	P
MACE	1.18	[0.94,1.47]	0.1588	0.98	[0.70,1.37]	0.9210
Ischemic heart disease	1.09	[0.71,1.66]	0.6928	0.80	[0.43,1.49]	0.4840
Cardiac arrhythmia	0.95	[0.66,1.37]	0.7846	0.73	[0.44,1.20]	0.2165
Cerebrovascular disorders	1.59	[0.96,2.63]	0.0740	0.76	[0.41,1.42]	0.3923
Glaucoma	0.69	[0.33,1.45]	0.3274	0.47	[0.18,1.26]	0.1354
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	0.99	[0.68,1.42]	0.9416	1.01	[0.58,1.75]	0.9843
Diabetes mellitus	1.10	[0.76,1.59]	0.6268	1.38	[0.74,2.58]	0.3117
Bronchospasm	.	[. , .]	.	.	[. , .]	.
Mortality	1.76	[1.36,2.28]	<.0001	1.99	[1.22,3.23]	0.0058

MACE=Major Adverse Cardiovascular Event

Pooled dataset	QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
Endpoint	HR	95% CI	P	HR	95% CI	P
MACE	0.99	[0.74,1.33]	0.9512	0.87	[0.76,1.00]	0.0534
Ischemic heart disease	0.98	[0.53,1.81]	0.9572	1.10	[0.83,1.47]	0.5003
Cardiac arrhythmia	0.77	[0.49,1.21]	0.2578	0.73	[0.57,0.93]	0.0118
Cerebrovascular disorders	0.79	[0.44,1.41]	0.4210	1.08	[0.79,1.49]	0.6197
Glaucoma	.	[. , .]	.	0.85	[0.47,1.51]	0.5744
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	1.52	[0.86,2.70]	0.1525	0.94	[0.73,1.22]	0.6530
Diabetes mellitus	1.73	[0.94,3.18]	0.0786	0.91	[0.70,1.18]	0.4770
Bronchospasm	0.32	[0.10,1.05]	0.0592	0.44	[0.19,1.05]	0.0647
Mortality	1.05	[0.75,1.46]	0.7696	0.81	[0.70,0.94]	0.0055

MACE=Major Adverse Cardiovascular Event

Pooled dataset	QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint	HR	95% CI	P	HR	95% CI	P
MACE	1.01	[0.83,1.24]	0.9158	1.39	[1.13,1.71]	0.0021
Ischemic heart disease	1.64	[1.09,2.46]	0.0166	1.43	[0.95,2.15]	0.0865
Cardiac arrhythmia	0.81	[0.57,1.15]	0.2437	1.24	[0.87,1.77]	0.2356
Cerebrovascular disorders	1.24	[0.81,1.89]	0.3296	1.08	[0.71,1.63]	0.7174
Glaucoma	0.93	[0.34,2.54]	0.8817	0.70	[0.34,1.43]	0.3226
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	1.18	[0.75,1.86]	0.4649	0.96	[0.69,1.33]	0.8051
Diabetes mellitus	0.80	[0.53,1.21]	0.2918	1.35	[0.94,1.94]	0.1039
Bronchospasm	.	[. , .]	.	0.89	[0.28,2.81]	0.8364
Mortality	1.41	[1.15,1.73]	0.0010	1.42	[1.14,1.76]	0.0014

MACE=Major Adverse Cardiovascular Event

Pooled dataset	QVA compared to LAMA		
Endpoint	HR	95% CI	P
MACE	0.99	[0.84,1.15]	0.8586
Ischemic heart disease	1.08	[0.79,1.47]	0.6301
Cardiac arrhythmia	0.77	[0.59,1.01]	0.0579
Cerebrovascular disorders	1.03	[0.73,1.44]	0.8794
Glaucoma	0.54	[0.30,0.98]	0.0436
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	0.89	[0.68,1.16]	0.3782
Diabetes mellitus	1.11	[0.84,1.47]	0.4691
Bronchospasm	1.17	[0.43,3.16]	0.7616
Mortality	1.20	[1.02,1.42]	0.0303

MACE=Major Adverse Cardiovascular Event

Table 15-12 Adjusted hazard ratios for QVA versus comparators (Model 1), pooled analysis

Pooled dataset	QVA compared to Free LABA+LAMA without ICS			QVA compared to Free LABA+LAMA with ICS		
Endpoint	HR	95% CI	P	HR	95% CI	P
MACE	1.19	[0.94,1.49]	0.1421	0.98	[0.70,1.37]	0.9041
Ischemic heart disease	1.09	[0.72,1.67]	0.6823	0.74	[0.40,1.38]	0.3492
Cardiac arrhythmia	0.96	[0.67,1.39]	0.8459	0.75	[0.45,1.24]	0.2582
Cerebrovascular disorders	1.62	[0.97,2.69]	0.0628	0.74	[0.40,1.38]	0.3438
Glaucoma	0.69	[0.33,1.46]	0.3352	0.50	[0.19,1.34]	0.1667
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	1.00	[0.69,1.44]	0.9942	0.97	[0.55,1.69]	0.9070
Diabetes mellitus	1.10	[0.76,1.59]	0.6166	1.37	[0.73,2.57]	0.3206
Bronchospasm	.	[. , .]	.	.	[. , .]	.
Mortality	1.71	[1.32,2.22]	<.0001	1.93	[1.18,3.15]	0.0083

MACE=Major Adverse Cardiovascular Event

Pooled dataset	QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
Endpoint	HR	95% CI	P	HR	95% CI	P
MACE	0.97	[0.71,1.30]	0.8170	0.85	[0.73,0.97]	0.0201
Ischemic heart disease	0.93	[0.50,1.73]	0.8114	1.07	[0.81,1.43]	0.6284
Cardiac arrhythmia	0.76	[0.47,1.22]	0.2575	0.72	[0.56,0.92]	0.0091
Cerebrovascular disorders	0.76	[0.42,1.38]	0.3670	1.06	[0.77,1.46]	0.7117
Glaucoma	.	[. , .]	.	0.88	[0.49,1.58]	0.6716
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	1.32	[0.74,2.35]	0.3549	0.83	[0.64,1.07]	0.1506
Diabetes mellitus	1.64	[0.88,3.05]	0.1201	0.85	[0.66,1.11]	0.2337
Bronchospasm	0.37	[0.11,1.29]	0.1183	0.49	[0.21,1.17]	0.1079
Mortality	0.99	[0.71,1.40]	0.9753	0.79	[0.69,0.92]	0.0018

MACE=Major Adverse Cardiovascular Event

Pooled dataset	QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint	HR	95% CI	P	HR	95% CI	P
MACE	0.99	[0.81,1.21]	0.9102	1.31	[1.05,1.63]	0.0160
Ischemic heart disease	1.64	[1.09,2.46]	0.0171	1.46	[0.96,2.23]	0.0760
Cardiac arrhythmia	0.79	[0.56,1.12]	0.1913	1.16	[0.80,1.69]	0.4246
Cerebrovascular disorders	1.22	[0.80,1.87]	0.3542	1.09	[0.71,1.66]	0.7012
Glaucoma	0.92	[0.34,2.53]	0.8745	0.73	[0.35,1.53]	0.4016
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	1.13	[0.72,1.78]	0.5913	0.86	[0.61,1.21]	0.3955
Diabetes mellitus	0.80	[0.53,1.21]	0.2948	1.30	[0.89,1.89]	0.1737
Bronchospasm	.	[. , .]	.	0.94	[0.27,3.23]	0.9160
Mortality	1.35	[1.10,1.66]	0.0043	1.22	[0.98,1.53]	0.0773

MACE=Major Adverse Cardiovascular Event

Pooled dataset	QVA compared to LAMA		
Endpoint	HR	95% CI	P
MACE	0.92	[0.79,1.08]	0.3251
Ischemic heart disease	1.06	[0.77,1.45]	0.7191
Cardiac arrhythmia	0.75	[0.57,0.99]	0.0406
Cerebrovascular disorders	1.00	[0.71,1.40]	0.9979
Glaucoma	0.55	[0.30,1.02]	0.0561
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	0.79	[0.60,1.05]	0.1047
Diabetes mellitus	1.03	[0.78,1.38]	0.8170
Bronchospasm	1.19	[0.43,3.33]	0.7377
Mortality	1.09	[0.92,1.29]	0.3396

MACE=Major Adverse Cardiovascular Event

Table 15-13 Hazard ratios for QVA versus comparators, IPTW model, pooled analysis

Pooled dataset	QVA compared to Free LABA+LAMA without ICS			QVA compared to Free LABA+LAMA with ICS		
Endpoint	HR	95% CI	P	HR	95% CI	P
MACE	1.18	[0.93,1.51]	0.1796	0.94	[0.59,1.48]	0.7784
Ischemic heart disease	1.22	[0.72,2.08]	0.4534	1.25	[0.64,2.44]	0.5039
Cardiac arrhythmia	1.31	[0.81,2.10]	0.2655	0.93	[0.54,1.60]	0.7991
Cerebrovascular disorders	1.52	[0.91,2.55]	0.1125	0.53	[0.20,1.43]	0.2094
Glaucoma	0.60	[0.30,1.24]	0.1673	0.29	[0.09,0.94]	0.0383
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	0.95	[0.64,1.41]	0.8097	1.81	[0.66,4.95]	0.2499
Diabetes mellitus	1.02	[0.70,1.50]	0.9028	1.60	[0.80,3.19]	0.1826
Bronchospasm	.	[. , .]	.	.	[. , .]	.
Mortality	1.56	[1.16,2.08]	0.0030	3.04	[1.79,5.17]	<.0001

MACE=Major Adverse Cardiovascular Event

Pooled dataset	QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
Endpoint	HR	95% CI	P	HR	95% CI	P
MACE	0.95	[0.68,1.33]	0.7627	0.94	[0.80,1.10]	0.4256
Ischemic heart disease	1.20	[0.62,2.35]	0.5888	1.21	[0.87,1.70]	0.2604
Cardiac arrhythmia	0.68	[0.39,1.18]	0.1658	0.84	[0.59,1.19]	0.3209
Cerebrovascular disorders	0.76	[0.37,1.55]	0.4512	1.16	[0.80,1.70]	0.4365
Glaucoma	.	[. , .]	.	0.89	[0.47,1.70]	0.7273
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	1.58	[0.71,3.49]	0.2590	0.86	[0.62,1.20]	0.3736
Diabetes mellitus	1.78	[0.82,3.89]	0.1456	0.87	[0.64,1.17]	0.3518
Bronchospasm	0.32	[0.10,0.98]	0.0451	0.48	[0.20,1.14]	0.0971
Mortality	0.88	[0.57,1.37]	0.5823	0.75	[0.62,0.90]	0.0021

MACE=Major Adverse Cardiovascular Event

Pooled dataset	QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint	HR	95% CI	P	HR	95% CI	P
MACE	1.03	[0.80,1.32]	0.8385	1.05	[0.81,1.37]	0.6924
Ischemic heart disease	1.60	[0.98,2.62]	0.0621	1.31	[0.83,2.08]	0.2481
Cardiac arrhythmia	0.79	[0.53,1.17]	0.2400	1.23	[0.81,1.87]	0.3251
Cerebrovascular disorders	1.02	[0.58,1.79]	0.9523	1.08	[0.70,1.69]	0.7226
Glaucoma	1.05	[0.37,2.97]	0.9230	0.64	[0.29,1.42]	0.2759
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	1.08	[0.62,1.86]	0.7899	0.85	[0.60,1.20]	0.3439
Diabetes mellitus	0.76	[0.47,1.25]	0.2781	1.18	[0.81,1.72]	0.3861
Bronchospasm	.	[. , .]	.	0.79	[0.24,2.56]	0.6958
Mortality	1.47	[1.16,1.86]	0.0014	0.91	[0.69,1.21]	0.5236

MACE=Major Adverse Cardiovascular Event

Pooled dataset	QVA compared to LAMA		
Endpoint	HR	95% CI	P
MACE	0.97	[0.82,1.15]	0.6994
Ischemic heart disease	1.12	[0.80,1.58]	0.5085
Cardiac arrhythmia	0.79	[0.57,1.10]	0.1649
Cerebrovascular disorders	0.98	[0.68,1.42]	0.9292
Glaucoma	0.52	[0.27,1.02]	0.0563
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	0.79	[0.59,1.07]	0.1221
Diabetes mellitus	0.98	[0.72,1.32]	0.8856
Bronchospasm	0.92	[0.34,2.46]	0.8607
Mortality	0.93	[0.75,1.14]	0.4910

MACE=Major Adverse Cardiovascular Event

Table 15-14 Sensitivity analysis 1, 2 and 3 on pooled dataset

		QVA compared to Free LABA+LAMA without ICS			QVA compared to Free LABA+LAMA with ICS		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
MACE	Main	1.20	[0.94,1.53]	0.1390	0.94	[0.59,1.50]	0.8010
	Ext 60	1.20	[0.95,1.53]	0.1324	0.91	[0.58,1.42]	0.6741
	Unr drugs	1.20	[0.95,1.52]	0.1321	0.93	[0.59,1.46]	0.7623
	Naive	1.23	[0.83,1.83]	0.2979	1.71	[0.96,3.04]	0.0685
	Smoke Never¥	1.19	[0.93,1.52]	0.1694	0.91	[0.56,1.48]	0.7165
	COPD Severe MildΩ	1.19	[0.93,1.52]	0.1664	0.93	[0.59,1.48]	0.7703
	COPD Severe VSevπ	1.18	[0.92,1.51]	0.1831	0.93	[0.59,1.48]	0.7652
Ischemic heart disease	Main	1.22	[0.72,2.06]	0.4612	1.26	[0.65,2.44]	0.5002
	Ext 60	1.25	[0.75,2.10]	0.3922	1.40	[0.72,2.74]	0.3259
	Unr drugs	1.14	[0.69,1.88]	0.6017	1.26	[0.65,2.45]	0.4942
	Naive	0.75	[0.34,1.66]	0.4828	1.02	[0.39,2.66]	0.9627
	Smoke Never¥	1.24	[0.73,2.10]	0.4250	1.27	[0.65,2.46]	0.4877
	COPD Severe MildΩ	1.23	[0.73,2.09]	0.4338	1.31	[0.67,2.54]	0.4271
	COPD Severe VSevπ	1.21	[0.71,2.06]	0.4772	1.24	[0.64,2.42]	0.5258

Sensitivity analysis 1= No censoring at start of other drug (= unr drugs), sensitivity analysis 2= wash-out period of 60 days (=Ext 60), sensitivity analysis 3= analysis in naïve patients. ¥= In case of missing smoking, all missing data imputed with “never smoker”, Ω In case of missing spirometry, all missing spirometru data imputed with “COPD mild”, π In case of missing spirometry, all missing data imputed with “COPD very severe”. Mace= Major adverse cardiovascular event, VSev= Very severe

		QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
MACE	Main	0.98	[0.70,1.37]	0.8940	1.03	[0.88,1.20]	0.7122
	Ext 60	0.99	[0.72,1.36]	0.9444	1.02	[0.88,1.18]	0.8119
	Unr drugs	0.96	[0.70,1.33]	0.8275	1.02	[0.87,1.18]	0.8430
	Naive	1.31	[0.78,2.19]	0.3030	1.07	[0.79,1.45]	0.6829
	Smoke Never¥	0.98	[0.70,1.37]	0.9019	0.94	[0.80,1.10]	0.4232
	COPD Severe MildΩ	0.94	[0.67,1.31]	0.7104	0.94	[0.81,1.10]	0.4414
	COPD Severe VSevπ	0.97	[0.70,1.35]	0.8605	0.93	[0.79,1.08]	0.3361
Ischemic heart disease	Main	1.21	[0.62,2.37]	0.5672	1.23	[0.88,1.73]	0.2231
	Ext 60	1.42	[0.73,2.75]	0.3063	1.21	[0.88,1.67]	0.2370
	Unr drugs	1.10	[0.58,2.08]	0.7659	1.17	[0.84,1.63]	0.3634
	Naive	1.83	[0.61,5.52]	0.2841	1.03	[0.62,1.71]	0.9134
	Smoke Never¥	1.29	[0.67,2.50]	0.4505	1.23	[0.88,1.72]	0.2337
	COPD Severe MildΩ	1.07	[0.55,2.10]	0.8382	1.20	[0.86,1.67]	0.2856
	COPD Severe VSevπ	1.26	[0.65,2.41]	0.4941	1.21	[0.87,1.69]	0.2625

Sensitivity analysis 1= No censoring at start of other drug (= unr drugs), sensitivity analysis 2= wash-out period of 60 days (=Ext 60), sensitivity analysis 3= analysis in naïve patients. ¥= In case of missing smoking, all missing data imputed with “never smoker”, Ω In case of missing spirometry, all missing spirometru data imputed with “COPD mild”, π In case of missing spirometry, all missing data imputed with “COPD very severe”. Mace= Major adverse cardiovascular event, VSev= Very severe

		QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
MACE	Main	1.03	[0.80,1.32]	0.8342	1.05	[0.81,1.37]	0.6932
	Ext 60	0.99	[0.78,1.27]	0.9599	1.06	[0.83,1.36]	0.6330
	Unr drugs	1.02	[0.80,1.31]	0.8615	0.91	[0.72,1.15]	0.4415
	Naive	1.28	[0.85,1.93]	0.2424	1.30	[0.93,1.81]	0.1265
	Smoke Never¥	1.02	[0.80,1.32]	0.8484	1.06	[0.82,1.38]	0.6585
	COPD Severe MildΩ	0.96	[0.73,1.26]	0.7719	1.06	[0.83,1.35]	0.6472
	COPD Severe VSevπ	0.99	[0.76,1.27]	0.9087	1.06	[0.84,1.35]	0.6211
Ischemic heart disease	Main	1.61	[0.98,2.65]	0.0610	1.27	[0.80,2.01]	0.3070
	Ext 60	1.56	[0.97,2.52]	0.0653	1.18	[0.78,1.79]	0.4406
	Unr drugs	1.51	[0.94,2.42]	0.0914	1.16	[0.77,1.76]	0.4709
	Naive	1.53	[0.42,5.58]	0.5222	1.17	[0.61,2.24]	0.6382
	Smoke Never¥	1.60	[0.97,2.63]	0.0638	1.32	[0.83,2.10]	0.2381
	COPD Severe MildΩ	1.56	[0.94,2.57]	0.0833	1.28	[0.81,2.02]	0.2898
	COPD Severe VSevπ	1.60	[0.98,2.63]	0.0619	1.26	[0.80,1.98]	0.3279

Sensitivity analysis 1= No censoring at start of other drug (= unr drugs), sensitivity analysis 2= wash-out period of 60 days (=Ext 60), sensitivity analysis 3= analysis in naïve patients. ¥= In case of missing smoking, all missing data imputed with “never smoker”, Ω In case of missing spirometry, all missing spirometru data imputed with “COPD mild”, π In case of missing spirometry, all missing data imputed with “COPD very severe”. Mace= Major adverse cardiovascular event, VSev= Very severe

Endpoint	Analysis	QVA compared to LAMA HR	95% CI	P
MACE	Main	1.04	[0.88,1.23]	0.6430
	Ext 60	1.05	[0.89,1.23]	0.5898
	Unr drugs	0.98	[0.83,1.15]	0.8036
	Naive	1.19	[0.92,1.55]	0.1860
	Smoke Never¥	0.97	[0.81,1.15]	0.6945
	COPD Severe MildΩ	0.97	[0.82,1.15]	0.7246
	COPD Severe VSevπ	0.96	[0.81,1.13]	0.6402
Ischemic heart disease	Main	1.08	[0.77,1.52]	0.6365
	Ext 60	1.08	[0.79,1.50]	0.6194
	Unr drugs	1.05	[0.76,1.45]	0.7720
	Naive	1.39	[0.85,2.28]	0.1868
	Smoke Never¥	1.12	[0.79,1.57]	0.5295
	COPD Severe MildΩ	1.09	[0.78,1.52]	0.6158
	COPD Severe VSevπ	1.13	[0.80,1.58]	0.4924

Sensitivity analysis 1= No censoring at start of other drug (= unr drugs), sensitivity analysis 2= wash-out period of 60 days (=Ext 60), sensitivity analysis 3= analysis in naïve patients. ¥= In case of missing smoking, all missing data imputed with “never smoker”, Ω In case of missing spirometry, all missing spirometru data imputed with “COPD mild”, π In case of missing spirometry, all missing data imputed with “COPD very severe”. Mace= Major adverse cardiovascular event, VSev= Very severe

		QVA compared to Free LABA+LAMA without ICS			QVA compared to Free LABA+LAMA with ICS		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
Cardiac arrhythmia	Main	1.31	[0.82,2.10]	0.2654	0.94	[0.55,1.61]	0.8245
	Ext 60	1.23	[0.78,1.93]	0.3783	0.96	[0.56,1.63]	0.8668
	Unr drugs	1.40	[0.89,2.20]	0.1411	1.03	[0.61,1.75]	0.9088
	Naive	0.77	[0.43,1.39]	0.3883	1.35	[0.57,3.22]	0.4922
	Smoke Never¥	1.30	[0.81,2.10]	0.2724	0.95	[0.56,1.62]	0.8539
	COPD Severe MildΩ	1.31	[0.82,2.09]	0.2673	0.95	[0.56,1.63]	0.8520
	COPD Severe VSevπ	1.32	[0.82,2.10]	0.2529	0.93	[0.55,1.59]	0.7925
Cerebrovascular disorders	Main	1.55	[0.92,2.62]	0.0987	0.54	[0.20,1.48]	0.2310
	Ext 60	1.58	[0.96,2.60]	0.0719	0.55	[0.21,1.43]	0.2201
	Unr drugs	1.56	[0.94,2.61]	0.0872	0.52	[0.20,1.35]	0.1793
	Naive	1.66	[0.62,4.44]	0.3151	1.91	[0.56,6.57]	0.3017
	Smoke Never¥	1.53	[0.91,2.56]	0.1074	0.49	[0.17,1.39]	0.1788
	COPD Severe MildΩ	1.56	[0.93,2.60]	0.0929	0.53	[0.20,1.46]	0.2211
	COPD Severe VSevπ	1.55	[0.92,2.60]	0.0980	0.52	[0.19,1.41]	0.1974

Sensitivity analysis 1= No censoring at start of other drug (= unr drugs), sensitivity analysis 2= wash-out period of 60 days (=Ext 60), sensitivity analysis 3= analysis in naïve patients. ¥= In case of missing smoking, all missing data imputed with “never smoker”, Ω In case of missing spirometry, all missing spirometru data imputed with “COPD mild”, π In case of missing spirometry, all missing data imputed with “COPD very severe”. Mace= Major adverse cardiovascular event, VSev= Very severe

Endpoint	Analysis	QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
		HR	95% CI	P	HR	95% CI	P
Cardiac arrhythmia	Main	0.68	[0.39,1.18]	0.1714	0.84	[0.59,1.20]	0.3359
	Ext 60	0.64	[0.38,1.07]	0.0880	0.83	[0.59,1.15]	0.2566
	Unr drugs	0.71	[0.42,1.19]	0.1928	0.95	[0.68,1.32]	0.7487
	Naive	0.90	[0.41,1.98]	0.7896	0.75	[0.43,1.32]	0.3167
	Smoke Never¥	0.69	[0.40,1.19]	0.1835	0.84	[0.59,1.20]	0.3357
	COPD Severe MildΩ	0.68	[0.40,1.15]	0.1494	0.83	[0.59,1.18]	0.3007
	COPD Severe VSevπ	0.69	[0.40,1.19]	0.1852	0.82	[0.59,1.16]	0.2684
Cerebrovascular disorders	Main	0.77	[0.37,1.58]	0.4772	1.15	[0.78,1.68]	0.4807
	Ext 60	0.80	[0.41,1.56]	0.5051	1.09	[0.77,1.55]	0.6139
	Unr drugs	0.83	[0.40,1.72]	0.6216	1.10	[0.75,1.61]	0.6300
	Naive	0.94	[0.38,2.31]	0.8885	1.62	[0.60,4.39]	0.3434
	Smoke Never¥	0.79	[0.38,1.62]	0.5126	1.13	[0.78,1.64]	0.5038
	COPD Severe MildΩ	0.80	[0.38,1.67]	0.5544	1.19	[0.81,1.75]	0.3661
	COPD Severe VSevπ	0.78	[0.39,1.57]	0.4822	1.17	[0.81,1.69]	0.4175

Sensitivity analysis 1= No censoring at start of other drug (= unr drugs), sensitivity analysis 2= wash-out period of 60 days (=Ext 60), sensitivity analysis 3= analysis in naïve patients. ¥= In case of missing smoking, all missing data imputed with “never smoker”, Ω In case of missing spirometry, all missing spirometru data imputed with “COPD mild”, π In case of missing spirometry, all missing data imputed with “COPD very severe”. Mace= Major adverse cardiovascular event, VSev= Very severe

		QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
Cardiac arrhythmia	Main	0.79	[0.53,1.18]	0.2531	1.25	[0.83,1.89]	0.2878
	Ext 60	0.82	[0.56,1.20]	0.3073	1.11	[0.76,1.62]	0.6063
	Unr drugs	0.85	[0.58,1.25]	0.4042	1.15	[0.76,1.72]	0.5078
	Naive	0.52	[0.26,1.03]	0.0609	1.10	[0.63,1.91]	0.7460
	Smoke Never¥	0.79	[0.53,1.18]	0.2414	1.23	[0.82,1.86]	0.3185
	COPD Severe MildΩ	0.74	[0.48,1.12]	0.1545	1.25	[0.83,1.88]	0.2805
	COPD Severe VSevπ	0.76	[0.51,1.14]	0.1790	1.25	[0.83,1.89]	0.2819
Cerebrovascular disorders	Main	0.98	[0.56,1.73]	0.9572	1.09	[0.70,1.70]	0.7041
	Ext 60	0.98	[0.57,1.69]	0.9486	1.05	[0.70,1.58]	0.8147
	Unr drugs	0.94	[0.53,1.65]	0.8231	1.01	[0.65,1.58]	0.9600
	Naive	1.30	[0.57,2.98]	0.5351	0.98	[0.51,1.90]	0.9560
	Smoke Never¥	1.01	[0.58,1.78]	0.9634	1.08	[0.70,1.68]	0.7168
	COPD Severe MildΩ	0.98	[0.54,1.80]	0.9513	1.15	[0.73,1.79]	0.5492
	COPD Severe VSevπ	0.99	[0.55,1.77]	0.9610	1.10	[0.71,1.70]	0.6697

Sensitivity analysis 1= No censoring at start of other drug (= unr drugs), sensitivity analysis 2= wash-out period of 60 days (=Ext 60), sensitivity analysis 3= analysis in naïve patients. ¥= In case of missing smoking, all missing data imputed with “never smoker”, Ω In case of missing spirometry, all missing spirometru data imputed with “COPD mild”, π In case of missing spirometry, all missing data imputed with “COPD very severe”. Mace= Major adverse cardiovascular event, VSev= Very severe

		QVA compared to LAMA		
Endpoint	Analysis	HR	95% CI	P
Cardiac arrhythmia	Main	0.82	[0.59,1.13]	0.2193
	Ext 60	0.80	[0.59,1.08]	0.1475
	Unr drugs	0.89	[0.66,1.20]	0.4493
	Naive	0.83	[0.51,1.36]	0.4693
	Smoke Never¥	0.80	[0.58,1.11]	0.1853
	COPD Severe MildΩ	0.78	[0.57,1.07]	0.1223
	COPD Severe VSevπ	0.81	[0.58,1.13]	0.2181
Cerebrovascular disorders	Main	0.97	[0.67,1.40]	0.8539
	Ext 60	1.01	[0.71,1.42]	0.9740
	Unr drugs	0.92	[0.64,1.31]	0.6365
	Naive	0.82	[0.42,1.61]	0.5605
	Smoke Never¥	0.97	[0.67,1.40]	0.8676
	COPD Severe MildΩ	1.02	[0.70,1.47]	0.9313
	COPD Severe VSevπ	1.00	[0.69,1.44]	0.9977

Sensitivity analysis 1= No censoring at start of other drug (= unr drugs), sensitivity analysis 2= wash-out period of 60 days (=Ext 60), sensitivity analysis 3= analysis in naïve patients. ¥= In case of missing smoking, all missing data imputed with “never smoker”, Ω In case of missing spirometry, all missing spirometru data imputed with “COPD mild”, π In case of missing spirometry, all missing data imputed with “COPD very severe”. Mace= Major adverse cardiovascular event, VSev= Very severe

Endpoint	Analysis	QVA compared to Free LABA+LAMA without ICS			QVA compared to Free LABA+LAMA with ICS		
		HR	95% CI	P	HR	95% CI	P
Glaucoma	Main	0.61	[0.30,1.24]	0.1692	0.29	[0.09,0.94]	0.0384
	Ext 60	0.61	[0.31,1.21]	0.1612	0.28	[0.10,0.83]	0.0222
	Unr drugs	0.59	[0.29,1.19]	0.1419	0.29	[0.09,0.93]	0.0371
	Smoke Never¥	0.61	[0.30,1.24]	0.1688	0.29	[0.09,0.96]	0.0427
	COPD Severe MildΩ	0.61	[0.30,1.25]	0.1807	0.24	[0.06,0.90]	0.0349
	COPD Severe VSevπ	0.61	[0.30,1.25]	0.1766	0.28	[0.08,0.95]	0.0418
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	Main	0.94	[0.64,1.38]	0.7394	0.97	[0.54,1.73]	0.9200
	Ext 60	0.95	[0.65,1.37]	0.7700	1.01	[0.57,1.80]	0.9607
	Unr drugs	0.91	[0.62,1.34]	0.6339	0.96	[0.55,1.69]	0.8921
	Naive	1.42	[0.73,2.76]	0.2945	1.97	[0.79,4.87]	0.1437
	Smoke Never¥	0.95	[0.64,1.41]	0.7985	1.58	[0.63,3.94]	0.3254
	COPD Severe MildΩ	0.93	[0.63,1.37]	0.7167	1.86	[0.69,5.00]	0.2212
	COPD Severe VSevπ	0.94	[0.64,1.38]	0.7414	1.76	[0.66,4.68]	0.2541

Sensitivity analysis 1= No censoring at start of other drug (= unr drugs), sensitivity analysis 2= wash-out period of 60 days (=Ext 60), sensitivity analysis 3= analysis in naïve patients. ¥= In case of missing smoking, all missing data imputed with “never smoker”, Ω In case of missing spirometry, all missing spirometru data imputed with “COPD mild”, π In case of missing spirometry, all missing data imputed with “COPD very severe”. Mace= Major adverse cardiovascular event, VSev= Very severe

Endpoint	Analysis	QVA compared to Free LABA+ICS HR	95% CI	P	QVA compared to Fixed LABA ICS HR	95% CI	P
Glaucoma	Main	.	[. , .]	.	0.85	[0.44,1.63]	0.6236
	Ext 60	.	[. , .]	.	0.88	[0.49,1.58]	0.6717
	Unr drugs	.	[. , .]	.	0.83	[0.43,1.58]	0.5653
	Smoke Never¥	.	[. , .]	.	0.89	[0.46,1.69]	0.7142
	COPD Severe MildΩ	.	[. , .]	.	0.91	[0.48,1.71]	0.7671
	COPD Severe VSevπ	.	[. , .]	.	0.86	[0.46,1.62]	0.6475
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	Main	1.27	[0.65,2.46]	0.4841	0.80	[0.60,1.07]	0.1293
	Ext 60	1.45	[0.76,2.78]	0.2650	0.87	[0.67,1.14]	0.3205
	Unr drugs	0.85	[0.42,1.74]	0.6660	0.82	[0.62,1.08]	0.1543
	Naive	2.00	[0.87,4.63]	0.1038	1.30	[0.67,2.51]	0.4367
	Smoke Never¥	1.50	[0.70,3.20]	0.2923	0.85	[0.62,1.16]	0.3025
	COPD Severe MildΩ	1.48	[0.69,3.17]	0.3101	0.87	[0.63,1.20]	0.3942
	COPD Severe VSevπ	1.56	[0.73,3.31]	0.2489	0.84	[0.62,1.13]	0.2509

Sensitivity analysis 1= No censoring at start of other drug (= unr drugs), sensitivity analysis 2= wash-out period of 60 days (=Ext 60), sensitivity analysis 3= analysis in naïve patients. ¥= In case of missing smoking, all missing data imputed with “never smoker”, Ω In case of missing spirometry, all missing spirometru data imputed with “COPD mild”, π In case of missing spirometry, all missing data imputed with “COPD very severe”. Mace= Major adverse cardiovascular event, VSev= Very severe

		QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
Glaucoma	Main	1.05	[0.37,2.96]	0.9313	0.64	[0.29,1.42]	0.2730
	Ext 60	1.11	[0.43,2.88]	0.8310	0.74	[0.36,1.54]	0.4274
	Unr drugs	0.68	[0.23,2.01]	0.4820	0.70	[0.33,1.49]	0.3597
	Smoke Never¥	1.07	[0.38,3.02]	0.8992	0.64	[0.29,1.42]	0.2699
	COPD Severe MildΩ	1.00	[0.35,2.87]	0.9934	0.66	[0.30,1.46]	0.3028
	COPD Severe VSevπ	1.01	[0.36,2.82]	0.9923	0.64	[0.29,1.41]	0.2662
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	Main	1.07	[0.62,1.85]	0.8003	0.86	[0.60,1.21]	0.3775
	Ext 60	1.19	[0.70,2.03]	0.5239	0.92	[0.66,1.28]	0.6063
	Unr drugs	1.12	[0.66,1.90]	0.6825	0.76	[0.54,1.06]	0.1095
	Naive	0.56	[0.13,2.48]	0.4452	1.18	[0.69,2.02]	0.5461
	Smoke Never¥	1.08	[0.62,1.86]	0.7900	0.84	[0.60,1.19]	0.3379
	COPD Severe MildΩ	1.09	[0.64,1.86]	0.7604	0.84	[0.60,1.18]	0.3178
	COPD Severe VSevπ	1.09	[0.64,1.87]	0.7428	0.82	[0.58,1.14]	0.2398

Sensitivity analysis 1= No censoring at start of other drug (= unr drugs), sensitivity analysis 2= wash-out period of 60 days (=Ext 60), sensitivity analysis 3= analysis in naïve patients. ¥= In case of missing smoking, all missing data imputed with “never smoker”, Ω In case of missing spirometry, all missing spirometru data imputed with “COPD mild”, π In case of missing spirometry, all missing data imputed with “COPD very severe”. Mace= Major adverse cardiovascular event, VSev= Very severe

		QVA compared to LAMA		
Endpoint	Analysis	HR	95% CI	P
Glaucoma	Main	0.54	[0.28,1.05]	0.0706
	Ext 60	0.58	[0.32,1.05]	0.0741
	Unr drugs	0.54	[0.29,1.03]	0.0605
	Smoke Never¥	0.52	[0.27,1.01]	0.0543
	COPD Severe MildΩ	0.55	[0.28,1.07]	0.0763
	COPD Severe VSevπ	0.52	[0.27,1.00]	0.0504
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	Main	0.80	[0.59,1.08]	0.1378
	Ext 60	0.85	[0.65,1.12]	0.2575
	Unr drugs	0.77	[0.58,1.02]	0.0693
	Naive	1.05	[0.64,1.73]	0.8482
	Smoke Never¥	0.79	[0.58,1.06]	0.1160
	COPD Severe MildΩ	0.78	[0.58,1.04]	0.0887
	COPD Severe VSevπ	0.76	[0.57,1.02]	0.0633

Sensitivity analysis 1= No censoring at start of other drug (= unr drugs), sensitivity analysis 2= wash-out period of 60 days (=Ext 60), sensitivity analysis 3= analysis in naïve patients. ¥= In case of missing smoking, all missing data imputed with “never smoker”, Ω In case of missing spirometry, all missing spirometru data imputed with “COPD mild”, π In case of missing spirometry, all missing data imputed with “COPD very severe”. Mace= Major adverse cardiovascular event, VSev= Very severe

		QVA compared to Free LABA+LAMA without ICS			QVA compared to Free LABA+LAMA with ICS		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
Diabetes mellitus	Main	1.02	[0.70,1.50]	0.9192	1.60	[0.80,3.19]	0.1833
	Ext 60	0.99	[0.68,1.44]	0.9620	1.60	[0.80,3.18]	0.1837
	Unr drugs	1.01	[0.70,1.46]	0.9504	1.57	[0.81,3.02]	0.1791
	Naive	1.22	[0.66,2.26]	0.5233	2.01	[0.74,5.46]	0.1703
	Smoke Never¥	1.02	[0.70,1.50]	0.9065	1.64	[0.82,3.27]	0.1639
	COPD Severe MildΩ	1.03	[0.70,1.51]	0.8861	1.61	[0.81,3.22]	0.1736
	COPD Severe VSevπ	1.03	[0.70,1.52]	0.8703	1.60	[0.81,3.14]	0.1772
Bronchospasm	Main	.	[. , .]	.	.	[. , .]	.
	Ext 60	.	[. , .]	.	.	[. , .]	.
	Unr drugs	.	[. , .]	.	.	[. , .]	.
	Smoke Never¥	.	[. , .]	.	.	[. , .]	.
	COPD Severe MildΩ	.	[. , .]	.	.	[. , .]	.
	COPD Severe VSevπ	.	[. , .]	.	.	[. , .]	.

Sensitivity analysis 1= No censoring at start of other drug (= unr drugs), sensitivity analysis 2= wash-out period of 60 days (=Ext 60), sensitivity analysis 3= analysis in naïve patients. ¥= In case of missing smoking, all missing data imputed with “never smoker”, Ω In case of missing spirometry, all missing spirometru data imputed with “COPD mild”, π In case of missing spirometry, all missing data imputed with “COPD very severe”. Mace= Major adverse cardiovascular event, VSev= Very severe

Endpoint	Analysis	QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
		HR	95% CI	P	HR	95% CI	P
Diabetes mellitus	Main	1.79	[0.82,3.89]	0.1446	0.86	[0.63,1.16]	0.3255
	Ext 60	1.43	[0.71,2.89]	0.3157	0.84	[0.62,1.12]	0.2311
	Unr drugs	1.60	[0.78,3.25]	0.1975	0.88	[0.66,1.18]	0.4030
	Naive	1.92	[0.80,4.60]	0.1437	1.16	[0.65,2.10]	0.6130
	Smoke Never¥	Smoke Never¥	[0.84,3.98]	0.1266	0.88	[0.65,1.20]	0.4223
	COPD Severe MildΩ	COPD Severe MildΩ	[0.73,3.66]	0.2338	0.88	[0.65,1.19]	0.3988
	COPD Severe VSevπ	COPD Severe VSevπ	[0.82,3.80]	0.1448	0.89	[0.66,1.22]	0.4711
Bronchospasm	Main	0.32	[0.10,0.98]	0.0454	0.50	[0.21,1.19]	0.1153
	Ext 60	0.42	[0.15,1.19]	0.1030	0.59	[0.28,1.23]	0.1594
	Unr drugs	0.37	[0.13,1.06]	0.0634	0.61	[0.27,1.37]	0.2318
	Smoke Never¥	0.32	[0.10,0.97]	0.0441	0.48	[0.20,1.14]	0.0947
	COPD Severe MildΩ	0.33	[0.11,1.01]	0.0524	0.52	[0.22,1.22]	0.1343
	COPD Severe VSevπ	0.35	[0.12,1.04]	0.0581	0.53	[0.22,1.26]	0.1514

Sensitivity analysis 1= No censoring at start of other drug (= unr drugs), sensitivity analysis 2= wash-out period of 60 days (=Ext 60), sensitivity analysis 3= analysis in naïve patients. ¥= In case of missing smoking, all missing data imputed with “never smoker”, Ω In case of missing spirometry, all missing spirometru data imputed with “COPD mild”, π In case of missing spirometry, all missing data imputed with “COPD very severe”. Mace= Major adverse cardiovascular event, VSev= Very severe

		QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
Diabetes mellitus	Main	0.76	[0.47,1.24]	0.2703	1.18	[0.81,1.72]	0.3972
	Ext 60	0.76	[0.47,1.23]	0.2583	1.17	[0.81,1.68]	0.4027
	Unr drugs	0.80	[0.50,1.29]	0.3574	1.20	[0.84,1.71]	0.3150
	Naive	0.67	[0.35,1.31]	0.2449	1.38	[0.80,2.40]	0.2462
	Smoke Never¥	0.76	[0.47,1.24]	0.2732	1.19	[0.82,1.74]	0.3548
	COPD Severe MildΩ	0.75	[0.46,1.23]	0.2515	1.19	[0.83,1.73]	0.3450
	COPD Severe VSevπ	0.75	[0.45,1.22]	0.2446	1.15	[0.79,1.66]	0.4640
Bronchospasm	Main	.	[. , .]	.	0.79	[0.24,2.56]	0.6958
	Ext 60	0.39	[0.13,1.20]	0.1007	1.14	[0.38,3.41]	0.8140
	Unr drugs	0.40	[0.11,1.50]	0.1722	0.58	[0.19,1.79]	0.3411
	Smoke Never¥	.	[. , .]	.	0.80	[0.25,2.58]	0.7035
	COPD Severe MildΩ	.	[. , .]	.	0.83	[0.26,2.62]	0.7487
	COPD Severe VSevπ	.	[. , .]	.	0.78	[0.25,2.44]	0.6756

Sensitivity analysis 1= No censoring at start of other drug (= unr drugs), sensitivity analysis 2= wash-out period of 60 days (=Ext 60), sensitivity analysis 3= analysis in naïve patients. ¥= In case of missing smoking, all missing data imputed with “never smoker”, Ω In case of missing spirometry, all missing spirometru data imputed with “COPD mild”, π In case of missing spirometry, all missing data imputed with “COPD very severe”. Mace= Major adverse cardiovascular event, VSev= Very severe

Endpoint	Analysis	QVA compared to LAMA HR	95% CI	P
Diabetes mellitus	Main	0.97	[0.72,1.31]	0.8284
	Ext 60	0.94	[0.70,1.26]	0.6643
	Unr drugs	1.01	[0.75,1.34]	0.9700
	Naive	1.19	[0.73,1.96]	0.4857
	Smoke Never¥	0.99	[0.73,1.33]	0.9269
	COPD Severe MildΩ	1.00	[0.74,1.35]	0.9905
	COPD Severe VSevπ	0.98	[0.73,1.33]	0.9176
Bronchospasm	Main	0.98	[0.36,2.65]	0.9689
	Ext 60	1.17	[0.49,2.77]	0.7265
	Unr drugs	0.75	[0.30,1.89]	0.5454
	Smoke Never¥	0.92	[0.34,2.46]	0.8609
	COPD Severe MildΩ	1.01	[0.38,2.69]	0.9796
	COPD Severe VSevπ	0.97	[0.36,2.59]	0.9491

Sensitivity analysis 1= No censoring at start of other drug (= unr drugs), sensitivity analysis 2= wash-out period of 60 days (=Ext 60), sensitivity analysis 3= analysis in naïve patients. ¥= In case of missing smoking, all missing data imputed with “never smoker”, Ω In case of missing spirometry, all missing spirometru data imputed with “COPD mild”, π In case of missing spirometry, all missing data imputed with “COPD very severe”. Mace= Major adverse cardiovascular event, VSev= Very severe

Endpoint	Analysis	QVA compared to Free LABA+LAMA without ICS			QVA compared to Free LABA+LAMA with ICS		
		HR	95% CI	P	HR	95% CI	P
Mortality	Main	1.60	[1.19,2.14]	0.0016	3.11	[1.83,5.30]	<.0001
	Ext 60	1.64	[1.25,2.15]	0.0003	2.98	[1.81,4.93]	<.0001
	Unr drugs	1.63	[1.23,2.17]	0.0007	2.55	[1.43,4.56]	0.0016
	Naive	2.50	[0.97,6.46]	0.0583	5.62	[2.14,14.7]	0.0004
	Smoke Never¥	1.58	[1.18,2.11]	0.0020	3.04	[1.79,5.16]	<.0001
	COPD Severe MildΩ	1.56	[1.17,2.09]	0.0027	3.04	[1.79,5.17]	<.0001
	COPD Severe VSevπ	1.56	[1.17,2.08]	0.0026	3.02	[1.77,5.16]	<.0001

Sensitivity analysis 1= No censoring at start of other drug (= unr drugs), sensitivity analysis 2= wash-out period of 60 days (=Ext 60), sensitivity analysis 3= analysis in naïve patients. ¥= In case of missing smoking, all missing data imputed with “never smoker”, Ω In case of missing spirometry, all missing spirometru data imputed with “COPD mild”, π In case of missing spirometry, all missing data imputed with “COPD very severe”. Mace= Major adverse cardiovascular event, VSev= Very severe

Endpoint	Analysis	QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
		HR	95% CI	P	HR	95% CI	P
Mortality	Main	0.90	[0.58,1.40]	0.6519	0.79	[0.66,0.95]	0.0127
	Ext 60	0.82	[0.56,1.19]	0.2971	0.79	[0.68,0.93]	0.0052
	Unr drugs	0.95	[0.63,1.44]	0.8235	0.81	[0.67,0.97]	0.0230
	Naive	1.96	[0.77,4.98]	0.1585	1.20	[0.51,2.83]	0.6771
	Smoke Never¥	0.88	[0.57,1.36]	0.5801	0.75	[0.62,0.90]	0.0019
	COPD Severe MildΩ	0.89	[0.58,1.37]	0.6031	0.79	[0.65,0.94]	0.0101
	COPD Severe VSevπ	0.94	[0.62,1.42]	0.7600	0.76	[0.63,0.91]	0.0024

Sensitivity analysis 1= No censoring at start of other drug (= unr drugs), sensitivity analysis 2= wash-out period of 60 days (=Ext 60), sensitivity analysis 3= analysis in naïve patients. ¥= In case of missing smoking, all missing data imputed with “never smoker”, Ω In case of missing spirometry, all missing spirometru data imputed with “COPD mild”, π In case of missing spirometry, all missing data imputed with “COPD very severe”. Mace= Major adverse cardiovascular event, VSev= Very severe

		QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
Mortality	Main	1.53	[1.21,1.92]	0.0003	0.91	[0.69,1.21]	0.5250
	Ext 60	1.40	[1.13,1.74]	0.0019	0.96	[0.75,1.22]	0.7175
	Unr drugs	1.46	[1.17,1.82]	0.0007	0.79	[0.61,1.02]	0.0690
	Naive	1.62	[1.04,2.53]	0.0322	1.15	[0.68,1.94]	0.5965
	Smoke Never¥	1.47	[1.16,1.87]	0.0013	0.91	[0.68,1.20]	0.4976
	COPD Severe MildΩ	1.44	[1.13,1.84]	0.0034	0.97	[0.75,1.27]	0.8301
	COPD Severe VSevπ	1.43	[1.12,1.82]	0.0040	0.94	[0.73,1.22]	0.6441

Sensitivity analysis 1= No censoring at start of other drug (= unr drugs), sensitivity analysis 2= wash-out period of 60 days (=Ext 60), sensitivity analysis 3= analysis in naïve patients. ¥= In case of missing smoking, all missing data imputed with “never smoker”, Ω In case of missing spirometry, all missing spirometru data imputed with “COPD mild”, π In case of missing spirometry, all missing data imputed with “COPD very severe”. Mace= Major adverse cardiovascular event, VSev= Very severe

Table 15-15 Sensitivity analysis 4 – Analysis of total follow-up time (pooled analysis)

	QVA compared to Free LABA+LAMA					QVA compared to Fixed LABA+LAMA			
Endpoint	N events during QVA exposure	N events during Free LABA+LAMA exposure	HR	95% CI	P	N events during Fixed LABA+LAMA exposure	HR	95% CI	P
MACE	344	250	1.12	[0.95,1.32]	0.1684	216	0.97	[0.82,1.15]	0.7148
Ischemic heart disease	92	95	0.91	[0.68,1.21]	0.5066	90	0.89	[0.67,1.20]	0.4589
Cardiac arrhythmia	149	146	0.94	[0.75,1.19]	0.6091	103	0.93	[0.72,1.20]	0.5767
Cerebrovascular disorders	92	79	1.17	[0.87,1.59]	0.3061	68	1.16	[0.85,1.60]	0.3501
Glaucoma	31	29	1.03	[0.62,1.71]	0.9185	15	0.88	[0.47,1.64]	0.6886
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	140	135	0.99	[0.78,1.25]	0.9270	58	1.00	[0.73,1.36]	0.9971
Diabetes mellitus	85	109	0.81	[0.61,1.08]	0.1452	70	0.85	[0.62,1.18]	0.3312
Bronchospasm	18	14	1.26	[0.63,2.54]	0.5186	7	0.41	[0.17,0.99]	0.0479
Mortality	318	209	1.28	[1.07,1.53]	0.0056	261	0.91	[0.78,1.08]	0.2866

Total follow-up in years (not censored by events) with exposure to QVA was 9,715, to Free LABA+LAMA 8,682 and to Fixed LABA+LAMA 6,570

MACE=Major Adverse Cardiovascular Event

Annex 2.2 – Event definition

1. Major adverse cardiovascular events (MACE)

Note: The identified codes as documented in this annex will be reviewed by all databases prior to data-extraction. As coding might change over time, relevant codes might be updated during the course of the project.

MACE includes the following:

- ***myocardial infarction***
- ***stroke***
- ***hospitalization due to acute coronary syndrome and/or heart failure***

The definitions of myocardial infarction and stroke (and relevant disease codes) are described under items 4 and 6 of this annex, respectively.

Hospitalization due to acute coronary syndrome is defined as patients being hospitalized for reasons of 1) unstable angina pectoris or 2) myocardial infarction (ST segment elevation or non-ST segment elevation). The definition and disease specific codes for (unstable) angina pectoris and myocardial infarction are described under items 3-4 of this annex.

Patients will be identified within the different databases based on a combination of disease specific codes for either unstable angina pectoris or myocardial infarction in combination with codes related to hospitalization. Hospitalization will be retrieved either via linkage with hospital admission/discharge database (SIDIAP and Aarhus), combination of disease codes with information from hospital referral and discharge letters) (HSD and IPCI) or combination of disease codes with source codes (hospital discharge letters) (THIN).

Hospitalization due to heart failure is defined as patients hospitalized for reasons of heart failure. The definition and disease specific codes for heart failure are described under item 4 of this annex

Patients will be identified within the different databases based on a combination of disease specific codes for heart failure in combination with codes related to hospitalization. Hospitalization will be retrieved either via linkage with hospital admission/discharge database (SIDIAP and Aarhus), combination of disease codes with information from hospital referral and discharge letters) (HSD and IPCI) or combination of disease codes with source codes (hospital discharge letters) (THIN).

2. Ischemic heart disease

Ischemic heart disease or myocardial ischemia is a disease characterized by ischemia of the heart muscle, usually due to atherosclerosis of the coronary arteries.

For this study, ischemic heart disease as endpoint encompasses angina pectoris (both stable and unstable) and myocardial infarction.

3. Angina pectoris (eventtype=AP)(eventtype=UNSTABLEAP)

According to the guidelines of the European Heart Association; angina pectoris is described as chest discomfort due to myocardial ischemia associated with coronary artery disease. Anginal symptoms are regarded as stable if they have been occurring over several weeks without major deterioration. They typically occur in conditions associated with increased myocardial oxygen consumption. Angina is said to be unstable if pre-existing angina worsens abruptly for no apparent reason or when new angina develops at a relatively low work load or at rest (Fox et al., 2006, Thygesen et al., 2012).

The following concepts of disease have been mapped through the Unified Medical Language System (UMLS) for the outcomes of angina pectoris.

Terms	ICD10	ICD9CM	Read Codes	ICPC
Angina pectoris	I20*	413*	G33..	K74
Angina pectoris, unspecified	I20.9	413.9	G33z.	
Angina of effort	I20.8			
Anginal syndrome	I20.9			
Cardiac angina	I20.9			
Ischemic chest pain	I20.9		G33z400	
Ischemic heart disease			G3...00	
			G3...13	
			G310.11	
			G31y.00	
			G34..00	
			G3y..00	
			G3z..00	
			Gyu3.00	
			Gyu3000	
Stenocardia			G33z1	
Unstable angina	I20.0		G311.00	K74.01
			G311.13	
			G311100	
			G330000	
Crescendo angina	I20.0		G311.11	
Intermediate coronary syndrome	I20.0	411.1		K76.01
Acute coronary syndrome				
			G311500	
			G33z000	
Angina at rest			G311.14	
			G311200	
Impending infarction			G311.12	
			G311000	
			G311011	
			G311z00	

Terms	ICD10	ICD9CM	Read Codes	ICPC
			G312.00	
			G31y100	
			G31y200	
			G31y300	
			G31yz00	
Worsening angina			G311400	
Angina pectoris with documented spasm	I20.1		G31y000	
			G332.00	
Nocturnal angina			G330000	
Stable angina			G33z700	
Other forms of angina pectoris	I20.8		Gyu30	
Exercise induced angina			G33z300	
Refractory angina			G311300	
Frequency of angina			187..00	
H/O angina pectoris#			14A5.	
			14AJ.00	
Canadian Cardiovascular Society classification of angina			388E.00	
Cardiovascular Limitations and			388F.00	
Angina self-management plan agreed			661M000	
Angina self-management plan re			661N000	
Angina control			662K.00	
			662K000	
			662K100	
			662K200	
			662K300	
			662Kz00	
Antianginal therapy			8B27.00	
Coronary artery bypass graft operation planned			8L40.00	
Coronary angioplasty planned			8L41.00	
Other chronic ischemic heart disease			G34..	

Not for acute event, will only be considered for angina pectoris as underlying comorbidity

4. Myocardial infarction (eventtype=MI)

Definition of Acute Myocardial Infarction (AMI)

Myocardial infarction is defined as necrosis of the myocardium caused by an obstruction of the blood supply to the heart (coronary circulation). Blockage of a coronary artery deprives the heart muscle of blood and oxygen, causing injury to the heart muscle Therefore, acute myocardial infarction is defined by the evidence of myocardial necrosis - in a clinical setting consistent with a) myocardial ischemia, including ST elevation b) myocardial infarction and c) non-ST elevation myocardial infarction. In this study, an acute MI event will be ascertained using specific diagnoses codes for acute transmural myocardial infarction, acute subendocardial myocardial infarction, or unspecified acute myocardial infarction (Thygesen et al., 2012).

The following concepts of disease have been mapped through the Unified Medical Language System (UMLS) for the outcomes of myocardial infarction.

Terms	ICD10	ICD9CM	Read Codes	ICPC
Cardiac infarction	I22*			
Cardiac infarction	I21*			
Acute myocardial infarction	I21*	410.*	G30z.	K75
Acute myocardial infarction, unspecified	I21.9	410.9		
Myocardial infarction (acute) NOS	I21.3	410		
Acute myocardial infarction, unspecified site, episode of care unspecified		410.90		
AMI NOS, unspecified		410.90		
Acute myocardial infarction, sub endocardial infarction		410.7		
Old myocardial infarction#	I25.2	412	G32..00	
Healed myocardial infarction#			G32..11	
Subsequent/recurrent myocardial infarction	I22		G35..	
Subsequent myocardial infarction of unspecified site	I22.9		Gyu36	
Subsequent myocardial infarction of other sites	I22.8		Gyu35 G353.	
Subsequent myocardial infarction of anterior wall	I22.0		G350.	
Subsequent myocardial infarction of inferior wall	I22.1		G351.]	
Subsequent acute sub endocardial myocardial infarction	I22.2			
Subsequent non transmural myocardial infarction NOS	I22.2			
Subsequent myocardial infarction (acute) NOS	I22.9			
Re-infarction of myocardium			G35..	
Acute sub endocardial myocardial infarction	I21.4			
Acute myocardial infarction, sub endocardial infarction, episode of care unspecified		410.70		
Non transmural myocardial infarction	I21.4			
Acute myocardial infarction, of antero lateral wall		410.0	G300.	
Acute antero septal myocardial infarction			G3011	
Acute inferior myocardial infarction		410.4	G308.00	
Acute myocardial infarction, true posterior wall infarction		410.6		
True posterior myocardial infarction			G306.	
Acute myocardial infarction, of inferoposterior wall		410.3	G303.]	
Other specified anterior myocardial infarction			G301.]	

Terms	ICD10	ICD9CM	Read Codes	ICPC
Acute transmural myocardial infarction of unspecified site	I21.3		Gyu34 G30X.00	
Acute transmural myocardial infarction of anterior wall	I21.0 122.0			
Acute transmural myocardial infarction of inferior wall	I21.1 I21.19 122.1			
Acute transmural myocardial infarction of other sites	I21.2 I21.29 122.8			
ECG: old myocardial infarction[#]			3232.	
Anterior myocard. infarct NOS		410.8	G301z	
Other acute myocardial infarct			G30y.	
Other acute myocardial inf.NOS			G30yz	
Inferior myocard. infarct NOS			G308.	
Acute myocardial infarction, of infero lateral wall		410.2	G302.	
Acute lateral myocardial infarction		410.5		
Lateral myocardial infarct NOS			G305.]	
Acute widespread myocardial infarction			X200S	
Acute posterior myocardial infarction		410.60 410.61 410.62		
Posterior myocard. infarct NOS			G304.]	
Silent myocardial infarct[#]			G30..17	
ECG: myocardial infarction			323..	
ECG: myocardial infarct NOS			323Z.	
Postoperative sub endocardial myocardial infarction			G384.00	
Postoperative myocardial infarction			G38z.00	
Acute anterior myocardial infarction		410.1		
Acute Q wave myocard infarct			G309.00	
Acute myocardial infarction, sub endocardial infarction		410.71 410.72		
Non-Q wave myocardial infarction NOS	I21.4 122.2			
Non-ST elevation (NSTEMI) myocardial infarction	I21.4 122.2			
History of MI[#]			14A3.00 14A4.00 14AH.00 14AT.00	K76.02
Diabetes mellitus insulin-glucose infuse acute myocardial infarct			889A.00	

[#] Not for acute event, will only be considered for angina pectoris as underlying comorbidity

5. Heart failure (eventtype=HF)

Definition of heart failure

HF is a syndrome in which the patients should have the following features: symptoms of HF, typically shortness of breath at rest or during exertion, and/or fatigue; signs of fluid retention such as pulmonary congestion or ankle swelling; and objective evidence of an abnormality of the structure or function of the heart at rest A clinical response to treatment directed at HF alone is not sufficient for the diagnosis, but is helpful when the diagnosis remains unclear after appropriate diagnostic investigations. Patients with HF would usually be expected to show some improvement in symptoms and signs in response to those treatments from which a relatively fast symptomatic improvement could be anticipated (e.g. diuretic or vasodilator administration) (Dickstein et al., 2008).

The following concepts of disease have been mapped through the Unified Medical Language System (UMLS) for heart failure.

Terms	ICD10	ICD9CM	Read Codes	ICPC
Heart failure	I50	428.*	G58..	K77
Heart failure, unspecified	I50.9	428.9		
Congestive heart failure	I50.0	428.0	G580.00	
Congestive heart disease	I50.9			
Left ventricular failure	I50.1	428.1	G581.00	
Acute heart failure			G582. G5800	
Admit heart failure emergency			8H2S.00	
Chronic congestive heart failure[#]			G5801	
H/O: heart failure[#]			14A6.00 14AM.00	
Hypertensive heart disease with (congestive) heart failure	I11.0	402.01 402.91	G21z011	
Hypertensive heart and renal disease with (congestive) heart failure	I13.0	402.11	G232.00	
Hypertensive heart and renal disease with both (congestive) heart failure and renal failure	I13.2	404.01 404.91		
Heart failure confirmed			1O1..00	
Heart failure management			661M500 661N500	
New York Heart Association classification - class II			662g.00	
New York Heart Association classification - class III			662h.00	
New York Heart Association classification - class IV			662i.00	
New York Heart Assoc classification heart failure symptoms				
Heart failure monitoring			662p.00 662T.00 662W.00 679W100	

Terms	ICD10	ICD9CM	Read Codes	ICPC
			679X.00	
			67D4.00	
			8CL3.00	
			8CMK.00	
Cardiac failure therapy			8B29.00	
Heart failure follow-up			8HBE.00	
			8HHb.00	
			8HHz.00	
			8Hk0.00	
			8HTL.00	
Heart failure quality indicators			9hH..00	
			9hH0.00	
			9hH1.00	
Cardiomegaly			G5y3.00	
Post cardiac operation heart failure NOS			G5y4z00	
Heart failure confirmed via echography			G5yy900	
			G5yyA00	
			G5yyC00	
Heart failure as a complication of care			SP11111	

[#] not for acute event, will only be considered for heart failure as underlying comorbidity

6. Stroke (eventtype=stroke)

Stroke is defined as rapidly developed clinical signs of focal (or global) disturbance of cerebral function lasting more than 24 hours (unless interrupted by surgery or death), with no apparent cause other than a vascular origin: it includes patients presenting clinical signs and symptoms suggestive of intracerebral haemorrhage or cerebral ischemic necrosis. It does not include transient cerebral ischemia or stroke events in cases of blood disease (e.g. leukemia, polycythaemia vera), brain tumour or brain metastases. Secondary stroke caused by trauma should also be excluded.

In this study, a stroke event is defined as any form of stroke due to haemorrhage (intracerebral) or infarction (i.e. ischemic) and stroke not specified as haemorrhage or infarction. Potential cases of acute stroke will be ascertained by specific and unspecific diagnosis codes (Goldstein et al., 2011).

The following concepts of disease have been mapped through the Unified Medical Language System (UMLS) for the outcomes of stroke.

Terms	ICD10	ICD9CM	Read Codes	ICPC
Stroke, not specified as hemorrhage or	I64			
Stroke NOS	I63.9			K90
Non-traumatic subarachnoidal bleeding	I60	430	G60..	
Intracerebral haemorrhage	I61	431	G61..	
Cerebrovascular accident (CVA)			G66..13	

Terms	ICD10	ICD9CM	Read Codes	ICPC
Stroke and cerebrovascular accident unspecified			G66..00	
Stroke NOS			G66..12	
Sequelae of stroke, not specified as hemorrhage or infarction#	I69	342	Gyu6C	
Brain stem stroke syndrome	G46.3		G663.	
Cerebellar stroke syndrome	G46.4		G664.	
Other and unspecified intracranial haemorrhage	I62	432.*	G62..00 G62z.00	
Cerebral infarction	I63		G64..	
Personal history of stroke#			ZV125	
Sequelae of stroke NOS#	I69.3			
H/O: Stroke§			14A7.00 14A7.11 14A7.12 14AK.00	
Cerebral infarct due to thrombosis of precerebral arteries		433*	G63y000 G63y000	
Personal history of transient ischemic attack (TIA), and cerebral infarction without residual deficits#	Z86.73	V12.54		
Management/monitoring of stroke			661M700 661N700 662e.00 662e.11 662M.00 662M100 662M200 662o.00 9Om..00 9Om0.00 9Om1.00 9Om2.00 9Om3.00 9Om4.00	
Delivery of rehabilitation for stroke			7P24200	
Stroke referral			8HBJ.00 8HTQ.00 8IEC.00	
Seen in stroke clinic			9N0p.00	
Quality indicators stroke			9h2..00 9h21.00 9h22.00	
Sequelae of cerebral infarction			G683.00	
Sequelae of stroke, not specified as haemorrhage or infarction#		438.*	G68X.00/Gyu6C00	
Cerebral infarction due unspecified occlusion/stenosis of pre-cerebral arteries		433.*	G6W..00/Gyu6300 G6X..00/Gyu6G00	

Terms	ICD10	ICD9CM	Read Codes	ICPC
Cerebral infarction due to unspecified occlusion/stenosis of cerebral arteries		434.*		
[X]Other cerebral infarction			Gyu6400	
[X]Occlusion and stenosis of other cerebral arteries			Gyu6600	
Discharge from stroke service			ZLEP.00	
Hemiplegia and hemiparesis		342.*		
Acute, but ill-defined, cerebrovascular disease		436.*		

not for acute event, will only be considered for stroke as underlying comorbidity

7. TIA (eventtype=TIA)

TIA is a transient episode of neurological dysfunction caused by focal brain, spinal cord, or retinal ischemia, without acute infarction (Easton et al., 2009).

The following concepts of disease have been mapped through the Unified Medical Language System (UMLS) for the outcomes of TIA.

Terms	ICD10	ICD9CM	Read Codes	ICPC
Transient cerebral ischemic attack, unspecified	G45.9			
TIA - Transient ischemic attack	G45	435.*	G65..12	K89
H/O: TIA			14AB.00	
			ZV12D00	
Amaurosis fugax			F423600	
Retinal transient arterial occlusion NOS			F423700	
Other transient cerebral ischemic attacks and related syndromes	G45.8		Fyu55	
Personal history of transient ischemic attack (TIA), and cerebral infarction without residual deficits#		V12.54		
Transient ischaemic attack clinical management plan			8CRB.00	
Transient cerebral ischaemia			G65..00	
Drop attack			G65..11	
Other transient cerebral ischaemia			G65y.00	
Transient cerebral ischaemia NOS			G65z.00	
Impending cerebral ischaemia			G65z000	
Intermittent cerebral ischaemia			G65z100	
Transient cerebral ischaemia NOS			G65zz00	

not for acute event, will only be considered for stroke as underlying comorbidity

8. Cardiac arrhythmia

Atrial flutter (AFL) (eventtype=AFIFLUT) is an abnormal heart rhythm that occurs in the atria of the heart. When it first occurs, it is usually associated with a fast heart rate or tachycardia (beats over 100 per minute). On ECG, AFL is defined as presence of flutter waves (Camm et al., 2010).

The following concepts of disease have been mapped through the Unified Medical Language System (UMLS) for the outcomes of atrial flutter.

Terms	ICD10	ICD9CM	Read Codes	ICPC
Atrial flutter		427.32	G5731	
Atrial fibrillation and flutter	I48	427.3	G573.	K78
Atrial fibrillation and flutter NOS			G573z	
Unspecified atrial fibrillation and atrial flutter	I48.9			
Type I atrial flutter	I48.3			
Type II atrial flutter	I48.4			
Atypical atrial flutter	I48.4			
Unspecified atrial flutter	I48.92			
ECG: atrial flutter			3273.00	
History of atrial flutter[#]			14AR.00	

[#] Not for acute event, will only be considered for atrial flutter as underlying comorbidity

Atrial fibrillation (AF) (eventtype=AFIFLUT) is the most common sustained cardiac arrhythmia, occurring in 1–2% of the general population. It is often associated with palpitations, fainting, chest pain, or congestive heart failure. By definition, the heart rate will be greater than 100 beats per minute. According to the ESC guidelines, the ECG shows absence of P waves, with disorganized electrical activity in their place, and irregular R-R intervals due to irregular conduction of impulses to the ventricles (Camm et al., 2010).

The following concepts of disease have been mapped through the Unified Medical Language System (UMLS) for the outcomes of atrial fibrillation.

Terms	ICD10	ICD9CM	Read Codes	ICPC
Atrial fibrillation		427.31	G5730	
Atrial fibrillation and flutter	I48	427.3	G573.	K78
Atrial fibrillation and flutter NOS			G573z	
Unspecified atrial fibrillation and atrial flutter	I48.9			
AF - Paroxysmal atrial fibrillation			G573200	K79.01
Chronic atrial fibrillation[#]	I48.2			
Persistent atrial fibrillation	I48.1		G573500	
Permanent atrial fibrillation	I48.2		G573400	
Non-rheumatic atrial fibrillation			G573300	
ECG: atrial fibrillation			3272.	
H/O: atrial fibrillation[#]			14AN.00	
Atrial fibrillation resolved[#]			212R.00	
Atrial fibrillation monitoring			662S.00	
			6A9..00	
			8HTy.00	
			9hF1.00	
			9Os..	

[#] Not for acute event, will only be considered for atrial fibrillation as underlying comorbidity

Ventricular tachycardia (*eventtype*=***VENTTACH***) is a rapid heartbeat that originates in one of the ventricles of the heart. To be classified as tachycardia, the heart rate is usually at least 100 beats per minute (Zipes et al., 2006).

Ventricular fibrillation (*eventtype*=***VENTFIBR***) is a very rapid, uncoordinated, ineffective series of contractions throughout the ventricles of the heart. Unless stopped, these chaotic impulses are fatal (Zipes et al., 2006).

Torsade de pointes *(eventtype=**TORSPOINT**)* is an uncommon and distinctive form of polymorphic ventricular tachycardia (VT) characterized by a gradual change in the amplitude and twisting of the QRS complexes around the isoelectric line. Torsade de pointes, is associated with a prolonged QT interval, which may be congenital or acquired. Torsade usually terminates spontaneously but frequently recurs and may degenerate into ventricular fibrillation (Zipes et al., 2006).

The following concepts of **ventricular arrhythmia** (ventricular tachycardia, ventricular fibrillation and Torsade de pointes) have been mapped through the Unified Medical Language System (UMLS).

Terms	ICD10	ICD9CM	Read Codes	ICPC
Ventricular tachycardia	I47.2		G571.11	K79.02
Paroxysmal ventricular tachycardia		427.1	G571.00	
ECG: ventricular tachycardia			3282.	
Ventricular fibrillation and flutter	I49.0	427.4	G574.	
ECG: ventricular fibrillation			3282.00	

Long QT syndrome (LQTS) (eventtype = LONGQT) is a congenital disorder characterized by a prolongation of the QT interval on electrocardiograms (ECGs) and a propensity to ventricular tachyarrhythmias, such as Torsade de Pointes, which may lead to syncope, cardiac arrest, or sudden death.

The following concepts of disease have been mapped through the Unified Medical Language System (UMLS) for the outcomes of long QT syndrome.

Terms	ICD10	ICD9CM	Read Codes	ICPC
Long QT syndrome	I45.81 147.2E	426.82	X202	
ECG: Q-T interval prolonged			32K3.00	

Supraventricular tachycardia (SVT) (eventtype =SVT) is a condition presenting as a rapid heart rhythm originating at or above the atrioventricular node. Supraventricular tachycardias can be contrasted with the potentially more dangerous ventricular tachycardias—rapid rhythms that originate within the ventricular tissue.

Although "SVT" can be due to any supraventricular cause, the term is most often used to refer to a specific example, paroxysmal supraventricular tachycardia (PSVT), two common types being atrioventricular reciprocating tachycardia and AV nodal reentrant tachycardia.

The following concepts of sinus tachycardia have been mapped through the Unified Medical Language System (UMLS).

Terms	ICD10	ICD9CM	Read Codes	ICPC
supraventricular tachycardia	I47.1			K79.01
paroxysmal supraventricular tachycardia		427.0		
paroxysmal tachycardia	147			K79
paroxysmal tachycardia, unspecified	147.9			
re-entry ventricular arrhythmia	147.0			
Wolf Parkinson White syndrome	145.6			
History of supraventricular tachycardia[#]			14AQ.00	
ECG: supraventricular arrhythmia			327..00	
Paroxysmal supraventricular tachycardia			G570.00	
ECG: paroxysmal atrial tachy.			3274.00	
ECG: supraventric. arryth. NOS			327Z.00	
Wolff-Parkinson-White syndrome			G567400	
Paroxysmal atrial tachycardia			G570000	
Paroxysmal atrioventricular tachycardia			G570100	
Paroxysmal atrioventricular tachycardia			G570100	
Paroxysmal junctional tachycardia			G570200	
Paroxysmal nodal tachycardia			G570300	
Paroxysmal supraventricular tachycardia NOS			G570z00	
Supraventricular tachycardia NOS			G57y900	
Re-entry ventricular arrhythmia			G57yA00	

[#] Not for acute event, will only be considered for SVT as underlying comorbidity

Sick Sinus Syndrome (eventtype=SICKSINUS) is characterized by dysfunction of the sinoatrial (SA) node that is often secondary to senescence of the SA node and surrounding atrial myocardium. It is characterized by chronic SA node dysfunction, a sluggish or absent SA nodal pacemaker after electrical electroversion, frequently depressed escape pacemakers, and/or atrioventricular (AV) nodal conduction disturbances. These abnormalities can result in profound sinus bradycardia, sinus pauses, sinus arrest, SA nodal exit block, and inappropriate responses to physiological demands during exercise or stress.

The following concepts of Sick Sinus Syndrome have been mapped through the Unified Medical Language System (UMLS).

Terms	ICD10	ICD9CM	Read Codes	ICPC
Sick sinus syndrome	149.5 I47.2E		G57y300	K79.02

Atrioventricular (AV) block (eventtype=AVBLOCK) is a partial or complete interruption of impulse transmission from the atria to the ventricles. The most common cause is idiopathic fibrosis and sclerosis of the conduction system. Diagnosis is by ECG; symptoms and treatment

depend on degree of block (first, second or third degree AV block), but treatment, when necessary, usually involves pacing.

The following concepts of atrioventricular block have been mapped through the Unified Medical Language System (UMLS).

Terms	ICD10	ICD9CM	Read codes	ICPC
Atrioventricular block, first degree	I44.0	426.11	G561311	
Atrioventricular block, complete	I44.2	426.0	G560.	
Third degree atrioventricular block			G560.	
Atrioventricular block, second degree	I44.1		G561400	
Other and unspecified atrioventricular block	I44.3	426.1	Gyu5U	
Unspecified atrioventricular block	I44.3	426.10	G561z	K84.02
			G5610	
Atrioventricular and left bundle-branch block	I44			
Mobitz (type) II atrioventricular block		426.12	G5612	
Other second degree atrioventricular block		426.13		
ECG: complete atrioventricular block			3298.	
Partial atrioventricular block			G561.	
ECG: partial atrioventricular block			3294.	
ECG: partial atrioventricular block - 2:1			3295.	
ECG: partial atrioventricular block - 3:1			3296.	
ECG: heart block			329..00	

Premature depolarization (eventtype=PREMATDEP) will include atrial premature depolarization, junctional premature depolarization and ventricular premature depolarization.

The following concepts of premature depolarization have been mapped through the Unified Medical Language System (UMLS).

Terms	ICD10	ICD9CM	Read codes	ICPC
Extrasystole	I49.4	427.6	G576z00	K80
	I49.40		G576011	
	I49.49			
Supraventricular extrasystole		427.61	G576100	K80.01
Ventricular extrasystole	I49.3		G576500	K80.02
			G576200	
Atrial premature depolarization	I49.1		G576300	
Junctional premature depolarization	I49.2		G576400	
[X]Other and unspecified premature depolarization			Gyu5Z00	
ECG: ectopic beats		427.6	326..00	
ECG: extrasystole			3262.00	
ECG: ventricular ectopics			3263.00	
ECG: atrial ectopics			3264.00	
ECG: ectopic beats NOS			326Z.00	
Ectopic beats			G576.00	
Premature beats			G576.11	
Ectopic beats unspecified			G576000	

9. Glaucoma (narrow angle glaucoma and other) (eventtype =NARGLAUC)

Definition of narrow angle glaucoma

Narrow angle glaucoma, also called acute angle closure glaucoma or closed angle glaucoma, is a rare type of glaucoma in which symptoms usually come on suddenly. Unlike most glaucoma, people with narrow angle glaucoma usually have severe symptoms including pain, blurry vision, redness and nausea. Some people also complain of seeing halos around lights.

Narrow angle glaucoma is caused by an acute blockage of the drainage canal where fluid normally flows freely out of the eye. A buildup of fluid causes a sudden increase in intraocular pressure.

Narrow angle glaucoma requires a quick diagnosis and rapid treatment, as significantly decreased vision or blindness can result within hours (Casson et al., 2012).

The following concepts of disease have been mapped through the Unified Medical Language System (UMLS) for the outcomes of narrow angle glaucoma.

Terms	ICD10	ICD9CM	Read Codes	ICPC
Anatomical narrow angle borderline glaucoma		365.02	F450200	
Acute angle-closure glaucoma	H40.21	365.22	F452	F93.02
Primary angle-closure glaucoma	H40.2		F452.00	
Closed angle glaucoma			F452.11	
Primary angle-closure glaucoma			F452..	
Glaucoma due to chamber angle anomaly			F454000	

Definitions of other glaucoma *(eventtype=OTHGLAUC)*

Open-angle glaucoma, the most common form of glaucoma, accounting for at least 90% of all glaucoma cases: It is caused by the slow clogging of the drainage canals, resulting in increased eye pressure. In contrast to narrow angle glaucoma, it has as wide and open angle between the iris and cornea. Open angle glaucoma develops slowly and is a lifelong condition and often has symptoms and eye damage that are not immediately noticed.

In normal tension glaucoma, the optic nerve is damaged even though the eye pressure is not very high.

The following concepts of disease have been mapped through the Unified Medical Language System (UMLS) for the outcomes of glaucoma.

Terms	ICD10	ICD9CM	Read Codes	ICPC
glaucoma	H40-H42.9	365	F45	F93
Glaucoma - absolute			F404211	
Glaucomatocyclitic crises			F442100	
[X]Glaucoma			FyuG.00	

10. Bladder obstruction/urinary retention/BPH

Definition of bladder obstruction/urinary retention *(eventtype=URINRETENTION)*

Urinary retention describes a bladder that does not empty completely or does not empty at all. Historically, urinary retention has been classified as either acute or chronic the latter is generally classified as high pressure or low pressure according to the bladder filling pressure on urodynamic (Verhamme et al., 2008).

Bladder outlet obstruction (BOO) is a blockage at the base of the bladder that reduces or prevents the flow of urine into the urethra, the tube that carries urine out of the body.Bladder outlet obstruction (BOO) can have many different causes, including benign prostatic hyperplasia (BPH), bladder stones, bladder tumors (cancer), pelvic tumors (cervix, prostate, uterus, rectum) and urethral stricture (scar tissue)

The following concepts of disease have been mapped through the Unified Medical Language System (UMLS) for the outcomes of urinary retention.

Terms	ICD10	ICD9CM	Read Codes	ICPC
Urinary Retention	R33	788.2 788.20	R082..	U05.02
Cannot pass urine - retention			1A32.00	
Acute retention of urine			R0822	
Retention symptoms			1A32.11	
Micturition stream poor			1A33.00	
Hesitancy			1A34.00	
Hesitancy of micturition			1A34.11	
BOO - Bladder outflow obstruction			K160.13	
Bladder outflow obstruction			K165200	
Bladder neck obstruction	N32.0	596.0		

Definition of BPH *(eventtype=BPH)*

Benign prostatic hyperplasia (BPH) is a histologic diagnosis that refers to the proliferation of smooth muscle and epithelial cells within the prostatic transition zone. The enlarged gland has been proposed to contribute to the overall lower urinary tract symptoms (LUTS) complex via at least two routes: (1) direct bladder outlet obstruction (BOO) from enlarged tissue (static component) and (2) from increased smooth muscle tone and resistance within the enlarged gland (dynamic component). Voiding symptoms have often been attributed to the physical presence of BOO. Detrusor overactivity is thought to be a contributor to the storage symptoms seen in LUTS.[Juliao, 2012 #127]

Terms	ICD10	ICD9CM	Read Codes	ICPC
Benign prostatic hypertrophy/ Benign prostatic hyperplasia	N40	600.0	K20*	Y85
Prostatic hyperplasia			K20z. K200.	
Benign neoplasm of prostate			B7C2.00	

11. Diabetes mellitus (eventtype=DM)

Definition of diabetes mellitus

Diabetes is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. The chronic hyperglycemia of diabetes is associated with long-term damage, dysfunction, and failure of different organs, especially the eyes, kidneys, nerves, heart, and blood vessels.

The vast majority of cases of diabetes fall into two broad etiopathogenetic categories (discussed in greater detail below). In one category, type 1 diabetes, the cause is an absolute deficiency of insulin secretion. Individuals at increased risk of developing this type of diabetes can often be identified by serological evidence of an autoimmune pathologic process occurring in the pancreatic islets and by genetic markers.

In the other, much more prevalent category, type 2 diabetes, the cause is a combination of resistance to insulin action and an inadequate compensatory insulin secretory response (ADA, 2012).

Criteria for the diagnosis of diabetes (based on lab results):

A1C ≥6.5%. The test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay.*

OR

FPG ≥126 mg/dl (7.0 mmol/l). Fasting is defined as no caloric intake for at least 8 h.*

OR

2-h plasma glucose ≥200 mg/dl (11.1 mmol/l) during an OGTT. The test should be performed as described by the World Health Organization, using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water.*

OR

In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥200 mg/dl (11.1 mmol/l).

*In the absence of unequivocal hyperglycemia, criteria 1–3 should be confirmed by repeat testing.

The following concepts of disease have been mapped through the Unified Medical Language System (UMLS) for diabetes mellitus.

Terms	ICD10	ICD9CM	Read Codes	ICPC
Diabetes mellitus	E10-E14.9	250	C10* Cyu2.00	T90
Diabetes mellitus due to underlying condition	E08			
Unspecified diabetes mellitus	E14			
diabetes NOS	E11			
Insulin-dependent diabetes mellitus	E10			
Non-insulin-dependent diabetes mellitus	E11			
Diabetes mellitus with ketoacidosis			C101. C101z	
Diabetes with renal manifestations		250.4		

Terms	ICD10	ICD9CM	Read Codes	ICPC
			C104z	
Nephrotic syndrome in diabetes mellitus			K01x1	
Diabetes with neurological manifestations		250.6		
Diabetes mellitus with neuropathy				
Unspecified diabetes mellitus without complications	E14.9	250.0	C100. C100z	
Secondary diabetes mellitus		249		
Diabetic mono/polyneuropathy	G63.2	357.2	F372* F3y0.00	
Diabetes with ophthalmic manifestations		250.5	C105. C105z 2BBF 7276.00 F420*	
Unspecified diabetes mellitus with unspecified complications	E14.8	250.9	C10z. C10zz	
History of diabetes mellitus			1434.00	
Diabetic foot			2G5*	
Diabetic monitoring			66A* 9OL*	

For those databases where information on lab results are available (THIN, HSD, SIDIAP and IPCI), a new diagnosis of diabetes mellitus will be made based on either the presence of diabetes mellitus disease codes and abnormal lab results (HbA1c, fasting plasma glucose, glucose tolerance test).

12. Bronchospasm (eventtype=BRONCHOSPASM)

Definition of bronchospasm

Bronchospasm is an abnormal contraction of the smooth muscle of the bronchi, resulting in an acute narrowing and obstruction of the respiratory airway. A cough with generalized wheezing usually indicates this condition. For this study, we are interested in bronchospasm as a result of administration of QVA149. As bronchospasm is much related to the indication of use, (paradoxal) bronchospasms will only be identified in those databases that allow free text validation (HSD, IPCI and SIDIAP). A free text search and a search on codes for bronchospasms will be done, maximum in the 1 month after start of QVA149 and the comparator medications. For those patients where potential hits have been identified, the complete medical file will be reviewed and only bronchospasms occurring short (within 1 hour) after administration of QVA149 (or comparators) will be considered. This manual validation will be conducted blinded to the treatment exposure.

Terms	ICD10	ICD9CM	Read Codes	ICPC
Acute bronchospasm	J98.01	519.11		
Dyspnea/shortness of breath				R02

13. Mortality (all-cause) (eventtype=DEATH)

Mortality will be assessed in the database either from the population table (death date and identification of death as reason for end of database follow-up) or via death specific codes. The following concepts of disease have been mapped through the Unified Medical Language System (UMLS) for the outcomes of death.

15.1.1.1 Terms	15.1.1.2 ICD10	15.1.1.3 ICD9CM	15.1.1.4 Read Codes	15.1.1.5 ICPC
Dead **Died** **Death** **Has died**			22J.	A96
Patient died at hospital			8HG	
Death administration			94.	
Instantaneous death	R96.0	798.1	R211. XM1AY Ua1q3	
Unattended death	R98	798.9	R213.	
Unattended death NOS			R213z	
Sudden cardiac death, so described	I46.1		G5751	
Other sudden death, cause unknown	R96	798	RyuC1 R21.. R21z. XM1Ac	
Death occurring less than 24 hours from onset of symptoms, not otherwise explained	R96.1	798.2	R212. R212z	

Annex 2.3 – Exposure definition – respiratory medication use

QVA149

	ATC code
QVA149	R03AL04

Concomitant use of other respiratory medications

Class of medication	ATC code	Description	UK	NL	DK	IT	SP
SAMA	R03BB01	Ipratropium bromide	x	x	x	x	x
	R03BB02	Oxitropium bromide	x	no	no	x	no
LAMA	R03BB04	Tiotropium bromide	x	x	x	x	x
	R03BB05	Aclidinium bromide	x	x	x	x	x
	R03BB06	Glycopyrronium bromide	x	x	x	x	x
	R03BB07	Umeclidinium bromide	x	x	x	x	x
SABA	R03AC02	Salbutamol	x	x	x	x	x
	R03AC03	Terbutaline	x	x	x	x	x
	R03AC04	Fenoterol	x	x	no	x	no
	R03AC05	Rimiterol	x	x	no	no	no
	R03AC06	Hexoprenaline	no	no	no	no	no
	R03AC07	Isoetarine	no	no	no	x	no
	R03AC08	Pirbuterol	x	no	no	no	no
	R03AC09	Tretoquinol	no	no	no	no	no
	R03AC10	Carbuterol	no	no	no	no	no
	R03AC15	Reproterol	x	no	no	no	no
	R03AC16	Procaterol	no	no	no	x	x
	R03AC17	Bitolterol	no	no	no	no	no
LABA	R03AC11	Tulobuterol	no	no	no	no	no
	R03AC12	Salmeterol	x	x	x	x	x
	R03AC13	Formoterol	x	x	x	x	x
	R03AC14	Clenbuterol	no	no	no	x	no
	R03AC18	Indacaterol	x	x	x	x	x
	R03AC19	Olodaterol	x	x	x	x	x
SABA+SAMA	R03AL01 ***(R03AK03 in past)***	Fenoterol and ipratropium bromide	x	x	x	x	no
	R03AL02 ***(R03AK04 in past)***	Salbutamol and ipratropium bromide	x	x	x	x	x
LABA+LAMA	R03AL03	Vilanterol and umeclidinium bromide	x	x	x	x	x
	R03AL04	Indacaterol and glycopyrronium bromide	x	x	x	x	x
	R03AL05	Formoterol and aclidinium bromide	x	x	x	x	x

Class of medication	ATC code	Description	UK	NL	DK	IT	SP
	R03AL06	Olodaterol and tiotropium bromide	x	x	x	x	no
LABA+ICS	R03AK06	Salmeterol and fluticasone	x	x	x	x	x
	R03AK07	Formoterol and budesonide	x	x	x	x	x
	R03AK08	Formoterol and beclomethasone	x	x	x	x	x
	R03AK09	Formoterol and momethasone	no	no	no	no	no
	R03AK10	Vilanterol and fluticasone furoate	x	x	x	x	x
	R03AK11	Formoterol and fluticasone	x	x	x	x	x
ICS	R03BA01	Beclometasone	x	x	x	x	x
	R03BA02	Budesonide	x	x	x	x	x
	R03BA03	Flunisolide	no	no	no	x	no
	R03BA04	Betamethasone	no	no	no	no	no
	R03BA05	Fluticasone	x	x	x	x	x
	R03BA06	Triamcinolone	no	no	no	no	no
	R03BA07	Mometasone	x	no	x	x	x
	R03BA08	Ciclesonide	x	x	x	x	x
	R03BA09	Fluticasone furoate	no	no	no	no	no
other fixed combinations	R03AK01	Epinephrine and other medications for obstructive airway diseases	no	no	no	no	no
	R03AK02	Isoprenaline and other medications for obstructive airway diseases	no	x	no	no	x
	R03AK04	Salbutamol and sodium cromoglicate	x	no	no	no	no
	R03AK05	Reproterol and sodium cromoglicate	no	no	no	no	no
xanthines	R03DA01	Diprophylline	no	no	no	x	no
	R03DA02	Choline theophyllinate	x	no	no	no	no
	R03DA03	Proxyphylline	no	no	no	no	no
	R03DA04	Theophylline	x	x	x	x	x
	R03DA05	Aminophylline	x	x	no	x	no
	R03DA06	Etamiphylline	no	no	no	no	x
	R03DA07	Theobromine	x	no	no	no	no
	R03DA08	Bamifylline	no	no	no	x	no
	R03DA09	Acefylline piperazine	no	no	no	no	no
	R03DA10	Bufylline	no	no	no	no	no
	R03DA11	Doxofylline	no	no	no	x	no
	R03DA20	Combinations of xanthines	no	no	no	no	no
	R03DA51	Diprophylline, combinations	no	no	no	no	no
	R03DA54	Theophylline, combinations excluding psycholeptics	no	no	no	no	no
	R03DA55	Aminophylline, combinations	no	no	no	no	no

Class of medication	ATC code	Description	UK	NL	DK	IT	SP
	R03DA57	Theobromine, combinations	no	no	no	no	no
	R03DA74	Theophylline, combinations with psycholeptics	no	no	no	no	no
Leukotriene receptor antagonists (LTRA)	R03DC01	Zafirlukast	x	no	no	x	x
	R03DC02	Pranlukast	no	no	no	no	no
	R03DC03	Montelukast	x	x	x	x	x
	R03DC04	Ibudilast	no	no	no	no	no
Oral phosphodiesterase-4 (PDE-4) inhibitors	R03DX07	roflumilast	x	x	x	x	x
Oral ß$_2$-adrenergic agonists	R03CC02	Salbutamol	x	x	x	x	x
	R03CC03	Terbutaline	x	x	x	no	x
	R03CC04	Fenoterol	no	x	no	x	x
	R03CC05	Hexoprenaline	no	no	no	no	no
	R03CC06	Isoetarine	no	no	no	no	no
	R03CC07	Pirbuterol	x	no	no	no	no
	R03CC08	Procaterol	no	no	no	no	no
	R03CC09	Tretoquinol	no	no	no	no	no
	R03CC10	Carbuterol	no	no	no	no	no
	R03CC11	Tulobuterol	x	no	no	no	no
	R03CC12	Bambuterol	x	no	x	no	x
	R03CC13	Clenbuterol	no	no	no	x	x
	R03CC14	Reproterol	no	no	no	no	no
	R03CC53	Terbutaline, combinations	no	no	no	no	no
	R03CC90	Clenbuterol, combinations	no	no	no	no	no
Systemic glucocorticosteroids	H02AB01	Betamethasone	x	x	x	x	x
	H02AB02	Dexamethasone	x	x	x	x	x
	H02AB03	Fluocortolone	no	no	no	x	no
	H02AB04	Methylprednisolone	x	x	x	x	x
	H02AB05	Paramethasone	no	no	no	no	x
	H02AB06	Prednisolone	x	x	x	x	x
	H02AB07	Prednisone	x	x	x	x	x
	H02AB08	Triamcinolone	x	x	x	x	x
	H02AB09	Hydrocortisone	x	x	x	x	x
	H02AB10	Cortisone	x	x	no	x	no
	H02AB11	Prednylidene	no	no	no	no	no
	H02AB12	Rimexolone	no	no	no	no	no
	H02AB13	Deflazacort	x	no	no	x	x
	H02AB14	Cloprednol	no	no	no	no	no
	H02AB15	Meprednisone	no	no	no	no	no

Class of medication	ATC code	Description	UK	NL	DK	IT	SP
	H02AB17	Cortivazol	no	no	no	no	no
	H02AB30	Combinations of glucocorticoids	no	no	no	no	no
	H02AB56	Prednisolone, combinations	no	no	no	no	no
	H02AB57	Prednisone, combinations	no	no	no	no	no
	H02AB90	Flumetasone	no	no	no	no	no

Annex 2.4 – COPD definition

According to GOLD (Global initiative of lung disease), COPD is a common preventable and treatable disease characterized by persistent airflow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the airways and the lung to noxious particles or gases. Exacerbations and comorbidities contribute to the overall severity in individual patients. A clinical diagnosis of COPD should be considered in any patient who has dyspnea, chronic cough or sputum production and/or a history of exposure to risk factors for the disease. Spirometry is required to make the diagnosis in this clinical context; the presence of a postbronchodilator FEV1/FVC < 0.70 confirms the presence of persistent airflow limitation and thus of COPD (GOLD 2016).

COPD will be identified within the databases both by COPD disease specific codes and via free text search for those databases where free text is available.

The following concepts of disease have been mapped through the Unified Medical Language System (UMLS) for the outcomes of COPD.

Terms	ICD10	ICD9CM	Read Codes	ICPC
Chronic obstructive pulmonary disease, unspecified	J44.9			R95
Chronic obstructive lung disease			H3*...	
Chronic obstructive airways disease			H3z..*	
Other chronic obstructive pulmonary disease	J44			
Other specified chronic obstructive pulmonary disease	J44.8		Hyu31*	
Other specified chronic obstructive airways disease			H3y..*	
Chronic obstructive pulmonary disease with acute exacerbation, unspecified	J44.1		H3y1.00*	
Mild chronic obstructive pulmonary disease			H36..00*	
Moderate chronic obstructive pulmonary disease			H37..00*	
Severe chronic obstructive pulmonary disease			H38..00*	

Terms	ICD10	ICD9CM	Read Codes	ICPC
Very severe chronic obstructive pulmonary disease			H39..00*	
chronic obstructive pulmonary disease and allied conditions		491.2 and 496		
Chronic obstructive pulmonary disease with acute lower respiratory infection	J44.0		H3y0.00.*	
COPD review/monitoring			66Y.*	
COPD quality indicators			9h5*	

*Read codes selected based on QoF codes for COPD as applied in the UK

COPD severity will be assessed at the index date for the three different exposure cohorts on the basis of spirometry data or on the basis of a severity classification if spirometry is not available.

- If spirometry is available:

Severity of COPD will be determined by spirometry, according to GOLD guidelines:

I. Mild COPD (GOLD stage I): $FEV_1/FVC<70\%$ and FEV_1 predicted > 80%
II. Moderate COPD (GOLD stage II): $FEV_1/FVC<70\%$ and $50\%<FEV_1\leq80\%$ predicted
III. Severe COPD (GOLD stage III): $FEV_1/FVC<70\%$ and $30\%<FEV_1\leq50\%$ predicted
IV. Very severe COPD (GOLD stage IV): $FEV_1/FVC<70\%$ and $FEV_1\leq30\%$ predicted or $FEV_1<50\%$ predicted and chronic respiratory failure.

Based on the suggestions/recommendations made by SAC (and subsequently endorsed by PRAC), COPD severity was assessed in all patients with information on FEV1 expected, even in patients with $FEV_1/FVC>=70\%$ and in patients with missing FVC; hence, severity was assessed as follows:

I. Mild COPD: FEV1 predicted > 80%
II. Moderate COPD: 50%<FEV1≤80% predicted
III. Severe COPD: 30%<FEV1≤50% predicted
IV. Very severe COPD: FEV1≤30% predicted or FEV1<50% predicted and chronic respiratory failure.

The most recently performed spirometry prior to the index date (for all cohorts) will be considered. In addition, in accordance with the updated GOLD guidelines (GOLD 2016),

patients will be further stratified upon the previous history of exacerbations (no, one or ≥ two exacerbations in the year prior to the index date [time of first prescription]) (Cazzola et al., 2011). A moderate COPD exacerbation is defined as need for oral corticosteroids and/or systemic antibiotics for COPD. A severe COPD exacerbation is defined as hospitalisation because of COPD exacerbation.

Since the COPD Assessment Test (CAT) is not performed routinely in clinical practice, and since a CAT score < 10 occurs only in the setting of screening programs in general populations, all patients will be considered as COPD GOLD B or D patients: COPD GOLD B if FEV1 > 50% AND a history of ≤ 1 exacerbation in the previous year; COPD GOLD D if FEV1 ≤ 50% OR a history of ≥ 2 exacerbations in the previous year.

- COPD severity by proxy

In all patients, COPD severity will also be categorized according to published literature on COPD severity scores using data from GP or health care databases. The COPD severity assessed closest to the index date (for all cohorts) will be considered.

1. Mild: Patients initially diagnosed with COPD
2. Moderate: Patients on regular treatment (defined as at least 2 prescriptions of the same medication group within 6 months) with inhaled/oral bronchodilators, xanthines or combination therapy. Patients are considered to have moderate COPD from the time of the second prescription onwards.
3. Severe: Patients with any of the following:
   - hospitalized for COPD during the past 365 days (prior to the index date)
   - requiring 3 or more courses of antibiotics for the treatment of respiratory infections in the past 365 days (prior to the index date)
   - two or more courses of systemic corticosteroids for the treatment of COPD exacerbations in the past 365 days (prior to the index date)
   - long term use of systemic corticosteroids in the past 365 days for the treatment of COPD (prior to the index date)
4. Very severe: Patients requiring chronic oxygen therapy.

Annex 2.5 – Concomitant medication use

- *Central nervous system medications (excl medications with anticholinergic effects)*

Use of opioids, hypnotics and sedatives, anxiolytics, antiepileptic medications, serotonin reuptake inhibitors.

Opioids **(N02A)**

N02AA Natural opium alkaloids
N02AA01 Morphine
N02AA02 Opium
N02AA03 Hydromorphone
N02AA04 Nicomorphine
N02AA05 Oxycodone
N02AA08 Dihydrocodeine
N02AA09 Diamorphine
N02AA10 Papaveretum
N02AA51 Morphine, combinations
N02AA55 Oxycodone, combinations
N02AA58 Dihydrocodeine, combinations
N02AA59 Codeine, combinations excluding psycholeptics
N02AA79 Codeine, combinations with psycholeptics
N02AB Phenylpiperidine derivatives
N02AB01 Ketobemidone
N02AB02 Pethidine
N02AB03 Fentanyl
N02AB52 Pethidine, combinations excluding psycholeptics
N02AB53 Fentanyl, combinations excluding psycholeptics
N02AB72 Pethidine, combinations with psycholeptics
N02AB73 Fentanyl, combinations with psycholeptics
N02AC Diphenylpropylamine derivatives
N02AC01 Dextromoramide
N02AC03 Piritramide
N02AC04 Dextropropoxyphene
N02AC05 Bezitramide
N02AC52 Methadone, combinations excluding psycholeptics
N02AC54 Dextropropoxyphene, combinations excluding psycholeptics
N02AC74 Dextropropoxyphene, combinations with psycholeptics
N02AD Benzomorphan derivatives
N02AD01 Pentazocine
N02AD02 Phenazocine
N02AE Oripavine derivatives

N02AE01 Buprenorphine
N02AE90 Etorphine
N02AE99 Oripavine derivatives, combinations
Morphinan derivatives
N02AF01 Butorphanol
N02AF02 Nalbuphine
N02AG Opioids in combination with antispasmodics
N02AG01 Morphine and antispasmodics
N02AG02 Ketobemidone and antispasmodics
N02AG03 Pethidine and antispasmodics
N02AG04 Hydromorphone and antispasmodics
N02AX Other opioids
N02AX01 Tilidine
N02AX02 Tramadol
N02AX03 Dezocine
N02AX05 Meptazinol
N02AX06 Tapentadol
N02AX52 Tramadol, combinations

Hypnotics and sedatives **(N05C)**
N05CA Barbiturates, plain
N05CA01 Pentobarbital
N05CA02 Amobarbital
N05CA03 Butobarbital
N05CA04 Barbital
N05CA05 Aprobarbital
N05CA06 Secobarbital
N05CA07 Talbutal
N05CA08 Vinylbital
N05CA09 Vinbarbital
N05CA10 Cyclobarbital
N05CA11 Heptabarbital
N05CA12 Reposal
N05CA15 Methohexital
N05CA16 Hexobarbital
N05CA19 Thiopental
N05CA20 Ethallobarbital
N05CA21 Allobarbital
N05CA22 Proxibarbal

N05CB Barbiturates, combinations
N05CB01 Combinations of barbiturates
N05CB02 Barbiturates in combination with other drugs
N05CC Aldehydes and derivatives
N05CC01 Chloral hydrate
N05CC02 Chloralodol
N05CC03 Acetylglycinamide chloral hydrate
N05CC04 Dichloralphenazone
N05CC05 Paraldehyde
N05CD Benzodiazepine derivatives
N05CD01 Flurazepam
N05CD02 Nitrazepam
N05CD03 Flunitrazepam
N05CD04 Estazolam
N05CD05 Triazolam
N05CD06 Lormetazepam
N05CD07 Temazepam
N05CD08 Midazolam
N05CD09 Brotizolam
N05CD10 Quazepam
N05CD11 Loprazolam
N05CD12 Doxefazepam
N05CD13 Cinolazepam
N05CD90 Climazolam
N05CE Piperidinedione derivatives
N05CE01 Glutethimide
N05CE02 Methyprylon
N05CE03 Pyrithyldione
N05CF Benzodiazepine related drugs
N05CF01 Zopiclone
N05CF02 Zolpidem
N05CF03 Zaleplon
N05CF04 Eszopiclone
N05CH Melatonin receptor agonists
N05CH01 Melatonin
N05CH02 Ramelteon
N05CM Other hypnotics and sedatives
N05CM01 Methaqualone
N05CM02 Clomethiazole

N05CM03 Bromisoval
N05CM04 Carbromal
N05CM05 Scopolamine
N05CM06 Propiomazine
N05CM07 Triclofos
N05CM08 Ethchlorvynol
N05CM09 Valerianae radix
N05CM10 Hexapropymate
N05CM11 Bromides
N05CM12 Apronal
N05CM13 Valnoctamide
N05CM15 Methylpentynol
N05CM16 Niaprazine
N05CM18 Dexmedetomidine
N05CM90 Detomidine
N05CM91 Medetomidine
N05CM92 Xylazine
N05CM93 Romifidine
N05CM94 Metomidate
N05CX Hypnotics and sedatives in combination, excluding barbiturates
N05CX01 Meprobamate, combinations
N05CX02 Methaqualone, combinations
N05CX03 Methylpentynol, combinations
N05CX04 Clomethiazole, combinations
N05CX05 Emepronium, combinations
N05CX06 Dipiperonylaminoethanol, combinations

Anxiolytics **(N05B)**
N05BA Benzodiazepine derivatives
N05BA01 Diazepam
N05BA02 Chlordiazepoxide
N05BA03 Medazepam
N05BA04 Oxazepam
N05BA05 Potassium clorazepate
N05BA06 Lorazepam
N05BA07 Adinazolam
N05BA08 Bromazepam
N05BA09 Clobazam
N05BA10 Ketazolam

N05BA11 Prazepam
N05BA12 Alprazolam
N05BA13 Halazepam
N05BA14 Pinazepam
N05BA15 Camazepam
N05BA16 Nordazepam
N05BA17 Fludiazepam
N05BA18 Ethyl loflazepate
N05BA19 Etizolam
N05BA21 Clotiazepam
N05BA22 Cloxazolam
N05BA23 Tofisopam
N05BA56 Lorazepam, combinations
N05BB Diphenylmethane derivatives
N05BB01 Hydroxyzine
N05BB02 Captodiame
N05BB51 Hydroxyzine, combinations
N05BC Carbamates
N05BC01 Meprobamate
N05BC03 Emylcamate
N05BC04 Mebutamate
N05BC51 Meprobamate, combinations
N05BD Dibenzo-bicyclo-octadiene derivatives
N05BD01 Benzoctamine
N05BE Azaspirodecanedione derivatives
N05BE01 Buspirone
N05BX Other anxiolytics
N05BX01 Mephenoxalone
N05BX02 Gedocarnil
N05BX03 Etifoxine

Antiepileptics **(N03A)**
N03AA Barbiturates and derivatives
N03AA01 Methylphenobarbital
N03AA02 Phenobarbital
N03AA03 Primidone
N03AA04 Barbexaclone
N03AA30 Metharbital
N03AB Hydantoin derivatives

N03AB01 Ethotoin
N03AB02 Phenytoin
N03AB03 Amino(diphenylhydantoin) valeric acid
N03AB04 Mephenytoin
N03AB05 Fosphenytoin
N03AB52 Phenytoin, combinations
N03AB54 Mephenytoin, combinations
N03AC Oxazolidine derivatives
N03AC01 Paramethadione
N03AC02 Trimethadione
N03AC03 Ethadione
N03AD Succinimide derivatives
N03AD01 Ethosuximide
N03AD02 Phensuximide
N03AD03 Mesuximide
N03AD51 Ethosuximide, combinations
N03AE Benzodiazepine derivatives
N03AE01 Clonazepam
N03AF Carboxamide derivatives
N03AF01 Carbamazepine
N03AF02 Oxcarbazepine
N03AF03 Rufinamide
N03AF04 Eslicarbazepine
N03AG Fatty acid derivatives
N03AG01 Valproic acid
N03AG02 Valpromide
N03AG03 Aminobutyric acid
N03AG04 Vigabatrin
N03AG05 Progabide
N03AG06 Tiagabine
N03AX Other antiepileptics
N03AX03 Sultiame
N03AX07 Phenacemide
N03AX09 Lamotrigine
N03AX10 Felbamate
N03AX11 Topiramate
N03AX12 Gabapentin
N03AX13 Pheneturide
N03AX14 Levetiracetam

N03AX15 Zonisamide
N03AX16 Pregabalin
N03AX17 Stiripentol
N03AX18 Lacosamide
N03AX19 Carisbamate
N03AX21 Retigabine
N03AX22 Perampanel
N03AX30 Beclamide
N03AX90 Imepitoin

Serotonin reuptake inhibitors **(N06A)**
N06AB Selective serotonin reuptake inhibitors
N06AB02 Zimelidine
N06AB03 Fluoxetine
N06AB04 Citalopram
N06AB05 Paroxetine
N06AB06 Sertraline
N06AB07 Alaproclate
N06AB08 Fluvoxamine
N06AB09 Etoperidone
N06AB10 Escitalopram

- *Anticholinergic medications*

Antipsychotic medications **(N05A)**
N05AA Phenothiazines with aliphatic side-chain
N05AA01 Chlorpromazine
N05AA02 Levomepromazine
N05AA03 Promazine
N05AA04 Acepromazine
N05AA05 Triflupromazine
N05AA06 Cyamemazine
N05AA07 Chlorproethazine
N05AB Phenothiazines with piperazine structure
N05AB01 Dixyrazine
N05AB02 Fluphenazine
N05AB03 Perphenazine
N05AB04 Prochlorperazine
N05AB05 Thiopropazate
N05AB06 Trifluoperazine

N05AB07 Acetophenazine
N05AB08 Thioproperazine
N05AB09 Butaperazine
N05AB10 Perazine
N05AC Phenothiazines with piperidine structure
N05AC01 Periciazine
N05AC02 Thioridazine
N05AC03 Mesoridazine
N05AC04 Pipotiazine
N05AD Butyrophenone derivatives
N05AD01 Haloperidol
N05AD02 Trifluperidol
N05AD03 Melperone
N05AD04 Moperone
N05AD05 Pipamperone
N05AD06 Bromperidol
N05AD07 Benperidol
N05AD08 Droperidol
N05AD09 Fluanisone
N05AD90 Azaperone
N05AE Indole derivatives
N05AE01 Oxypertine
N05AE02 Molindone
N05AE03 Sertindole
N05AE04 Ziprasidone
N05AF Thioxanthene derivative
N05AF01 Flupentixol
N05AF02 Clopenthixol
N05AF03 Chlorprothixene
N05AF04 Thiothixene
N05AF05 Zuclopenthixol
N05AG Diphenylbutylpiperidine derivatives
N05AG01 Fluspirilene
N05AG02 Pimozide
N05AG03 Penfluridol
N05AH Diazepines, oxazepines, thiazepines and oxepines
N05AH01 Loxapine
N05AH02 Clozapine
N05AH03 Olanzapine

N05AH04 Quetiapine
N05AH05 Asenapine
N05AH06 Clotiapine
N05AK Neuroleptics, in tardive dyskinesia
N05AL Benzamides
N05AL01 Sulpiride
N05AL02 Sultopride
N05AL03 Tiapride
N05AL04 Remoxipride
N05AL05 Amisulpride
N05AL06 Veralipride
N05AL07 Levosulpiride
N05AN Lithium
N05AN01 Lithium
N05AX Other antipsychotics
N05AX07 Prothipendyl
N05AX08 Risperidone
N05AX10 Mosapramine
N05AX11 Zotepine
N05AX12 Aripiprazole
N05AX13 Paliperidone
N05AX14 Iloperidone
N05AX90 Amperozide

Tricyclic and tetracyclic antidepressant agents **(N06A)**
N06AA Non-selective monoamine reuptake inhibitors
N06AA01 Desipramine
N06AA02 Imipramine
N06AA03 Imipramine oxide
N06AA04 Clomipramine
N06AA05 Opipramol
N06AA06 Trimipramine
N06AA07 Lofepramine
N06AA08 Dibenzepin
N06AA09 Amitriptyline
N06AA10 Nortriptyline
N06AA11 Protriptyline
N06AA12 Doxepin
N06AA13 Iprindole

N06AA14 Melitracen
N06AA15 Butriptyline
N06AA16 Dosulepin
N06AA17 Amoxapine
N06AA18 Dimetacrine
N06AA19 Amineptine
N06AA21 Maprotiline
N06AA23 Quinupramine
N06AX Other antidepressants
N06AX01 Oxitriptan
N06AX02 Tryptophan
N06AX03 Mianserin
N06AX04 Nomifensine
N06AX05 Trazodone
N06AX06 Nefazodone
N06AX07 Minaprine
N06AX08 Bifemelane
N06AX09 Viloxazine
N06AX10 Oxaflozane
N06AX11 Mirtazapine
N06AX12 Bupropion
N06AX13 Medifoxamine
N06AX14 Tianeptine
N06AX15 Pivagabine
N06AX16 Venlafaxine
N06AX17 Milnacipran
N06AX18 Reboxetine
N06AX19 Gepirone
N06AX21 Duloxetine
N06AX22 Agomelatine
N06AX23 Desvenlafaxine
N06AX24 Vilazodone
N06AX25 Hyperici herba
N06AX90 Selegiline

Disopyramide **(C01BA)**
C01BA03 Disopyramide

Antispasmodics **(A03A)**

A03AA Synthetic anticholinergics, esters with tertiary amino group
A03AA01 Oxyphencyclimine
A03AA03 Camylofin
A03AA04 Mebeverine
A03AA05 Trimebutine
A03AA06 Rociverine
A03AA07 Dicycloverine
A03AA08 Dihexyverine
A03AA09 Difemerine
A03AA30 Piperidolate
A03AB Synthetic anticholinergics, quaternary ammonium compounds
A03AB01 Benzilone
A03AB02 Glycopyrronium
A03AB03 Oxyphenonium
A03AB04 Penthienate
A03AB05 Propantheline
A03AB06 Otilonium bromide
A03AB07 Methantheline
A03AB08 Tridihexethyl
A03AB09 Isopropamide
A03AB10 Hexocyclium
A03AB11 Poldine
A03AB12 Mepenzolate
A03AB13 Bevonium
A03AB14 Pipenzolate
A03AB15 Diphemanil
A03AB16 (2-benzhydryloxyethyl)diethyl-methylammonium iodide
A03AB17 Tiemonium iodide
A03AB18 Prifinium bromide
A03AB19 Timepidium bromide
A03AB21 Fenpiverinium
A03AB53 Oxyphenonium, combinations
A03AB90 Benzetimide
A03AB92 Carbachol
A03AB93 Neostigmin

Anti Parkinson medications
N04A Anticholinergic agents
N04AA Tertiary amines

N04AA01 Trihexyphenidyl
N04AA02 Biperiden
N04AA03 Metixene
N04AA04 Procyclidine
N04AA05 Profenamine
N04AA08 Dexetimide
N04AA09 Phenglutarimide
N04AA10 Mazaticol
N04AA11 Bornaprine
N04AA12 Tropatepine
N04AB Ethers chemically close to antihistamines
N04AB01 Etanautine
N04AB02 Orphenadrine (chloride)
N04AC Ethers of tropine or tropine derivatives
N04AC01 Benzatropine
N04AC30 Etybenzatropine

Choline-esterase inhibitors **(N07A)**
N07AA Anticholinesterases
N07AA01 Neostigmine
N07AA02 Pyridostigmine
N07AA03 Distigmine
N07AA30 Ambenonium
N07AA51 Neostigmine, combinations

Atropine **(A03BA)**
A03BA01 Atropine

H1-antihistamines **(R06A)**
R06AA Aminoalkyl ethers
R06AA01 Bromazine
R06AA02 Diphenhydramine
R06AA04 Clemastine
R06AA06 Chlorphenoxamine
R06AA07 Diphenylpyraline
R06AA08 Carbinoxamine
R06AA09 Doxylamine
R06AA52 Diphenhydramine, combinations
R06AA54 Clemastine, combinations

R06AA56 Chlorphenoxamine, combinations
R06AA57 Diphenylpyraline, combinations
R06AA59 Doxylamine, combinations
R06AB Substituted alkylamines
R06AB01 Brompheniramine
R06AB02 Dexchlorpheniramine
R06AB03 Dimetindene
R06AB04 Chlorphenamine
R06AB05 Pheniramine
R06AB06 Dexbrompheniramine
R06AB07 Talastine
R06AB51 Brompheniramine, combinations
R06AB52 Dexchlorpheniramine, combinations
R06AB54 Chlorphenamine, combinations
R06AB56 Dexbrompheniramine, combinations
R06AC Substituted ethylene diamines
R06AC01 Mepyramine
R06AC02 Histapyrrodine
R06AC03 Chloropyramine
R06AC04 Tripelennamine
R06AC05 Methapyrilene
R06AC06 Thonzylamine
R06AC52 Histapyrrodine, combinations
R06AC53 Chloropyramine, combinations
R06AD Phenothiazine derivatives
R06AD01 Alimemazine
R06AD02 Promethazine
R06AD03 Thiethylperazine
R06AD04 Methdilazine
R06AD05 Hydroxyethylpromethazine
R06AD06 Thiazinam
R06AD07 Mequitazine
R06AD08 Oxomemazine
R06AD09 Isothipendyl
R06AD52 Promethazine, combinations
R06AD55 Hydroxyethylpromethazine, combinations
R06AE Piperazine derivatives
R06AE01 Buclizine
R06AE03 Cyclizine

R06AE04 Chlorcyclizine
R06AE05 Meclozine
R06AE06 Oxatomide
R06AE07 Cetirizine
R06AE09 Levocetirizine
R06AE51 Buclizine, combinations
R06AE53 Cyclizine, combinations
R06AE55 Meclozine, combinations
R06AK Combinations of antihistamines
R06AX Other antihistamines for systemic use
R06AX01 Bamipine
R06AX02 Cyproheptadine
R06AX03 Thenalidine
R06AX04 Phenindamine
R06AX05 Antazoline
R06AX07 Triprolidine
R06AX08 Pyrrobutamine
R06AX09 Azatadine
R06AX11 Astemizole
R06AX12 Terfenadine
R06AX13 Loratadine
R06AX15 Mebhydrolin
R06AX16 Deptropine
R06AX17 Ketotifen
R06AX18 Acrivastine
R06AX19 Azelastine
R06AX21 Tritoqualine
R06AX22 Ebastine
R06AX23 Pimethixene
R06AX24 Epinastine
R06AX25 Mizolastine
R06AX26 Fexofenadine
R06AX27 Desloratadine
R06AX28 Rupatadine
R06AX29 Bilastine
R06AX53 Thenalidine, combinations
R06AX58 Pyrrobutamine, combinations

Anticholinergics for treatment of overactive bladder

G04BD Urinary antispasmodics
G04BD01 Emepronium
G04BD02 Flavoxate
G04BD03 Meladrazine
G04BD04 Oxybutynin
G04BD05 Terodiline
G04BD06 Propiverine
G04BD07 Tolterodine
G04BD08 Solifenacin
G04BD09 Trospium
G04BD10 Darifenacin
G04BD11 Fesoterodine

- *Medications affecting cerebrovascular and cardiovascular disease*

Systemic glucocorticosteroids
H02AB Glucocorticoids
H02AB01 Betamethasone
H02AB02 Dexamethasone
H02AB03 Fluocortolone
H02AB04 Methylprednisolone
H02AB05 Paramethasone
H02AB06 Prednisolone
H02AB07 Prednisone
H02AB08 Triamcinolone
H02AB09 Hydrocortisone
H02AB10 Cortisone
H02AB11 Prednylidene
H02AB12 Rimexolone
H02AB13 Deflazacort
H02AB14 Cloprednol
H02AB15 Meprednisone
H02AB17 Cortivazol
H02AB30 Combinations of glucocorticoids
H02AB56 Prednisolone, combinations
H02AB57 Prednisone, combinations
H02AB90 Flumetasone

NSAIDs **(M01A)**
M01AA Butylpyrazolidines

M01AA01 Phenylbutazone
M01AA02 Mofebutazone
M01AA03 Oxyphenbutazone
M01AA05 Clofezone
M01AA06 Kebuzone
M01AA90 Suxibuzone
M01AA99 Combinations
M01AB Acetic acid derivatives and related substances
M01AB01 Indometacin
M01AB02 Sulindac
M01AB03 Tolmetin
M01AB04 Zomepirac
M01AB05 Diclofenac
M01AB06 Alclofenac
M01AB07 Bumadizone
M01AB08 Etodolac
M01AB09 Lonazolac
M01AB10 Fentiazac
M01AB11 Acemetacin
M01AB12 Difenpiramide
M01AB13 Oxametacin
M01AB14 Proglumetacin
M01AB15 Ketorolac
M01AB16 Aceclofenac
M01AB17 Bufexamac
M01AB51 Indometacin, combinations
M01AB55 Diclofenac, combinations
M01AC Oxicams
M01AC01 Piroxicam
M01AC02 Tenoxicam
M01AC04 Droxicam
M01AC05 Lornoxicam
M01AC06 Meloxicam
M01AC56 Meloxicam, combinations
M01AE Propionic acid derivatives
M01AE01 Ibuprofen
M01AE02 Naproxen
M01AE03 Ketoprofen
M01AE04 Fenoprofen

M01AE05 Fenbufen
M01AE06 Benoxaprofen
M01AE07 Suprofen
M01AE08 Pirprofen
M01AE09 Flurbiprofen
M01AE10 Indoprofen
M01AE11 Tiaprofenic acid
M01AE12 Oxaprozin
M01AE13 Ibuproxam
M01AE14 Dexibuprofen
M01AE15 Flunoxaprofen
M01AE16 Alminoprofen
M01AE17 Dexketoprofen
M01AE18 Naproxcinod
M01AE51 Ibuprofen, combinations
M01AE52 Naproxen and esomeprazole
M01AE53 Ketoprofen, combinations
M01AE56 Naproxen and misoprostol
M01AE90 Vedaprofen
M01AE91 Carprofen
M01AE92 Tepoxalin
M01AG Fenamates
M01AG01 Mefenamic acid
M01AG02 Tolfenamic acid
M01AG03 Flufenamic acid
M01AG04 Meclofenamic acid
M01AG90 Flunixin
M01AH Coxibs
M01AH01 Celecoxib
M01AH02 Rofecoxib
M01AH03 Valdecoxib
M01AH04 Parecoxib
M01AH05 Etoricoxib
M01AH06 Lumiracoxib
M01AH90 Firocoxib
M01AH91 Robenacoxib
M01AH92 Mavacoxib
M01AH93 Cimicoxib
M01AX Other anti-inflammatory and antirheumatic agents, non-steroids

M01AX01 Nabumetone
M01AX02 Niflumic acid
M01AX04 Azapropazone
M01AX05 Glucosamine
M01AX07 Benzydamine
M01AX12 Glucosaminoglycan polysulfate
M01AX13 Proquazone
M01AX14 Orgotein
M01AX17 Nimesulide
M01AX18 Feprazone
M01AX21 Diacerein
M01AX22 Morniflumate
M01AX23 Tenidap
M01AX24 Oxaceprol
M01AX25 Chondroitin sulfate
M01AX26 Avocado and soyabean oil, unsaponifiables
M01AX52 Niflumic acid, combinations
M01AX68 Feprazone, combinations
M01AX90 Pentosan polysulfate
M01AX91 Aminopropionitrile
M01AX99 Combinations

Antithrombotic agents (B01A)
B01AA Vitamin K antagonists
B01AA01 Dicoumarol
B01AA02 Phenindione
B01AA03 Warfarin
B01AA04 Phenprocoumon
B01AA07 Acenocoumarol
B01AA08 Ethyl biscoumacetate
B01AA09 Clorindione
B01AA10 Diphenadione
B01AA11 Tioclomarol
B01AA12 Fluindione

B01AE Direct thrombin inhibitors
B01AE01 Desirudin
B01AE02 Lepirudin
B01AE03 Argatroban

B01AE04 Melagatran
B01AE05 Ximelagatran
B01AE06 Bivalirudin
B01AE07 Dabigatran etexilate

B01AF Direct factor Xa inhibitors
B01AF01 Rivaroxaban
B01AF02 Apixaban

B01AX Other antithrombotic agents
B01AX01 Defibrotide
B01AX04 Dermatan sulfate
B01AX05 Fondaparinux

Lipid lowering medications **(C10A, C10B))**
C10AA HMG CoA reductase inhibitors
C10AA01 Simvastatin
C10AA02 Lovastatin
C10AA03 Pravastatin
C10AA04 Fluvastatin
C10AA05 Atorvastatin
C10AA06 Cerivastatin
C10AA07 Rosuvastatin
C10AA08 Pitavastatin
C10AB Fibrates
C10AB01 Clofibrate
C10AB02 Bezafibrate
C10AB03 Aluminium clofibrate
C10AB04 Gemfibrozil
C10AB05 Fenofibrate
C10AB06 Simfibrate
C10AB07 Ronifibrate
C10AB08 Ciprofibrate
C10AB09 Etofibrate
C10AB10 Clofibride
C10AB11 Choline fenofibrate
C10AC Bile acid sequestrants
C10AC01 Colestyramine
C10AC02 Colestipol

C10AC03 Colextran
C10AC04 Colesevelam
C10AD Nicotinic acid and derivatives
C10AD01 Niceritrol
C10AD02 Nicotinic acid
C10AD03 Nicofuranose
C10AD04 Aluminium nicotinate
C10AD05 Nicotinyl alcohol (pyridylcarbinol)
C10AD06 Acipimox
C10AD52 Nicotinic acid, combinations
C10AX Other lipid modifying agents
C10AX01 Dextrothyroxine
C10AX02 Probucol
C10AX03 Tiadenol
C10AX05 Meglutol
C10AX06 Omega-3-triglycerides
C10AX07 Magnesium pyridoxal 5-phosphate glutamate
C10AX08 Policosanol
C10AX09 Ezetimibe
C10AX10 Alipogene tiparvovec
C10AX11 Mipomersen
C10B Lipid modifying agents, combinations
C10BA HMG CoA reductase inhibitors in combination with other lipid modifying agents
C10BA01 Lovastatin and nicotinic acid
C10BA02 Simvastatin and ezetimibe
C10BA03 Pravastatin and fenofibrate
C10BX HMG CoA reductase inhibitors, other combinations
C10BX01 Simvastatin and acetylsalicylic acid
C10BX02 Pravastatin and acetylsalicylic acid
C10BX03 Atorvastatin and amlodipine
C10BX04 Simvastatin, acetylsalicylic acid and ramipril

Platelet aggregation inhibitors **(B01AC)**
B01AC Platelet aggregation inhibitors excluding heparin
B01AC01 Ditazole
B01AC02 Cloricromen
B01AC03 Picotamide
B01AC04 Clopidogrel
B01AC05 Ticlopidine

B01AC06 Acetylsalicylic acid
B01AC07 Dipyridamole
B01AC08 Carbasalate calcium
B01AC09 Epoprostenol
B01AC10 Indobufen
B01AC11 Iloprost
B01AC13 Abciximab
B01AC15 Aloxiprin
B01AC16 Eptifibatide
B01AC17 Tirofiban
B01AC18 Triflusal
B01AC19 Beraprost
B01AC21 Treprostinil
B01AC22 Prasugrel
B01AC23 Cilostazol
B01AC24 Ticagrelor
B01AC30 Combinations
B01AC56 Acetylsalicylic acid and esomeprazole

Nitrates **(C01DA)**
C01DA Organic nitrates
C01DA02 Glyceryl trinitrate
C01DA04 Methylpropylpropanediol dinitrate
C01DA05 Pentaerithrityl tetranitrate
C01DA07 Propatylnitrate
C01DA08 Isosorbide dinitrate
C01DA09 Trolnitrate
C01DA13 Eritrityl tetranitrate
C01DA14 Isosorbide mononitrate
C01DA20 Organic nitrates in combination
C01DA38 Tenitramine
C01DA52 Glyceryl trinitrate, combinations
C01DA54 Methylpropylpropanediol dinitrate, combinations
C01DA55 Pentaerithrityl tetranitrate, combinations
C01DA57 Propatylnitrate, combinations
C01DA58 Isosorbide dinitrate, combinations
C01DA59 Trolnitrate, combinations
C01DA63 Eritrityl tetranitrate, combinations
C01DA70 Organic nitrates in combination with psycholeptics

Cardiac glycosides **(C01AA, C01AB, C01AC, C01AX)**
C01AA Digitalis glycosides
C01AA01 Acetyldigitoxin
C01AA02 Acetyldigoxin
C01AA03 Digitalis leaves
C01AA04 Digitoxin
C01AA05 Digoxin
C01AA06 Lanatoside C
C01AA07 Deslanoside
C01AA08 Metildigoxin
C01AA09 Gitoformate
C01AA52 Acetyldigoxin, combinations
C01AB Scilla glycosides
C01AB01 Proscillaridin
C01AB51 Proscillaridin, combinations
C01AC Strophanthus glycosides
C01AC01 G-strophanthin
C01AC03 Cymarin
C01AX Other cardiac glycosides
C01AX02 Peruvoside

Anti-arrhythmics **(C01B)**
C01BA Antiarrhythmics, class Ia
C01BA01 Quinidine
C01BA02 Procainamide
C01BA03 Disopyramide
C01BA04 Sparteine
C01BA05 Ajmaline
C01BA08 Prajmaline
C01BA12 Lorajmine
C01BA51 Quinidine, combinations excluding psycholeptics
C01BA71 Quinidine, combinations with psycholeptics
C01BB Antiarrhythmics, class Ib
C01BB01 Lidocaine
C01BB02 Mexiletine
C01BB03 Tocainide
C01BB04 Aprindine
C01BC Antiarrhythmics, class Ic

C01BC03 Propafenone
C01BC04 Flecainide
C01BC07 Lorcainide
C01BC08 Encainide
C01BD Antiarrhythmics, class III
C01BD01 Amiodarone
C01BD02 Bretylium tosilate
C01BD03 Bunaftine
C01BD04 Dofetilide
C01BD05 Ibutilide
C01BD06 Tedisamil
C01BD07 Dronedarone
C01BG Other antiarrhythmics, class I and III
C01BG01 Moracizine
C01BG07 Cibenzoline
C01BG11 Vernakalant

Anti-hypertensive medications **(C03, C07, C08, C09)**
C03AA Thiazides, plain
C03AA01 Bendroflumethiazide
C03AA02 Hydroflumethiazide
C03AA03 Hydrochlorothiazide
C03AA04 Chlorothiazide
C03AA05 Polythiazide
C03AA06 Trichlormethiazide
C03AA07 Cyclopenthiazide
C03AA08 Methyclothiazide
C03AA09 Cyclothiazide
C03AA13 Mebutizide
C03AA56 Trichlormethiazide, combinations
C03AB Thiazides and potassium in combination
C03AB01 Bendroflumethiazide and potassium
C03AB02 Hydroflumethiazide and potassium
C03AB03 Hydrochlorothiazide and potassium
C03AB04 Chlorothiazide and potassium
C03AB05 Polythiazide and potassium
C03AB06 Trichlormethiazide and potassium
C03AB07 Cyclopenthiazide and potassium
C03AB08 Methyclothiazide and potassium

C03AB09 Cyclothiazide and potassium
C03AH Thiazides, combinations with psycholeptics and/or analgesics
C03AH01 Chlorothiazide, combinations
C03AH02 Hydroflumethiazide, combinations
C03AX Thiazides, combinations with other drugs
C03AX01 Hydrochlorothiazide, combinations
C03B Low-ceiling diuretics, excluding thiazides
C03BA Sulfonamides, plain
C03BA02 Quinethazone
C03BA03 Clopamide
C03BA04 Chlortalidone
C03BA05 Mefruside
C03BA07 Clofenamide
C03BA08 Metolazone
C03BA09 Meticrane
C03BA10 Xipamide
C03BA11 Indapamide
C03BA12 Clorexolone
C03BA13 Fenquizone
C03BA82 Clorexolone, combinations with psycholeptics
C03BB Sulfonamides and potassium in combination
C03BB02 Quinethazone and potassium
C03BB03 Clopamide and potassium
C03BB04 Chlortalidone and potassium
C03BB05 Mefruside and potassium
C03BB07 Clofenamide and potassium
C03BC Mercurial diuretics
C03BC01 Mersalyl
C03BD Xanthine derivatives
C03BD01 Theobromine
C03BK Sulfonamides, combinations with other drugs
C03BX Other low-ceiling diuretics
C03BX03 Cicletanine
C03C High-ceiling diuretics
C03CA Sulfonamides, plain
C03CA01 Furosemide
C03CA02 Bumetanide
C03CA03 Piretanide
C03CA04 Torasemide

C03CB Sulfonamides and potassium in combination
C03CB01 Furosemide and potassium
C03CB02 Bumetanide and potassium
C03CC Aryloxyacetic acid derivatives
C03CC01 Etacrynic acid
C03CC02 Tienilic acid
C03CD Pyrazolone derivatives
C03CD01 Muzolimine
C03CX Other high-ceiling diuretics
C03CX01 Etozolin
C03D Potassium-sparing agents
C03DA Aldosterone antagonists
C03DA01 Spironolactone
C03DA02 Potassium canrenoate
C03DA03 Canrenone
C03DA04 Eplerenone
C03DB Other potassium-sparing agents
C03DB01 Amiloride
C03DB02 Triamterene
C03E Diuretics and potassium-sparing agents in combination
C03EA Low-ceiling diuretics and potassium-sparing agents
C03EA01 Hydrochlorothiazide and potassium-sparing agents
C03EA02 Trichlormethiazide and potassium-sparing agents
C03EA03 Epitizide and potassium-sparing agents
C03EA04 Altizide and potassium-sparing agents
C03EA05 Mebutizide and potassium-sparing agents
C03EA06 Chlortalidone and potassium-sparing agents
C03EA07 Cyclopenthiazide and potassium-sparing agents
C03EA12 Metolazone and potassium-sparing agents
C03EA13 Bendroflumethiazide and potassium-sparing agents
C03EA14 Butizide and potassium-sparing agents
C03EB High-ceiling diuretics and potassium-sparing agents
C03EB01 Furosemide and potassium-sparing agents
C03EB02 Bumetanide and potassium-sparing agents
C07A Beta blocking agents
C07AA Beta blocking agents, non-selective
C07AA01 Alprenolol
C07AA02 Oxprenolol
C07AA03 Pindolol

C07AA05 Propranolol
C07AA06 Timolol
C07AA07 Sotalol
C07AA12 Nadolol
C07AA14 Mepindolol
C07AA15 Carteolol
C07AA16 Tertatolol
C07AA17 Bopindolol
C07AA19 Bupranolol
C07AA23 Penbutolol
C07AA27 Cloranolol
C07AA57 Sotalol, combinations
C07AA90 Carazolol
C07AB Beta blocking agents, selective
C07AB01 Practolol
C07AB02 Metoprolol
C07AB03 Atenolol
C07AB04 Acebutolol
C07AB05 Betaxolol
C07AB06 Bevantolol
C07AB07 Bisoprolol
C07AB08 Celiprolol
C07AB09 Esmolol
C07AB10 Epanolol
C07AB11 S-atenolol
C07AB12 Nebivolol
C07AB13 Talinolol
C07AB52 Metoprolol, combinations
C07AB57 Bisoprolol, combinations
C07AG Alpha and beta blocking agents
C07AG01 Labetalol
C07AG02 Carvedilol
C07B Beta blocking agents and thiazides
C07BA Beta blocking agents, non-selective, and thiazides
C07BA02 Oxprenolol and thiazides
C07BA05 Propranolol and thiazides
C07BA06 Timolol and thiazides
C07BA07 Sotalol and thiazides
C07BA12 Nadolol and thiazides

C07BA68 Metipranolol and thiazides, combinations
C07BB Beta blocking agents, selective, and thiazides
C07BB02 Metoprolol and thiazides
C07BB03 Atenolol and thiazides
C07BB04 Acebutolol and thiazides
C07BB06 Bevantolol and thiazides
C07BB07 Bisoprolol and thiazides
C07BB12 Nebivolol and thiazides
C07BB52 Metoprolol and thiazides, combinations
C07BG Alpha and beta blocking agents and thiazides
C07BG01 Labetalol and thiazides
C07C Beta blocking agents and other diuretics
C07CA Beta blocking agents, non-selective, and other diuretics
C07CA02 Oxprenolol and other diuretics
C07CA03 Pindolol and other diuretics
C07CA17 Bopindolol and other diuretics
C07CA23 Penbutolol and other diuretics
C07CB Beta blocking agents, selective, and other diuretics
C07CB02 Metoprolol and other diuretics
C07CB03 Atenolol and other diuretics
C07CB53 Atenolol and other diuretics, combinations
C07CG Alpha and beta blocking agents and other diuretics
C07CG01 Labetalol and other diuretics
C07D Beta blocking agents, thiazides and other diuretics
C07DA Beta blocking agents, non-selective, thiazides and other diuretics
C07DA06 Timolol, thiazides and other diuretics
C07DB Beta blocking agents, selective, thiazides and other diuretics
C07DB01 Atenolol, thiazides and other diuretics
C07E Beta blocking agents and vasodilators
C07EA Beta blocking agents, non-selective, and vasodilators
C07EB Beta blocking agents, selective, and vasodilators
C07F Beta blocking agents and other antihypertensives
C07FA Beta blocking agents, non-selective, and other antihypertensives
C07FA05 Propranolol and other antihypertensives
C07FB Beta blocking agents, selective, and other antihypertensives
C07FB02 Metoprolol and other antihypertensives
C07FB03 Atenolol and other antihypertensives
C07FB07 Bisoprolol and other antihypertensives
C08C Selective calcium channel blockers with mainly vascular effects

C08CA Dihydropyridine derivatives
C08CA01 Amlodipine
C08CA02 Felodipine
C08CA03 Isradipine
C08CA04 Nicardipine
C08CA05 Nifedipine
C08CA06 Nimodipine
C08CA07 Nisoldipine
C08CA08 Nitrendipine
C08CA09 Lacidipine
C08CA10 Nilvadipine
C08CA11 Manidipine
C08CA12 Barnidipine
C08CA13 Lercanidipine
C08CA14 Cilnidipine
C08CA15 Benidipine
C08CA16 Clevidipine
C08CA55 Nifedipine, combinations
C08CX Other selective calcium channel blockers with mainly vascular effects
C08CX01 Mibefradil
C08D Selective calcium channel blockers with direct cardiac effects
C08DA Phenylalkylamine derivatives
C08DA01 Verapamil
C08DA02 Gallopamil
C08DA51 Verapamil, combinations
C08DB Benzothiazepine derivatives
C08DB01 Diltiazem
C08E Non-selective calcium channel blockers
C08EA Phenylalkylamine derivatives
C08EA01 Fendiline
C08EA02 Bepridil
C08EX Other non-selective calcium channel blockers
C08EX01 Lidoflazine
C08EX02 Perhexiline
C08G Calcium channel blockers and diuretics
C08GA Calcium channel blockers and diuretics
C08GA01 Nifedipine and diuretics
C09A ACE inhibitors, plain
C09AA ACE inhibitors, plain

C09AA01 Captopril
C09AA02 Enalapril
C09AA03 Lisinopril
C09AA04 Perindopril
C09AA05 Ramipril
C09AA06 Quinapril
C09AA07 Benazepril
C09AA08 Cilazapril
C09AA09 Fosinopril
C09AA10 Trandolapril
C09AA11 Spirapril
C09AA12 Delapril
C09AA13 Moexipril
C09AA14 Temocapril
C09AA15 Zofenopril
C09AA16 Imidapril
C09B ACE inhibitors, combinations
C09BA ACE inhibitors and diuretics
C09BA01 Captopril and diuretics
C09BA02 Enalapril and diuretics
C09BA03 Lisinopril and diuretics
C09BA04 Perindopril and diuretics
C09BA05 Ramipril and diuretics
C09BA06 Quinapril and diuretics
C09BA07 Benazepril and diuretics
C09BA08 Cilazapril and diuretics
C09BA09 Fosinopril and diuretics
C09BA12 Delapril and diuretics
C09BA13 Moexipril and diuretics
C09BA15 Zofenopril and diuretics
C09BB ACE inhibitors and calcium channel blockers
C09BB02 Enalapril and lercanidipine
C09BB03 Lisinopril and amlodipine
C09BB04 Perindopril and amlodipine
C09BB05 Ramipril and felodipine
C09BB06 Enalapril and nitrendipine
C09BB07 Ramipril and amlodipine
C09BB10 Trandolapril and verapamil
C09BB12 Delapril and manidipine

C09C Angiotensin II antagonists, plain
C09CA Angiotensin II antagonists, plain
C09CA01 Losartan
C09CA02 Eprosartan
C09CA03 Valsartan
C09CA04 Irbesartan
C09CA05 Tasosartan
C09CA06 Candesartan
C09CA07 Telmisartan
C09CA08 Olmesartan medoxomil
C09CA09 Azilsartan medoxomil
C09D Angiotensin II antagonists, combinations
C09DA Angiotensin II antagonists and diuretics
C09DA01 Losartan and diuretics
C09DA02 Eprosartan and diuretics
C09DA03 Valsartan and diuretics
C09DA04 Irbesartan and diuretics
C09DA06 Candesartan and diuretics
C09DA07 Telmisartan and diuretics
C09DA08 Olmesartan medoxomil and diuretics
C09DB Angiotensin II antagonists and calcium channel blockers
C09DB01 Valsartan and amlodipine
C09DB02 Olmesartan medoxomil and amlodipine
C09DB04 Telmisartan and amlodipine
C09DB05 Irbesartan and amlodipine
C09DB06 Losartan and amlodipine
C09DX Angiotensin II antagonists, other combinations
C09DX01 Valsartan, amlodipine and hydrochlorothiazide
C09DX02 Valsartan and aliskiren
C09DX03 Olmesartan medoxomil, amlodipine and hydrochlorothiazide
C09X Other agents acting on the renin-angiotensin system
C09XA Renin-inhibitors
C09XA01 Remikiren
C09XA02 Aliskiren
C09XA52 Aliskiren and hydrochlorothiazide
C09XA53 Aliskiren and amlodipine
C09XA54 Aliskiren, amlodipine and hydrochlorothiazide

Anti-diabetic medications **(A10)**

A10A Insulins and analogues
A10AB Insulins and analogues for injection, fast-acting
A10AB01 Insulin (human)
A10AB02 Insulin (beef)
A10AB03 Insulin (pork)
A10AB04 Insulin lispro
A10AB05 Insulin aspart
A10AB06 Insulin glulisine
A10AB30 Combinations
A10AC Insulins and analogues for injection, intermediate-acting
A10AC01 Insulin (human)
A10AC02 Insulin (beef)
A10AC03 Insulin (pork)
A10AC04 Insulin lispro
A10AC30 Combinations
A10AD Insulins and analogues for injection, intermediate-acting combined with fast-acting
A10AD01 Insulin (human)
A10AD02 Insulin (beef)
A10AD03 Insulin (pork)
A10AD04 Insulin lispro
A10AD05 Insulin aspart
A10AD30 Combinations
A10AE Insulins and analogues for injection, long-acting
A10AE01 Insulin (human)
A10AE02 Insulin (beef)
A10AE03 Insulin (pork)
A10AE04 Insulin glargine
A10AE05 Insulin detemir
A10AE30 Combinations
A10AF Insulins and analogues for inhalation
A10AF01 Insulin (human)
A10B Blood glucose lowering drugs, excluding insulins
A10BA Biguanides
A10BA01 Phenformin
A10BA02 Metformin
A10BA03 Buformin
A10BB Sulfonamides, urea derivatives
A10BB01 Glibenclamide
A10BB02 Chlorpropamide

A10BB03 Tolbutamide
A10BB04 Glibornuride
A10BB05 Tolazamide
A10BB06 Carbutamide
A10BB07 Glipizide
A10BB08 Gliquidone
A10BB09 Gliclazide
A10BB10 Metahexamide
A10BB11 Glisoxepide
A10BB12 Glimepiride
A10BB31 Acetohexamide
A10BC Sulfonamides (heterocyclic)
A10BC01 Glymidine
A10BD Combinations of oral blood glucose lowering drugs
A10BD01 Phenformin and sulfonamides
A10BD02 Metformin and sulfonamides
A10BD03 Metformin and rosiglitazone
A10BD04 Glimepiride and rosiglitazone
A10BD05 Metformin and pioglitazone
A10BD06 Glimepiride and pioglitazone
A10BD07 Metformin and sitagliptin
A10BD08 Metformin and vildagliptin
A10BD09 Pioglitazone and alogliptin
A10BD10 Metformin and saxagliptin
A10BD11 Metformin and linagliptin
A10BF Alpha glucosidase inhibitors
A10BF01 Acarbose
A10BF02 Miglitol
A10BF03 Voglibose
A10BG Thiazolidinediones
A10BG01 Troglitazone
A10BG02 Rosiglitazone
A10BG03 Pioglitazone
A10BH Dipeptidyl peptidase 4 (DPP-4) inhibitors
A10BH01 Sitagliptin
A10BH02 Vildagliptin
A10BH03 Saxagliptin
A10BH04 Alogliptin
A10BH05 Linagliptin

A10BX Other blood glucose lowering drugs, excluding insulins
A10BX01 Guar gum
A10BX02 Repaglinide
A10BX03 Nateglinide
A10BX04 Exenatide
A10BX05 Pramlintide
A10BX06 Benfluorex
A10BX07 Liraglutide
A10BX08 Mitiglinide
A10BX09 Dapagliflozin
A10X Other drugs used in diabetes
A10XA Aldose reductase inhibitors
A10XA01 Tolrestat

- Antibiotics (if given for the treatment of lower respiratory tract infections = acute bronchitis, pneumonia) (J01)

J01AA Tetracyclines (J01A)
J01AA01 Demeclocycline
J01AA02 Doxycycline
J01AA03 Chlortetracycline
J01AA04 Lymecycline
J01AA05 Metacycline
J01AA06 Oxytetracycline
J01AA07 Tetracycline
J01AA08 Minocycline
J01AA09 Rolitetracycline
J01AA10 Penimepicycline
J01AA11 Clomocycline
J01AA12 Tigecycline
J01AA20 Combinations of tetracyclines
J01AA53 Chlortetracycline, combinations
J01AA56 Oxytetracycline, combinations

J01B Amphenicols (J01B)
J01BA
J01BA01 Chloramphenicol
J01BA02 Thiamphenicol
J01BA52 Thiamphenicol, combinations
J01BA90 Florfenicol
J01BA99 Amphenicols, combinations

J01C Beta-lactam antibacterials, penicillins (J01C)
J01CA Penicillins with extended spectrum
J01CA01 Ampicillin
J01CA02 Pivampicillin
J01CA03 Carbenicillin
J01CA04 Amoxicillin
J01CA05 Carindacillin
J01CA06 Bacampicillin
J01CA07 Epicillin
J01CA08 Pivmecillinam
J01CA09 Azlocillin
J01CA10 Mezlocillin
J01CA11 Mecillinam
J01CA12 Piperacillin
J01CA13 Ticarcillin
J01CA14 Metampicillin
J01CA15 Talampicillin
J01CA16 Sulbenicillin
J01CA17 Temocillin
J01CA18 Hetacillin
J01CA19 Aspoxicillin
J01CA20 Combinations
J01CA51 Ampicillin, combinations
J01CE Beta-lactamase-sensitive penicillin
J01CE01 Benzylpenicillin
J01CE02 Phenoxymethylpenicillin
J01CE03 Propicillin
J01CE04 Azidocillin
J01CE05 Pheneticillin
J01CE06 Penamecillin
J01CE07 Clometocillin
J01CE08 Benzathine benzylpenicillin
J01CE09 Procaine benzylpenicillin
J01CE10 Benzathine phenoxymethylpenicillin
J01CE30 Combinations
J01CE90 Penethamate hydroiodide
J01CE91 Benethamine penicillin
J01CF Beta-lactamase-resistant penicillins
J01CF01 Dicloxacillin

J01CF02 Cloxacillin
J01CF03 Methicillin
J01CF04 Oxacillin
J01CF05 Flucloxacillin
J01CF06 Nafcillin
J01CG Beta-lactamase inhibitors
J01CG01 Sulbactam
J01CG02 Tazobactam
J01CR Combinations of penicillins, including beta-lactamase inhibitors
J01CR01 Ampicillin and enzyme inhibitor
J01CR02 Amoxicillin and enzyme inhibitor
J01CR03 Ticarcillin and enzyme inhibitor
J01CR04 Sultamicillin
J01CR05 Piperacillin and enzyme inhibitor
J01CR50 Combinations of penicillins

J01D Other beta-lactam antibacterials (J01D)
J01DB First-generation cephalosporins
J01DB01 Cefalexin
J01DB02 Cefaloridine
J01DB03 Cefalotin
J01DB04 Cefazolin
J01DB05 Cefadroxil
J01DB06 Cefazedone
J01DB07 Cefatrizine
J01DB08 Cefapirin
J01DB09 Cefradine
J01DB10 Cefacetrile
J01DB11 Cefroxadine
J01DB12 Ceftezole
J01DC Second-generation cephalosporins
J01DC01 Cefoxitin
J01DC02 Cefuroxime
J01DC03 Cefamandole
J01DC04 Cefaclor
J01DC05 Cefotetan
J01DC06 Cefonicide
J01DC07 Cefotiam
J01DC08 Loracarbef

J01DC09 Cefmetazole
J01DC10 Cefprozil
J01DC11 Ceforanide
J01DC12 Cefminox
J01DC13 Cefbuperazone
J01DC14 Flomoxef
J01DD Third-generation cephalosporins
J01DD01 Cefotaxime
J01DD02 Ceftazidime
J01DD03 Cefsulodin
J01DD04 Ceftriaxone
J01DD05 Cefmenoxime
J01DD06 Latamoxef
J01DD07 Ceftizoxime
J01DD08 Cefixime
J01DD09 Cefodizime
J01DD10 Cefetamet
J01DD11 Cefpiramide
J01DD12 Cefoperazone
J01DD13 Cefpodoxime
J01DD14 Ceftibuten
J01DD15 Cefdinir
J01DD16 Cefditoren
J01DD17 Cefcapene
J01DD54 Ceftriaxone, combinations
J01DD62 Cefoperazone, combinations
J01DD90 Ceftiofur
J01DD91 Cefovecin
J01DE Fourth-generation cephalosporins
J01DE01 Cefepime
J01DE02 Cefpirome
J01DE03 Cefozopran
J01DE90 Cefquinome
J01DF Monobactams
J01DF01 Aztreonam
J01DF02 Carumonam
J01DH Carbapenems
J01DH02 Meropenem
J01DH03 Ertapenem

J01DH04 Doripenem
J01DH05 Biapenem
J01DH51 Imipenem and enzyme inhibitor
J01DH55 Panipenem and betamipron
J01DI Other cephalosporins and penems
J01DI01 Ceftobiprole medocaril
J01DI02 Ceftaroline fosamil
J01DI03 Faropenem

J01E Sulfonamides and trimethoprim (J01E)
J01EA Trimethoprim and derivatives
J01EA01 Trimethoprim
J01EA02 Brodimoprim
J01EA03 Iclaprim
J01EB Short-acting sulfonamides
J01EB01 Sulfaisodimidine
J01EB02 Sulfamethizole
J01EB03 Sulfadimidine
J01EB04 Sulfapyridine
J01EB05 Sulfafurazole
J01EB06 Sulfanilamide
J01EB07 Sulfathiazole
J01EB08 Sulfathiourea
J01EB20 Combinations
J01EC Intermediate-acting sulfonamides
J01EC01 Sulfamethoxazole
J01EC02 Sulfadiazine
J01EC03 Sulfamoxole
J01EC20 Combinations
J01ED Long-acting sulfonamides
J01ED01 Sulfadimethoxine
J01ED02 Sulfalene
J01ED03 Sulfametomidine
J01ED04 Sulfametoxydiazine
J01ED05 Sulfamethoxypyridazine
J01ED06 Sulfaperin
J01ED07 Sulfamerazine
J01ED08 Sulfaphenazole
J01ED09 Sulfamazon

J01ED20 Combinations
J01EE Combinations of sulfonamides and trimethoprim, including derivatives
J01EE01 Sulfamethoxazole and trimethoprim
J01EE02 Sulfadiazine and trimethoprim
J01EE03 Sulfametrole and trimethoprim
J01EE04 Sulfamoxole and trimethoprim
J01EE05 Sulfadimidine and trimethoprim
J01EE06 Sulfadiazine and tetroxoprim
J01EE07 Sulfamerazine and trimethoprim
J01EQ Sulfonamides
J01EQ01 Sulfapyrazole
J01EQ02 Sulfamethizole
J01EQ03 Sulfadimidine
J01EQ04 Sulfapyridine
J01EQ05 Sulfafurazole
J01EQ06 Sulfanilamide
J01EQ07 Sulfathiazole
J01EQ08 Sulfaphenazole
J01EQ09 Sulfadimethoxine
J01EQ10 Sulfadiazine
J01EQ11 Sulfamethoxazole
J01EQ12 Sulfachlorpyridazine
J01EQ13 Sulfadoxine
J01EQ14 Sulfatroxazol
J01EQ15 Sulfamethoxypyridazine
J01EQ16 Sulfazuinoxaline
J01EQ17 Sulfamerazine
J01EQ18 Sulfamonomethoxine
J01EQ19 Sulfalene
J01EQ21 Sulfacetamide
J01EQ30 Combinations of sulfonamides
J01EQ59 Sulfadimethoxine, combinations
J01EW Combinations of sulfonamides and trimethoprim, including derivatives
J01EW03 Sulfadimidine and trimethoprim
J01EW09 Sulfadimethoxine and trimethoprim
J01EW10 Sulfadiazine and trimethoprim
J01EW11 Sulfamethoxazole and trimethoprime
J01EW12 Sulfachlorpyridazine and trimethoprim
J01EW13 Sulfadoxine and trimethoprim

J01EW14 Sulfatroxazol and trimethoprim
J01EW15 Sulfamethoxypyridazine and trimethoprim
J01EW16 Sulfaquinoxaline and trimethoprim
J01EW17 Sulfamonomethoxine and trimethoprim
J01EW18 Sulfamerazine and trimethoprim
J01EW30 Combinations of sulfonamides and trimethoprim

J01F Macrolides, lincosamides and streptogramins (J01F)
J01FA Macrolides
J01FA01 Erythromycin
J01FA02 Spiramycin
J01FA03 Midecamycin
J01FA05 Oleandomycin
J01FA06 Roxithromycin
J01FA07 Josamycin
J01FA08 Troleandomycin
J01FA09 Clarithromycin
J01FA10 Azithromycin
J01FA11 Miocamycin
J01FA12 Rokitamycin
J01FA13 Dirithromycin
J01FA14 Flurithromycin
J01FA15 Telithromycin
J01FA90 Tylosin
J01FA91 Tilmicosin
J01FA92 Tylvalosin
J01FA93 Kitasamycin
J01FA94 Tulathromycin
J01FA95 Gamithromycin
J01FA96 Tildipirosin
J01FF Lincosamides
J01FF01 Clindamycin
J01FF02 Lincomycin
J01FF52 Lincomycin, combinations
J01FG Streptogramins
J01FG01 Pristinamycin
J01FG02 Quinupristin/dalfopristin
J01FG90 Virginiamycin

J01G Aminoglycoside antibacterials (J01G)
J01GA Streptomycins
J01GA01 Streptomycin
J01GA02 Streptoduocin
J01GA90 Dihydrostreptomycin
J01GB Other aminoglycosides
J01GB01 Tobramycin
J01GB03 Gentamicin
J01GB04 Kanamycin
J01GB05 Neomycin
J01GB06 Amikacin
J01GB07 Netilmicin
J01GB08 Sisomicin
J01GB09 Dibekacin
J01GB10 Ribostamycin
J01GB11 Isepamicin
J01GB12 Arbekacin
J01GB13 Bekanamycin
J01GB90 Apramycin
J01GB91 Framycetin

J01M Quinolone antibacterials (J01M)
J01MA Fluoroquinolones
J01MA01 Ofloxacin
J01MA02 Ciprofloxacin
J01MA03 Pefloxacin
J01MA04 Enoxacin
J01MA05 Temafloxacin
J01MA06 Norfloxacin
J01MA07 Lomefloxacin
J01MA08 Fleroxacin
J01MA09 Sparfloxacin
J01MA10 Rufloxacin
J01MA11 Grepafloxacin
J01MA12 Levofloxacin
J01MA13 Trovafloxacin
J01MA14 Moxifloxacin
J01MA15 Gemifloxacin
J01MA16 Gatifloxacin

J01MA17 Prulifloxacin
J01MA18 Pazufloxacin
J01MA19 Garenoxacin
J01MA21 Sitafloxacin
J01MA90 Enrofloxacin
J01MA92 Danofloxacin
J01MA93 Marbofloxacin
J01MA94 Difloxacin
J01MA95 Orbifloxacin
J01MA96 Ibafloxacin
J01MA97 Pradofloxacin
J01MB Other quinolones
J01MB01 Rosoxacin
J01MB02 Nalidixic acid
J01MB03 Piromidic acid
J01MB04 Pipemidic acid
J01MB05 Oxolinic acid
J01MB06 Cinoxacin
J01MB07 Flumequine
J01MQ Quinoxalines
J01MQ01 Olaquindox

J01R Combinations of antibacterials (J01R)
J01RA Combinations of antibacterials
J01RA01 Penicillins, combinations with other antibacterials
J01RA02 Sulfonamides, combinations with other antibacterials (excluding trimethoprim)
J01RA03 Cefuroxime, combinations with other antibacterials
J01RA04 Spiramycin, combinations with other antibacterials
J01RA90 Tetracyclines, combinations with other antibacterials
J01RA91 Macrolides, combinations with other antibacterials
J01RA92 Amphenicols, combinations with other antibacterials
J01RA94 Lincosamides, combinations with other antibacterials
J01RA95 Polymyxins, combinations with other antibacterials
J01RA96 Quinolones, combinations with other antibacterials
J01RA97 Aminoglycosides, combinations with other antibacterials
J01RV Combinations of antibacterials and other substances
J01RV01 Antibacterials and corticosteroids

J01X Other antibacterials (J01X)

J01XA Glycopeptide antibacterials
J01XA01 Vancomycin
J01XA02 Teicoplanin
J01XA03 Telavancin
J01XA04 Dalbavancin
J01XA05 Oritavancin
J01XB Polymyxins
J01XB01 Colistin
J01XB02 Polymyxin B
J01XC Steroid antibacterials
J01XC01 Fusidic acid
J01XD Imidazole derivatives
J01XD01 Metronidazole
J01XD02 Tinidazole
J01XD03 Ornidazole
J01XE Nitrofuran derivatives
J01XE01 Nitrofurantoin
J01XE02 Nifurtoinol
QJ01XE90 Furazolidine
QJ01XQ Pleuromutilins
QJ01XQ01 Tiamulin
QJ01XQ02 Valnemulin
J01XX Other antibacterials
J01XX01 Fosfomycin
J01XX02 Xibornol
J01XX03 Clofoctol
J01XX04 Spectinomycin
J01XX05 Methenamine
J01XX06 Mandelic acid
J01XX07 Nitroxoline
J01XX08 Linezolid
J01XX09 Daptomycin
J01XX10 Bacitracin
QJ01XX55 Methenamine, combinations
QJ01XX93 Furaltadone
QJ01XX95 Novobiocin

Annex 2.6 – Comorbidity definition

History of any of the endpoints of interest will also be considered as comorbidity. These events are described in Annex 2.2. In addition, the following diseases will also be captured under comorbidity:

1. Definition of asthma (eventtype=ASTHMA)

According to the GINA (Global Initiative for Asthma) guidelines, asthma is a disorder defined by its clinical, physiological and pathological characteristics. The predominant feature of the clinical history is episodic shortness of breath, particularly at night often accompanied by cough (Bateman et al., 2008).

The following concepts of disease have been mapped through the UMLS for the outcomes of asthma.

Terms	ICD10	ICD9CM	Read Codes	ICPC
Asthma	J45*	493.*	H33..	R96
Asthma, unspecified	J45.9	493.90	H33z	
Nonallergic asthma	J45.1	493.1	H331z	
Intrinsic asthma			H331z	
Mixed asthma	J45.8		H332.	
Atopic asthma	J45			
extrinsic allergic asthma	J45	493.0	H330z	
Predominantly allergic asthma	J45.0			
Confirmed asthma			1O2..00	
Extrinsic asthma with asthma attack		493.02	663d.00	
			663m.00	
Intrinsic asthma + attack		493.12		
Number of asthma exacerbations in past year			663y.00	
Emergency admission, asthma			8H2P.00	
Status asthmaticus	J46	493.91		
Extrinsic asthma with status asthmaticus		493.01		
Intrinsic asthma NOS		493.10		
Intrinsic asthma with status asthmaticus		493.11		
chronic obstructive asthma		493.2		
Other forms of asthma		493.8		
Asthma severity			663V.00	
Mild asthma			663V100	
Moderate asthma			663V200	
Severe asthma			663V300	
History of asthma			14B4.00	
Asthma quality indicators			9hA..00	
			9hA1.00	
			9hA2.00	

2 Definition of arterial hypertension (eventtype=AHT)

According to the European Society of Hypertension (ESH) and European Society of Cardiology (ESC) Guidelines for the Management of Arterial Hypertension, a patient is defined as having hypertension when the systolic blood pressure is above 140 mm Hg and the diastolic blood pressure is above 90 mm Hg(2007).

	Blood pressure (mmHg)				
Other risk factors, OD or Disease	Normal SBP 120–129 or DBP 80–84	High normal SBP 130–139 or DBP 85–89	Grade 1 HT SBP 140–159 or DBP 90–99	Grade 2 HT SBP 160–179 or DBP 100–109	Grade 3 HT SBP ≥180 or DBP ≥110
No other risk factors	Average risk	Average risk	Low added risk	Moderate added risk	High added risk
1–2 risk factors	Low added risk	Low added risk	Moderate added risk	Moderate added risk	Very high added risk
3 or more risk factors, MS, OD or Diabetes	Moderate added risk	High added risk	High added risk	High added risk	Very high added risk
Established CV or renal disease	Very high added risk	Very high added risk	Very high added risk	Very high added risk	Very high added risk

The following concepts of disease have been mapped through the Unified Medical Language System (UMLS) for arterial hypertension.

Terms	ICD10	ICD9CM	Read Codes	ICPC
Hypertensive diseases	I10-I15.9	401-405.99	Gyu2.	
high blood pressure	I10		XE0Ub	
			XM02V	
High blood pressure disorder			XE0Ub	
Uncomplicated hypertension				K86
Hypertension with involvement target organs				K87
Renovascular hypertension	I15.0			
Secondary hypertension	I15	405	G24..	
Secondary hypertension, unspecified	I15.9		G24z.	
Malignant essential hypertension		401.0	G200.	
Essential (primary) hypertension	I10	401	XE0Uc	
Hypertension NOS		401.9	XE0Ud	
Benign hypertension		401.1	G201.	
Other secondary hypertension	I15.8	405.99	Gyu20	
Malignant secondary hypertension		405.0	G240.	
		405.09	G240z	
Benign secondary hypertension		405.1	G241	
		405.19	G241z	

Terms	ICD10	ICD9CM	Read Codes	ICPC
Malignant hypertension			Xa3fQ	

3 Definition of hyperlipidemia/dyslipidemia (eventtype=LIPID)

Dyslipidemia is defined as an elevation of plasma cholesterol, triglycerides (TGs), or both, or a low high-density lipoprotein level that contributes to the development of atherosclerosis. Causes may be primary (genetic) or secondary. Diagnosis is by measuring plasma levels of total cholesterol, TGs, and individual lipoproteins.

The following concepts of disease have been mapped through the Unified Medical Language System (UMLS) for hyperlipidemia.

Terms	ICD10	ICD9CM	Read Codes	ICPC
Mixed hyperlipidaemia	E78.2	272.2	XE11U	T93.03
Fam hyperlipoproteinaemia IIb			X40Vm	T93.04
Familial combined hyperlipidaemia				
Hyper apo beta lipoproteinaemia				
Other hyperlipidemia	E78.4	272.4	Cyu8D	
hypercholesterolaemia	E78.0	272.0	XE11S	T93.01
			C320z	

4 Definition of chronic kidney disease (eventtype=CKD)

Chronic kidney disease is defined as either kidney damage or glomerular filtration rate <60 mL/min/1.73 m2 for at least 3 months. Kidney damage is defined as pathologic abnormalities or markers of damage, including abnormalities in blood or urine tests or imaging studies (Levey and Coresh, 2012).

The different stages of chronic kidney disease are described in the table below:

Stage	Description	GFR (mL/min/1.73 m^2)
1	Kidney damage with normal or ↑ GFR	≥ 90
2	Kidney damage with mild ↓ GFR	60-89
3	Moderate ↓ GFR	30-59
4	Severe ↓ GFR	15-29
5	Kidney failure	< 15 or dialysis

The following concepts of disease have been mapped through the Unified Medical Language System (UMLS) for the outcomes of chronic kidney disease.

Terms	ICD10	ICD9CM	Read Codes	ICPC
Chronic kidney disease	N18	585.9	1Z1..	U99
	N18.9	583*	K05..13	
		585*		
		586*		
Hypertensive chronic kidney disease	I12	403		
Chronic kidney disease, Stage I		585.1	1Z10.00	
			1Z17.00	
			1Z18.00	

Terms	ICD10	ICD9CM	Read Codes	ICPC
			1Z18.11	
			K051.00	
End stage renal disease		585.6	K050.00	
			K0D..00	
Chronic kidney disease, Stage 5		585.5	1Z14.00	
			1Z1K.00	
			1Z1K.11	
			1Z1L.00	
			1Z1L.11	
			K055.00	
Hypertensive chronic kidney disease, malignant		403.0		
Hypertensive heart and chronic kidney disease	I13	404		
Chronic kidney disease, stage 2 (mild)	N18.2	585.2	1Z11.00	
			1Z19.00	
			1Z19.11	
			1Z1A.00	
			1Z1A.11	
			K052.00	
Chronic kidney disease, stage 3 (moderate)	N18.3	585.3	1Z12.00	
			1Z15.00	
			1Z16.00	
			1Z1B.00	
			1Z1B.11	
			1Z1C.00	
			1Z1C.11	
			1Z1D.00	
			1Z1D.11	
			1Z1E.00	
			1Z1E.11	
			1Z1F.00	
			1Z1F.11	
			1Z1G.00	
			1Z1G.11	
			K053.00	
Chronic kidney disease, stage 4 (severe)	N18.4	585.4	1Z13.00	
			1Z1H.00	
			1Z1H.11	
			1Z1J.00	
			1Z1J.11	
			K054.00	
Hypertensive heart and chronic kidney disease, malignant		404.0		
		403.xx, 404.xx		
Renal failure	N17-N19.9	586	D215.00	
			D215000	
			K05..00	
			K05..12	
			K050.00	

Terms	ICD10	ICD9CM	Read Codes	ICPC
			K06..00	
			K06..12	
Other chronic renal failure	N18.8		Kyu21	
Chronic kidney diseases monitoring/self-management			661M200	
			661N200	
			66i..00	
			6AA..00	
			9Ni9.00	
			9Ot..00	
			9Ot0.00	
			9Ot1.00	
			9Ot2.00	
			9Ot3.00	
			9Ot4.00	
Dialysis		V45.1	7L1..	
		V56.0	SP06B00	
		V56.8	Z1A..	
			Z91A.00	
			Z91A100	
			ZV45100	
			ZV56..	
			ZVu3G00	
CKD quality indicators			9hE..00	
			9hE0.00	
			9hE1.00	
Predicted stage chronic kidney			9Ot5.00	
Renal impairment			K060.00	
Impaired renal function			K060.11	
Acute-on-chronic renal failure			K0E..00	
Kidney transplantation		V42.0, 996.81	SP08300	
		250.4x	SP08C00	
			SP08D00	
			SP08E00	
			SP08F00	
			SP08G00	
			SP08H00	

If available, kidney function will be derived from the lab results (calculation of glomerular filtration rate = creatinine clearance) using the following formula:

$$GFR = 141 \times \min(Scr/\kappa,1)^{\alpha} \times \max(Scr/\kappa,1)^{-1.209} \times 0.993^{Age} \times 1.018 \text{ [if female]} \times 1.159 \text{ [if black]}$$

Where Scr is serum creatinine (mg/dL), κ is 0.7 for females and 0.9 for males, α is –0.329 for females and –0.411 for males, min indicates the minimum of Scr/κ or 1, and max indicates the maximum of Scr/κ or 1 (Levey et al., 2009).

Based on the actual value of the GFR, it will be possible to describe the stage of chronic kidney disease. In addition, code specific terms by stage (see above) will be used.

5 Definition of hepatic impairment (eventtype=HEPAR)

Hepatic function decreases with age, but due to the high capacity of the liver this is considered not to change the pharmacokinetics to a clinically relevant extent. Liver disease, however, is known to be a common cause of altered pharmacokinetics of medications. Hepatic function can be decreased through different pathophysiological mechanisms. Worldwide, chronic infections with hepatitis B or C are the most common causes of chronic liver disease, whereas in the western world, chronic and excessive alcohol ingestion is one of the major causes of liver disease. Other causes are uncommon diseases such as primary biliary cirrhosis, primary sclerosing cholangitis and autoimmune chronic active hepatitis. Ongoing destruction of the liver parenchyma in chronic liver diseases ultimately leads to liver cirrhosis and the development of portal hypertension. However, even if liver cirrhosis is established, the residual metabolic function of the liver may be rather well preserved for many years because of regeneration of hepatocytes. Clinical symptoms related to hepato-cellular failure and portal hypertensions are most importantly ascites, oesophageal varices and encephalopathy. Serum markers of liver failure are low serum albumin and a prothrombin deficiency. Serum bilirubin as well as other liver tests may or may not be affected to a varying degree, e.g. depending on the liver disease (cholestatic versus hepatocellular). Liver cirrhosis is irreversible in nature, but progression can be modified by e.g. abstinence of alcohol in alcohol liver cirrhosis (EMA, 2005).

Terms	ICD10	ICD9CM	Read Codes	ICPC
Liver enzymes abnormal	R94.5 R74	794.8	44G2. R148. 44D2. 44G3100 44G4100 44H5100 44H5200 R148.00	
Hepatic failure, unspecified	K72.9			
Liver failure			7L1f.00 7L1fy00 7L1fz00 J625.00 J625.11 J62y.11 J62y.12 J62y.13	
Cirrhosis; liver	K74.60	571.5	J615..	D97
Hepatic failure, unspecified				
Nonspecific elevation of levels of transaminase or LDH		790.4		
Inflammatory liver disease, unspecified	K75.9			
Hepatitis NOS		573.3	J633.	
Hepatitis unspecified				

Terms	ICD10	ICD9CM	Read Codes	ICPC
Unspecified viral hepatitis	B19	070	A70z.	D72
Viral hepatitis	B19.9		A70..	
			A72x000	
			A785200	
			AyuB..	
			J63..	
Chronic hepatitis, unspecified	K73.9	571.4	J614..	
			J614y	
Alcoholic cirrhosis or fibrosis	K70.2			
	K70.3			
	K70.4			
Primary or secondary biliary cirrhosis	K74.3			
	K74.4			
	K74.5			
History of hepatitis			141E.00	
			141F.00	
			2126700	
H/O: liver disease			14C5.00	
Hepatitis A - current infection			2J23.00	
Chronic hepatitis			9kR..00	
			9kR..11	
Hepatitis screening positive			9kV..00	
			9kV..11	
			9kZ..00	
			9kZ..11	
Sequelae of viral hepatitis			AE23.00	
			AyuJ900	
Acute liver failure			J600011	
Acute hepatitis - noninfective			J600100	
Necrosis of liver			J600z00	
			J601.00	
Cirrhosis and chronic liver disease			J61..	
Other sequelae of chronic liver			J62y.00	
[X]Diseases of the liver			Jyu7..	
Liver transplant failure and rejection			SP08600	
Liver failure as a complication of care			SP14211	

6 Definition of lung cancer (eventtype=LUNGCAN)

The definition of lung cancer is a cancer (malignancy) that originates in the tissues of the lungs or the cells lining the airways. Lung cancer originates when normal lung cells become abnormal, usually after a series of mutations, and begin to divide out of control.

The following concepts of disease have been mapped through the Unified Medical Language System (UMLS) for lung cancer.

Terms	ICD10	ICD9CM	Read Codes	ICPC
Lung cancer	C34.9	162	Xa0KG	R84
Malignant neoplasm of bronchus and lung		162.9	B22.. Byu20 XE1vc	
Oat cell carcinoma of			X78QO	
Small cell carcinoma of lung			X78QN	
Secondary malignant neoplasm of lung	C78.0	197.0	B570	
Non-small cell lung cancer			X78QS	
Malignant neoplasm of hilus of lung			B2211	
Malignant neoplasm of upper lobe of lung			B2221	
Malignant neoplasm of middle lobe of lung			B2231	
Malignant neoplasm of lower lobe of lung			B2241	
Malignant neoplasm of upper lobe, bronchus or lung	C34.1	162.3	B222z XE1vb	
Malignant neoplasm of middle lobe, bronchus or lung	C34.2	162.4	B223. B223z	
Malignant neoplasm of lower lobe, bronchus or lung	C34.3	162.5	B224. B224z	
Malignant neoplasm of other parts of bronchus or lung		162.8	B22y.	
Malignant neoplasm overlapping bronchus and lung sites	C34.8		B225.	
Personal history of malignant neoplasm of lung			ZV101	

7 Definition of cancer (eventtype=CANCER)

The following concepts of disease have been mapped through the Unified Medical Language System (UMLS) for cancer. **For skin cancer, basocellular epithelioma and spinocellular epithelioma are excluded**

Terms	ICD10	ICD9CM	Read Codes	ICPC
Malignancy	C* (excluding lung cancer)			
Malignant neoplasm without specification of site	C80	199	ByuC8 XE20H B59..	A79
Cancer			X78ef	
Malignant neoplasm				
Malignant neoplasm of bladder	C67	188	B49..	U76
Malignant neoplasm of breast	C50-C50.9		Byu6.	X76
Breast cancer			X78WM	
Malignant tumor of breast			XE1zL	
Malignant neoplasm of colon	C18	153	B13..	D75
Malignant tumour of colon			XE1xd XE1vV	
Malignant neoplasm of larynx	C32	161	B21.. XE1yD	
Carcinoma of the rectum			XE1vW X78OK	

Terms	ICD10	ICD9CM	Read Codes	ICPC
Malignant neoplasm of skin (excluding basocellular epithelioma/spinocellular epithelioma)			Byu43 X78gs B33z.	S77
Malignant neoplasm of thyroid gland	C73	193	B53..	T71
Malignant neoplasm of cervix uteri	C53	180	XE1vi B41z.	X75
Malignant neoplasm of stomach Gastric cancer	C16	151	X78gA XE1vR XE1xJ B11z.	D74
Malignant neoplasm of vagina	C52	184.0	B450.	
Malignant neoplasm of oropharynx	C10	146	B06..	
Malignant neoplasm of nasopharynx	C11	147	B07..	
Malignant neoplasm of pharynx	C14	149.0	X78fO	
Malignant neoplasm of duodenum	C17	152.0	/B120.	
Malignant neoplasm of caecum	C18.0	153.4	XE1vU	
Malignant neoplasm of peritoneum	C48.2	158.9	Byu57 X78Pq	
Malignant neoplasm of trachea	C33	162.0	B220.	
Malignant neoplasm of pleura	C38.4	163	B23..	
Bone cancer			XE1vd	
Malignant neoplasm of liver	C22	155	Xa97q B152.	
Malignant neoplasm of intestinal tract, part unspecified	C26.0	159.0	Byu12 X78gK B1z0.	
Malignant neoplasm of pancreas	C25	157	B17.. XE1y5	D76
Malignant neoplasm of vertebral column	C41.2		B302.	
Malignant neoplasm of prostate	C61	185	B46..	Y77
Malignant neoplasm of oesophagus	C15	150.9	B10.. X78g3 XE1vQ	
Malignant neoplasm of ovary	C56	183.0	B440.	
Malignant neoplasm of uterus	C55	179	B43..	
Malignant melanoma of skin	C43	172	Byu41 B32..	
Malignant neoplasm of brain	C71	191	B51z. XE2vS	N74
Malignant tumor of kidney	C64	189.0	X78iu	U75
Hodgkin's disease	C81	201	B61.. XaC2n BBjA.	B72
Leukemia	C95	208	BBr00 X78e2	B73

Annex 2.7 – Codes for COPD exacerbation as indication of use of systemic corticosteroids and antibiotics

Codes in annex 2.4 and 2.7 were used to identify use of systemic corticosteroids or antibiotics for reason of "COPD exacerbation"

Terms	ICD10	ICD9CM	Read Codes	ICPC
COPD exacerbation	J44.0		66Yd.00	
	J44.1		66Ye.00	
			66Yf.00	
			8H2R.00	
			H3y1.00	
			H312200	
Chronic obstructive pulmonary disease disturbs sleep			66Yg.00	
Chronic obstructive pulmonary disease does not disturb sleep			66Yh.00	
Attends respiratory support group			66YH.00	
COPD self-management plan given			66YI.00	
Multiple COPD emergency hospitalisations			66Yi.00	
Chronic obstructive pulmonary disease follow-up/monitoring			66YL.00	
			66YL.11	
			66YL.12	
			66YM.00	
			66YS.00	
			66YT.00	
COPD quality indicators			9h5..00	
			9h51.00	
			9h52.00	
Chronic bronchitis		491*	H31..00	R91
Simple and mucopurulent chronic bronchitis	J41			
Unspecified chronic bronchitis	J42			
Simple chronic bronchitis			H310.00	
Simple chronic bronchitis NOS			H310z00	
Mucopurulent chronic bronchitis			H311.00	
Purulent chronic bronchitis			H311000	
Fetid chronic bronchitis			H311100	
Mucopurulent chronic bronchitis NOS			H311z00	
Obstructive chronic bronchitis			H312.00	
Chronic wheezy bronchitis			H312011	
Emphysematous bronchitis			H312100	
Mixed simple and mucopurulent chronic bronchitis			H313.00	
Other chronic bronchitis			H31y.00	
Other chronic bronchitis NOS			H31yz00	
Chronic bronchitis NOS			H31z.00	
Bronchitis, not specified as acute or chronic	J40	490		

Terms	ICD10	ICD9CM	Read Codes	ICPC
Emphysema	J43	492*	H32..00	R95
interstitial emphysema		518.1		
Compensatory emphysema		518.2		
Chronic bullous emphysema			H320.00	
Segmental bullous emphysema			H320000	
Zonal bullous emphysema			H320100	
Giant bullous emphysema			H320200	
Bullous emphysema with collapse			H320300	
Chronic bullous emphysema NOS			H320z00	
Panlobular emphysema			H321.00	
Centrilobular emphysema			H322.00	
Other emphysema			H32y.00	
Acute vesicular emphysema			H32y000	
Atrophic (senile) emphysema			H32y100	
MacLeod's unilateral emphysema			H32y200	
Other emphysema NOS			H32yz00	
Emphysema NOS			H32z.00	

Annex 2.8 - Definition of LRTI (indication of use of antibiotics)

Lower respiratory tract infection consists of both pneumonia and (acute) bronchitis
The following concepts of disease have been mapped through the Unified Medical Language System (UMLS) for lower respiratory tract infection.

Terms	ICD10	ICD9CM	Read Codes	ICPC
Pneumonia, (unspecified)	J18*		X100E H2*	R81
Bacterial pneumonia, (unspecified)	J15.9	482.9	X100H H22z.	
Atypical pneumonia	J16.8		H28.00	
Viral pneumonia	J12.9 J10.0	480 480.9	XE0YG H2*.	
Acute bronchitis	J20	466	H06..	R78
Acute tracheo-bronchitis	J20.9	466.0	XE0Xr H060z H0605	

Annex 2.9 – Data sources

IPCI Database

In 1992 the Integrated Primary Care Information Project (IPCI) was started by the Department of Medical Informatics of the Erasmus University Medical Center. IPCI is a longitudinal observational database that contains data from computer-based patient records of a selected group of general practitioners (GPs) throughout The Netherlands, who voluntarily chose to supply data to the database. Collaborating practices are located throughout The Netherlands and the collaborating GPs are comparable to other GPs in the country according to age and gender. In the Netherlands, all citizens are registered with a GP practice, which forms the point of care and acts as a gatekeeper in a two-way exchange of information with secondary care. The medical records of each patient can therefore be assumed to contain all relevant medical information including medical findings and diagnosis from secondary care.

The database contains information on about 2.2 million patients. This is the cumulative amount of patients who have ever been part of the dynamic cohort of patients who have been registered. The International Classification of Primary Care (ICPC) is the coding system for patient complaints and diagnoses, but diagnoses and complaints can also be entered as free text. Prescription data such as product name, quantity prescribed, dosage regimens, strength and indication are entered into the computer (Vlug et al., 1999). The National Database of Drugs, maintained by the Royal Dutch Association for the Advancement of Pharmacy, enables the coding of prescriptions, according to the Anatomical Therapeutic Chemical (ATC) classification scheme recommended by the WHO (WHO, 2008).

As this is a primary care database, information on specialist prescribing, medication dispensing and actual medication intake is missing.

IPCI is listed under the ENCePP resources database. (www.encepp.eu/encepp/resourcesDatabase.jsp)

THIN Database

The Health Improvement Network (THIN) is a database of primary care medical records from the United Kingdom. General practitioners are trained to complete their medical records using the Vision general practice computer system (InPractice Systems, London, UK). This electronic record serves as the primary medical records for the practice.

Data recorded in THIN include demographics, details from general practitioners' visits such as medical diagnoses and prescriptions written by the general practitioners, diagnoses from specialist referrals and hospital admissions, some results of laboratory tests, some lifestyle characteristics and other measurements as taken in the practice. Within the database, diagnoses are recorded using READ codes. Prospective data collection for THIN began in September 2002, with electronic medical records that date back to 1985. In addition, practices may retrospectively enter significant medical events into the electronic medical record. Currently, the database has 2.7 million active patients registered. Recently a validation study was conducted by Lewis et al which concluded that "THIN data that are collected outside of the Clinical Practice Research Datalink (CPRD) appear as valid as the data collected as part of the CPRD (Lewis et al., 2007).

As the primary aim of the collection of data in the THIN database is patient management, data will reflect only those events that are deemed to be relevant to patient's care. In addition; use of THIN data is not appropriate in studies where individual ethnicity, occupation, employment, and/or socio-economic status are important variables. As for all prescription databases, OTC medication use and non-compliance to medication prescriptions might be an issue. As the average follow-up within the THIN database is 7.3 years, the THIN database is not suitable to conduct long-term follow-up studies.

THIN is listed under the ENCePP resources database. (www.encepp.eu/encepp/resourcesDatabase.jsp)

Aarhus Database

The Aarhus University Prescription Database comprises clinical and prescription data on the population of former North-Jutland, Aarhus, Rinkjebing and Viborg counties, which since 2007 are called the Central Denmark Region and the North Denmark Region. This population covers a total of 1.4 million inhabitants and is representative of the population of Denmark (Ehrenstein et al., 2010). Data available on these subjects comprise their eligibility, dispensing data, hospitalizations and procedures and the population can also be linked to other National Danish registries. Dispensing data comprise the filled prescriptions for all ambulatory patients and contains information on name of the medication, ATC code, package identifier (strength and route of administration), and the date of refill. These data can be linked to the national registry of patients that comprises information on admissions to Danish somatic hospitals, emergency rooms and outpatient clinics, diagnosis codes and procedures are registered. These databases have been used in numerous studies and are proven valid for pharmacoepidemiological research (Sorensen and Larsen, 1994).

Dose must be inferred from the strength, assuming a once daily administration for QVA149 and according the dosing regimens of the respective Summary of Product Characteristics of the other medications. The main drawbacks of the Aarhus University Prescription Database are a lack of nationwide coverage and the absence of data of certain medication types (non-reimbursed medications, OTC medications or medications dispensed directly to hospital patients or outpatient clinics).

HSD CSD Longitudinal Patient Database

The Italian arm of the study uses the Health Search CSD Longitudinal Patient Database (HSD), a longitudinal observational database that is representative of the Italian general population. It was established in 1998 by the Italian College of General Practitioners (Filippi et al., 2005). The HSD contains data from computer-based patient records from a selected group of GPs (covering a total of 1.7 million patients) located throughout Italy. These GPs voluntarily agreed to collect data for the database and attend specified training courses. The database includes information on the age, gender, and identification of the patient, and GP registration information, which is linked to prescription information, clinical events and diagnoses, hospital admission, and causes of death. All diagnoses are coded according to the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM). Medication names are coded according to the ATC classification system (WHO, 2008). To be included in the study, GPs must have provided data for at least 1 year and meet standard quality criteria pertaining to:

levels of coding, prevalence of well-known diseases, and mortality rates (Cricelli et al., 2003). The HSD complies with EU, guidelines on the use of medical data for research. The HSD has been used as data source for a number of peer-reviewed publications on the prevalence of disease conditions, drug safety and prescription patterns in Italian primary care (Cazzola et al., 2011). Approval for use of data is obtained from the Italian College of General Practitioners.

Dose must be inferred from the strength, assuming a once daily administration for QVA149 and according to the dosing regimens of the respective SmPC for the other medications. Around 50% of prescription dosage is also imputed by GPs.

HSD is listed under the ENCePP resources database. (www.encepp.eu/encepp/resourcesDatabase.jsp)

SIDIAP Database

General practitioners (GPs) play an essential role in the public health care system of Spain, as they are responsible for primary health care, long-term prescriptions and specialist and hospital referrals.

The Spanish public health care system covers more than 98% of the population. SIDIAP Database comprises of electronic medical records of a representative sample of patients attended by GPs in Catalonia (North-East Spain), covering a population of more than 5.6 million patients (about 80% of the total of 7.5 million population of Catalonia) from 274 primary care practices with 3,414 participating GPs.

The SIDIAP data comprises the clinical and referral events registered by primary care health professionals (GPs and nurses) and administrative staff in electronic medical records, comprehensive demographic information, prescription and corresponding pharmacy invoicing data, specialist referrals, primary care laboratory test results, and hospital admissions and their major outcomes. Health professionals gather this information using ICD-10 codes, and structured forms designed for the collection of variables relevant for primary care clinical management, such as country of origin, sex, age, height, weight, body mass index, tobacco and alcohol use, blood pressure measurements, blood and urine test results. Only GPs who meet quality control standards can participate in the SIDIAP database. Encoding personal and clinic identifiers ensures the confidentiality of the information in the SIDIAP Database. Recent reports have shown the SIDIAP data to be useful for epidemiological research (Garcia-Gil Mdel et al., 2011).

Additional Statistical table set

QVA149A2402

Table 15-16-1 (Page 1 of 20)
Continuous baseline characteristics by exposure cohorts
THIN - Total analysis population

		QVA149	Free LABA+LAMA without ICS	Std Dif	Free LABA+LAMA with ICS	Std Dif
Cohort time	N	1346	2586	0.410	394	0.691
	Mean (SD)	200.4 (183.6)	157.4 (198.3)	.	113.3 (144.8)	.
	Median (IQR)	134.0 (60.0-283.0)	77.0 (35.0-187.3)	.	60.0 (30.0-127.0)	.
	Min-Max	1.0-950.0	1.0-1376	.	4.0-1014	.
Cohort time extended	N	1346	2586	0.457	394	0.750
	Mean (SD)	208.9 (182.3)	160.3 (198.6)	.	114.9 (145.2)	.
	Median (IQR)	148.0 (88.0-290.0)	87.0 (35.0-190.0)	.	60.0 (30.0-131.3)	.
	Min-Max	1.0-950.0	1.0-1376	.	4.0-1014	.
Cohort time unrestricted	N	1346	2586	0.473	394	0.778
	Mean (SD)	214.6 (185.6)	166.9 (204.8)	.	120.9 (157.3)	.
	Median (IQR)	154.0 (73.0-299.0)	86.0 (44.0-200.3)	.	60.0 (33.8-133.0)	.
	Min-Max	3.0-950.0	1.0-1376	.	4.0-1136	.

Note: Run date and time 22NOV2018 13:58:58,

QVA149A2402

Table 15-16-1 (Page 2 of 20)
Continuous baseline characteristics by exposure cohorts
THIN - Total analysis population

		QVA149	Free LABA+ICS	Std Dif	Fixed LABA/ICS	Std Dif
Cohort time	N	1346	583	0.605	21315	-0.086
	Mean (SD)	200.4 (183.6)	116.9 (151.1)	.	246.5 (272.7)	.
	Median (IQR)	134.0 (60.0-283.0)	73.0 (54.0-117.0)	.	129.0 (62.0-309.0)	.
	Min-Max	1.0-950.0	1.0-1232	.	1.0-1421	.
Cohort time extended	N	1346	583	0.556	21315	-0.177
	Mean (SD)	208.9 (182.3)	129.6 (152.0)	.	265.7 (268.3)	.
	Median (IQR)	148.0 (88.0-290.0)	90.0 (55.0-133.0)	.	150.0 (90.0-327.0)	.
	Min-Max	1.0-950.0	1.0-1232	.	1.0-1421	.
Cohort time unrestricted	N	1346	583	0.624	21315	0.012
	Mean (SD)	214.6 (185.6)	130.3 (159.0)	.	249.4 (274.0)	.
	Median (IQR)	154.0 (73.0-299.0)	85.0 (60.0-126.0)	.	131.0 (67.0-313.0)	.
	Min-Max	3.0-950.0	14.0-1360	.	1.0-1421	.

Note: Run date and time 22NOV2018 13:58:58,

QVA149A2402

Table 15-16-1 (Page 3 of 20)
Continuous baseline characteristics by exposure cohorts
THIN - Total analysis population

		QVA149	Fixed LABA/LAMA	Std Dif	LABA	Std Dif
Cohort time	N	1346	4921	0.089	3006	0.419
	Mean (SD)	200.4 (183.6)	185.6 (175.9)	.	146.9 (183.5)	.
	Median (IQR)	134.0 (60.0-283.0)	118.0 (60.0-256.0)	.	81.0 (59.0-159.0)	.
	Min-Max	1.0-950.0	1.0-1070	.	1.0-1397	.
Cohort time extended	N	1346	4921	0.076	3006	0.351
	Mean (SD)	208.9 (182.3)	195.4 (174.6)	.	161.1 (182.9)	.
	Median (IQR)	148.0 (88.0-290.0)	133.0 (81.0-266.0)	.	94.0 (62.0-181.0)	.
	Min-Max	1.0-950.0	1.0-1070	.	1.0-1397	.
Cohort time unrestricted	N	1346	4921	0.097	3006	0.259
	Mean (SD)	214.6 (185.6)	198.0 (176.4)	.	185.9 (208.3)	.
	Median (IQR)	154.0 (73.0-299.0)	134.0 (60.0-276.5)	.	97.0 (60.0-210.0)	.
	Min-Max	3.0-950.0	1.0-1070	.	1.0-1397	.

Note: Run date and time 22NOV2018 13:58:58,

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Continuous baseline characteristics by exposure cohorts
THIN - Total analysis population

		QVA149	LAMA	Std Dif
Cohort time	N	1346	18598	0.264
	Mean (SD)	200.4 (183.6)	176.8 (214.9)	.
	Median (IQR)	134.0 (60.0-283.0)	90.0 (60.0-210.0)	.
	Min-Max	1.0-950.0	1.0-1424	.
Cohort time extended	N	1346	18598	0.200
	Mean (SD)	208.9 (182.3)	191.4 (213.9)	.
	Median (IQR)	148.0 (88.0-290.0)	111.0 (78.0-229.0)	.
	Min-Max	1.0-950.0	1.0-1424	.
Cohort time unrestricted	N	1346	18598	0.071
	Mean (SD)	214.6 (185.6)	236.5 (262.4)	.
	Median (IQR)	154.0 (73.0-299.0)	122.0 (60.0-297.0)	.
	Min-Max	3.0-950.0	1.0-1424	.

Note: Run date and time 22NOV2018 13:58:58,

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Table 15-16-1 (Page 5 of 20)
Continuous baseline characteristics by exposure cohorts
THIN - Total analysis population

		QVA149	Free LABA+LAMA without ICS	Std Dif	Free LABA+LAMA with ICS	Std Dif
Follow-up time	N	1346	2586	-1.074	394	-1.086
	Mean (SD)	354.8 (246.0)	707.2 (393.3)	.	714.8 (399.3)	.
	Median (IQR)	306.0 (158.0-544.3)	707.5 (363.0-1038)	.	677.5 (385.5-1049)	.
	Min-Max	3.0-980.0	1.0-1425	.	29.0-1422	.
Age at cohort entry	N	1346	2586	0.053	394	0.043
	Mean (SD)	70.3 (10.4)	69.7 (10.1)	.	69.8 (10.0)	.
	Median (IQR)	71.0 (63.5-77.8)	70.2 (62.9-77.1)	.	70.3 (63.0-76.9)	.
	Min-Max	40.6-101.0	40.9-97.8	.	44.2-97.3	.
Number of contacts with GP at practice	N	1346	2586	-0.111	394	-0.309
	Mean (SD)	7.5 (6.2)	8.2 (6.5)	.	9.7 (7.7)	.
	Median (IQR)	6.0 (3.0-10.0)	7.0 (4.0-11.0)	.	8.0 (4.0-13.0)	.
	Min-Max	0.0-53.0	0.0-92.0	.	0.0-63.0	.

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Table 15-16-1 (Page 6 of 20)
Continuous baseline characteristics by exposure cohorts
THIN - Total analysis population

		QVA149	Free LABA+ICS	Std Dif	Fixed LABA/ICS	Std Dif
Follow-up time	N	1346	583	-0.956	21315	-0.766
	Mean (SD)	354.8 (246.0)	672.3 (400.2)	.	606.3 (393.6)	.
	Median (IQR)	306.0 (158.0-544.3)	630.0 (335.0-1022)	.	565.0 (258.0-921.0)	.
	Min-Max	3.0-980.0	14.0-1420	.	1.0-1425	.
Age at cohort entry	N	1346	583	0.139	21315	0.115
	Mean (SD)	70.3 (10.4)	68.7 (11.8)	.	69.0 (11.1)	.
	Median (IQR)	71.0 (63.5-77.8)	69.5 (60.5-77.3)	.	69.5 (61.4-77.2)	.
	Min-Max	40.6-101.0	40.8-100.3	.	40.0-102.9	.
Number of contacts with GP at practice	N	1346	583	-0.177	21315	-0.018
	Mean (SD)	7.5 (6.2)	8.7 (7.2)	.	7.6 (7.0)	.
	Median (IQR)	6.0 (3.0-10.0)	8.0 (4.0-12.0)	.	6.0 (3.0-10.0)	.
	Min-Max	0.0-53.0	0.0-92.0	.	0.0-140.0	.

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Continuous baseline characteristics by exposure cohorts
THIN - Total analysis population

		QVA149	Fixed LABA/LAMA	Std Dif	LABA	Std Dif
Follow-up time	N	1346	4921	0.083	3006	-0.843
	Mean (SD)	354.8 (246.0)	335.0 (233.1)	.	635.7 (402.1)	.
	Median (IQR)	306.0 (158.0-544.3)	297.0 (143.0-490.0)	.	592.5 (289.0-979.0)	.
	Min-Max	3.0-980.0	1.0-1152	.	1.0-1420	.
Age at cohort entry	N	1346	4921	0.052	3006	0.108
	Mean (SD)	70.3 (10.4)	69.7 (10.2)	.	69.1 (10.8)	.
	Median (IQR)	71.0 (63.5-77.8)	70.2 (62.9-77.1)	.	69.9 (61.9-77.0)	.
	Min-Max	40.6-101.0	40.6-98.3	.	40.1-99.9	.
Number of contacts with GP at practice	N	1346	4921	0.023	3006	-0.007
	Mean (SD)	7.5 (6.2)	7.4 (6.3)	.	7.6 (6.5)	.
	Median (IQR)	6.0 (3.0-10.0)	6.0 (3.0-10.0)	.	6.0 (3.0-10.0)	.
	Min-Max	0.0-53.0	0.0-76.0	.	0.0-91.0	.

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Continuous baseline characteristics by exposure cohorts
THIN - Total analysis population

		QVA149	LAMA	Std Dif
Follow-up time	N	1346	18598	-0.781
	Mean (SD)	354.8 (246.0)	611.1 (393.7)	.
	Median (IQR)	306.0 (158.0-544.3)	572.0 (269.0-922.0)	.
	Min-Max	3.0-980.0	1.0-1425	.
Age at cohort entry	N	1346	18598	0.112
	Mean (SD)	70.3 (10.4)	69.1 (10.8)	.
	Median (IQR)	71.0 (63.5-77.8)	69.7 (61.7-77.0)	.
	Min-Max	40.6-101.0	40.0-100.1	.
Number of contacts with GP at practice	N	1346	18598	0.018
	Mean (SD)	7.5 (6.2)	7.4 (6.4)	.
	Median (IQR)	6.0 (3.0-10.0)	6.0 (3.0-10.0)	.
	Min-Max	0.0-53.0	0.0-102.0	.

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Continuous baseline characteristics by exposure cohorts
THIN - Total analysis population

		QVA149	Free LABA+LAMA without ICS	Std Dif	Free LABA+LAMA with ICS	Std Dif
Number of contacts with GP at home	N	1346	2586	0.076	394	0.019
	Mean (SD)	0.5 (1.7)	0.4 (1.6)	.	0.4 (1.1)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.	0.0 (0.0-0.0)	.
	Min-Max	0.0-21.0	0.0-20.0	.	0.0-10.0	.
Days from spirometry to index date	N	1123	2206	0.143	354	0.081
	Mean (SD)	337.5 (426.4)	244.0 (337.7)	.	252.7 (339.1)	.
	Median (IQR)	153.0 (2.0-504.0)	107.0 (4.0-338.3)	.	125.0 (13.8-345.5)	.
	Min-Max	0.0-1805	0.0-1766	.	0.0-1806	.
FEV1 percentage	N	1123	2206	-0.134	354	0.086
	Mean (SD)	62.2 (19.7)	64.8 (18.9)	.	60.5 (19.1)	.
	Median (IQR)	61.8 (47.2-76.1)	64.0 (51.9-76.2)	.	60.9 (46.5-73.0)	.
	Min-Max	20.1-169.5	19.6-204.7	.	21.2-117.2	.

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Continuous baseline characteristics by exposure cohorts
THIN - Total analysis population

		QVA149	Free LABA+ICS	Std Dif	Fixed LABA/ICS	Std Dif
Number of contacts with GP at home	N	1346	583	0.039	21315	0.074
	Mean (SD)	0.5 (1.7)	0.5 (1.8)	.	0.5 (2.1)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.	0.0 (0.0-0.0)	.
	Min-Max	0.0-21.0	0.0-29.0	.	0.0-69.0	.
Days from spirometry to index date	N	1123	459	0.050	16660	0.114
	Mean (SD)	337.5 (426.4)	300.8 (406.0)	.	288.1 (400.5)	.
	Median (IQR)	153.0 (2.0-504.0)	142.0 (8.0-379.0)	.	106.0 (0.0-408.0)	.
	Min-Max	0.0-1805	0.0-1731	.	0.0-1826	.
FEV1 percentage	N	1123	459	-0.409	16660	-0.096
	Mean (SD)	62.2 (19.7)	70.2 (19.5)	.	64.1 (20.3)	.
	Median (IQR)	61.8 (47.2-76.1)	69.8 (56.8-82.1)	.	63.0 (49.3-76.9)	.
	Min-Max	20.1-169.5	21.6-130.7	.	15.2-379.8	.

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Continuous baseline characteristics by exposure cohorts
THIN - Total analysis population

		QVA149	Fixed LABA/LAMA	Std Dif	LABA	Std Dif
Number of contacts with GP at home	N	1346	4921	0.127	3006	0.116
	Mean (SD)	0.5 (1.7)	0.4 (2.2)	.	0.4 (1.9)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.	0.0 (0.0-0.0)	.
	Min-Max	0.0-21.0	0.0-94.0	.	0.0-38.0	.
Days from spirometry to index date	N	1123	4047	0.221	2471	0.355
	Mean (SD)	337.5 (426.4)	268.5 (392.3)	.	201.9 (339.4)	.
	Median (IQR)	153.0 (2.0-504.0)	57.0 (0.0-390.0)	.	33.0 (0.0-268.0)	.
	Min-Max	0.0-1805	0.0-1819	.	0.0-1821	.
FEV1 percentage	N	1123	4047	-0.103	2471	-0.329
	Mean (SD)	62.2 (19.7)	64.2 (19.9)	.	68.7 (19.9)	.
	Median (IQR)	61.8 (47.2-76.1)	63.6 (50.7-76.5)	.	68.1 (56.0-80.1)	.
	Min-Max	20.1-169.5	17.5-405.4	.	18.3-379.8	.

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Continuous baseline characteristics by exposure cohorts
THIN - Total analysis population

		QVA149	LAMA	Std Dif
Number of contacts with GP at home	N	1346	18598	0.142
	Mean (SD)	0.5 (1.7)	0.4 (2.0)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.
	Min-Max	0.0-21.0	0.0-100.0	.
Days from spirometry to index date	N	1123	14158	0.369
	Mean (SD)	337.5 (426.4)	204.8 (351.0)	.
	Median (IQR)	153.0 (2.0-504.0)	22.0 (0.0-272.0)	.
	Min-Max	0.0-1805	0.0-1823	.
FEV1 percentage	N	1123	14158	-0.232
	Mean (SD)	62.2 (19.7)	66.7 (19.7)	.
	Median (IQR)	61.8 (47.2-76.1)	66.0 (53.5-78.5)	.
	Min-Max	20.1-169.5	18.4-347.5	.

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Continuous baseline characteristics by exposure cohorts
THIN - Total analysis population

		QVA149	Free LABA+LAMA without ICS	Std Dif	Free LABA+LAMA with ICS	Std Dif
FEV1/FVC	N	989	2002	-0.004	322	0.039
	Mean (SD)	59.8 (14.5)	59.9 (13.2)	.	59.3 (15.0)	.
	Median (IQR)	60.0 (49.0-69.0)	60.0 (51.0-69.0)	.	60.0 (49.0-68.0)	.
	Min-Max	25.0-100.0	18.9-99.0	.	26.0-99.0	.
Duration of COPD (yrs)	N	1346	2586	0.107	394	-0.208
	Mean (SD)	6.1 (6.6)	5.1 (5.5)	.	6.7 (5.8)	.
	Median (IQR)	4.1 (1.0-9.1)	3.3 (0.9-7.6)	.	5.5 (2.3-10.0)	.
	Min-Max	0.0-47.6	0.0-49.7	.	0.0-34.0	.
Number of hospitalizations for COPD exac	N	1346	2586	0.136	394	0.166
	Mean (SD)	0.1 (0.4)	0.1 (0.3)	.	0.1 (0.3)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.	0.0 (0.0-0.0)	.
	Min-Max	0.0-6.0	0.0-3.0	.	0.0-2.0	.

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Continuous baseline characteristics by exposure cohorts
THIN - Total analysis population

		QVA149	Free LABA+ICS	Std Dif	Fixed LABA/ICS	Std Dif
FEV1/FVC	N	989	418	-0.392	15144	-0.145
	Mean (SD)	59.8 (14.5)	65.3 (13.4)	.	61.9 (14.3)	.
	Median (IQR)	60.0 (49.0-69.0)	65.0 (56.4-74.0)	.	62.0 (52.0-71.0)	.
	Min-Max	25.0-100.0	28.6-99.0	.	18.9-310.3	.
Duration of COPD (yrs)	N	1346	583	0.134	21315	0.301
	Mean (SD)	6.1 (6.6)	5.5 (6.6)	.	4.5 (5.7)	.
	Median (IQR)	4.1 (1.0-9.1)	3.5 (0.4-8.1)	.	2.6 (0.2-6.9)	.
	Min-Max	0.0-47.6	0.0-49.9	.	0.0-49.8	.
Number of hospitalizations for COPD exac	N	1346	583	0.291	21315	0.204
	Mean (SD)	0.1 (0.4)	0.1 (0.3)	.	0.1 (0.3)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.	0.0 (0.0-0.0)	.
	Min-Max	0.0-6.0	0.0-4.0	.	0.0-10.0	.

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Continuous baseline characteristics by exposure cohorts
THIN - Total analysis population

		QVA149	Fixed LABA/LAMA	Std Dif	LABA	Std Dif
FEV1/FVC	N	989	3763	-0.026	2273	-0.214
	Mean (SD)	59.8 (14.5)	60.2 (13.3)	.	62.8 (13.2)	.
	Median (IQR)	60.0 (49.0-69.0)	61.0 (52.0-68.0)	.	63.0 (55.0-69.2)	.
	Min-Max	25.0-100.0	23.0-100.0	.	17.9-310.3	.
Duration of COPD (yrs)	N	1346	4921	0.196	3006	0.451
	Mean (SD)	6.1 (6.6)	4.9 (5.8)	.	3.8 (5.0)	.
	Median (IQR)	4.1 (1.0-9.1)	3.1 (0.4-7.5)	.	1.7 (0.1-5.7)	.
	Min-Max	0.0-47.6	0.0-49.2	.	0.0-47.2	.
Number of hospitalizations for COPD exac	N	1346	4921	0.200	3006	0.284
	Mean (SD)	0.1 (0.4)	0.1 (0.3)	.	0.1 (0.3)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.	0.0 (0.0-0.0)	.
	Min-Max	0.0-6.0	0.0-4.0	.	0.0-5.0	.

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Continuous baseline characteristics by exposure cohorts
THIN - Total analysis population

		QVA149	LAMA	Std Dif
FEV1/FVC	N	989	12895	-0.180
	Mean (SD)	59.8 (14.5)	62.4 (13.9)	.
	Median (IQR)	60.0 (49.0-69.0)	63.0 (54.0-70.0)	.
	Min-Max	25.0-100.0	18.9-633.8	.
Duration of COPD (yrs)	N	1346	18598	0.665
	Mean (SD)	6.1 (6.6)	3.3 (5.1)	.
	Median (IQR)	4.1 (1.0-9.1)	0.8 (0.0-4.9)	.
	Min-Max	0.0-47.6	0.0-49.4	.
Number of hospitalizations for COPD exac	N	1346	18598	0.275
	Mean (SD)	0.1 (0.4)	0.1 (0.3)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.
	Min-Max	0.0-6.0	0.0-7.0	.

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Continuous baseline characteristics by exposure cohorts
THIN - Total analysis population

		QVA149	Free LABA+LAMA without ICS	Std Dif	Free LABA+LAMA with ICS	Std Dif
Number of systemic steroids episodes	N	1346	2586	0.021	394	-0.194
	Mean (SD)	0.2 (0.5)	0.2 (0.5)	.	0.3 (0.7)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.	0.0 (0.0-0.0)	.
	Min-Max	0.0-4.0	0.0-4.0	.	0.0-4.0	.
Number of Antibiotic courses	N	1346	2586	-0.014	394	-0.157
	Mean (SD)	0.3 (0.8)	0.3 (0.8)	.	0.5 (1.1)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.	0.0 (0.0-1.0)	.
	Min-Max	0.0-7.0	0.0-6.0	.	0.0-8.0	.

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Continuous baseline characteristics by exposure cohorts
THIN - Total analysis population

		QVA149	Free LABA+ICS	Std Dif	Fixed LABA/ICS	Std Dif
Number of systemic steroids episodes	N	1346	583	0.074	21315	0.026
	Mean (SD)	0.2 (0.5)	0.2 (0.5)	.	0.2 (0.5)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.	0.0 (0.0-0.0)	.
	Min-Max	0.0-4.0	0.0-4.0	.	0.0-5.0	.
Number of Antibiotic courses	N	1346	583	0.045	21315	0.036
	Mean (SD)	0.3 (0.8)	0.3 (0.8)	.	0.3 (0.7)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.	0.0 (0.0-0.0)	.
	Min-Max	0.0-7.0	0.0-9.0	.	0.0-9.0	.

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Continuous baseline characteristics by exposure cohorts
THIN - Total analysis population

		QVA149	Fixed LABA/LAMA	Std Dif	LABA	Std Dif
Number of systemic steroids episodes	N	1346	4921	0.128	3006	0.163
	Mean (SD)	0.2 (0.5)	0.1 (0.4)	.	0.1 (0.4)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.	0.0 (0.0-0.0)	.
	Min-Max	0.0-4.0	0.0-4.0	.	0.0-4.0	.
Number of Antibiotic courses	N	1346	4921	0.121	3006	0.170
	Mean (SD)	0.3 (0.8)	0.2 (0.7)	.	0.2 (0.7)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.	0.0 (0.0-0.0)	.
	Min-Max	0.0-7.0	0.0-9.0	.	0.0-12.0	.

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Continuous baseline characteristics by exposure cohorts
THIN - Total analysis population

		QVA149	LAMA	Std Dif
Number of systemic steroids episodes	N	1346	18598	0.188
	Mean (SD)	0.2 (0.5)	0.1 (0.4)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.
	Min-Max	0.0-4.0	0.0-4.0	.
Number of Antibiotic courses	N	1346	18598	0.187
	Mean (SD)	0.3 (0.8)	0.2 (0.6)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.
	Min-Max	0.0-7.0	0.0-8.0	.

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Continuous baseline characteristics by exposure cohorts
IPCI - Total analysis population

		QVA149	Free LABA+LAMA without ICS	Std Dif	Free LABA+LAMA with ICS	Std Dif
Cohort time	N	699	1148	0.579	496	0.671
	Mean (SD)	193.7 (200.3)	117.0 (144.2)	.	104.9 (128.9)	.
	Median (IQR)	115.0 (60.0-256.0)	61.0 (30.0-130.8)	.	60.0 (30.0-107.8)	.
	Min-Max	1.0-1047	1.0-1106	.	1.0-909.0	.
Cohort time extended	N	699	1148	0.756	496	0.874
	Mean (SD)	209.5 (197.7)	118.7 (145.1)	.	105.9 (129.3)	.
	Median (IQR)	133.0 (90.0-270.0)	65.0 (30.0-137.8)	.	60.0 (30.0-110.0)	.
	Min-Max	1.0-1047	1.0-1106	.	1.0-909.0	.
Cohort time unrestricted	N	699	1148	0.590	496	0.778
	Mean (SD)	208.9 (207.9)	128.3 (150.2)	.	107.5 (129.2)	.
	Median (IQR)	120.0 (60.0-269.0)	74.0 (36.3-146.5)	.	60.0 (31.3-112.5)	.
	Min-Max	3.0-1076	2.0-1106	.	4.0-909.0	.

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Continuous baseline characteristics by exposure cohorts
IPCI - Total analysis population

		QVA149	Free LABA+ICS	Std Dif	Fixed LABA/ICS	Std Dif
Cohort time	N	699	597	0.592	7001	0.127
	Mean (SD)	193.7 (200.3)	91.3 (80.6)	.	148.0 (157.9)	.
	Median (IQR)	115.0 (60.0-256.0)	68.0 (50.0-111.5)	.	90.0 (60.0-156.0)	.
	Min-Max	1.0-1047	1.0-727.0	.	1.0-1146	.
Cohort time extended	N	699	597	0.650	7001	0.084
	Mean (SD)	209.5 (197.7)	104.4 (84.2)	.	170.4 (155.7)	.
	Median (IQR)	133.0 (90.0-270.0)	90.0 (52.0-131.0)	.	120.0 (90.0-180.0)	.
	Min-Max	1.0-1047	1.0-727.0	.	1.0-1146	.
Cohort time unrestricted	N	699	597	0.588	7001	0.231
	Mean (SD)	208.9 (207.9)	104.1 (91.3)	.	150.6 (158.7)	.
	Median (IQR)	120.0 (60.0-269.0)	80.0 (60.0-120.0)	.	90.0 (60.0-160.0)	.
	Min-Max	3.0-1076	2.0-781.0	.	1.0-1146	.

Note: Run date and time 22NOV2018 13:59:17,

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Continuous baseline characteristics by exposure cohorts
IPCI - Total analysis population

		QVA149	Fixed LABA/LAMA	Std Dif	LABA	Std Dif
Cohort time	N	699	1081	0.122	1526	0.496
	Mean (SD)	193.7 (200.3)	149.6 (127.3)	.	108.0 (121.6)	.
	Median (IQR)	115.0 (60.0-256.0)	104.0 (60.0-207.5)	.	67.0 (55.0-120.0)	.
	Min-Max	1.0-1047	1.0-682.0	.	1.0-1124	.
Cohort time extended	N	699	1081	0.182	1526	0.488
	Mean (SD)	209.5 (197.7)	160.2 (126.2)	.	124.6 (122.9)	.
	Median (IQR)	133.0 (90.0-270.0)	120.0 (79.0-222.0)	.	90.0 (62.0-144.0)	.
	Min-Max	1.0-1047	1.0-682.0	.	1.0-1124	.
Cohort time unrestricted	N	699	1081	0.135	1526	0.379
	Mean (SD)	208.9 (207.9)	158.4 (125.8)	.	133.2 (140.0)	.
	Median (IQR)	120.0 (60.0-269.0)	116.0 (60.0-219.0)	.	90.0 (60.0-138.3)	.
	Min-Max	3.0-1076	1.0-682.0	.	2.0-1124	.

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Continuous baseline characteristics by exposure cohorts
IPCI - Total analysis population

		QVA149	LAMA	Std Dif
Cohort time	N	699	5006	0.228
	Mean (SD)	193.7 (200.3)	148.3 (169.7)	.
	Median (IQR)	115.0 (60.0-256.0)	90.0 (60.0-160.0)	.
	Min-Max	1.0-1047	1.0-1146	.
Cohort time extended	N	699	5006	0.221
	Mean (SD)	209.5 (197.7)	165.6 (169.2)	.
	Median (IQR)	133.0 (90.0-270.0)	116.0 (76.0-181.0)	.
	Min-Max	1.0-1047	1.0-1152	.
Cohort time unrestricted	N	699	5006	0.110
	Mean (SD)	208.9 (207.9)	182.4 (193.3)	.
	Median (IQR)	120.0 (60.0-269.0)	120.0 (60.0-215.0)	.
	Min-Max	3.0-1076	1.0-1146	.

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Continuous baseline characteristics by exposure cohorts
IPCI - Total analysis population

		QVA149	Free LABA+LAMA without ICS	Std Dif	Free LABA+LAMA with ICS	Std Dif
Follow-up time	N	699	1148	-0.079	496	-0.141
	Mean (SD)	497.5 (304.3)	522.1 (316.3)	.	541.4 (318.5)	.
	Median (IQR)	485.0 (237.0-748.0)	520.5 (258.0-761.0)	.	534.5 (270.8-788.3)	.
	Min-Max	3.0-1145	2.0-1157	.	4.0-1152	.
Age at cohort entry	N	699	1148	-0.125	496	-0.090
	Mean (SD)	68.2 (10.1)	69.4 (10.2)	.	69.1 (10.2)	.
	Median (IQR)	68.5 (61.2-75.5)	69.3 (62.2-77.2)	.	69.4 (61.5-76.7)	.
	Min-Max	41.0-94.7	42.7-98.3	.	40.0-91.6	.
Number of contacts with GP at practice	N	699	1148	-0.101	496	-0.183
	Mean (SD)	7.3 (5.5)	7.9 (6.0)	.	8.4 (6.2)	.
	Median (IQR)	6.0 (3.0-10.0)	6.0 (4.0-11.0)	.	7.0 (4.0-11.0)	.
	Min-Max	0.0-42.0	0.0-54.0	.	0.0-33.0	.

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Continuous baseline characteristics by exposure cohorts
IPCI - Total analysis population

		QVA149	Free LABA+ICS	Std Dif	Fixed LABA/ICS	Std Dif
Follow-up time	N	699	597	-0.049	7001	-0.104
	Mean (SD)	497.5 (304.3)	513.1 (331.7)	.	530.6 (329.0)	.
	Median (IQR)	485.0 (237.0-748.0)	451.0 (228.0-778.0)	.	507.0 (247.5-796.0)	.
	Min-Max	3.0-1145	2.0-1150	.	1.0-1157	.
Age at cohort entry	N	699	597	-0.075	7001	0.114
	Mean (SD)	68.2 (10.1)	69.0 (11.0)	.	66.9 (11.5)	.
	Median (IQR)	68.5 (61.2-75.5)	69.6 (60.5-77.1)	.	66.9 (58.5-75.5)	.
	Min-Max	41.0-94.7	40.0-95.6	.	40.2-101.6	.
Number of contacts with GP at practice	N	699	597	-0.181	7001	0.030
	Mean (SD)	7.3 (5.5)	8.4 (6.9)	.	7.1 (5.9)	.
	Median (IQR)	6.0 (3.0-10.0)	7.0 (4.0-11.0)	.	6.0 (3.0-10.0)	.
	Min-Max	0.0-42.0	0.0-62.0	.	0.0-91.0	.

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Continuous baseline characteristics by exposure cohorts
IPCI - Total analysis population

		QVA149	Fixed LABA/LAMA	Std Dif	LABA	Std Dif
Follow-up time	N	699	1081	0.975	1526	0.054
	Mean (SD)	497.5 (304.3)	259.1 (164.6)	.	480.7 (320.2)	.
	Median (IQR)	485.0 (237.0-748.0)	247.0 (116.5-381.0)	.	446.0 (213.0-723.0)	.
	Min-Max	3.0-1145	1.0-726.0	.	2.0-1157	.
Age at cohort entry	N	699	1081	-0.063	1526	0.009
	Mean (SD)	68.2 (10.1)	68.8 (10.0)	.	68.1 (11.3)	.
	Median (IQR)	68.5 (61.2-75.5)	69.2 (62.1-76.3)	.	68.1 (59.8-76.5)	.
	Min-Max	41.0-94.7	40.5-93.6	.	40.2-97.8	.
Number of contacts with GP at practice	N	699	1081	-0.126	1526	0.029
	Mean (SD)	7.3 (5.5)	8.0 (6.5)	.	7.1 (5.7)	.
	Median (IQR)	6.0 (3.0-10.0)	7.0 (4.0-11.0)	.	6.0 (3.0-10.0)	.
	Min-Max	0.0-42.0	0.0-59.0	.	0.0-41.0	.

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Continuous baseline characteristics by exposure cohorts
IPCI - Total analysis population

		QVA149	LAMA	Std Dif
Follow-up time	N	699	5006	-0.094
	Mean (SD)	497.5 (304.3)	527.0 (323.7)	.
	Median (IQR)	485.0 (237.0-748.0)	503.0 (256.8-787.0)	.
	Min-Max	3.0-1145	1.0-1157	.
Age at cohort entry	N	699	5006	0.017
	Mean (SD)	68.2 (10.1)	68.0 (10.8)	.
	Median (IQR)	68.5 (61.2-75.5)	67.8 (60.3-76.0)	.
	Min-Max	41.0-94.7	40.0-97.9	.
Number of contacts with GP at practice	N	699	5006	0.029
	Mean (SD)	7.3 (5.5)	7.1 (5.8)	.
	Median (IQR)	6.0 (3.0-10.0)	6.0 (3.0-10.0)	.
	Min-Max	0.0-42.0	0.0-64.0	.

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Continuous baseline characteristics by exposure cohorts
IPCI - Total analysis population

		QVA149	Free LABA+LAMA without ICS	Std Dif	Free LABA+LAMA with ICS	Std Dif
Number of contacts with GP at home	N	699	1148	0.042	496	-0.034
	Mean (SD)	1.0 (2.7)	1.1 (3.1)	.	1.4 (4.2)	.
	Median (IQR)	0.0 (0.0-1.0)	0.0 (0.0-1.0)	.	0.0 (0.0-1.0)	.
	Min-Max	0.0-29.0	0.0-26.0	.	0.0-56.0	.
Days from spirometry to index date	N	351	710	-0.001	206	-0.227
	Mean (SD)	339.0 (453.8)	330.3 (439.3)	.	404.0 (459.1)	.
	Median (IQR)	133.0 (7.0-490.0)	145.0 (7.0-480.0)	.	270.0 (34.8-602.8)	.
	Min-Max	0.0-1808	0.0-1760	.	0.0-1763	.
FEV1 percentage	N	351	710	-0.120	206	-0.126
	Mean (SD)	63.6 (18.4)	65.8 (18.2)	.	65.9 (18.1)	.
	Median (IQR)	62.4 (49.0-75.4)	65.3 (53.0-78.0)	.	66.0 (53.8-78.1)	.
	Min-Max	20.6-114.0	23.2-149.7	.	25.8-128.6	.

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Continuous baseline characteristics by exposure cohorts
IPCI - Total analysis population

		QVA149	Free LABA+ICS	Std Dif	Fixed LABA/ICS	Std Dif
Number of contacts with GP at home	N	699	597	-0.063	7001	0.079
	Mean (SD)	1.0 (2.7)	1.5 (3.8)	.	1.0 (3.1)	.
	Median (IQR)	0.0 (0.0-1.0)	0.0 (0.0-1.0)	.	0.0 (0.0-0.0)	.
	Min-Max	0.0-29.0	0.0-26.0	.	0.0-55.0	.
Days from spirometry to index date	N	351	291	-0.286	3485	-0.100
	Mean (SD)	339.0 (453.8)	434.9 (474.3)	.	391.6 (481.0)	.
	Median (IQR)	133.0 (7.0-490.0)	287.0 (30.0-644.0)	.	180.0 (7.0-636.5)	.
	Min-Max	0.0-1808	0.0-1824	.	0.0-1818	.
FEV1 percentage	N	351	291	-0.652	3485	-0.490
	Mean (SD)	63.6 (18.4)	76.1 (19.8)	.	72.7 (18.7)	.
	Median (IQR)	62.4 (49.0-75.4)	76.1 (63.0-89.0)	.	73.0 (60.0-85.0)	.
	Min-Max	20.6-114.0	22.8-127.2	.	20.3-232.9	.

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Continuous baseline characteristics by exposure cohorts
IPCI - Total analysis population

		QVA149	Fixed LABA/LAMA	Std Dif	LABA	Std Dif
Number of contacts with GP at home	N	699	1081	-0.007	1526	0.094
	Mean (SD)	1.0 (2.7)	1.1 (3.3)	.	1.1 (3.3)	.
	Median (IQR)	0.0 (0.0-1.0)	0.0 (0.0-1.0)	.	0.0 (0.0-0.0)	.
	Min-Max	0.0-29.0	0.0-40.0	.	0.0-44.0	.
Days from spirometry to index date	N	351	530	-0.151	935	0.164
	Mean (SD)	339.0 (453.8)	383.8 (457.8)	.	285.1 (439.0)	.
	Median (IQR)	133.0 (7.0-490.0)	178.0 (24.0-628.8)	.	51.0 (4.0-404.0)	.
	Min-Max	0.0-1808	0.0-1815	.	0.0-1825	.
FEV1 percentage	N	351	530	0.071	935	-0.506
	Mean (SD)	63.6 (18.4)	62.3 (18.3)	.	72.8 (17.9)	.
	Median (IQR)	62.4 (49.0-75.4)	61.9 (49.2-74.1)	.	72.8 (60.4-84.4)	.
	Min-Max	20.6-114.0	18.7-118.0	.	28.3-128.6	.

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Continuous baseline characteristics by exposure cohorts
IPCI - Total analysis population

		QVA149	LAMA	Std Dif
Number of contacts with GP at home	N	699	5006	0.131
	Mean (SD)	1.0 (2.7)	1.0 (3.0)	.
	Median (IQR)	0.0 (0.0-1.0)	0.0 (0.0-0.0)	.
	Min-Max	0.0-29.0	0.0-45.0	.
Days from spirometry to index date	N	351	2890	0.293
	Mean (SD)	339.0 (453.8)	259.8 (420.8)	.
	Median (IQR)	133.0 (7.0-490.0)	21.0 (0.0-369.5)	.
	Min-Max	0.0-1808	0.0-1822	.
FEV1 percentage	N	351	2890	-0.427
	Mean (SD)	63.6 (18.4)	71.3 (17.7)	.
	Median (IQR)	62.4 (49.0-75.4)	71.0 (60.0-82.4)	.
	Min-Max	20.6-114.0	18.7-184.9	.

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Continuous baseline characteristics by exposure cohorts
IPCI - Total analysis population

		QVA149	Free LABA+LAMA without ICS	Std Dif	Free LABA+LAMA with ICS	Std Dif
FEV1/FVC	N	350	713	-0.057	209	-0.040
	Mean (SD)	55.1 (12.5)	55.8 (12.6)	.	55.5 (12.2)	.
	Median (IQR)	55.9 (46.0-64.6)	56.0 (47.0-64.0)	.	55.8 (47.0-64.0)	.
	Min-Max	24.7-96.5	25.6-173.2	.	28.9-87.0	.
Duration of COPD (yrs)	N	699	1148	-0.259	496	-0.550
	Mean (SD)	5.6 (5.8)	6.6 (5.5)	.	8.0 (5.7)	.
	Median (IQR)	4.1 (1.0-8.2)	5.6 (2.5-9.0)	.	7.2 (3.9-10.4)	.
	Min-Max	0.0-45.1	0.0-43.9	.	0.0-44.9	.
Number of hospitalizations for COPD exac	N	699	1148	0.115	496	-0.058
	Mean (SD)	0.1 (0.4)	0.1 (0.3)	.	0.1 (0.5)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.	0.0 (0.0-0.0)	.
	Min-Max	0.0-4.0	0.0-3.0	.	0.0-6.0	.

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Continuous baseline characteristics by exposure cohorts
IPCI - Total analysis population

		QVA149	Free LABA+ICS	Std Dif	Fixed LABA/ICS	Std Dif
FEV1/FVC	N	350	287	-0.581	3488	-0.496
	Mean (SD)	55.1 (12.5)	62.0 (11.5)	.	61.3 (12.6)	.
	Median (IQR)	55.9 (46.0-64.6)	63.3 (54.3-70.0)	.	62.0 (53.2-69.0)	.
	Min-Max	24.7-96.5	28.0-92.6	.	15.4-210.6	.
Duration of COPD (yrs)	N	699	597	-0.488	7001	-0.205
	Mean (SD)	5.6 (5.8)	7.9 (6.3)	.	6.5 (5.9)	.
	Median (IQR)	4.1 (1.0-8.2)	6.7 (3.6-10.5)	.	5.6 (2.2-9.0)	.
	Min-Max	0.0-45.1	0.0-49.5	.	0.0-48.9	.
Number of hospitalizations for COPD exac	N	699	597	-0.032	7001	0.182
	Mean (SD)	0.1 (0.4)	0.1 (0.5)	.	0.0 (0.2)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.	0.0 (0.0-0.0)	.
	Min-Max	0.0-4.0	0.0-4.0	.	0.0-4.0	.

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Continuous baseline characteristics by exposure cohorts
IPCI - Total analysis population

		QVA149	Fixed LABA/LAMA	Std Dif	LABA	Std Dif
FEV1/FVC	N	350	530	-0.010	936	-0.412
	Mean (SD)	55.1 (12.5)	55.2 (14.5)	.	60.0 (11.4)	.
	Median (IQR)	55.9 (46.0-64.6)	55.0 (46.4-63.9)	.	60.7 (52.8-67.0)	.
	Min-Max	24.7-96.5	15.4-217.1	.	28.7-106.7	.
Duration of COPD (yrs)	N	699	1081	-0.165	1526	-0.020
	Mean (SD)	5.6 (5.8)	6.4 (6.0)	.	5.6 (5.4)	.
	Median (IQR)	4.1 (1.0-8.2)	5.6 (1.5-9.5)	.	4.6 (1.2-8.1)	.
	Min-Max	0.0-45.1	0.0-43.1	.	0.0-45.3	.
Number of hospitalizations for COPD exac	N	699	1081	0.063	1526	0.222
	Mean (SD)	0.1 (0.4)	0.1 (0.3)	.	0.0 (0.3)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.	0.0 (0.0-0.0)	.
	Min-Max	0.0-4.0	0.0-3.0	.	0.0-6.0	.

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Continuous baseline characteristics by exposure cohorts
IPCI - Total analysis population

		QVA149	LAMA	Std Dif
FEV1/FVC	N	350	2888	-0.396
	Mean (SD)	55.1 (12.5)	59.8 (11.6)	.
	Median (IQR)	55.9 (46.0-64.6)	60.3 (52.6-67.0)	.
	Min-Max	24.7-96.5	15.4-155.0	.
Duration of COPD (yrs)	N	699	5006	0.086
	Mean (SD)	5.6 (5.8)	5.2 (5.6)	.
	Median (IQR)	4.1 (1.0-8.2)	4.0 (0.4-7.8)	.
	Min-Max	0.0-45.1	0.0-49.9	.
Number of hospitalizations for COPD exac	N	699	5006	0.234
	Mean (SD)	0.1 (0.4)	0.0 (0.2)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.
	Min-Max	0.0-4.0	0.0-5.0	.

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Continuous baseline characteristics by exposure cohorts
IPCI - Total analysis population

		QVA149	Free LABA+LAMA without ICS	Std Dif	Free LABA+LAMA with ICS	Std Dif
Number of systemic steroids episodes	N	699	1148	-0.052	496	-0.444
	Mean (SD)	0.4 (0.8)	0.4 (0.9)	.	0.8 (1.0)	.
	Median (IQR)	0.0 (0.0-1.0)	0.0 (0.0-1.0)	.	0.0 (0.0-1.0)	.
	Min-Max	0.0-5.0	0.0-6.0	.	0.0-5.0	.
Number of Antibiotic courses	N	699	1148	-0.074	496	-0.253
	Mean (SD)	0.5 (0.9)	0.6 (1.1)	.	0.9 (1.4)	.
	Median (IQR)	0.0 (0.0-1.0)	0.0 (0.0-1.0)	.	0.0 (0.0-1.0)	.
	Min-Max	0.0-7.0	0.0-7.0	.	0.0-13.0	.

Note: Run date and time 22NOV2018 13:59:17,

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Table 15-16-2 (Page 18 of 20)
Continuous baseline characteristics by exposure cohorts
IPCI - Total analysis population

		QVA149	Free LABA+ICS	Std Dif	Fixed LABA/ICS	Std Dif
Number of systemic steroids episodes	N	699	597	-0.076	7001	0.084
	Mean (SD)	0.4 (0.8)	0.5 (0.9)	.	0.3 (0.7)	.
	Median (IQR)	0.0 (0.0-1.0)	0.0 (0.0-1.0)	.	0.0 (0.0-0.0)	.
	Min-Max	0.0-5.0	0.0-6.0	.	0.0-7.0	.
Number of Antibiotic courses	N	699	597	-0.048	7001	0.029
	Mean (SD)	0.5 (0.9)	0.7 (1.3)	.	0.5 (1.0)	.
	Median (IQR)	0.0 (0.0-1.0)	0.0 (0.0-1.0)	.	0.0 (0.0-1.0)	.
	Min-Max	0.0-7.0	0.0-12.0	.	0.0-11.0	.

Note: Run date and time 22NOV2018 13:59:17,

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Table 15-16-2 (Page 19 of 20)
Continuous baseline characteristics by exposure cohorts
IPCI - Total analysis population

		QVA149	Fixed LABA/LAMA	Std Dif	LABA	Std Dif
Number of systemic steroids episodes	N	699	1081	-0.123	1526	0.192
	Mean (SD)	0.4 (0.8)	0.5 (1.0)	.	0.3 (0.6)	.
	Median (IQR)	0.0 (0.0-1.0)	0.0 (0.0-1.0)	.	0.0 (0.0-0.0)	.
	Min-Max	0.0-5.0	0.0-8.0	.	0.0-6.0	.
Number of Antibiotic courses	N	699	1081	-0.166	1526	0.109
	Mean (SD)	0.5 (0.9)	0.8 (1.4)	.	0.4 (0.9)	.
	Median (IQR)	0.0 (0.0-1.0)	0.0 (0.0-1.0)	.	0.0 (0.0-1.0)	.
	Min-Max	0.0-7.0	0.0-9.0	.	0.0-9.0	.

Note: Run date and time 22NOV2018 13:59:17,

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Table 15-16-2 (Page 20 of 20)
Continuous baseline characteristics by exposure cohorts
IPCI - Total analysis population

		QVA149	LAMA	Std Dif
Number of systemic steroids episodes	N	699	5006	0.183
	Mean (SD)	0.4 (0.8)	0.3 (0.7)	.
	Median (IQR)	0.0 (0.0-1.0)	0.0 (0.0-0.0)	.
	Min-Max	0.0-5.0	0.0-6.0	.
Number of Antibiotic courses	N	699	5006	0.097
	Mean (SD)	0.5 (0.9)	0.5 (0.9)	.
	Median (IQR)	0.0 (0.0-1.0)	0.0 (0.0-1.0)	.
	Min-Max	0.0-7.0	0.0-9.0	.

Note: Run date and time 22NOV2018 13:59:17,

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Table 15-16-3 (Page 1 of 20)
Continuous baseline characteristics by exposure cohorts
AUH - Total analysis population

		QVA149	Free LABA+LAMA without ICS	Std Dif	Free LABA+LAMA with ICS	Std Dif
Cohort time	N	1807	671	0.724	242	0.816
	Mean (SD)	245.2 (252.2)	115.6 (147.1)	.	108.2 (145.0)	.
	Median (IQR)	136.0 (60.0-335.0)	63.0 (30.0-122.0)	.	59.5 (30.0-109.8)	.
	Min-Max	1.0-1111	1.0-1014	.	8.0-999.0	.
Cohort time extended	N	1807	671	0.837	242	0.917
	Mean (SD)	257.1 (250.4)	117.2 (147.4)	.	109.0 (145.5)	.
	Median (IQR)	152.0 (90.0-352.0)	69.0 (30.0-125.0)	.	59.5 (30.0-112.3)	.
	Min-Max	1.0-1111	1.0-1014	.	8.0-999.0	.
Cohort time unrestricted	N	1807	671	0.771	242	0.951
	Mean (SD)	270.6 (259.1)	135.2 (167.8)	.	113.4 (147.6)	.
	Median (IQR)	161.0 (73.0-383.0)	72.0 (35.0-151.0)	.	60.0 (30.0-125.3)	.
	Min-Max	2.0-1122	2.0-1014	.	13.0-999.0	.

Note: Run date and time 22NOV2018 13:59:31,

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Table 15-16-3 (Page 2 of 20)
Continuous baseline characteristics by exposure cohorts
AUH - Total analysis population

		QVA149	Free LABA+ICS	Std Dif	Fixed LABA/ICS	Std Dif
Cohort time	N	1807	273	0.916	3481	0.346
	Mean (SD)	245.2 (252.2)	93.0 (118.2)	.	159.0 (178.9)	.
	Median (IQR)	136.0 (60.0-335.0)	60.0 (45.0-100.0)	.	90.0 (60.0-179.0)	.
	Min-Max	1.0-1111	2.0-1063	.	2.0-1133	.
Cohort time extended	N	1807	273	0.922	3481	0.250
	Mean (SD)	257.1 (250.4)	101.6 (120.0)	.	179.9 (176.4)	.
	Median (IQR)	152.0 (90.0-352.0)	75.0 (47.5-120.0)	.	114.0 (90.0-201.5)	.
	Min-Max	1.0-1111	2.0-1063	.	2.0-1133	.
Cohort time unrestricted	N	1807	273	0.964	3481	0.518
	Mean (SD)	270.6 (259.1)	110.3 (137.2)	.	163.4 (181.6)	.
	Median (IQR)	161.0 (73.0-383.0)	61.0 (50.0-120.0)	.	90.0 (60.0-183.5)	.
	Min-Max	2.0-1122	10.0-1063	.	2.0-1133	.

Note: Run date and time 22NOV2018 13:59:31,

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Table 15-16-3 (Page 3 of 20)
Continuous baseline characteristics by exposure cohorts
AUH - Total analysis population

		QVA149	Fixed LABA/LAMA	Std Dif	LABA	Std Dif
Cohort time	N	1807	1758	0.202	1078	0.571
	Mean (SD)	245.2 (252.2)	174.1 (157.3)	.	129.9 (165.4)	.
	Median (IQR)	136.0 (60.0-335.0)	120.0 (60.0-247.0)	.	81.0 (56.0-128.0)	.
	Min-Max	1.0-1111	1.0-835.0	.	1.0-1144	.
Cohort time extended	N	1807	1758	0.210	1078	0.544
	Mean (SD)	257.1 (250.4)	184.5 (156.2)	.	143.9 (165.6)	.
	Median (IQR)	152.0 (90.0-352.0)	135.0 (80.0-262.0)	.	90.0 (59.0-150.0)	.
	Min-Max	1.0-1111	1.0-835.0	.	1.0-1144	.
Cohort time unrestricted	N	1807	1758	0.277	1078	0.465
	Mean (SD)	270.6 (259.1)	184.7 (158.0)	.	164.1 (181.0)	.
	Median (IQR)	161.0 (73.0-383.0)	121.5 (60.0-261.0)	.	90.0 (60.0-186.0)	.
	Min-Max	2.0-1122	1.0-835.0	.	3.0-1144	.

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Table 15-16-3 (Page 4 of 20)
Continuous baseline characteristics by exposure cohorts
AUH - Total analysis population

		QVA149	LAMA	Std Dif
Cohort time	N	1807	2095	0.563
	Mean (SD)	245.2 (252.2)	132.1 (163.0)	.
	Median (IQR)	136.0 (60.0-335.0)	65.0 (59.0-134.0)	.
	Min-Max	1.0-1111	1.0-1087	.
Cohort time extended	N	1807	2095	0.524
	Mean (SD)	257.1 (250.4)	146.6 (163.5)	.
	Median (IQR)	152.0 (90.0-352.0)	90.0 (59.0-150.0)	.
	Min-Max	1.0-1111	1.0-1087	.
Cohort time unrestricted	N	1807	2095	0.389
	Mean (SD)	270.6 (259.1)	181.9 (194.1)	.
	Median (IQR)	161.0 (73.0-383.0)	109.0 (60.0-215.0)	.
	Min-Max	2.0-1122	1.0-1094	.

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Table 15-16-3 (Page 5 of 20)
Continuous baseline characteristics by exposure cohorts
AUH - Total analysis population

		QVA149	Free LABA+LAMA without ICS	Std Dif	Free LABA+LAMA with ICS	Std Dif
Follow-up time	N	1807	671	-0.209	242	-0.258
	Mean (SD)	540.6 (319.1)	609.0 (333.7)	.	625.9 (340.8)	.
	Median (IQR)	557.0 (256.0-815.0)	642.0 (322.0-893.0)	.	648.0 (329.5-942.0)	.
	Min-Max	2.0-1123	2.0-1157	.	17.0-1157	.
Age at cohort entry	N	1807	671	-0.130	242	0.111
	Mean (SD)	71.5 (10.0)	72.8 (9.8)	.	70.4 (10.1)	.
	Median (IQR)	72.1 (65.2-78.6)	73.2 (66.7-80.0)	.	70.7 (63.9-77.6)	.
	Min-Max	40.1-95.8	41.3-94.8	.	42.5-94.0	.
Number of contacts with GP at practice	N	1807	671	-0.123	242	-0.210
	Mean (SD)	17.7 (15.2)	19.6 (14.4)	.	20.9 (15.2)	.
	Median (IQR)	14.0 (7.0-25.0)	17.0 (9.0-26.0)	.	18.0 (10.0-29.0)	.
	Min-Max	0.0-143.0	0.0-114.0	.	0.0-95.0	.

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Table 15-16-3 (Page 6 of 20)
Continuous baseline characteristics by exposure cohorts
AUH - Total analysis population

		QVA149	Free LABA+ICS	Std Dif	Fixed LABA/ICS	Std Dif
Follow-up time	N	1807	273	-0.162	3481	-0.011
	Mean (SD)	540.6 (319.1)	594.9 (350.6)	.	544.1 (337.1)	.
	Median (IQR)	557.0 (256.0-815.0)	625.0 (263.5-893.0)	.	548.0 (248.0-823.5)	.
	Min-Max	2.0-1123	13.0-1153	.	2.0-1157	.
Age at cohort entry	N	1807	273	0.182	3481	0.053
	Mean (SD)	71.5 (10.0)	69.6 (10.9)	.	70.9 (11.7)	.
	Median (IQR)	72.1 (65.2-78.6)	70.9 (61.9-77.3)	.	71.7 (62.6-80.1)	.
	Min-Max	40.1-95.8	40.5-93.9	.	40.1-98.6	.
Number of contacts with GP at practice	N	1807	273	-0.062	3481	-0.018
	Mean (SD)	17.7 (15.2)	18.7 (14.7)	.	18.0 (15.6)	.
	Median (IQR)	14.0 (7.0-25.0)	15.0 (8.0-24.0)	.	15.0 (7.0-25.0)	.
	Min-Max	0.0-143.0	0.0-81.0	.	0.0-179.0	.

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Table 15-16-3 (Page 7 of 20)
Continuous baseline characteristics by exposure cohorts
AUH - Total analysis population

		QVA149	Fixed LABA/LAMA	Std Dif	LABA	Std Dif
Follow-up time	N	1807	1758	0.832	1078	-0.074
	Mean (SD)	540.6 (319.1)	314.1 (215.2)	.	565.0 (341.0)	.
	Median (IQR)	557.0 (256.0-815.0)	285.5 (129.8-451.3)	.	564.0 (264.5-860.5)	.
	Min-Max	2.0-1123	1.0-850.0	.	3.0-1157	.
Age at cohort entry	N	1807	1758	-0.009	1078	0.004
	Mean (SD)	71.5 (10.0)	71.6 (9.8)	.	71.4 (10.7)	.
	Median (IQR)	72.1 (65.2-78.6)	71.9 (65.1-78.9)	.	72.3 (64.3-78.9)	.
	Min-Max	40.1-95.8	41.9-99.9	.	40.3-97.7	.
Number of contacts with GP at practice	N	1807	1758	0.269	1078	0.047
	Mean (SD)	17.7 (15.2)	13.7 (14.5)	.	17.0 (15.4)	.
	Median (IQR)	14.0 (7.0-25.0)	10.0 (2.0-20.0)	.	13.0 (6.0-23.0)	.
	Min-Max	0.0-143.0	0.0-111.0	.	0.0-112.0	.

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Table 15-16-3 (Page 8 of 20)
Continuous baseline characteristics by exposure cohorts
AUH - Total analysis population

		QVA149	LAMA	Std Dif
Follow-up time	N	1807	2095	-0.075
	Mean (SD)	540.6 (319.1)	565.0 (333.8)	.
	Median (IQR)	557.0 (256.0-815.0)	563.0 (277.0-836.0)	.
	Min-Max	2.0-1123	1.0-1157	.
Age at cohort entry	N	1807	2095	0.029
	Mean (SD)	71.5 (10.0)	71.2 (10.9)	.
	Median (IQR)	72.1 (65.2-78.6)	71.8 (63.7-79.4)	.
	Min-Max	40.1-95.8	40.9-96.1	.
Number of contacts with GP at practice	N	1807	2095	0.047
	Mean (SD)	17.7 (15.2)	17.0 (14.6)	.
	Median (IQR)	14.0 (7.0-25.0)	14.0 (6.0-24.0)	.
	Min-Max	0.0-143.0	0.0-106.0	.

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Table 15-16-3 (Page 9 of 20)
Continuous baseline characteristics by exposure cohorts
AUH - Total analysis population

		QVA149	Free LABA+LAMA without ICS	Std Dif	Free LABA+LAMA with ICS	Std Dif
Number of contacts with GP at home	N	1807	671	0.041	242	0.038
	Mean (SD)	1.0 (2.8)	1.0 (2.8)	.	1.2 (3.7)	.
	Median (IQR)	0.0 (0.0-1.0)	0.0 (0.0-1.0)	.	0.0 (0.0-1.0)	.
	Min-Max	0.0-38.0	0.0-36.0	.	0.0-36.0	.
Days from spirometry to index date	N	989	351	-0.192	143	-0.328
	Mean (SD)	316.1 (452.8)	376.8 (470.9)	.	386.7 (477.5)	.
	Median (IQR)	57.0 (4.0-476.5)	148.0 (15.0-627.0)	.	147.0 (25.0-625.0)	.
	Min-Max	0.0-1813	0.0-1787	.	0.0-1794	.
FEV1 percentage	N	989	351	-0.115	143	0.178
	Mean (SD)	51.8 (17.5)	53.8 (17.3)	.	48.7 (16.5)	.
	Median (IQR)	50.0 (38.0-63.0)	53.0 (40.0-65.0)	.	46.0 (35.0-58.0)	.
	Min-Max	18.3-184.0	25.0-106.0	.	18.3-99.0	.

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Table 15-16-3 (Page 10 of 20)
Continuous baseline characteristics by exposure cohorts
AUH - Total analysis population

		QVA149	Free LABA+ICS	Std Dif	Fixed LABA/ICS	Std Dif
Number of contacts with GP at home	N	1807	273	-0.021	3481	-0.094
	Mean (SD)	1.0 (2.8)	1.0 (2.4)	.	1.3 (3.3)	.
	Median (IQR)	0.0 (0.0-1.0)	0.0 (0.0-1.0)	.	0.0 (0.0-1.0)	.
	Min-Max	0.0-38.0	0.0-18.0	.	0.0-54.0	.
Days from spirometry to index date	N	989	104	-0.516	1584	0.049
	Mean (SD)	316.1 (452.8)	484.2 (499.4)	.	323.9 (469.2)	.
	Median (IQR)	57.0 (4.0-476.5)	288.0 (46.0-837.3)	.	48.5 (2.0-539.0)	.
	Min-Max	0.0-1813	0.0-1759	.	0.0-1824	.
FEV1 percentage	N	989	104	-0.324	1584	-0.124
	Mean (SD)	51.8 (17.5)	57.4 (17.2)	.	54.0 (18.4)	.
	Median (IQR)	50.0 (38.0-63.0)	56.5 (45.0-69.0)	.	52.0 (39.0-67.0)	.
	Min-Max	18.3-184.0	24.0-105.0	.	22.5-122.0	.

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Continuous baseline characteristics by exposure cohorts
AUH - Total analysis population

		QVA149	Fixed LABA/LAMA	Std Dif	LABA	Std Dif
Number of contacts with GP at home	N	1807	1758	0.204	1078	0.112
	Mean (SD)	1.0 (2.8)	0.7 (2.3)	.	0.9 (2.5)	.
	Median (IQR)	0.0 (0.0-1.0)	0.0 (0.0-0.0)	.	0.0 (0.0-1.0)	.
	Min-Max	0.0-38.0	0.0-34.0	.	0.0-25.0	.
Days from spirometry to index date	N	989	1239	0.465	466	-0.261
	Mean (SD)	316.1 (452.8)	205.5 (402.5)	.	452.6 (498.7)	.
	Median (IQR)	57.0 (4.0-476.5)	7.0 (1.0-176.0)	.	257.0 (8.0-818.0)	.
	Min-Max	0.0-1813	0.0-1824	.	0.0-1811	.
FEV1 percentage	N	989	1239	0.006	466	-0.528
	Mean (SD)	51.8 (17.5)	51.7 (16.5)	.	60.9 (17.1)	.
	Median (IQR)	50.0 (38.0-63.0)	51.0 (38.0-62.0)	.	61.0 (50.0-73.0)	.
	Min-Max	18.3-184.0	22.1-117.0	.	18.9-115.0	.

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Continuous baseline characteristics by exposure cohorts
AUH - Total analysis population

		QVA149	LAMA	Std Dif
Number of contacts with GP at home	N	1807	2095	0.019
	Mean (SD)	1.0 (2.8)	1.0 (2.9)	.
	Median (IQR)	0.0 (0.0-1.0)	0.0 (0.0-1.0)	.
	Min-Max	0.0-38.0	0.0-47.0	.
Days from spirometry to index date	N	989	998	0.102
	Mean (SD)	316.1 (452.8)	324.8 (475.6)	.
	Median (IQR)	57.0 (4.0-476.5)	35.5 (2.0-581.3)	.
	Min-Max	0.0-1813	0.0-1826	.
FEV1 percentage	N	989	998	-0.395
	Mean (SD)	51.8 (17.5)	58.8 (17.9)	.
	Median (IQR)	50.0 (38.0-63.0)	59.0 (46.0-71.0)	.
	Min-Max	18.3-184.0	24.0-123.0	.

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Table 15-16-3 (Page 13 of 20)
Continuous baseline characteristics by exposure cohorts
AUH - Total analysis population

		QVA149	Free LABA+LAMA without ICS	Std Dif	Free LABA+LAMA with ICS	Std Dif
FEV1/FVC	N	373	98	-0.052	39	0.455
	Mean (SD)	53.2 (14.7)	54.0 (15.1)	.	47.1 (11.8)	.
	Median (IQR)	52.0 (41.3-64.6)	54.9 (41.0-65.0)	.	43.0 (39.3-54.0)	.
	Min-Max	24.0-96.0	25.4-88.0	.	27.0-74.0	.
Duration of COPD (yrs)	N	1807	671	-0.177	242	-0.468
	Mean (SD)	4.3 (5.1)	5.1 (5.4)	.	6.7 (5.8)	.
	Median (IQR)	2.4 (0.1-6.8)	3.2 (0.6-7.6)	.	5.3 (1.4-11.4)	.
	Min-Max	0.0-21.8	0.0-21.9	.	0.0-21.4	.
Number of hospitalizations for COPD exac	N	1807	671	0.167	242	0.045
	Mean (SD)	0.3 (0.8)	0.2 (0.7)	.	0.3 (1.0)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.	0.0 (0.0-0.0)	.
	Min-Max	0.0-10.0	0.0-7.0	.	0.0-10.0	.

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Continuous baseline characteristics by exposure cohorts
AUH - Total analysis population

		QVA149	Free LABA+ICS	Std Dif	Fixed LABA/ICS	Std Dif
FEV1/FVC	N	373	20	-0.033	316	-0.397
	Mean (SD)	53.2 (14.7)	53.6 (12.3)	.	58.7 (13.2)	.
	Median (IQR)	52.0 (41.3-64.6)	52.0 (42.8-64.2)	.	59.0 (49.0-67.0)	.
	Min-Max	24.0-96.0	31.5-75.1	.	26.0-92.0	.
Duration of COPD (yrs)	N	1807	273	-0.292	3481	0.024
	Mean (SD)	4.3 (5.1)	5.6 (5.3)	.	4.4 (5.4)	.
	Median (IQR)	2.4 (0.1-6.8)	4.3 (1.0-8.5)	.	2.2 (0.1-7.2)	.
	Min-Max	0.0-21.8	0.0-21.4	.	0.0-22.6	.
Number of hospitalizations for COPD exac	N	1807	273	0.149	3481	0.010
	Mean (SD)	0.3 (0.8)	0.2 (0.5)	.	0.3 (0.7)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.	0.0 (0.0-0.0)	.
	Min-Max	0.0-10.0	0.0-4.0	.	0.0-12.0	.

Note: Run date and time 22NOV2018 13:59:31,

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Table 15-16-3 (Page 15 of 20)
Continuous baseline characteristics by exposure cohorts
AUH - Total analysis population

		QVA149	Fixed LABA/LAMA	Std Dif	LABA	Std Dif
FEV1/FVC	N	373	254	-0.021	129	-0.370
	Mean (SD)	53.2 (14.7)	53.5 (13.6)	.	58.2 (12.3)	.
	Median (IQR)	52.0 (41.3-64.6)	53.0 (43.0-64.0)	.	59.0 (49.6-67.0)	.
	Min-Max	24.0-96.0	26.0-94.1	.	24.6-86.3	.
Duration of COPD (yrs)	N	1807	1758	-0.016	1078	-0.012
	Mean (SD)	4.3 (5.1)	4.5 (5.4)	.	4.5 (5.2)	.
	Median (IQR)	2.4 (0.1-6.8)	2.5 (0.1-7.2)	.	2.7 (0.1-7.2)	.
	Min-Max	0.0-21.8	0.0-22.2	.	0.0-21.9	.
Number of hospitalizations for COPD exac	N	1807	1758	0.031	1078	0.301
	Mean (SD)	0.3 (0.8)	0.3 (0.9)	.	0.1 (0.6)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.	0.0 (0.0-0.0)	.
	Min-Max	0.0-10.0	0.0-13.0	.	0.0-12.0	.

Note: Run date and time 22NOV2018 13:59:31,

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Table 15-16-3 (Page 16 of 20)
Continuous baseline characteristics by exposure cohorts
AUH - Total analysis population

		QVA149	LAMA	Std Dif
FEV1/FVC	N	373	206	-0.638
	Mean (SD)	53.2 (14.7)	62.0 (12.8)	.
	Median (IQR)	52.0 (41.3-64.6)	61.8 (55.0-70.0)	.
	Min-Max	24.0-96.0	30.0-98.5	.
Duration of COPD (yrs)	N	1807	2095	0.171
	Mean (SD)	4.3 (5.1)	3.8 (5.0)	.
	Median (IQR)	2.4 (0.1-6.8)	1.5 (0.0-5.9)	.
	Min-Max	0.0-21.8	0.0-21.7	.
Number of hospitalizations for COPD exac	N	1807	2095	0.211
	Mean (SD)	0.3 (0.8)	0.1 (0.5)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.
	Min-Max	0.0-10.0	0.0-5.0	.

Note: Run date and time 22NOV2018 13:59:31,

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Table 15-16-3 (Page 17 of 20)
Continuous baseline characteristics by exposure cohorts
AUH - Total analysis population

		QVA149	Free LABA+LAMA without ICS	Std Dif	Free LABA+LAMA with ICS	Std Dif
Number of systemic steroids episodes	N	1807	671	0.040	242	-0.133
	Mean (SD)	0.2 (0.5)	0.2 (0.5)	.	0.3 (0.7)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.	0.0 (0.0-0.0)	.
	Min-Max	0.0-3.0	0.0-3.0	.	0.0-3.0	.
Number of Antibiotic courses	N	1807	671	0.089	242	-0.087
	Mean (SD)	0.4 (0.8)	0.4 (0.9)	.	0.6 (1.0)	.
	Median (IQR)	0.0 (0.0-1.0)	0.0 (0.0-0.0)	.	0.0 (0.0-1.0)	.
	Min-Max	0.0-7.0	0.0-10.0	.	0.0-7.0	.

Note: Run date and time 22NOV2018 13:59:31,

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Table 15-16-3 (Page 18 of 20)
Continuous baseline characteristics by exposure cohorts
AUH - Total analysis population

		QVA149	Free LABA+ICS	Std Dif	Fixed LABA/ICS	Std Dif
Number of systemic steroids episodes	N	1807	273	0.044	3481	-0.016
	Mean (SD)	0.2 (0.5)	0.2 (0.4)	.	0.2 (0.5)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.	0.0 (0.0-0.0)	.
	Min-Max	0.0-3.0	0.0-2.0	.	0.0-3.0	.
Number of Antibiotic courses	N	1807	273	0.225	3481	0.008
	Mean (SD)	0.4 (0.8)	0.3 (0.7)	.	0.4 (0.8)	.
	Median (IQR)	0.0 (0.0-1.0)	0.0 (0.0-0.0)	.	0.0 (0.0-1.0)	.
	Min-Max	0.0-7.0	0.0-3.0	.	0.0-8.0	.

Note: Run date and time 22NOV2018 13:59:31,

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Table 15-16-3 (Page 19 of 20)
Continuous baseline characteristics by exposure cohorts
AUH - Total analysis population

		QVA149	Fixed LABA/LAMA	Std Dif	LABA	Std Dif
Number of systemic steroids episodes	N	1807	1758	-0.120	1078	0.241
	Mean (SD)	0.2 (0.5)	0.3 (0.5)	.	0.1 (0.4)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.	0.0 (0.0-0.0)	.
	Min-Max	0.0-3.0	0.0-3.0	.	0.0-3.0	.
Number of Antibiotic courses	N	1807	1758	-0.134	1078	0.316
	Mean (SD)	0.4 (0.8)	0.6 (1.1)	.	0.2 (0.7)	.
	Median (IQR)	0.0 (0.0-1.0)	0.0 (0.0-1.0)	.	0.0 (0.0-0.0)	.
	Min-Max	0.0-7.0	0.0-9.0	.	0.0-8.0	.

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Table 15-16-3 (Page 20 of 20)
Continuous baseline characteristics by exposure cohorts
AUH - Total analysis population

		QVA149	LAMA	Std Dif
Number of systemic steroids episodes	N	1807	2095	0.131
	Mean (SD)	0.2 (0.5)	0.2 (0.4)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.
	Min-Max	0.0-3.0	0.0-3.0	.
Number of Antibiotic courses	N	1807	2095	0.132
	Mean (SD)	0.4 (0.8)	0.3 (0.7)	.
	Median (IQR)	0.0 (0.0-1.0)	0.0 (0.0-0.0)	.
	Min-Max	0.0-7.0	0.0-6.0	.

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Table 15-16-4 (Page 1 of 20)
Continuous baseline characteristics by exposure cohorts
HSD - Total analysis population

		QVA149	Free LABA+LAMA without ICS	Std Dif	Free LABA+LAMA with ICS	Std Dif
Cohort time	N	385	995	0.667	335	1.875
	Mean (SD)	189.8 (181.4)	121.5 (165.5)	.	44.7 (85.6)	.
	Median (IQR)	119.0 (60.0-231.5)	60.0 (30.0-120.0)	.	21.0 (10.0-42.0)	.
	Min-Max	1.0-809.0	1.0-1313	.	3.0-668.0	.
Cohort time extended	N	385	995	0.772	335	1.983
	Mean (SD)	211.7 (184.2)	128.8 (167.0)	.	45.6 (86.6)	.
	Median (IQR)	134.0 (90.0-259.0)	87.0 (30.0-128.0)	.	21.0 (10.0-42.0)	.
	Min-Max	1.0-839.0	1.0-1313	.	3.0-668.0	.
Cohort time unrestricted	N	385	995	0.738	335	2.147
	Mean (SD)	208.5 (184.7)	138.8 (185.1)	.	45.7 (86.5)	.
	Median (IQR)	134.0 (60.0-262.5)	60.0 (39.0-146.0)	.	21.0 (10.0-43.0)	.
	Min-Max	14.0-809.0	5.0-1313	.	3.0-702.0	.

Note: Run date and time 22NOV2018 13:59:49,

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Table 15-16-4 (Page 2 of 20)
Continuous baseline characteristics by exposure cohorts
HSD - Total analysis population

		QVA149	Free LABA+ICS	Std Dif	Fixed LABA/ICS	Std Dif
Cohort time	N	385	437	2.028	5897	0.521
	Mean (SD)	189.8 (181.4)	34.3 (45.7)	.	114.2 (135.9)	.
	Median (IQR)	119.0 (60.0-231.5)	21.0 (10.0-45.5)	.	60.0 (60.0-97.0)	.
	Min-Max	1.0-809.0	1.0-456.0	.	1.0-1389	.
Cohort time extended	N	385	437	2.043	5897	0.389
	Mean (SD)	211.7 (184.2)	38.7 (51.5)	.	142.4 (136.1)	.
	Median (IQR)	134.0 (90.0-259.0)	21.0 (10.0-47.5)	.	90.0 (90.0-126.0)	.
	Min-Max	1.0-839.0	1.0-486.0	.	1.0-1419	.
Cohort time unrestricted	N	385	437	2.122	5897	0.777
	Mean (SD)	208.5 (184.7)	43.7 (76.1)	.	116.2 (138.5)	.
	Median (IQR)	134.0 (60.0-262.5)	25.0 (10.0-60.0)	.	60.0 (60.0-100.0)	.
	Min-Max	14.0-809.0	3.0-764.0	.	1.0-1389	.

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Table 15-16-4 (Page 3 of 20)
Continuous baseline characteristics by exposure cohorts
HSD - Total analysis population

		QVA149	Fixed LABA/LAMA	Std Dif	LABA	Std Dif
Cohort time	N	385	426	0.025	875	0.746
	Mean (SD)	189.8 (181.4)	160.7 (127.9)	.	94.6 (111.6)	.
	Median (IQR)	119.0 (60.0-231.5)	114.0 (60.0-216.0)	.	60.0 (58.0-90.0)	.
	Min-Max	1.0-809.0	3.0-682.0	.	1.0-1065	.
Cohort time extended	N	385	426	0.000	875	0.699
	Mean (SD)	211.7 (184.2)	185.3 (130.4)	.	115.4 (114.7)	.
	Median (IQR)	134.0 (90.0-259.0)	140.5 (90.0-243.0)	.	90.0 (75.0-120.0)	.
	Min-Max	1.0-839.0	3.0-712.0	.	1.0-1095	.
Cohort time unrestricted	N	385	426	0.084	875	0.681
	Mean (SD)	208.5 (184.7)	173.2 (132.2)	.	126.7 (152.8)	.
	Median (IQR)	134.0 (60.0-262.5)	126.5 (79.0-225.5)	.	80.0 (60.0-117.0)	.
	Min-Max	14.0-809.0	18.0-682.0	.	2.0-1367	.

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Table 15-16-4 (Page 4 of 20)
Continuous baseline characteristics by exposure cohorts
HSD - Total analysis population

		QVA149	LAMA	Std Dif
Cohort time	N	385	3595	0.492
	Mean (SD)	189.8 (181.4)	123.6 (159.0)	.
	Median (IQR)	119.0 (60.0-231.5)	67.0 (60.0-111.0)	.
	Min-Max	1.0-809.0	1.0-1388	.
Cohort time extended	N	385	3595	0.439
	Mean (SD)	211.7 (184.2)	146.4 (161.4)	.
	Median (IQR)	134.0 (90.0-259.0)	90.0 (90.0-136.0)	.
	Min-Max	1.0-839.0	1.0-1418	.
Cohort time unrestricted	N	385	3595	0.465
	Mean (SD)	208.5 (184.7)	153.6 (191.8)	.
	Median (IQR)	134.0 (60.0-262.5)	90.0 (60.0-145.0)	.
	Min-Max	14.0-809.0	1.0-1459	.

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Table 15-16-4 (Page 5 of 20)
Continuous baseline characteristics by exposure cohorts
HSD - Total analysis population

		QVA149	Free LABA+LAMA without ICS	Std Dif	Free LABA+LAMA with ICS	Std Dif
Follow-up time	N	385	995	-0.766	335	-0.781
	Mean (SD)	602.4 (232.7)	852.5 (398.9)	.	862.1 (408.5)	.
	Median (IQR)	634.0 (413.0-794.0)	852.0 (537.0-1175)	.	913.0 (491.0-1193)	.
	Min-Max	14.0-1098	5.0-1518	.	27.0-1510	.
Age at cohort entry	N	385	995	-0.084	335	-0.119
	Mean (SD)	73.9 (8.8)	74.6 (9.1)	.	75.0 (9.3)	.
	Median (IQR)	74.3 (68.0-79.8)	75.3 (68.8-81.3)	.	75.1 (69.2-81.4)	.
	Min-Max	48.8-97.1	41.1-99.9	.	41.6-98.9	.
Number of contacts with GP at practice	N	385	995	0.183	335	0.149
	Mean (SD)	16.5 (12.3)	14.3 (11.3)	.	14.8 (10.1)	.
	Median (IQR)	13.0 (7.0-23.0)	12.0 (6.0-20.0)	.	13.0 (7.0-21.0)	.
	Min-Max	0.0-66.0	0.0-90.0	.	0.0-55.0	.

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Table 15-16-4 (Page 6 of 20)
Continuous baseline characteristics by exposure cohorts
HSD - Total analysis population

		QVA149	Free LABA+ICS	Std Dif	Fixed LABA/ICS	Std Dif
Follow-up time	N	385	437	-0.916	5897	-0.683
	Mean (SD)	602.4 (232.7)	905.9 (406.5)	.	828.3 (405.9)	.
	Median (IQR)	634.0 (413.0-794.0)	942.0 (582.0-1279)	.	810.0 (479.0-1165)	.
	Min-Max	14.0-1098	14.0-1515	.	1.0-1518	.
Age at cohort entry	N	385	437	-0.036	5897	0.111
	Mean (SD)	73.9 (8.8)	74.2 (9.9)	.	72.8 (11.0)	.
	Median (IQR)	74.3 (68.0-79.8)	75.2 (67.3-81.1)	.	73.8 (65.5-81.0)	.
	Min-Max	48.8-97.1	42.1-97.2	.	41.3-102.4	.
Number of contacts with GP at practice	N	385	437	0.242	5897	0.346
	Mean (SD)	16.5 (12.3)	13.8 (10.0)	.	12.5 (10.7)	.
	Median (IQR)	13.0 (7.0-23.0)	11.0 (7.0-19.0)	.	10.0 (5.0-18.0)	.
	Min-Max	0.0-66.0	0.0-57.0	.	0.0-116.0	.

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Table 15-16-4 (Page 7 of 20)
Continuous baseline characteristics by exposure cohorts
HSD - Total analysis population

		QVA149	Fixed LABA/LAMA	Std Dif	LABA	Std Dif
Follow-up time	N	385	426	0.850	875	-0.861
	Mean (SD)	602.4 (232.7)	425.3 (180.8)	.	884.2 (399.8)	.
	Median (IQR)	634.0 (413.0-794.0)	389.0 (291.8-557.3)	.	921.0 (580.0-1222)	.
	Min-Max	14.0-1098	18.0-825.0	.	2.0-1519	.
Age at cohort entry	N	385	426	0.093	875	0.170
	Mean (SD)	73.9 (8.8)	73.1 (9.0)	.	72.2 (10.5)	.
	Median (IQR)	74.3 (68.0-79.8)	73.3 (67.2-80.3)	.	72.8 (65.3-79.9)	.
	Min-Max	48.8-97.1	46.4-93.8	.	44.2-97.5	.
Number of contacts with GP at practice	N	385	426	0.041	875	0.325
	Mean (SD)	16.5 (12.3)	16.0 (11.5)	.	12.8 (10.2)	.
	Median (IQR)	13.0 (7.0-23.0)	14.0 (8.0-21.0)	.	10.0 (5.0-18.0)	.
	Min-Max	0.0-66.0	0.0-73.0	.	0.0-74.0	.

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Continuous baseline characteristics by exposure cohorts
HSD - Total analysis population

		QVA149	LAMA	Std Dif
Follow-up time	N	385	3595	-0.738
	Mean (SD)	602.4 (232.7)	847.2 (407.3)	.
	Median (IQR)	634.0 (413.0-794.0)	846.0 (520.0-1187)	.
	Min-Max	14.0-1098	1.0-1518	.
Age at cohort entry	N	385	3595	-0.026
	Mean (SD)	73.9 (8.8)	74.1 (10.3)	.
	Median (IQR)	74.3 (68.0-79.8)	75.0 (67.5-81.9)	.
	Min-Max	48.8-97.1	43.6-99.8	.
Number of contacts with GP at practice	N	385	3595	0.278
	Mean (SD)	16.5 (12.3)	13.3 (10.8)	.
	Median (IQR)	13.0 (7.0-23.0)	11.0 (6.0-19.0)	.
	Min-Max	0.0-66.0	0.0-105.0	.

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Table 15-16-4 (Page 9 of 20)
Continuous baseline characteristics by exposure cohorts
HSD - Total analysis population

		QVA149	Free LABA+LAMA without ICS	Std Dif	Free LABA+LAMA with ICS	Std Dif
Number of contacts with GP at home	N	385	995	-0.080	335	-0.261
	Mean (SD)	0.4 (2.5)	0.6 (2.4)	.	0.9 (3.2)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.	0.0 (0.0-0.0)	.
	Min-Max	0.0-41.0	0.0-30.0	.	0.0-24.0	.
Days from spirometry to index date	N	149	340	-0.221	119	-0.538
	Mean (SD)	388.4 (491.5)	491.2 (513.6)	.	588.8 (487.4)	.
	Median (IQR)	170.0 (20.0-706.0)	305.5 (36.3-872.8)	.	471.0 (168.0-963.0)	.
	Min-Max	0.0-1762	0.0-1799	.	0.0-1763	.
FEV1 percentage	N	149	340	0.133	119	0.222
	Mean (SD)	68.8 (16.7)	66.5 (17.0)	.	64.9 (18.1)	.
	Median (IQR)	69.1 (54.8-81.0)	67.2 (55.6-76.1)	.	61.2 (51.0-75.0)	.
	Min-Max	31.0-115.2	26.0-119.0	.	30.0-113.1	.

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Continuous baseline characteristics by exposure cohorts
HSD - Total analysis population

		QVA149	Free LABA+ICS	Std Dif	Fixed LABA/ICS	Std Dif
Number of contacts with GP at home	N	385	437	-0.098	5897	-0.007
	Mean (SD)	0.4 (2.5)	0.8 (3.3)	.	0.6 (3.3)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.	0.0 (0.0-0.0)	.
	Min-Max	0.0-41.0	0.0-27.0	.	0.0-58.0	.
Days from spirometry to index date	N	149	149	-0.658	1340	-0.362
	Mean (SD)	388.4 (491.5)	641.1 (499.9)	.	601.5 (561.5)	.
	Median (IQR)	170.0 (20.0-706.0)	582.0 (192.5-1010)	.	493.5 (43.5-1048)	.
	Min-Max	0.0-1762	0.0-1799	.	0.0-1821	.
FEV1 percentage	N	149	149	-0.336	1340	-0.290
	Mean (SD)	68.8 (16.7)	74.5 (17.6)	.	73.7 (17.6)	.
	Median (IQR)	69.1 (54.8-81.0)	73.9 (63.8-82.7)	.	73.0 (62.1-84.9)	.
	Min-Max	31.0-115.2	31.0-121.6	.	25.0-125.0	.

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Table 15-16-4 (Page 11 of 20)
Continuous baseline characteristics by exposure cohorts
HSD - Total analysis population

		QVA149	Fixed LABA/LAMA	Std Dif	LABA	Std Dif
Number of contacts with GP at home	N	385	426	0.018	875	0.002
	Mean (SD)	0.4 (2.5)	0.4 (1.9)	.	0.6 (3.2)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.	0.0 (0.0-0.0)	.
	Min-Max	0.0-41.0	0.0-26.0	.	0.0-60.0	.
Days from spirometry to index date	N	149	161	-0.036	271	-0.189
	Mean (SD)	388.4 (491.5)	419.7 (532.7)	.	488.1 (535.5)	.
	Median (IQR)	170.0 (20.0-706.0)	135.0 (23.0-688.0)	.	244.0 (34.0-889.0)	.
	Min-Max	0.0-1762	0.0-1811	.	0.0-1780	.
FEV1 percentage	N	149	161	0.154	271	-0.400
	Mean (SD)	68.8 (16.7)	66.1 (17.8)	.	75.6 (17.2)	.
	Median (IQR)	69.1 (54.8-81.0)	65.5 (55.0-77.0)	.	74.0 (63.0-85.1)	.
	Min-Max	31.0-115.2	25.0-115.8	.	37.6-124.0	.

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Table 15-16-4 (Page 12 of 20)
Continuous baseline characteristics by exposure cohorts
HSD - Total analysis population

		QVA149	LAMA	Std Dif
Number of contacts with GP at home	N	385	3595	-0.038
	Mean (SD)	0.4 (2.5)	0.6 (3.3)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.
	Min-Max	0.0-41.0	0.0-61.0	.
Days from spirometry to index date	N	149	918	-0.112
	Mean (SD)	388.4 (491.5)	489.7 (543.8)	.
	Median (IQR)	170.0 (20.0-706.0)	238.5 (20.0-907.8)	.
	Min-Max	0.0-1762	0.0-1825	.
FEV1 percentage	N	149	918	-0.405
	Mean (SD)	68.8 (16.7)	75.4 (16.2)	.
	Median (IQR)	69.1 (54.8-81.0)	74.0 (64.9-85.2)	.
	Min-Max	31.0-115.2	27.0-125.0	.

Note: Run date and time 22NOV2018 13:59:49,

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Table 15-16-4 (Page 13 of 20)
Continuous baseline characteristics by exposure cohorts
HSD - Total analysis population

		QVA149	Free LABA+LAMA without ICS	Std Dif	Free LABA+LAMA with ICS	Std Dif
FEV1/FVC	N	140	321	0.115	111	0.145
	Mean (SD)	69.0 (13.7)	67.4 (14.3)	.	66.7 (18.0)	.
	Median (IQR)	68.9 (59.3-79.0)	68.0 (57.5-76.5)	.	65.5 (55.0-75.0)	.
	Min-Max	33.0-98.0	28.0-100.0	.	35.9-179.2	.
Duration of COPD (yrs)	N	385	995	0.107	335	-0.023
	Mean (SD)	7.8 (4.7)	7.2 (4.5)	.	7.9 (4.6)	.
	Median (IQR)	7.3 (4.3-11.5)	7.0 (3.7-10.8)	.	7.8 (3.8-12.1)	.
	Min-Max	0.0-17.1	0.0-17.2	.	0.0-17.0	.
Number of hospitalizations for COPD exac	N	385	995	0.075	335	0.102
	Mean (SD)	0.0 (0.1)	0.0 (0.0)	.	0.0 (0.0)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.	0.0 (0.0-0.0)	.
	Min-Max	0.0-1.0	0.0-1.0	.	0.0-0.0	.

Note: Run date and time 22NOV2018 13:59:49,

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Table 15-16-4 (Page 14 of 20)
Continuous baseline characteristics by exposure cohorts
HSD - Total analysis population

		QVA149	Free LABA+ICS	Std Dif	Fixed LABA/ICS	Std Dif
FEV1/FVC	N	140	141	-0.113	1193	-0.183
	Mean (SD)	69.0 (13.7)	70.5 (12.6)	.	71.6 (15.1)	.
	Median (IQR)	68.9 (59.3-79.0)	70.2 (63.5-78.4)	.	72.5 (63.0-79.3)	.
	Min-Max	33.0-98.0	32.0-100.0	.	31.0-223.1	.
Duration of COPD (yrs)	N	385	437	0.112	5897	0.114
	Mean (SD)	7.8 (4.7)	7.2 (4.3)	.	7.2 (4.6)	.
	Median (IQR)	7.3 (4.3-11.5)	7.1 (3.6-10.8)	.	7.0 (3.5-10.9)	.
	Min-Max	0.0-17.1	0.0-16.5	.	0.0-17.4	.
Number of hospitalizations for COPD exac	N	385	437	0.102	5897	0.056
	Mean (SD)	0.0 (0.1)	0.0 (0.0)	.	0.0 (0.0)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.	0.0 (0.0-0.0)	.
	Min-Max	0.0-1.0	0.0-0.0	.	0.0-1.0	.

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Table 15-16-4 (Page 15 of 20)
Continuous baseline characteristics by exposure cohorts
HSD - Total analysis population

		QVA149	Fixed LABA/LAMA	Std Dif	LABA	Std Dif
FEV1/FVC	N	140	147	0.215	248	-0.235
	Mean (SD)	69.0 (13.7)	65.9 (14.7)	.	72.0 (12.1)	.
	Median (IQR)	68.9 (59.3-79.0)	66.0 (57.0-77.0)	.	73.0 (64.0-79.0)	.
	Min-Max	33.0-98.0	28.9-98.6	.	26.0-98.4	.
Duration of COPD (yrs)	N	385	426	-0.070	875	0.079
	Mean (SD)	7.8 (4.7)	8.1 (5.1)	.	7.4 (4.5)	.
	Median (IQR)	7.3 (4.3-11.5)	8.0 (4.2-12.1)	.	7.4 (3.7-11.1)	.
	Min-Max	0.0-17.1	0.0-17.4	.	0.0-17.2	.
Number of hospitalizations for COPD exac	N	385	426	0.102	875	0.102
	Mean (SD)	0.0 (0.1)	0.0 (0.0)	.	0.0 (0.0)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.	0.0 (0.0-0.0)	.
	Min-Max	0.0-1.0	0.0-0.0	.	0.0-0.0	.

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Table 15-16-4 (Page 16 of 20)
Continuous baseline characteristics by exposure cohorts
HSD - Total analysis population

		QVA149	LAMA	Std Dif
FEV1/FVC	N	140	830	-0.259
	Mean (SD)	69.0 (13.7)	72.4 (12.2)	.
	Median (IQR)	68.9 (59.3-79.0)	72.0 (64.0-80.0)	.
	Min-Max	33.0-98.0	35.5-121.6	.
Duration of COPD (yrs)	N	385	3595	0.215
	Mean (SD)	7.8 (4.7)	6.7 (4.6)	.
	Median (IQR)	7.3 (4.3-11.5)	6.5 (2.9-10.5)	.
	Min-Max	0.0-17.1	0.0-17.1	.
Number of hospitalizations for COPD exac	N	385	3595	0.038
	Mean (SD)	0.0 (0.1)	0.0 (0.1)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.
	Min-Max	0.0-1.0	0.0-2.0	.

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Table 15-16-4 (Page 17 of 20)
Continuous baseline characteristics by exposure cohorts
HSD - Total analysis population

		QVA149	Free LABA+LAMA without ICS	Std Dif	Free LABA+LAMA with ICS	Std Dif
Number of systemic steroids episodes	N	385	995	-0.067	335	-0.135
	Mean (SD)	0.1 (0.3)	0.1 (0.3)	.	0.1 (0.4)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.	0.0 (0.0-0.0)	.
	Min-Max	0.0-3.0	0.0-3.0	.	0.0-3.0	.
Number of Antibiotic courses	N	385	995	-0.000	335	-0.055
	Mean (SD)	0.3 (0.9)	0.2 (0.7)	.	0.3 (0.9)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.	0.0 (0.0-0.0)	.
	Min-Max	0.0-8.0	0.0-8.0	.	0.0-6.0	.

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Table 15-16-4 (Page 18 of 20)
Continuous baseline characteristics by exposure cohorts
HSD - Total analysis population

		QVA149	Free LABA+ICS	Std Dif	Fixed LABA/ICS	Std Dif
Number of systemic steroids episodes	N	385	437	-0.071	5897	-0.045
	Mean (SD)	0.1 (0.3)	0.1 (0.3)	.	0.1 (0.3)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.	0.0 (0.0-0.0)	.
	Min-Max	0.0-3.0	0.0-2.0	.	0.0-4.0	.
Number of Antibiotic courses	N	385	437	-0.068	5897	0.018
	Mean (SD)	0.3 (0.9)	0.3 (0.7)	.	0.2 (0.6)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.	0.0 (0.0-0.0)	.
	Min-Max	0.0-8.0	0.0-6.0	.	0.0-8.0	.

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Table 15-16-4 (Page 19 of 20)
Continuous baseline characteristics by exposure cohorts
HSD - Total analysis population

		QVA149	Fixed LABA/LAMA	Std Dif	LABA	Std Dif
Number of systemic steroids episodes	N	385	426	-0.095	875	0.029
	Mean (SD)	0.1 (0.3)	0.1 (0.3)	.	0.1 (0.3)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.	0.0 (0.0-0.0)	.
	Min-Max	0.0-3.0	0.0-4.0	.	0.0-3.0	.
Number of Antibiotic courses	N	385	426	0.020	875	0.097
	Mean (SD)	0.3 (0.9)	0.2 (0.7)	.	0.2 (0.6)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.	0.0 (0.0-0.0)	.
	Min-Max	0.0-8.0	0.0-7.0	.	0.0-6.0	.

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Continuous baseline characteristics by exposure cohorts
HSD - Total analysis population

		QVA149	LAMA	Std Dif
Number of systemic steroids episodes	N	385	3595	-0.019
	Mean (SD)	0.1 (0.3)	0.1 (0.3)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.
	Min-Max	0.0-3.0	0.0-4.0	.
Number of Antibiotic courses	N	385	3595	-0.015
	Mean (SD)	0.3 (0.9)	0.3 (0.7)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.
	Min-Max	0.0-8.0	0.0-8.0	.

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Table 15-16-5 (Page 1 of 20)
Continuous baseline characteristics by exposure cohorts
SIDIAP - Total analysis population

		QVA149	Free LABA+LAMA without ICS	Std Dif	Free LABA+LAMA with ICS	Std Dif
Cohort time	N	5561	4219	0.683	1725	1.036
	Mean (SD)	168.3 (154.3)	95.4 (118.7)	.	74.0 (91.3)	.
	Median (IQR)	92.0 (59.0-213.0)	60.0 (30.0-119.0)	.	50.0 (30.0-88.0)	.
	Min-Max	2.0-975.0	1.0-1156	.	2.0-882.0	.
Cohort time extended	N	5561	4219	0.828	1725	1.216
	Mean (SD)	185.4 (152.6)	100.9 (120.5)	.	76.3 (93.0)	.
	Median (IQR)	120.0 (89.0-242.0)	61.0 (30.0-121.0)	.	50.0 (30.0-90.0)	.
	Min-Max	2.0-975.0	1.0-1156	.	2.0-882.0	.
Cohort time unrestricted	N	5561	4219	0.671	1725	1.092
	Mean (SD)	176.0 (156.5)	102.6 (127.8)	.	76.1 (94.1)	.
	Median (IQR)	120.0 (59.0-240.0)	60.0 (30.0-121.0)	.	50.0 (30.0-89.0)	.
	Min-Max	2.0-975.0	1.0-1156	.	2.0-882.0	.

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Table 15-16-5 (Page 2 of 20)
Continuous baseline characteristics by exposure cohorts
SIDIAP - Total analysis population

		QVA149	Free LABA+ICS	Std Dif	Fixed LABA/ICS	Std Dif
Cohort time	N	5561	2738	1.021	20638	0.452
	Mean (SD)	168.3 (154.3)	66.9 (57.6)	.	103.9 (104.0)	.
	Median (IQR)	92.0 (59.0-213.0)	60.0 (31.0-61.0)	.	60.0 (55.0-111.0)	.
	Min-Max	2.0-975.0	6.0-699.0	.	1.0-1156	.
Cohort time extended	N	5561	2738	1.046	20638	0.362
	Mean (SD)	185.4 (152.6)	79.3 (62.4)	.	128.4 (102.3)	.
	Median (IQR)	120.0 (89.0-242.0)	71.0 (31.0-90.0)	.	90.0 (82.0-121.0)	.
	Min-Max	2.0-975.0	6.0-729.0	.	1.0-1156	.
Cohort time unrestricted	N	5561	2738	1.032	20638	0.533
	Mean (SD)	176.0 (156.5)	71.9 (63.1)	.	105.2 (105.0)	.
	Median (IQR)	120.0 (59.0-240.0)	60.0 (50.0-81.0)	.	60.0 (60.0-113.0)	.
	Min-Max	2.0-975.0	6.0-699.0	.	1.0-1156	.

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Table 15-16-5 (Page 3 of 20)
Continuous baseline characteristics by exposure cohorts
SIDIAP - Total analysis population

		QVA149	Fixed LABA/LAMA	Std Dif	LABA	Std Dif
Cohort time	N	5561	964	0.128	5879	0.441
	Mean (SD)	168.3 (154.3)	129.1 (110.4)	.	98.2 (98.9)	.
	Median (IQR)	92.0 (59.0-213.0)	90.0 (60.0-183.0)	.	60.0 (60.0-91.0)	.
	Min-Max	2.0-975.0	29.0-640.0	.	14.0-1095	.
Cohort time extended	N	5561	964	0.249	5879	0.441
	Mean (SD)	185.4 (152.6)	139.9 (110.0)	.	118.2 (99.5)	.
	Median (IQR)	120.0 (89.0-242.0)	95.0 (60.0-183.0)	.	90.0 (74.0-121.0)	.
	Min-Max	2.0-975.0	29.0-640.0	.	14.0-1125	.
Cohort time unrestricted	N	5561	964	0.117	5879	0.310
	Mean (SD)	176.0 (156.5)	134.9 (111.9)	.	116.6 (115.7)	.
	Median (IQR)	120.0 (59.0-240.0)	91.0 (60.0-183.0)	.	60.0 (60.0-121.0)	.
	Min-Max	2.0-975.0	30.0-640.0	.	14.0-1095	.

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Continuous baseline characteristics by exposure cohorts
SIDIAP - Total analysis population

		QVA149	LAMA	Std Dif
Cohort time	N	5561	13678	0.451
	Mean (SD)	168.3 (154.3)	103.0 (108.7)	.
	Median (IQR)	92.0 (59.0-213.0)	60.0 (38.0-119.0)	.
	Min-Max	2.0-975.0	11.0-1126	.
Cohort time extended	N	5561	13678	0.439
	Mean (SD)	185.4 (152.6)	122.8 (109.5)	.
	Median (IQR)	120.0 (89.0-242.0)	90.0 (68.0-130.0)	.
	Min-Max	2.0-975.0	11.0-1126	.
Cohort time unrestricted	N	5561	13678	0.332
	Mean (SD)	176.0 (156.5)	121.4 (123.2)	.
	Median (IQR)	120.0 (59.0-240.0)	68.0 (60.0-138.0)	.
	Min-Max	2.0-975.0	11.0-1156	.

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Table 15-16-5 (Page 5 of 20)
Continuous baseline characteristics by exposure cohorts
SIDIAP - Total analysis population

		QVA149	Free LABA+LAMA without ICS	Std Dif	Free LABA+LAMA with ICS	Std Dif
Follow-up time	N	5561	4219	-0.392	1725	-0.488
	Mean (SD)	398.8 (240.8)	504.3 (294.2)	.	530.7 (297.3)	.
	Median (IQR)	364.0 (213.0-560.0)	487.0 (274.0-699.0)	.	517.0 (305.0-730.0)	.
	Min-Max	2.0-975.0	1.0-1156	.	30.0-1156	.
Age at cohort entry	N	5561	4219	-0.041	1725	-0.221
	Mean (SD)	71.3 (10.3)	71.7 (10.3)	.	73.5 (9.8)	.
	Median (IQR)	71.6 (64.2-79.3)	72.3 (64.8-79.5)	.	74.3 (67.0-80.7)	.
	Min-Max	40.1-103.4	40.0-98.8	.	42.2-101.4	.
Number of contacts with GP at practice	N	5561	4219	0.022	1725	-0.198
	Mean (SD)	9.2 (7.0)	9.1 (6.7)	.	10.7 (7.7)	.
	Median (IQR)	8.0 (4.0-12.0)	8.0 (5.0-12.0)	.	9.0 (6.0-14.0)	.
	Min-Max	0.0-115.0	0.0-90.0	.	0.0-113.0	.

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Continuous baseline characteristics by exposure cohorts
SIDIAP - Total analysis population

		QVA149	Free LABA+ICS	Std Dif	Fixed LABA/ICS	Std Dif
Follow-up time	N	5561	2738	-0.489	20638	-0.257
	Mean (SD)	398.8 (240.8)	531.9 (300.5)	.	466.4 (283.2)	.
	Median (IQR)	364.0 (213.0-560.0)	518.0 (305.0-730.0)	.	425.5 (244.0-671.0)	.
	Min-Max	2.0-975.0	11.0-1156	.	1.0-1156	.
Age at cohort entry	N	5561	2738	-0.143	20638	0.006
	Mean (SD)	71.3 (10.3)	72.9 (11.4)	.	71.2 (11.6)	.
	Median (IQR)	71.6 (64.2-79.3)	74.2 (65.8-81.3)	.	72.0 (63.3-80.2)	.
	Min-Max	40.1-103.4	40.5-101.8	.	40.1-105.1	.
Number of contacts with GP at practice	N	5561	2738	-0.047	20638	0.069
	Mean (SD)	9.2 (7.0)	9.5 (6.9)	.	8.7 (7.1)	.
	Median (IQR)	8.0 (4.0-12.0)	8.0 (5.0-13.0)	.	7.0 (4.0-12.0)	.
	Min-Max	0.0-115.0	0.0-55.0	.	0.0-227.0	.

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Continuous baseline characteristics by exposure cohorts
SIDIAP - Total analysis population

		QVA149	Fixed LABA/LAMA	Std Dif	LABA	Std Dif
Follow-up time	N	5561	964	0.898	5879	-0.350
	Mean (SD)	398.8 (240.8)	219.3 (148.1)	.	491.7 (289.0)	.
	Median (IQR)	364.0 (213.0-560.0)	213.0 (91.0-305.0)	.	457.0 (274.0-698.0)	.
	Min-Max	2.0-975.0	30.0-640.0	.	14.0-1156	.
Age at cohort entry	N	5561	964	0.046	5879	0.119
	Mean (SD)	71.3 (10.3)	70.8 (9.9)	.	70.0 (11.2)	.
	Median (IQR)	71.6 (64.2-79.3)	71.0 (63.8-78.5)	.	70.5 (62.3-78.7)	.
	Min-Max	40.1-103.4	41.7-96.3	.	40.0-101.1	.
Number of contacts with GP at practice	N	5561	964	-0.030	5879	0.150
	Mean (SD)	9.2 (7.0)	9.4 (7.1)	.	8.2 (6.3)	.
	Median (IQR)	8.0 (4.0-12.0)	7.0 (4.0-13.0)	.	7.0 (4.0-11.0)	.
	Min-Max	0.0-115.0	0.0-49.0	.	0.0-100.0	.

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Continuous baseline characteristics by exposure cohorts
SIDIAP - Total analysis population

		QVA149	LAMA	Std Dif
Follow-up time	N	5561	13678	-0.251
	Mean (SD)	398.8 (240.8)	464.9 (285.2)	.
	Median (IQR)	364.0 (213.0-560.0)	426.0 (244.0-670.0)	.
	Min-Max	2.0-975.0	11.0-1156	.
Age at cohort entry	N	5561	13678	0.094
	Mean (SD)	71.3 (10.3)	70.3 (10.9)	.
	Median (IQR)	71.6 (64.2-79.3)	70.7 (62.6-78.8)	.
	Min-Max	40.1-103.4	40.0-101.4	.
Number of contacts with GP at practice	N	5561	13678	0.152
	Mean (SD)	9.2 (7.0)	8.2 (6.3)	.
	Median (IQR)	8.0 (4.0-12.0)	7.0 (4.0-11.0)	.
	Min-Max	0.0-115.0	0.0-107.0	.

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Continuous baseline characteristics by exposure cohorts
SIDIAP - Total analysis population

		QVA149	Free LABA+LAMA without ICS	Std Dif	Free LABA+LAMA with ICS	Std Dif
Number of contacts with GP at home	N	5561	4219	0.042	1725	-0.100
	Mean (SD)	0.3 (1.3)	0.3 (1.2)	.	0.4 (1.6)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.	0.0 (0.0-0.0)	.
	Min-Max	0.0-26.0	0.0-26.0	.	0.0-21.0	.
Days from spirometry to index date	N	3807	3098	0.027	1277	-0.134
	Mean (SD)	438.4 (420.7)	432.4 (424.8)	.	479.0 (422.3)	.
	Median (IQR)	319.0 (104.0-651.0)	309.5 (96.0-629.0)	.	370.0 (153.0-654.0)	.
	Min-Max	0.0-1824	0.0-1824	.	0.0-1822	.
FEV1 percentage	N	3807	3098	-0.109	1277	0.082
	Mean (SD)	56.5 (17.2)	58.3 (16.3)	.	55.1 (16.9)	.
	Median (IQR)	56.0 (44.0-67.7)	58.0 (46.8-68.4)	.	54.0 (42.2-67.0)	.
	Min-Max	25.0-124.0	25.0-124.0	.	25.0-122.4	.

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Continuous baseline characteristics by exposure cohorts
SIDIAP - Total analysis population

		QVA149	Free LABA+ICS	Std Dif	Fixed LABA/ICS	Std Dif
Number of contacts with GP at home	N	5561	2738	-0.110	20638	-0.031
	Mean (SD)	0.3 (1.3)	0.5 (1.9)	.	0.3 (1.5)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.	0.0 (0.0-0.0)	.
	Min-Max	0.0-26.0	0.0-49.0	.	0.0-57.0	.
Days from spirometry to index date	N	3807	1785	-0.148	12076	-0.124
	Mean (SD)	438.4 (420.7)	484.5 (418.9)	.	497.0 (451.7)	.
	Median (IQR)	319.0 (104.0-651.0)	382.0 (150.0-691.0)	.	376.0 (126.3-739.8)	.
	Min-Max	0.0-1824	0.0-1821	.	0.0-1826	.
FEV1 percentage	N	3807	1785	-0.422	12076	-0.417
	Mean (SD)	56.5 (17.2)	64.0 (18.4)	.	64.0 (18.9)	.
	Median (IQR)	56.0 (44.0-67.7)	63.0 (51.0-76.8)	.	63.3 (50.0-77.0)	.
	Min-Max	25.0-124.0	25.0-124.8	.	25.0-125.0	.

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Table 15-16-5 (Page 11 of 20)
Continuous baseline characteristics by exposure cohorts
SIDIAP - Total analysis population

		QVA149	Fixed LABA/LAMA	Std Dif	LABA	Std Dif
Number of contacts with GP at home	N	5561	964	-0.055	5879	0.050
	Mean (SD)	0.3 (1.3)	0.3 (1.2)	.	0.3 (1.2)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.	0.0 (0.0-0.0)	.
	Min-Max	0.0-26.0	0.0-17.0	.	0.0-30.0	.
Days from spirometry to index date	N	3807	692	-0.140	3813	0.060
	Mean (SD)	438.4 (420.7)	492.6 (435.8)	.	441.2 (446.5)	.
	Median (IQR)	319.0 (104.0-651.0)	373.5 (157.0-721.8)	.	313.0 (59.0-691.5)	.
	Min-Max	0.0-1824	0.0-1824	.	0.0-1824	.
FEV1 percentage	N	3807	692	0.022	3813	-0.568
	Mean (SD)	56.5 (17.2)	56.1 (17.0)	.	66.4 (17.6)	.
	Median (IQR)	56.0 (44.0-67.7)	55.7 (43.0-67.8)	.	66.0 (54.8-78.0)	.
	Min-Max	25.0-124.0	25.0-124.3	.	25.0-125.0	.

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Continuous baseline characteristics by exposure cohorts
SIDIAP - Total analysis population

		QVA149	LAMA	Std Dif
Number of contacts with GP at home	N	5561	13678	0.063
	Mean (SD)	0.3 (1.3)	0.2 (1.3)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.
	Min-Max	0.0-26.0	0.0-40.0	.
Days from spirometry to index date	N	3807	8615	0.117
	Mean (SD)	438.4 (420.7)	421.7 (442.5)	.
	Median (IQR)	319.0 (104.0-651.0)	274.0 (52.0-656.0)	.
	Min-Max	0.0-1824	0.0-1826	.
FEV1 percentage	N	3807	8615	-0.506
	Mean (SD)	56.5 (17.2)	65.2 (17.3)	.
	Median (IQR)	56.0 (44.0-67.7)	65.0 (53.1-76.0)	.
	Min-Max	25.0-124.0	25.0-125.0	.

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Continuous baseline characteristics by exposure cohorts
SIDIAP - Total analysis population

		QVA149	Free LABA+LAMA without ICS	Std Dif	Free LABA+LAMA with ICS	Std Dif
FEV1/FVC	N	3900	3147	-0.053	1313	0.096
	Mean (SD)	60.9 (14.9)	61.6 (12.8)	.	59.5 (13.9)	.
	Median (IQR)	61.8 (51.8-70.0)	62.0 (53.0-70.0)	.	60.1 (49.8-69.0)	.
	Min-Max	20.1-452.4	13.6-99.5	.	20.7-100.0	.
Duration of COPD (yrs)	N	5561	4219	0.018	1725	-0.296
	Mean (SD)	5.6 (5.7)	5.3 (5.3)	.	6.8 (5.7)	.
	Median (IQR)	3.8 (0.9-9.1)	3.8 (1.0-8.3)	.	5.7 (2.2-9.9)	.
	Min-Max	0.0-49.9	0.0-47.7	.	0.0-39.9	.
Number of hospitalizations for COPD exac	N	5561	4219	0.114	1725	-0.060
	Mean (SD)	0.1 (0.4)	0.1 (0.3)	.	0.2 (0.6)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.	0.0 (0.0-0.0)	.
	Min-Max	0.0-9.0	0.0-7.0	.	0.0-9.0	.

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Continuous baseline characteristics by exposure cohorts
SIDIAP - Total analysis population

		QVA149	Free LABA+ICS	Std Dif	Fixed LABA/ICS	Std Dif
FEV1/FVC	N	3900	1820	-0.314	12296	-0.310
	Mean (SD)	60.9 (14.9)	65.4 (14.0)	.	65.3 (13.8)	.
	Median (IQR)	61.8 (51.8-70.0)	66.3 (57.0-73.9)	.	66.0 (57.0-74.0)	.
	Min-Max	20.1-452.4	24.7-288.4	.	20.7-452.4	.
Duration of COPD (yrs)	N	5561	2738	-0.076	20638	0.116
	Mean (SD)	5.6 (5.7)	6.0 (5.9)	.	5.1 (5.6)	.
	Median (IQR)	3.8 (0.9-9.1)	4.4 (1.2-9.2)	.	3.3 (0.4-8.3)	.
	Min-Max	0.0-49.9	0.0-44.2	.	0.0-48.6	.
Number of hospitalizations for COPD exac	N	5561	2738	0.137	20638	0.115
	Mean (SD)	0.1 (0.4)	0.1 (0.4)	.	0.1 (0.3)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.	0.0 (0.0-0.0)	.
	Min-Max	0.0-9.0	0.0-13.0	.	0.0-9.0	.

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Continuous baseline characteristics by exposure cohorts
SIDIAP - Total analysis population

		QVA149	Fixed LABA/LAMA	Std Dif	LABA	Std Dif
FEV1/FVC	N	3900	708	-0.029	3878	-0.344
	Mean (SD)	60.9 (14.9)	61.3 (14.3)	.	65.5 (11.9)	.
	Median (IQR)	61.8 (51.8-70.0)	61.5 (52.2-71.3)	.	66.3 (58.3-73.0)	.
	Min-Max	20.1-452.4	25.0-100.0	.	18.8-100.0	.
Duration of COPD (yrs)	N	5561	964	-0.100	5879	0.315
	Mean (SD)	5.6 (5.7)	6.0 (6.0)	.	4.2 (5.3)	.
	Median (IQR)	3.8 (0.9-9.1)	4.5 (1.4-9.4)	.	2.3 (0.0-6.9)	.
	Min-Max	0.0-49.9	0.0-49.8	.	0.0-49.1	.
Number of hospitalizations for COPD exac	N	5561	964	-0.107	5879	0.258
	Mean (SD)	0.1 (0.4)	0.2 (0.5)	.	0.0 (0.3)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.	0.0 (0.0-0.0)	.
	Min-Max	0.0-9.0	0.0-6.0	.	0.0-12.0	.

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Continuous baseline characteristics by exposure cohorts
SIDIAP - Total analysis population

		QVA149	LAMA	Std Dif
FEV1/FVC	N	3900	8714	-0.343
	Mean (SD)	60.9 (14.9)	65.5 (11.9)	.
	Median (IQR)	61.8 (51.8-70.0)	66.1 (58.1-73.0)	.
	Min-Max	20.1-452.4	20.8-175.0	.
Duration of COPD (yrs)	N	5561	13678	0.384
	Mean (SD)	5.6 (5.7)	4.0 (5.1)	.
	Median (IQR)	3.8 (0.9-9.1)	1.9 (0.0-6.5)	.
	Min-Max	0.0-49.9	0.0-49.4	.
Number of hospitalizations for COPD exac	N	5561	13678	0.214
	Mean (SD)	0.1 (0.4)	0.0 (0.3)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.
	Min-Max	0.0-9.0	0.0-7.0	.

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Continuous baseline characteristics by exposure cohorts
SIDIAP - Total analysis population

		QVA149	Free LABA+LAMA without ICS	Std Dif	Free LABA+LAMA with ICS	Std Dif
Number of systemic steroids episodes	N	5561	4219	0.035	1725	-0.104
	Mean (SD)	0.1 (0.2)	0.0 (0.2)	.	0.1 (0.3)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.	0.0 (0.0-0.0)	.
	Min-Max	0.0-2.0	0.0-3.0	.	0.0-4.0	.
Number of Antibiotic courses	N	5561	4219	0.021	1725	-0.067
	Mean (SD)	0.2 (0.6)	0.2 (0.6)	.	0.3 (0.7)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.	0.0 (0.0-0.0)	.
	Min-Max	0.0-5.0	0.0-10.0	.	0.0-6.0	.

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Continuous baseline characteristics by exposure cohorts
SIDIAP - Total analysis population

		QVA149	Free LABA+ICS	Std Dif	Fixed LABA/ICS	Std Dif
Number of systemic steroids episodes	N	5561	2738	-0.032	20638	-0.003
	Mean (SD)	0.1 (0.2)	0.1 (0.3)	.	0.1 (0.2)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.	0.0 (0.0-0.0)	.
	Min-Max	0.0-2.0	0.0-2.0	.	0.0-3.0	.
Number of Antibiotic courses	N	5561	2738	-0.115	20638	-0.088
	Mean (SD)	0.2 (0.6)	0.3 (0.6)	.	0.3 (0.6)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.	0.0 (0.0-0.0)	.
	Min-Max	0.0-5.0	0.0-6.0	.	0.0-9.0	.

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Continuous baseline characteristics by exposure cohorts
SIDIAP - Total analysis population

		QVA149	Fixed LABA/LAMA	Std Dif	LABA	Std Dif
Number of systemic steroids episodes	N	5561	964	-0.079	5879	0.061
	Mean (SD)	0.1 (0.2)	0.1 (0.3)	.	0.0 (0.2)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.	0.0 (0.0-0.0)	.
	Min-Max	0.0-2.0	0.0-3.0	.	0.0-2.0	.
Number of Antibiotic courses	N	5561	964	-0.063	5879	-0.032
	Mean (SD)	0.2 (0.6)	0.3 (0.6)	.	0.2 (0.6)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.	0.0 (0.0-0.0)	.
	Min-Max	0.0-5.0	0.0-4.0	.	0.0-5.0	.

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Continuous baseline characteristics by exposure cohorts
SIDIAP - Total analysis population

		QVA149	LAMA	Std Dif
Number of systemic steroids episodes	N	5561	13678	0.080
	Mean (SD)	0.1 (0.2)	0.0 (0.2)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.
	Min-Max	0.0-2.0	0.0-2.0	.
Number of Antibiotic courses	N	5561	13678	-0.032
	Mean (SD)	0.2 (0.6)	0.2 (0.6)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.
	Min-Max	0.0-5.0	0.0-7.0	.

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Table 15-16-6 (Page 1 of 20)
Continuous baseline characteristics by exposure cohorts
POOLED - Total analysis population

		QVA149	Free LABA+LAMA without ICS	Std Dif	Free LABA+LAMA with ICS	Std Dif
Cohort time	N	9798	9619	0.598	3192	0.975
	Mean (SD)	189.5 (186.7)	118.7 (155.6)	.	83.2 (111.6)	.
	Median (IQR)	120.0 (60.0-244.0)	60.0 (30.0-129.0)	.	50.0 (30.0-90.0)	.
	Min-Max	1.0-1111	1.0-1376	.	1.0-1014	.
Cohort time extended	N	9798	9619	0.717	3192	1.118
	Mean (SD)	204.6 (184.9)	123.1 (156.4)	.	84.9 (112.6)	.
	Median (IQR)	137.0 (89.0-270.0)	67.0 (30.0-142.0)	.	50.0 (30.0-90.0)	.
	Min-Max	1.0-1111	1.0-1376	.	1.0-1014	.
Cohort time unrestricted	N	9798	9619	0.613	3192	1.062
	Mean (SD)	202.4 (191.6)	129.0 (165.3)	.	86.1 (115.6)	.
	Median (IQR)	120.0 (60.0-271.0)	61.0 (30.0-150.0)	.	50.0 (30.0-90.8)	.
	Min-Max	2.0-1122	1.0-1376	.	2.0-1136	.

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Continuous baseline characteristics by exposure cohorts
POOLED - Total analysis population

		QVA149	Free LABA+ICS	Std Dif	Fixed LABA/ICS	Std Dif
Cohort time	N	9798	4628	0.973	58332	0.176
	Mean (SD)	189.5 (186.7)	74.8 (84.6)	.	165.7 (204.5)	.
	Median (IQR)	120.0 (60.0-244.0)	60.0 (31.0-85.0)	.	90.0 (60.0-174.0)	.
	Min-Max	1.0-1111	1.0-1232	.	1.0-1421	.
Cohort time extended	N	9798	4628	0.980	58332	0.101
	Mean (SD)	204.6 (184.9)	86.3 (88.0)	.	188.1 (200.9)	.
	Median (IQR)	137.0 (89.0-270.0)	76.0 (31.0-100.0)	.	118.0 (90.0-195.0)	.
	Min-Max	1.0-1111	1.0-1232	.	1.0-1421	.
Cohort time unrestricted	N	9798	4628	0.997	58332	0.273
	Mean (SD)	202.4 (191.6)	83.0 (94.1)	.	167.9 (205.9)	.
	Median (IQR)	120.0 (60.0-271.0)	60.0 (50.0-90.0)	.	90.0 (60.0-176.0)	.
	Min-Max	2.0-1122	2.0-1360	.	1.0-1421	.

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Continuous baseline characteristics by exposure cohorts
POOLED - Total analysis population

		QVA149	Fixed LABA/LAMA	Std Dif	LABA	Std Dif
Cohort time	N	9798	9150	0.042	12364	0.482
	Mean (SD)	189.5 (186.7)	172.0 (160.3)	.	113.8 (135.5)	.
	Median (IQR)	120.0 (60.0-244.0)	113.0 (60.0-236.0)	.	60.0 (60.0-120.0)	.
	Min-Max	1.0-1111	1.0-1070	.	1.0-1397	.
Cohort time extended	N	9798	9150	0.089	12364	0.457
	Mean (SD)	204.6 (184.9)	182.8 (159.2)	.	131.4 (135.5)	.
	Median (IQR)	137.0 (89.0-270.0)	125.0 (80.0-246.0)	.	90.0 (68.0-143.0)	.
	Min-Max	1.0-1111	1.0-1070	.	1.0-1397	.
Cohort time unrestricted	N	9798	9150	0.021	12364	0.340
	Mean (SD)	202.4 (191.6)	183.0 (161.1)	.	140.4 (157.1)	.
	Median (IQR)	120.0 (60.0-271.0)	121.0 (60.0-248.0)	.	90.0 (60.0-150.0)	.
	Min-Max	2.0-1122	1.0-1070	.	1.0-1397	.

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Continuous baseline characteristics by exposure cohorts
POOLED - Total analysis population

		QVA149	LAMA	Std Dif
Cohort time	N	9798	42972	0.323
	Mean (SD)	189.5 (186.7)	143.3 (177.7)	.
	Median (IQR)	120.0 (60.0-244.0)	73.0 (60.0-152.0)	.
	Min-Max	1.0-1111	1.0-1424	.
Cohort time extended	N	9798	42972	0.302
	Mean (SD)	204.6 (184.9)	160.6 (177.0)	.
	Median (IQR)	137.0 (89.0-270.0)	90.0 (68.0-179.0)	.
	Min-Max	1.0-1111	1.0-1424	.
Cohort time unrestricted	N	9798	42972	0.153
	Mean (SD)	202.4 (191.6)	184.0 (215.5)	.
	Median (IQR)	120.0 (60.0-271.0)	91.0 (60.0-211.0)	.
	Min-Max	2.0-1122	1.0-1459	.

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Continuous baseline characteristics by exposure cohorts
POOLED - Total analysis population

		QVA149	Free LABA+LAMA without ICS	Std Dif	Free LABA+LAMA with ICS	Std Dif
Follow-up time	N	9798	9619	-0.534	3192	-0.522
	Mean (SD)	433.9 (271.6)	604.3 (360.7)	.	597.1 (348.4)	.
	Median (IQR)	395.0 (213.0-625.0)	579.0 (305.0-858.0)	.	579.0 (328.8-822.0)	.
	Min-Max	2.0-1145	1.0-1518	.	4.0-1510	.
Age at cohort entry	N	9798	9619	-0.021	3192	-0.120
	Mean (SD)	71.1 (10.3)	71.3 (10.2)	.	72.3 (10.1)	.
	Median (IQR)	71.5 (64.2-78.8)	71.7 (64.5-78.9)	.	73.0 (65.7-79.7)	.
	Min-Max	40.1-103.4	40.0-99.9	.	40.0-101.4	.
Number of contacts with GP at practice	N	9798	9619	0.079	3192	-0.073
	Mean (SD)	10.7 (9.9)	10.0 (8.5)	.	11.4 (9.1)	.
	Median (IQR)	8.0 (4.0-14.0)	8.0 (4.0-13.0)	.	9.0 (5.0-15.0)	.
	Min-Max	0.0-143.0	0.0-114.0	.	0.0-113.0	.

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Continuous baseline characteristics by exposure cohorts
POOLED - Total analysis population

		QVA149	Free LABA+ICS	Std Dif	Fixed LABA/ICS	Std Dif
Follow-up time	N	9798	4628	-0.485	58332	-0.412
	Mean (SD)	433.9 (271.6)	586.2 (351.5)	.	566.4 (364.2)	.
	Median (IQR)	395.0 (213.0-625.0)	575.0 (305.0-791.0)	.	528.0 (274.0-805.0)	.
	Min-Max	2.0-1145	2.0-1515	.	1.0-1518	.
Age at cohort entry	N	9798	4628	-0.065	58332	0.093
	Mean (SD)	71.1 (10.3)	71.8 (11.4)	.	70.1 (11.5)	.
	Median (IQR)	71.5 (64.2-78.8)	73.0 (64.3-80.3)	.	70.5 (62.0-78.8)	.
	Min-Max	40.1-103.4	40.0-101.8	.	40.0-105.1	.
Number of contacts with GP at practice	N	9798	4628	0.052	58332	0.176
	Mean (SD)	10.7 (9.9)	10.2 (8.3)	.	9.1 (8.5)	.
	Median (IQR)	8.0 (4.0-14.0)	8.0 (5.0-13.0)	.	7.0 (4.0-12.0)	.
	Min-Max	0.0-143.0	0.0-92.0	.	0.0-227.0	.

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Continuous baseline characteristics by exposure cohorts
POOLED - Total analysis population

		QVA149	Fixed LABA/LAMA	Std Dif	LABA	Std Dif
Follow-up time	N	9798	9150	0.488	12364	-0.398
	Mean (SD)	433.9 (271.6)	314.0 (217.4)	.	559.5 (353.4)	.
	Median (IQR)	395.0 (213.0-625.0)	279.0 (137.0-450.0)	.	531.5 (274.0-790.0)	.
	Min-Max	2.0-1145	1.0-1152	.	1.0-1519	.
Age at cohort entry	N	9798	9150	0.081	12364	0.115
	Mean (SD)	71.1 (10.3)	70.2 (10.1)	.	69.8 (11.0)	.
	Median (IQR)	71.5 (64.2-78.8)	70.6 (63.5-77.7)	.	70.3 (62.3-78.1)	.
	Min-Max	40.1-103.4	40.5-99.9	.	40.0-101.1	.
Number of contacts with GP at practice	N	9798	9150	0.147	12364	0.185
	Mean (SD)	10.7 (9.9)	9.3 (9.3)	.	9.0 (8.3)	.
	Median (IQR)	8.0 (4.0-14.0)	7.0 (3.0-12.0)	.	7.0 (4.0-12.0)	.
	Min-Max	0.0-143.0	0.0-111.0	.	0.0-112.0	.

Note: Run date and time 22NOV2018 14:00:19,

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Table 15-16-6 (Page 8 of 20)
Continuous baseline characteristics by exposure cohorts
POOLED - Total analysis population

		QVA149	LAMA	Std Dif
Follow-up time	N	9798	42972	-0.428
	Mean (SD)	433.9 (271.6)	572.3 (367.9)	.
	Median (IQR)	395.0 (213.0-625.0)	541.0 (274.0-822.0)	.
	Min-Max	2.0-1145	1.0-1518	.
Age at cohort entry	N	9798	42972	0.113
	Mean (SD)	71.1 (10.3)	69.9 (10.9)	.
	Median (IQR)	71.5 (64.2-78.8)	70.3 (62.2-78.1)	.
	Min-Max	40.1-103.4	40.0-101.4	.
Number of contacts with GP at practice	N	9798	42972	0.238
	Mean (SD)	10.7 (9.9)	8.6 (7.8)	.
	Median (IQR)	8.0 (4.0-14.0)	7.0 (4.0-11.0)	.
	Min-Max	0.0-143.0	0.0-107.0	.

Note: Run date and time 22NOV2018 14:00:19,

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Table 15-16-6 (Page 9 of 20)
Continuous baseline characteristics by exposure cohorts
POOLED - Total analysis population

		QVA149	Free LABA+LAMA without ICS	Std Dif	Free LABA+LAMA with ICS	Std Dif
Number of contacts with GP at home	N	9798	9619	0.050	3192	-0.056
	Mean (SD)	0.5 (1.9)	0.5 (1.9)	.	0.7 (2.6)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.	0.0 (0.0-0.0)	.
	Min-Max	0.0-41.0	0.0-36.0	.	0.0-56.0	.
Days from spirometry to index date	N	6419	6705	0.090	2099	-0.150
	Mean (SD)	395.3 (433.5)	359.7 (417.1)	.	433.4 (430.8)	.
	Median (IQR)	243.0 (42.0-604.0)	211.0 (35.0-529.0)	.	313.0 (92.0-621.0)	.
	Min-Max	0.0-1824	0.0-1824	.	0.0-1822	.
FEV1 percentage	N	6419	6705	-0.221	2099	0.013
	Mean (SD)	57.4 (18.2)	61.4 (17.9)	.	57.2 (18.0)	.
	Median (IQR)	56.0 (44.0-69.0)	61.0 (49.0-72.8)	.	56.0 (44.0-69.1)	.
	Min-Max	18.3-184.0	19.6-204.7	.	18.3-128.6	.

Note: Run date and time 22NOV2018 14:00:19,

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Table 15-16-6 (Page 10 of 20)
Continuous baseline characteristics by exposure cohorts
POOLED - Total analysis population

		QVA149	Free LABA+ICS	Std Dif	Fixed LABA/ICS	Std Dif
Number of contacts with GP at home	N	9798	4628	-0.033	58332	0.020
	Mean (SD)	0.5 (1.9)	0.7 (2.4)	.	0.6 (2.3)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.	0.0 (0.0-0.0)	.
	Min-Max	0.0-41.0	0.0-49.0	.	0.0-69.0	.
Days from spirometry to index date	N	6419	2788	-0.199	35145	0.101
	Mean (SD)	395.3 (433.5)	457.4 (437.9)	.	383.7 (449.1)	.
	Median (IQR)	243.0 (42.0-604.0)	334.0 (104.0-683.0)	.	214.0 (19.0-597.5)	.
	Min-Max	0.0-1824	0.0-1824	.	0.0-1826	.
FEV1 percentage	N	6419	2788	-0.490	35145	-0.388
	Mean (SD)	57.4 (18.2)	66.6 (19.2)	.	64.8 (19.9)	.
	Median (IQR)	56.0 (44.0-69.0)	65.6 (53.0-79.0)	.	64.0 (50.2-78.0)	.
	Min-Max	18.3-184.0	21.6-130.7	.	15.2-379.8	.

Note: Run date and time 22NOV2018 14:00:19,

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Table 15-16-6 (Page 11 of 20)
Continuous baseline characteristics by exposure cohorts
POOLED - Total analysis population

		QVA149	Fixed LABA/LAMA	Std Dif	LABA	Std Dif
Number of contacts with GP at home	N	9798	9150	0.009	12364	0.082
	Mean (SD)	0.5 (1.9)	0.5 (2.3)	.	0.5 (2.1)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.	0.0 (0.0-0.0)	.
	Min-Max	0.0-41.0	0.0-94.0	.	0.0-60.0	.
Days from spirometry to index date	N	6419	6669	0.422	7956	0.187
	Mean (SD)	395.3 (433.5)	292.8 (416.6)	.	350.8 (436.8)	.
	Median (IQR)	243.0 (42.0-604.0)	75.0 (1.0-434.0)	.	165.5 (13.0-546.0)	.
	Min-Max	0.0-1824	0.0-1824	.	0.0-1825	.
FEV1 percentage	N	6419	6669	-0.185	7956	-0.566
	Mean (SD)	57.4 (18.2)	60.9 (19.5)	.	67.8 (18.6)	.
	Median (IQR)	56.0 (44.0-69.0)	60.1 (47.0-73.4)	.	67.9 (55.6-79.0)	.
	Min-Max	18.3-184.0	17.5-405.4	.	18.3-379.8	.

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Table 15-16-6 (Page 12 of 20)
Continuous baseline characteristics by exposure cohorts
POOLED - Total analysis population

		QVA149	LAMA	Std Dif
Number of contacts with GP at home	N	9798	42972	0.089
	Mean (SD)	0.5 (1.9)	0.5 (2.2)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.
	Min-Max	0.0-41.0	0.0-100.0	.
Days from spirometry to index date	N	6419	27579	0.407
	Mean (SD)	395.3 (433.5)	292.1 (414.2)	.
	Median (IQR)	243.0 (42.0-604.0)	78.0 (4.0-431.0)	.
	Min-Max	0.0-1824	0.0-1826	.
FEV1 percentage	N	6419	27579	-0.503
	Mean (SD)	57.4 (18.2)	66.8 (18.8)	.
	Median (IQR)	56.0 (44.0-69.0)	66.2 (54.0-78.0)	.
	Min-Max	18.3-184.0	18.4-347.5	.

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Continuous baseline characteristics by exposure cohorts
POOLED - Total analysis population

		QVA149	Free LABA+LAMA without ICS	Std Dif	Free LABA+LAMA with ICS	Std Dif
FEV1/FVC	N	5752	6281	-0.038	1994	0.058
	Mean (SD)	60.1 (14.9)	60.6 (13.3)	.	59.2 (14.4)	.
	Median (IQR)	60.8 (50.0-69.5)	61.0 (51.4-69.2)	.	59.9 (49.0-68.8)	.
	Min-Max	20.1-452.4	13.6-173.2	.	20.7-179.2	.
Duration of COPD (yrs)	N	9798	9619	-0.069	3192	-0.375
	Mean (SD)	5.5 (5.7)	5.6 (5.4)	.	7.1 (5.7)	.
	Median (IQR)	3.8 (0.8-8.7)	4.2 (1.2-8.6)	.	6.1 (2.7-10.2)	.
	Min-Max	0.0-49.9	0.0-49.7	.	0.0-44.9	.
Number of hospitalizations for COPD exac	N	9798	9619	0.156	3192	0.041
	Mean (SD)	0.1 (0.5)	0.1 (0.3)	.	0.1 (0.6)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.	0.0 (0.0-0.0)	.
	Min-Max	0.0-10.0	0.0-7.0	.	0.0-10.0	.

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Continuous baseline characteristics by exposure cohorts
POOLED - Total analysis population

		QVA149	Free LABA+ICS	Std Dif	Fixed LABA/ICS	Std Dif
FEV1/FVC	N	5752	2686	-0.361	32437	-0.236
	Mean (SD)	60.1 (14.9)	65.2 (13.7)	.	63.5 (14.1)	.
	Median (IQR)	60.8 (50.0-69.5)	66.0 (56.8-73.8)	.	64.0 (54.4-72.5)	.
	Min-Max	20.1-452.4	24.7-288.4	.	15.4-452.4	.
Duration of COPD (yrs)	N	9798	4628	-0.161	58332	0.061
	Mean (SD)	5.5 (5.7)	6.3 (5.9)	.	5.2 (5.6)	.
	Median (IQR)	3.8 (0.8-8.7)	4.9 (1.5-9.4)	.	3.7 (0.4-8.3)	.
	Min-Max	0.0-49.9	0.0-49.9	.	0.0-49.8	.
Number of hospitalizations for COPD exac	N	9798	4628	0.184	58332	0.167
	Mean (SD)	0.1 (0.5)	0.1 (0.4)	.	0.1 (0.3)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.	0.0 (0.0-0.0)	.
	Min-Max	0.0-10.0	0.0-13.0	.	0.0-12.0	.

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Continuous baseline characteristics by exposure cohorts
POOLED - Total analysis population

		QVA149	Fixed LABA/LAMA	Std Dif	LABA	Std Dif
FEV1/FVC	N	5752	5402	0.025	7464	-0.294
	Mean (SD)	60.1 (14.9)	59.7 (13.8)	.	64.1 (12.5)	.
	Median (IQR)	60.8 (50.0-69.5)	60.0 (50.0-68.2)	.	64.9 (56.6-71.5)	.
	Min-Max	20.1-452.4	15.4-217.1	.	17.9-310.3	.
Duration of COPD (yrs)	N	9798	9150	0.048	12364	0.209
	Mean (SD)	5.5 (5.7)	5.3 (5.8)	.	4.5 (5.3)	.
	Median (IQR)	3.8 (0.8-8.7)	3.6 (0.5-8.4)	.	2.7 (0.1-7.4)	.
	Min-Max	0.0-49.9	0.0-49.8	.	0.0-49.1	.
Number of hospitalizations for COPD exac	N	9798	9150	0.060	12364	0.278
	Mean (SD)	0.1 (0.5)	0.1 (0.5)	.	0.0 (0.3)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.	0.0 (0.0-0.0)	.
	Min-Max	0.0-10.0	0.0-13.0	.	0.0-12.0	.

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Continuous baseline characteristics by exposure cohorts
POOLED - Total analysis population

		QVA149	LAMA	Std Dif
FEV1/FVC	N	5752	25533	-0.244
	Mean (SD)	60.1 (14.9)	63.5 (13.2)	.
	Median (IQR)	60.8 (50.0-69.5)	64.0 (55.5-71.0)	.
	Min-Max	20.1-452.4	15.4-633.8	.
Duration of COPD (yrs)	N	9798	42972	0.357
	Mean (SD)	5.5 (5.7)	4.0 (5.2)	.
	Median (IQR)	3.8 (0.8-8.7)	1.9 (0.0-6.6)	.
	Min-Max	0.0-49.9	0.0-49.9	.
Number of hospitalizations for COPD exac	N	9798	42972	0.249
	Mean (SD)	0.1 (0.5)	0.0 (0.3)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.
	Min-Max	0.0-10.0	0.0-7.0	.

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Continuous baseline characteristics by exposure cohorts
POOLED - Total analysis population

		QVA149	Free LABA+LAMA without ICS	Std Dif	Free LABA+LAMA with ICS	Std Dif
Number of systemic steroids episodes	N	9798	9619	-0.023	3192	-0.188
	Mean (SD)	0.1 (0.4)	0.1 (0.5)	.	0.2 (0.6)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.	0.0 (0.0-0.0)	.
	Min-Max	0.0-5.0	0.0-6.0	.	0.0-5.0	.
Number of Antibiotic courses	N	9798	9619	0.002	3192	-0.108
	Mean (SD)	0.3 (0.7)	0.3 (0.8)	.	0.4 (1.0)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.	0.0 (0.0-0.0)	.
	Min-Max	0.0-8.0	0.0-10.0	.	0.0-13.0	.

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Continuous baseline characteristics by exposure cohorts
POOLED - Total analysis population

		QVA149	Free LABA+ICS	Std Dif	Fixed LABA/ICS	Std Dif
Number of systemic steroids episodes	N	9798	4628	0.001	58332	-0.041
	Mean (SD)	0.1 (0.4)	0.1 (0.5)	.	0.1 (0.4)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.	0.0 (0.0-0.0)	.
	Min-Max	0.0-5.0	0.0-6.0	.	0.0-7.0	.
Number of Antibiotic courses	N	9798	4628	-0.038	58332	-0.019
	Mean (SD)	0.3 (0.7)	0.3 (0.8)	.	0.3 (0.7)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.	0.0 (0.0-0.0)	.
	Min-Max	0.0-8.0	0.0-12.0	.	0.0-11.0	.

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Table 15-16-6 (Page 19 of 20)
Continuous baseline characteristics by exposure cohorts
POOLED - Total analysis population

		QVA149	Fixed LABA/LAMA	Std Dif	LABA	Std Dif
Number of systemic steroids episodes	N	9798	9150	-0.149	12364	0.094
	Mean (SD)	0.1 (0.4)	0.2 (0.6)	.	0.1 (0.4)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.	0.0 (0.0-0.0)	.
	Min-Max	0.0-5.0	0.0-8.0	.	0.0-6.0	.
Number of Antibiotic courses	N	9798	9150	-0.068	12364	0.073
	Mean (SD)	0.3 (0.7)	0.4 (0.9)	.	0.2 (0.7)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.	0.0 (0.0-0.0)	.
	Min-Max	0.0-8.0	0.0-9.0	.	0.0-12.0	.

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Continuous baseline characteristics by exposure cohorts
POOLED - Total analysis population

		QVA149	LAMA	Std Dif
Number of systemic steroids episodes	N	9798	42972	0.064
	Mean (SD)	0.1 (0.4)	0.1 (0.4)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.
	Min-Max	0.0-5.0	0.0-6.0	.
Number of Antibiotic courses	N	9798	42972	0.075
	Mean (SD)	0.3 (0.7)	0.2 (0.6)	.
	Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.
	Min-Max	0.0-8.0	0.0-9.0	.

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Table 15-17-1 (Page 1 of 12)
Incidence rates (per 1,000 PY) of events during cohort time by exposure cohorts
THIN - Total analysis population

	QVA149				Free LABA+LAMA without ICS				Free LABA+LAMA with ICS			
Endpoint	Events	PY	IR	95% CI	Events	PY	IR	95% CI	Events	PY	IR	95% CI
MACE	19	732	25.9	[17.1,37.8]	27	1103	24.5	[17.3,33.6]	3	121	24.8	[6.8,62.9]
Ischemic heart disease	15	734	20.4	[12.6,31.3]	19	1104	17.2	[11.3,25.1]	2	121	16.5	[2.9,51.0]
Cardiac arrhythmia	7	738	9.5	[4.5,17.8]	11	1112	9.9	[5.6,16.3]	0	122	0.0	[0.0,24.2]
Cerebrovascular disorders	8	736	10.9	[5.4,19.5]	10	1107	9.0	[4.9,15.3]	1	122	8.2	[0.4,38.4]
Glaucoma	3	737	4.1	[1.1,10.5]	1	1114	0.9	[0.0, 4.3]	2	121	16.5	[2.9,51.0]
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	7	736	9.5	[4.5,17.8]	14	1109	12.6	[7.6,19.7]	1	122	8.2	[0.4,38.2]
Diabetes mellitus	9	617	14.6	[7.6,25.3]	20	959	20.9	[13.9,30.2]	2	110	18.2	[3.2,56.1]
Bronchospasm	0	739	0.0	[0.0, 4.0]	0	1114	0.0	[0.0, 2.7]	0	122	0.0	[0.0,24.2]
Mortality	71	739	96.1	[78.8, 116]	34	1114	30.5	[22.5,40.4]	4	122	32.7	[11.3,73.3]

Note: Run date and time 01NOV2018 11:20:02,

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Table 15-17-1 (Page 2 of 12)
Incidence rates (per 1,000 PY) of events during cohort time by exposure cohorts
THIN - Total analysis population

	Free LABA+ICS				Fixed LABA ICS				Fixed LABA LAMA			
Endpoint	Events	PY	IR	95% CI	Events	PY	IR	95% CI	Events	PY	IR	95% CI
MACE	5	186	26.9	[10.7,55.8]	307	14225	21.6	[19.6,23.7]	41	2487	16.5	[12.5,21.3]
Ischemic heart disease	1	186	5.4	[0.3,25.2]	185	14280	13.0	[11.4,14.6]	27	2485	10.9	[7.7,15.0]
Cardiac arrhythmia	3	185	16.2	[4.4,41.4]	232	14242	16.3	[14.6,18.1]	32	2489	12.9	[9.4,17.2]
Cerebrovascular disorders	2	186	10.7	[1.9,33.4]	190	14277	13.3	[11.8,15.0]	33	2488	13.3	[9.7,17.7]
Glaucoma	0	187	0.0	[0.0,15.9]	33	14363	2.3	[1.7, 3.1]	4	2500	1.6	[0.5, 3.7]
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	0	187	0.0	[0.0,15.9]	121	14295	8.5	[7.2, 9.8]	18	2493	7.2	[4.7,10.7]
Diabetes mellitus	3	159	18.9	[5.2,48.0]	186	12400	15.0	[13.2,16.9]	33	2124	15.5	[11.4,20.7]
Bronchospasm	0	187	0.0	[0.0,15.9]	0	14386	0.0	[0.0, 0.2]	0	2501	0.0	[0.0, 1.2]
Mortality	8	187	42.9	[21.5,76.1]	817	14386	56.8	[53.6,60.1]	117	2501	46.8	[40.0,54.3]

Note: Run date and time 01NOV2018 11:20:02,

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Table 15-17-1 (Page 3 of 12)
Incidence rates (per 1,000 PY) of events during cohort time by exposure cohorts
THIN - Total analysis population

	LABA				LAMA			
Endpoint	Events	PY	IR	95% CI	Events	PY	IR	95% CI
MACE	27	1197	22.6	[16.0,31.0]	199	8919	22.3	[19.8,25.1]
Ischemic heart disease	18	1202	15.0	[9.7,22.1]	128	8940	14.3	[12.3,16.6]
Cardiac arrhythmia	16	1198	13.4	[8.4,20.2]	129	8941	14.4	[12.4,16.7]
Cerebrovascular disorders	20	1200	16.7	[11.1,24.1]	133	8942	14.9	[12.8,17.2]
Glaucoma	5	1207	4.1	[1.6, 8.7]	24	8989	2.7	[1.8, 3.8]
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	12	1202	10.0	[5.8,16.1]	77	8962	8.6	[7.1,10.4]
Diabetes mellitus	19	1042	18.2	[12.0,26.7]	120	7740	15.5	[13.3,18.0]
Bronchospasm	0	1209	0.0	[0.0, 2.5]	0	9000	0.0	[0.0, 0.3]
Mortality	53	1209	43.8	[34.6,54.8]	356	9000	39.6	[36.2,43.1]

Note: Run date and time 01NOV2018 11:20:02,

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Table 15-17-1 (Page 4 of 12)
Incidence rates (per 1,000 PY) of events during cohort time by exposure cohorts
THIN - Total analysis population

	QVA149				Free LABA+LAMA without ICS				Free LABA+LAMA with ICS			
Endpoint	Events	PY	IR	95% CI	Events	PY	IR	95% CI	Events	PY	IR	95% CI
Atrial fibrillation/flutter	7	651	10.8	[5.1,20.1]	11	1025	10.7	[6.0,17.7]	0	116	0.0	[0.0,25.5]
Angina pectoris	5	594	8.4	[3.3,17.6]	7	946	7.4	[3.5,13.9]	0	109	0.0	[0.0,27.2]
AV block	1	736	1.4	[0.1, 6.4]	0	1109	0.0	[0.0, 2.7]	0	122	0.0	[0.0,24.2]
Incident benign prostatic hyperplasia	1	673	1.5	[0.1, 7.0]	6	1029	5.8	[2.5,11.5]	1	113	8.9	[0.5,41.4]
Hospitalization for acute coronary syndrome	4	738	5.4	[1.9,12.4]	7	1111	6.3	[3.0,11.8]	0	122	0.0	[0.0,24.2]
Hospitalization for heart failure	3	737	4.1	[1.1,10.5]	5	1113	4.5	[1.8, 9.4]	1	122	8.2	[0.4,38.3]
Myocardial infarction	9	736	12.2	[6.4,21.2]	9	1112	8.1	[4.2,14.1]	1	122	8.2	[0.4,38.4]
Long QT	0	739	0.0	[0.0, 4.0]	0	1114	0.0	[0.0, 2.7]	0	122	0.0	[0.0,24.2]
Narrow angle glaucoma	0	739	0.0	[0.0, 4.0]	0	1112	0.0	[0.0, 2.7]	0	122	0.0	[0.0,24.2]

Note: Run date and time 01NOV2018 11:20:02,

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Table 15-17-1 (Page 5 of 12)
Incidence rates (per 1,000 PY) of events during cohort time by exposure cohorts
THIN - Total analysis population

	Free LABA+ICS				Fixed LABA ICS				Fixed LABA LAMA			
Endpoint	Events	PY	IR	95% CI	Events	PY	IR	95% CI	Events	PY	IR	95% CI
Atrial fibrillation/flutter	3	175	17.1	[4.7,43.7]	224	13076	17.1	[15.3,19.1]	30	2256	13.3	[9.6,18.0]
Angina pectoris	1	163	6.1	[0.3,28.8]	84	12266	6.8	[5.7, 8.2]	14	2076	6.7	[4.1,10.5]
AV block	0	186	0.0	[0.0,15.9]	3	14367	0.2	[0.1, 0.5]	0	2494	0.0	[0.0, 1.2]
Incident benign prostatic hyperplasia	0	173	0.0	[0.0,17.1]	58	13354	4.3	[3.5, 5.4]	9	2303	3.9	[2.0, 6.8]
Hospitalization for acute coronary syndrome	1	186	5.4	[0.3,25.2]	52	14360	3.6	[2.8, 4.6]	5	2500	2.0	[0.8, 4.2]
Hospitalization for heart failure	2	186	10.7	[1.9,33.4]	63	14353	4.4	[3.5, 5.4]	11	2499	4.4	[2.5, 7.3]
Myocardial infarction	0	187	0.0	[0.0,15.9]	91	14343	6.3	[5.3, 7.5]	10	2496	4.0	[2.2, 6.8]
Long QT	0	187	0.0	[0.0,15.9]	0	14386	0.0	[0.0, 0.2]	1	2501	0.4	[0.0, 1.9]
Narrow angle glaucoma	0	187	0.0	[0.0,15.9]	1	14380	0.1	[0.0, 0.3]	0	2497	0.0	[0.0, 1.2]

Note: Run date and time 01NOV2018 11:20:02,

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Table 15-17-1 (Page 6 of 12)
Incidence rates (per 1,000 PY) of events during cohort time by exposure cohorts
THIN - Total analysis population

	LABA				LAMA			
Endpoint	Events	PY	IR	95% CI	Events	PY	IR	95% CI
Atrial fibrillation/flutter	16	1089	14.7	[9.2,22.2]	125	8150	15.3	[13.2,17.8]
Angina pectoris	9	1028	8.8	[4.6,15.2]	67	7616	8.8	[7.1,10.8]
AV block	0	1207	0.0	[0.0, 2.5]	0	8984	0.0	[0.0, 0.3]
Incident benign prostatic hyperplasia	5	1112	4.5	[1.8, 9.4]	33	8395	3.9	[2.9, 5.3]
Hospitalization for acute coronary syndrome	4	1207	3.3	[1.1, 7.6]	32	8986	3.6	[2.6, 4.8]
Hospitalization for heart failure	7	1205	5.8	[2.7,10.9]	37	8987	4.1	[3.1, 5.4]
Myocardial infarction	7	1206	5.8	[2.7,10.9]	56	8980	6.2	[4.9, 7.8]
Long QT	0	1209	0.0	[0.0, 2.5]	0	9000	0.0	[0.0, 0.3]
Narrow angle glaucoma	0	1208	0.0	[0.0, 2.5]	0	8993	0.0	[0.0, 0.3]

Note: Run date and time 01NOV2018 11:20:02,

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Table 15-17-1 (Page 7 of 12)
Incidence rates (per 1,000 PY) of events during cohort time by exposure cohorts
THIN - Total analysis population

	QVA149				Free LABA+LAMA without ICS				Free LABA+LAMA with ICS			
Endpoint	Events	PY	IR	95% CI	Events	PY	IR	95% CI	Events	PY	IR	95% CI
Other glaucoma	3	710	4.2	[1.2,10.9]	1	1056	0.9	[0.0, 4.5]	2	115	17.4	[3.1,53.8]
Premature depolarization	1	730	1.4	[0.1, 6.5]	0	1106	0.0	[0.0, 2.7]	0	122	0.0	[0.0,24.3]
Sick sinus	0	739	0.0	[0.0, 4.0]	0	1113	0.0	[0.0, 2.7]	0	122	0.0	[0.0,24.2]
Stroke	4	737	5.4	[1.9,12.4]	9	1108	8.1	[4.2,14.1]	1	122	8.2	[0.4,38.4]
Supraventricular tachycardia	1	730	1.4	[0.1, 6.5]	0	1105	0.0	[0.0, 2.7]	0	121	0.0	[0.0,24.5]
TIA	4	737	5.4	[1.9,12.4]	1	1114	0.9	[0.0, 4.3]	1	122	8.2	[0.4,38.4]
Torsades de Pointes	0	739	0.0	[0.0, 4.0]	0	1114	0.0	[0.0, 2.7]	0	122	0.0	[0.0,24.2]
Unstable angina pectoris	2	738	2.7	[0.5, 8.5]	3	1113	2.7	[0.7, 7.0]	1	122	8.2	[0.4,38.3]
Urinary retention	6	736	8.2	[3.6,16.0]	9	1110	8.1	[4.2,14.1]	0	122	0.0	[0.0,24.2]

Note: Run date and time 01NOV2018 11:20:02,

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Table 15-17-1 (Page 8 of 12)
Incidence rates (per 1,000 PY) of events during cohort time by exposure cohorts
THIN - Total analysis population

	Free LABA+ICS				Fixed LABA ICS				Fixed LABA LAMA			
Endpoint	Events	PY	IR	95% CI	Events	PY	IR	95% CI	Events	PY	IR	95% CI
Other glaucoma	0	171	0.0	[0.0,17.4]	32	13692	2.3	[1.7, 3.1]	4	2398	1.7	[0.6, 3.8]
Premature depolarization	0	186	0.0	[0.0,16.0]	9	14299	0.6	[0.3, 1.1]	0	2490	0.0	[0.0, 1.2]
Sick sinus	0	187	0.0	[0.0,15.9]	1	14365	0.1	[0.0, 0.3]	0	2500	0.0	[0.0, 1.2]
Stroke	2	186	10.7	[1.9,33.4]	144	14306	10.1	[8.7,11.5]	21	2494	8.4	[5.6,12.1]
Supraventricular tachycardia	1	184	5.4	[0.3,25.5]	17	14209	1.2	[0.8, 1.8]	1	2473	0.4	[0.0, 1.9]
TIA	2	186	10.7	[1.9,33.4]	57	14352	4.0	[3.1, 4.9]	14	2494	5.6	[3.4, 8.8]
Torsades de Pointes	0	187	0.0	[0.0,15.9]	0	14386	0.0	[0.0, 0.2]	0	2501	0.0	[0.0, 1.2]
Unstable angina pectoris	1	186	5.4	[0.3,25.2]	28	14378	1.9	[1.4, 2.7]	7	2497	2.8	[1.3, 5.3]
Urinary retention	0	187	0.0	[0.0,15.9]	66	14336	4.6	[3.7, 5.6]	9	2497	3.6	[1.9, 6.3]

Note: Run date and time 01NOV2018 11:20:02,

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Table 15-17-1 (Page 9 of 12)
Incidence rates (per 1,000 PY) of events during cohort time by exposure cohorts
THIN - Total analysis population

	LABA				LAMA			
Endpoint	Events	PY	IR	95% CI	Events	PY	IR	95% CI
Other glaucoma	5	1136	4.4	[1.7, 9.2]	24	8619	2.8	[1.9, 3.9]
Premature depolarization	1	1201	0.8	[0.0, 3.9]	3	8927	0.3	[0.1, 0.9]
Sick sinus	0	1209	0.0	[0.0, 2.5]	1	8993	0.1	[0.0, 0.5]
Stroke	12	1204	10.0	[5.8,16.1]	95	8958	10.6	[8.9,12.6]
Supraventricular tachycardia	0	1200	0.0	[0.0, 2.5]	4	8886	0.5	[0.2, 1.0]
TIA	10	1204	8.3	[4.5,14.0]	47	8980	5.2	[4.0, 6.7]
Torsades de Pointes	0	1209	0.0	[0.0, 2.5]	0	9000	0.0	[0.0, 0.3]
Unstable angina pectoris	4	1208	3.3	[1.1, 7.6]	14	8994	1.6	[0.9, 2.4]
Urinary retention	7	1204	5.8	[2.7,10.9]	48	8980	5.3	[4.1, 6.8]

Note: Run date and time 01NOV2018 11:20:02,

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Table 15-17-1 (Page 10 of 12)
Incidence rates (per 1,000 PY) of events during cohort time by exposure cohorts
THIN - Total analysis population

	QVA149				Free LABA+LAMA without ICS				Free LABA+LAMA with ICS			
Endpoint	Events	PY	IR	95% CI	Events	PY	IR	95% CI	Events	PY	IR	95% CI
Ventricular tachycardia	0	739	0.0	[0.0, 4.0]	0	1114	0.0	[0.0, 2.7]	0	122	0.0	[0.0,24.2]
Ventricular fibrillation	0	739	0.0	[0.0, 4.0]	0	1114	0.0	[0.0, 2.7]	0	122	0.0	[0.0,24.2]
Cardiovascular death	2	739	2.7	[0.5, 8.5]	1	1114	0.9	[0.0, 4.3]	0	122	0.0	[0.0,24.2]
Respiratory death	0	739	0.0	[0.0, 4.0]	0	1114	0.0	[0.0, 2.7]	0	122	0.0	[0.0,24.2]
Cardiovascular and respiratory death	0	739	0.0	[0.0, 4.0]	0	1114	0.0	[0.0, 2.7]	0	122	0.0	[0.0,24.2]
Cerebrovascular death	0	739	0.0	[0.0, 4.0]	0	1114	0.0	[0.0, 2.7]	0	122	0.0	[0.0,24.2]
Cancer death (excluding lungcancer)	0	739	0.0	[0.0, 4.0]	0	1114	0.0	[0.0, 2.7]	0	122	0.0	[0.0,24.2]
Death due to other causes	1	739	1.4	[0.1, 6.4]	0	1114	0.0	[0.0, 2.7]	0	122	0.0	[0.0,24.2]
Death with cause unknown	68	739	92.1	[75.1, 111]	33	1114	29.6	[21.8,39.4]	4	122	32.7	[11.3,73.3]

Note: Run date and time 01NOV2018 11:20:02,

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Table 15-17-1 (Page 11 of 12)
Incidence rates (per 1,000 PY) of events during cohort time by exposure cohorts
THIN - Total analysis population

	Free LABA+ICS				Fixed LABA ICS				Fixed LABA LAMA			
Endpoint	Events	PY	IR	95% CI	Events	PY	IR	95% CI	Events	PY	IR	95% CI
Ventricular tachycardia	0	187	0.0	[0.0,15.9]	7	14381	0.5	[0.2, 0.9]	1	2501	0.4	[0.0, 1.9]
Ventricular fibrillation	0	187	0.0	[0.0,15.9]	1	14386	0.1	[0.0, 0.3]	1	2501	0.4	[0.0, 1.9]
Cardiovascular death	0	187	0.0	[0.0,15.9]	7	14386	0.5	[0.2, 0.9]	1	2501	0.4	[0.0, 1.9]
Respiratory death	0	187	0.0	[0.0,15.9]	7	14386	0.5	[0.2, 0.9]	1	2501	0.4	[0.0, 1.9]
Cardiovascular and respiratory death	0	187	0.0	[0.0,15.9]	1	14386	0.1	[0.0, 0.3]	0	2501	0.0	[0.0, 1.2]
Cerebrovascular death	0	187	0.0	[0.0,15.9]	0	14386	0.0	[0.0, 0.2]	0	2501	0.0	[0.0, 1.2]
Cancer death (excluding lungcancer)	0	187	0.0	[0.0,15.9]	4	14386	0.3	[0.1, 0.6]	0	2501	0.0	[0.0, 1.2]
Death due to other causes	0	187	0.0	[0.0,15.9]	1	14386	0.1	[0.0, 0.3]	0	2501	0.0	[0.0, 1.2]
Death with cause unknown	8	187	42.9	[21.5,76.1]	798	14386	55.5	[52.4,58.7]	115	2501	46.0	[39.3,53.5]

Note: Run date and time 01NOV2018 11:20:02,

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Table 15-17-1 (Page 12 of 12)
Incidence rates (per 1,000 PY) of events during cohort time by exposure cohorts
THIN - Total analysis population

	LABA				LAMA			
Endpoint	Events	PY	IR	95% CI	Events	PY	IR	95% CI
Ventricular tachycardia	0	1209	0.0	[0.0, 2.5]	4	8997	0.4	[0.2, 1.0]
Ventricular fibrillation	0	1209	0.0	[0.0, 2.5]	0	9000	0.0	[0.0, 0.3]
Cardiovascular death	1	1209	0.8	[0.0, 3.9]	5	9000	0.6	[0.2, 1.2]
Respiratory death	1	1209	0.8	[0.0, 3.9]	6	9000	0.7	[0.3, 1.3]
Cardiovascular and respiratory death	0	1209	0.0	[0.0, 2.5]	0	9000	0.0	[0.0, 0.3]
Cerebrovascular death	0	1209	0.0	[0.0, 2.5]	0	9000	0.0	[0.0, 0.3]
Cancer death (excluding lungcancer)	0	1209	0.0	[0.0, 2.5]	4	9000	0.4	[0.2, 1.0]
Death due to other causes	1	1209	0.8	[0.0, 3.9]	1	9000	0.1	[0.0, 0.5]
Death with cause unknown	50	1209	41.4	[32.4,52.1]	341	9000	37.9	[34.6,41.4]

Note: Run date and time 01NOV2018 11:20:02,

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Table 15-17-2 (Page 1 of 12)
Incidence rates (per 1,000 PY) of events during cohort time by exposure cohorts
IPCI - Total analysis population

	QVA149				Free LABA+LAMA without ICS				Free LABA+LAMA with ICS			
Endpoint	Events	PY	IR	95% CI	Events	PY	IR	95% CI	Events	PY	IR	95% CI
MACE	16	365	43.8	[27.7,65.8]	17	361	47.1	[30.2,69.8]	6	141	42.6	[18.7,82.4]
Ischemic heart disease	5	369	13.6	[5.4,28.3]	7	365	19.2	[9.0,35.7]	4	140	28.5	[9.8,64.0]
Cardiac arrhythmia	9	367	24.5	[12.9,42.4]	7	366	19.1	[9.0,35.7]	7	141	49.8	[23.6,91.4]
Cerebrovascular disorders	13	365	35.6	[21.2,56.0]	6	366	16.4	[7.2,32.1]	4	142	28.2	[9.7,63.4]
Glaucoma	1	370	2.7	[0.1,12.8]	0	368	0.0	[0.0, 8.1]	1	142	7.0	[0.4,32.9]
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	11	365	30.1	[17.0,49.4]	5	367	13.6	[5.4,28.4]	4	141	28.4	[9.8,63.8]
Diabetes mellitus	6	307	19.6	[8.6,38.2]	5	304	16.4	[6.5,34.2]	1	123	8.1	[0.4,38.1]
Bronchospasm	1	371	2.7	[0.1,12.7]	0	368	0.0	[0.0, 8.1]	0	142	0.0	[0.0,20.8]
Mortality	20	371	53.9	[36.0,77.4]	23	368	62.6	[43.1,87.5]	8	142	56.2	[28.2,99.1]

Note: Run date and time 01NOV2018 11:20:14,

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Table 15-17-2 (Page 2 of 12)
Incidence rates (per 1,000 PY) of events during cohort time by exposure cohorts
IPCI - Total analysis population

	Free LABA+ICS				Fixed LABA ICS				Fixed LABA LAMA			
Endpoint	Events	PY	IR	95% CI	Events	PY	IR	95% CI	Events	PY	IR	95% CI
MACE	11	148	74.6	[42.4, 120]	142	2797	50.8	[44.1,58.1]	20	438	45.7	[30.5,65.6]
Ischemic heart disease	4	149	26.9	[9.2,60.5]	41	2821	14.5	[11.0,18.8]	6	441	13.6	[5.9,26.7]
Cardiac arrhythmia	6	149	40.4	[17.7,78.1]	57	2818	20.2	[16.1,25.2]	7	439	15.9	[7.5,29.7]
Cerebrovascular disorders	5	148	33.7	[13.4,69.6]	53	2818	18.8	[14.8,23.6]	4	442	9.1	[3.1,20.6]
Glaucoma	0	149	0.0	[0.0,19.9]	5	2833	1.8	[0.7, 3.7]	0	443	0.0	[0.0, 6.7]
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	4	149	26.9	[9.2,60.4]	51	2818	18.1	[14.2,22.8]	9	437	20.6	[10.8,35.6]
Diabetes mellitus	2	121	16.5	[2.9,50.9]	26	2317	11.2	[7.9,15.5]	5	367	13.6	[5.4,28.4]
Bronchospasm	0	149	0.0	[0.0,19.9]	0	2838	0.0	[0.0, 1.1]	1	442	2.3	[0.1,10.7]
Mortality	13	149	87.1	[52.3, 135]	179	2838	63.1	[55.7,71.1]	19	443	42.9	[28.3,62.4]

Note: Run date and time 01NOV2018 11:20:14,

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Table 15-17-2 (Page 3 of 12)
Incidence rates (per 1,000 PY) of events during cohort time by exposure cohorts
IPCI - Total analysis population

	LABA				LAMA			
Endpoint	Events	PY	IR	95% CI	Events	PY	IR	95% CI
MACE	18	449	40.1	[26.1,58.9]	90	1995	45.1	[37.7,53.5]
Ischemic heart disease	3	451	6.7	[1.8,17.1]	43	2006	21.4	[16.4,27.6]
Cardiac arrhythmia	4	449	8.9	[3.0,20.2]	50	2018	24.8	[19.4,31.3]
Cerebrovascular disorders	12	449	26.7	[15.5,43.0]	41	2011	20.4	[15.5,26.4]
Glaucoma	0	451	0.0	[0.0, 6.6]	5	2027	2.5	[1.0, 5.2]
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	6	449	13.4	[5.8,26.2]	44	2017	21.8	[16.7,28.0]
Diabetes mellitus	1	387	2.6	[0.1,12.2]	16	1711	9.4	[5.9,14.2]
Bronchospasm	0	451	0.0	[0.0, 6.6]	2	2032	1.0	[0.2, 3.1]
Mortality	32	451	70.9	[52.1,94.1]	85	2032	41.8	[34.8,49.9]

Note: Run date and time 01NOV2018 11:20:14,

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Table 15-17-2 (Page 4 of 12)
Incidence rates (per 1,000 PY) of events during cohort time by exposure cohorts
IPCI - Total analysis population

	QVA149				Free LABA+LAMA without ICS				Free LABA+LAMA with ICS			
Endpoint	Events	PY	IR	95% CI	Events	PY	IR	95% CI	Events	PY	IR	95% CI
Atrial fibrillation/flutter	8	322	24.9	[12.4,44.4]	7	322	21.7	[10.2,40.4]	5	128	39.1	[15.5,80.4]
Angina pectoris	1	325	3.1	[0.2,14.5]	2	309	6.5	[1.2,20.2]	1	116	8.6	[0.4,40.2]
AV block	0	370	0.0	[0.0, 8.1]	1	363	2.8	[0.1,13.0]	0	142	0.0	[0.0,20.9]
Incident benign prostatic hyperplasia	2	334	6.0	[1.1,18.7]	0	333	0.0	[0.0, 9.0]	0	129	0.0	[0.0,23.0]
Hospitalization for acute coronary syndrome	4	369	10.8	[3.7,24.6]	7	363	19.3	[9.1,35.9]	3	141	21.3	[5.8,54.1]
Hospitalization for heart failure	4	370	10.8	[3.7,24.6]	8	366	21.8	[10.9,39.0]	3	142	21.1	[5.8,53.6]
Myocardial infarction	3	370	8.1	[2.2,20.8]	4	365	10.9	[3.7,24.9]	3	141	21.3	[5.8,54.1]
Long QT	0	371	0.0	[0.0, 8.0]	1	368	2.7	[0.1,12.8]	0	142	0.0	[0.0,20.8]
Narrow angle glaucoma	0	369	0.0	[0.0, 8.1]	0	367	0.0	[0.0, 8.1]	0	142	0.0	[0.0,20.9]

Note: Run date and time 01NOV2018 11:20:14,

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Table 15-17-2 (Page 5 of 12)
Incidence rates (per 1,000 PY) of events during cohort time by exposure cohorts
IPCI - Total analysis population

	Free LABA+ICS				Fixed LABA ICS				Fixed LABA LAMA			
Endpoint	Events	PY	IR	95% CI	Events	PY	IR	95% CI	Events	PY	IR	95% CI
Atrial fibrillation/flutter	6	126	47.8	[21.0,92.2]	53	2503	21.2	[16.7,26.6]	6	379	15.8	[6.9,31.0]
Angina pectoris	0	130	0.0	[0.0,22.8]	10	2454	4.1	[2.2, 6.9]	1	380	2.6	[0.1,12.4]
AV block	1	147	6.8	[0.3,31.8]	10	2807	3.6	[1.9, 6.0]	2	438	4.6	[0.8,14.3]
Incident benign prostatic hyperplasia	2	136	14.7	[2.6,45.7]	14	2596	5.4	[3.3, 8.4]	3	393	7.6	[2.1,19.6]
Hospitalization for acute coronary syndrome	4	149	26.9	[9.2,60.5]	30	2826	10.6	[7.7,14.4]	5	441	11.3	[4.5,23.7]
Hospitalization for heart failure	5	149	33.6	[13.3,69.4]	79	2819	28.0	[23.1,33.7]	13	439	29.6	[17.6,46.6]
Myocardial infarction	2	149	13.4	[2.4,41.7]	23	2830	8.1	[5.6,11.5]	3	441	6.8	[1.9,17.5]
Long QT	0	149	0.0	[0.0,19.9]	0	2838	0.0	[0.0, 1.1]	0	443	0.0	[0.0, 6.7]
Narrow angle glaucoma	0	149	0.0	[0.0,19.9]	0	2826	0.0	[0.0, 1.1]	0	439	0.0	[0.0, 6.8]

Note: Run date and time 01NOV2018 11:20:14,

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Table 15-17-2 (Page 6 of 12)
Incidence rates (per 1,000 PY) of events during cohort time by exposure cohorts
IPCI - Total analysis population

	LABA				LAMA			
Endpoint	Events	PY	IR	95% CI	Events	PY	IR	95% CI
Atrial fibrillation/flutter	4	395	10.1	[3.5,23.0]	43	1754	24.5	[18.8,31.5]
Angina pectoris	1	406	2.5	[0.1,11.6]	9	1723	5.2	[2.7, 9.1]
AV block	0	446	0.0	[0.0, 6.7]	5	1994	2.5	[1.0, 5.3]
Incident benign prostatic hyperplasia	3	413	7.3	[2.0,18.7]	16	1830	8.7	[5.5,13.3]
Hospitalization for acute coronary syndrome	2	451	4.4	[0.8,13.9]	29	2017	14.4	[10.3,19.6]
Hospitalization for heart failure	8	450	17.8	[8.9,31.8]	44	2019	21.8	[16.7,27.9]
Myocardial infarction	2	451	4.4	[0.8,13.9]	22	2019	10.9	[7.4,15.5]
Long QT	0	451	0.0	[0.0, 6.6]	0	2032	0.0	[0.0, 1.5]
Narrow angle glaucoma	0	450	0.0	[0.0, 6.6]	1	2025	0.5	[0.0, 2.3]

Note: Run date and time 01NOV2018 11:20:14,

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Table 15-17-2 (Page 7 of 12)
Incidence rates (per 1,000 PY) of events during cohort time by exposure cohorts
IPCI - Total analysis population

	QVA149				Free LABA+LAMA without ICS				Free LABA+LAMA with ICS			
Endpoint	Events	PY	IR	95% CI	Events	PY	IR	95% CI	Events	PY	IR	95% CI
Other glaucoma	1	359	2.8	[0.1,13.1]	0	353	0.0	[0.0, 8.4]	1	139	7.2	[0.4,33.7]
Premature depolarization	0	362	0.0	[0.0, 8.2]	1	358	2.8	[0.1,13.2]	1	138	7.2	[0.4,33.8]
Sick sinus	0	370	0.0	[0.0, 8.1]	0	367	0.0	[0.0, 8.1]	0	142	0.0	[0.0,20.8]
Stroke	8	368	21.8	[10.9,38.9]	4	366	10.9	[3.7,24.8]	0	142	0.0	[0.0,20.8]
Supraventricular tachycardia	1	365	2.7	[0.1,12.9]	3	361	8.3	[2.3,21.3]	0	139	0.0	[0.0,21.3]
TIA	6	368	16.3	[7.1,31.9]	3	367	8.2	[2.2,21.0]	4	142	28.2	[9.7,63.4]
Torsades de Pointes	0	371	0.0	[0.0, 8.0]	0	368	0.0	[0.0, 8.1]	0	142	0.0	[0.0,20.8]
Unstable angina pectoris	1	370	2.7	[0.1,12.8]	1	368	2.7	[0.1,12.8]	0	142	0.0	[0.0,20.8]
Urinary retention	10	367	27.3	[14.9,45.8]	5	367	13.6	[5.4,28.4]	4	141	28.4	[9.8,63.8]

Note: Run date and time 01NOV2018 11:20:14,

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Table 15-17-2 (Page 8 of 12)
Incidence rates (per 1,000 PY) of events during cohort time by exposure cohorts
IPCI - Total analysis population

	Free LABA+ICS				Fixed LABA ICS				Fixed LABA LAMA			
Endpoint	Events	PY	IR	95% CI	Events	PY	IR	95% CI	Events	PY	IR	95% CI
Other glaucoma	0	143	0.0	[0.0,20.7]	5	2722	1.8	[0.7, 3.9]	0	427	0.0	[0.0, 7.0]
Premature depolarization	0	146	0.0	[0.0,20.3]	6	2764	2.2	[0.9, 4.3]	0	435	0.0	[0.0, 6.9]
Sick sinus	0	148	0.0	[0.0,20.0]	0	2831	0.0	[0.0, 1.1]	0	441	0.0	[0.0, 6.8]
Stroke	3	149	20.2	[5.5,51.3]	36	2827	12.7	[9.5,16.8]	4	442	9.1	[3.1,20.6]
Supraventricular tachycardia	0	145	0.0	[0.0,20.4]	13	2772	4.7	[2.8, 7.4]	0	435	0.0	[0.0, 6.9]
TIA	2	149	13.4	[2.4,41.7]	18	2828	6.4	[4.1, 9.4]	0	443	0.0	[0.0, 6.7]
Torsades de Pointes	0	149	0.0	[0.0,19.9]	0	2838	0.0	[0.0, 1.1]	0	443	0.0	[0.0, 6.7]
Unstable angina pectoris	2	149	13.4	[2.4,41.6]	9	2833	3.2	[1.7, 5.5]	3	442	6.8	[1.9,17.4]
Urinary retention	2	149	13.4	[2.4,41.6]	39	2824	13.8	[10.4,18.0]	8	438	18.2	[9.1,32.7]

Note: Run date and time 01NOV2018 11:20:14,

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Table 15-17-2 (Page 9 of 12)
Incidence rates (per 1,000 PY) of events during cohort time by exposure cohorts
IPCI - Total analysis population

	LABA				LAMA			
Endpoint	Events	PY	IR	95% CI	Events	PY	IR	95% CI
Other glaucoma	0	436	0.0	[0.0, 6.9]	4	1957	2.0	[0.7, 4.7]
Premature depolarization	1	440	2.3	[0.1,10.7]	4	1978	2.0	[0.7, 4.6]
Sick sinus	0	451	0.0	[0.0, 6.6]	0	2027	0.0	[0.0, 1.5]
Stroke	8	450	17.8	[8.9,31.9]	19	2024	9.4	[6.2,13.7]
Supraventricular tachycardia	2	441	4.5	[0.8,14.2]	6	1994	3.0	[1.3, 5.9]
TIA	5	450	11.1	[4.4,23.2]	24	2019	11.9	[8.2,16.7]
Torsades de Pointes	0	451	0.0	[0.0, 6.6]	0	2032	0.0	[0.0, 1.5]
Unstable angina pectoris	0	451	0.0	[0.0, 6.6]	12	2026	5.9	[3.4, 9.6]
Urinary retention	3	449	6.7	[1.8,17.2]	31	2024	15.3	[11.1,20.6]

Note: Run date and time 01NOV2018 11:20:14,

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Table 15-17-2 (Page 10 of 12)
Incidence rates (per 1,000 PY) of events during cohort time by exposure cohorts
IPCI - Total analysis population

	QVA149				Free LABA+LAMA without ICS				Free LABA+LAMA with ICS			
Endpoint	Events	PY	IR	95% CI	Events	PY	IR	95% CI	Events	PY	IR	95% CI
Ventricular tachycardia	1	370	2.7	[0.1,12.7]	0	368	0.0	[0.0, 8.1]	1	142	7.0	[0.4,32.9]
Ventricular fibrillation	0	371	0.0	[0.0, 8.0]	0	368	0.0	[0.0, 8.1]	1	142	7.0	[0.4,32.9]
Cardiovascular death	1	371	2.7	[0.1,12.7]	6	368	16.3	[7.1,32.0]	0	142	0.0	[0.0,20.8]
Respiratory death	7	371	18.9	[8.9,35.2]	6	368	16.3	[7.1,32.0]	2	142	14.0	[2.5,43.5]
Cardiovascular and respiratory death	2	371	5.4	[1.0,16.9]	3	368	8.2	[2.2,21.0]	2	142	14.0	[2.5,43.5]
Cerebrovascular death	0	371	0.0	[0.0, 8.0]	0	368	0.0	[0.0, 8.1]	0	142	0.0	[0.0,20.8]
Cancer death (excluding lungcancer)	3	371	8.1	[2.2,20.8]	2	368	5.4	[1.0,17.0]	1	142	7.0	[0.4,32.9]
Death due to other causes	1	371	2.7	[0.1,12.7]	3	368	8.2	[2.2,21.0]	2	142	14.0	[2.5,43.5]
Death with cause unknown	6	371	16.2	[7.1,31.7]	3	368	8.2	[2.2,21.0]	1	142	7.0	[0.4,32.9]

Note: Run date and time 01NOV2018 11:20:14,

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Table 15-17-2 (Page 11 of 12)
Incidence rates (per 1,000 PY) of events during cohort time by exposure cohorts
IPCI - Total analysis population

	Free LABA+ICS				Fixed LABA ICS				Fixed LABA LAMA			
Endpoint	Events	PY	IR	95% CI	Events	PY	IR	95% CI	Events	PY	IR	95% CI
Ventricular tachycardia	0	149	0.0	[0.0,19.9]	3	2837	1.1	[0.3, 2.7]	1	442	2.3	[0.1,10.7]
Ventricular fibrillation	0	149	0.0	[0.0,19.9]	3	2838	1.1	[0.3, 2.7]	0	443	0.0	[0.0, 6.7]
Cardiovascular death	1	149	6.7	[0.3,31.4]	20	2838	7.0	[4.7,10.2]	1	443	2.3	[0.1,10.7]
Respiratory death	6	149	40.2	[17.7,77.8]	65	2838	22.9	[18.5,28.1]	7	443	15.8	[7.4,29.5]
Cardiovascular and respiratory death	0	149	0.0	[0.0,19.9]	13	2838	4.6	[2.7, 7.3]	1	443	2.3	[0.1,10.7]
Cerebrovascular death	1	149	6.7	[0.3,31.4]	4	2838	1.4	[0.5, 3.2]	1	443	2.3	[0.1,10.7]
Cancer death (excluding lungcancer)	1	149	6.7	[0.3,31.4]	19	2838	6.7	[4.4, 9.8]	0	443	0.0	[0.0, 6.7]
Death due to other causes	0	149	0.0	[0.0,19.9]	11	2838	3.9	[2.2, 6.4]	4	443	9.0	[3.1,20.6]
Death with cause unknown	4	149	26.8	[9.2,60.3]	47	2838	16.6	[12.8,21.1]	5	443	11.3	[4.5,23.6]

Note: Run date and time 01NOV2018 11:20:14,

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Table 15-17-2 (Page 12 of 12)
Incidence rates (per 1,000 PY) of events during cohort time by exposure cohorts
IPCI - Total analysis population

	LABA				LAMA			
Endpoint	Events	PY	IR	95% CI	Events	PY	IR	95% CI
Ventricular tachycardia	0	451	0.0	[0.0, 6.6]	3	2032	1.5	[0.4, 3.8]
Ventricular fibrillation	0	451	0.0	[0.0, 6.6]	4	2031	2.0	[0.7, 4.5]
Cardiovascular death	4	451	8.9	[3.0,20.2]	9	2032	4.4	[2.3, 7.7]
Respiratory death	10	451	22.2	[12.1,37.3]	28	2032	13.8	[9.8,18.8]
Cardiovascular and respiratory death	0	451	0.0	[0.0, 6.6]	10	2032	4.9	[2.7, 8.3]
Cerebrovascular death	1	451	2.2	[0.1,10.5]	2	2032	1.0	[0.2, 3.1]
Cancer death (excluding lungcancer)	4	451	8.9	[3.0,20.2]	16	2032	7.9	[4.9,11.9]
Death due to other causes	3	451	6.6	[1.8,17.1]	7	2032	3.4	[1.6, 6.5]
Death with cause unknown	10	451	22.2	[12.1,37.3]	13	2032	6.4	[3.8,10.2]

Note: Run date and time 01NOV2018 11:20:14,

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Table 15-17-3 (Page 1 of 12)
Incidence rates (per 1,000 PY) of events during cohort time by exposure cohorts
AUH - Total analysis population

	QVA149				Free LABA+LAMA without ICS				Free LABA+LAMA with ICS			
Endpoint	Events	PY	IR	95% CI	Events	PY	IR	95% CI	Events	PY	IR	95% CI
MACE	139	1139	122	[106, 139]	30	207	145	[107, 192]	14	69	203	[127, 299]
Ischemic heart disease	39	1189	32.8	[24.8,42.6]	4	212	18.9	[6.5,42.6]	2	71	28.1	[5.0,85.7]
Cardiac arrhythmia	32	1193	26.8	[19.6,35.9]	6	211	28.4	[12.4,55.3]	2	72	27.9	[5.0,85.3]
Cerebrovascular disorders	20	1203	16.6	[11.0,24.1]	2	212	9.4	[1.7,29.4]	2	71	28.0	[5.0,85.6]
Glaucoma	0	1213	0.0	[0.0, 2.5]	1	212	4.7	[0.2,22.2]	0	72	0.0	[0.0,40.9]
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	9	1207	7.5	[3.9,13.0]	2	212	9.5	[1.7,29.5]	0	72	0.0	[0.0,40.9]
Diabetes mellitus	7	1087	6.4	[3.0,12.1]	0	195	0.0	[0.0,15.3]	0	66	0.0	[0.0,44.5]
Bronchospasm	0	1213	0.0	[0.0, 2.5]	0	212	0.0	[0.0,14.0]	0	72	0.0	[0.0,40.9]
Mortality	138	1213	114	[99.1, 130]	16	212	75.3	[47.8, 112]	2	72	27.9	[5.0,85.2]

Note: Run date and time 01NOV2018 11:20:25,

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Table 15-17-3 (Page 2 of 12)
Incidence rates (per 1,000 PY) of events during cohort time by exposure cohorts
AUH - Total analysis population

	Free LABA+ICS				Fixed LABA ICS				Fixed LABA LAMA			
Endpoint	Events	PY	IR	95% CI	Events	PY	IR	95% CI	Events	PY	IR	95% CI
MACE	13	65	201	[123, 300]	234	1431	164	[148, 180]	121	794	152	[132, 175]
Ischemic heart disease	5	67	74.6	[29.9, 150]	42	1492	28.1	[21.5,36.3]	16	831	19.3	[12.1,29.1]
Cardiac arrhythmia	2	69	28.8	[5.1,88.0]	52	1504	34.6	[27.2,43.4]	35	830	42.2	[31.3,55.5]
Cerebrovascular disorders	2	69	29.1	[5.2,88.7]	22	1508	14.6	[9.9,20.8]	19	834	22.8	[15.0,33.3]
Glaucoma	0	70	0.0	[0.0,42.2]	2	1514	1.3	[0.2, 4.2]	4	836	4.8	[1.6,10.9]
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	1	69	14.4	[0.7,66.5]	11	1512	7.3	[4.1,12.0]	7	835	8.4	[3.9,15.7]
Diabetes mellitus	0	62	0.0	[0.0,46.8]	16	1320	12.1	[7.6,18.4]	10	741	13.5	[7.3,22.8]
Bronchospasm	0	70	0.0	[0.0,42.2]	0	1516	0.0	[0.0, 2.0]	0	838	0.0	[0.0, 3.6]
Mortality	5	70	71.9	[28.8, 145]	236	1516	156	[141, 172]	82	838	97.8	[81.4, 116]

Note: Run date and time 01NOV2018 11:20:25,

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Table 15-17-3 (Page 3 of 12)
Incidence rates (per 1,000 PY) of events during cohort time by exposure cohorts
AUH - Total analysis population

	LABA				LAMA			
Endpoint	Events	PY	IR	95% CI	Events	PY	IR	95% CI
MACE	43	372	116	[89.3, 146]	133	718	185	[162, 211]
Ischemic heart disease	11	377	29.2	[16.4,47.8]	15	753	19.9	[12.3,30.5]
Cardiac arrhythmia	10	380	26.3	[14.4,44.3]	32	750	42.7	[31.2,56.9]
Cerebrovascular disorders	5	382	13.1	[5.2,27.3]	13	753	17.3	[10.2,27.3]
Glaucoma	0	383	0.0	[0.0, 7.8]	3	757	4.0	[1.1,10.2]
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	1	383	2.6	[0.1,12.3]	7	756	9.3	[4.4,17.3]
Diabetes mellitus	1	325	3.1	[0.2,14.5]	7	669	10.5	[4.9,19.6]
Bronchospasm	0	383	0.0	[0.0, 7.8]	0	757	0.0	[0.0, 3.9]
Mortality	28	383	73.0	[52.4,98.8]	86	757	114	[95.1, 134]

Note: Run date and time 01NOV2018 11:20:25,

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Table 15-17-3 (Page 4 of 12)
Incidence rates (per 1,000 PY) of events during cohort time by exposure cohorts
AUH - Total analysis population

	QVA149				Free LABA+LAMA without ICS				Free LABA+LAMA with ICS			
Endpoint	Events	PY	IR	95% CI	Events	PY	IR	95% CI	Events	PY	IR	95% CI
Atrial fibrillation/flutter	30	955	31.4	[22.7,42.4]	6	181	33.1	[14.5,64.3]	2	64	31.1	[5.6,94.6]
Angina pectoris	19	916	20.7	[13.6,30.3]	2	164	12.2	[2.2,38.0]	0	53	0.0	[0.0,55.1]
AV block	5	1188	4.2	[1.7, 8.8]	1	210	4.8	[0.2,22.4]	0	70	0.0	[0.0,41.8]
Incident benign prostatic hyperplasia	5	1135	4.4	[1.7, 9.2]	1	203	4.9	[0.3,23.2]	0	69	0.0	[0.0,42.6]
Hospitalization for acute coronary syndrome	30	1197	25.1	[18.1,33.8]	3	212	14.1	[3.9,36.1]	3	71	42.2	[11.6, 105]
Hospitalization for heart failure	108	1153	93.6	[79.9, 109]	26	207	126	[89.6, 170]	9	70	129	[68.8, 214]
Myocardial infarction	18	1202	15.0	[9.7,22.1]	2	212	9.4	[1.7,29.4]	2	71	28.1	[5.0,85.7]
Long QT	0	1213	0.0	[0.0, 2.5]	0	212	0.0	[0.0,14.0]	0	72	0.0	[0.0,40.9]
Narrow angle glaucoma	0	1205	0.0	[0.0, 2.5]	0	208	0.0	[0.0,14.3]	0	72	0.0	[0.0,40.9]

Note: Run date and time 01NOV2018 11:20:25,

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Table 15-17-3 (Page 5 of 12)
Incidence rates (per 1,000 PY) of events during cohort time by exposure cohorts
AUH - Total analysis population

	Free LABA+ICS				Fixed LABA ICS				Fixed LABA LAMA			
Endpoint	Events	PY	IR	95% CI	Events	PY	IR	95% CI	Events	PY	IR	95% CI
Atrial fibrillation/flutter	2	52	38.3	[6.9, 116]	52	1248	41.7	[32.8,52.2]	34	687	49.5	[36.6,65.3]
Angina pectoris	1	49	20.3	[1.0,92.8]	28	1176	23.8	[17.0,32.5]	5	651	7.7	[3.0,16.1]
AV block	0	63	0.0	[0.0,46.1]	3	1478	2.0	[0.6, 5.2]	2	818	2.4	[0.4, 7.7]
Incident benign prostatic hyperplasia	1	66	15.2	[0.8,70.3]	7	1436	4.9	[2.3, 9.1]	4	778	5.1	[1.8,11.7]
Hospitalization for acute coronary syndrome	5	67	74.3	[29.7, 150]	34	1499	22.7	[16.7,30.1]	14	832	16.8	[10.2,26.2]
Hospitalization for heart failure	8	68	118	[60.2, 203]	192	1449	132	[118, 148]	97	802	121	[102, 142]
Myocardial infarction	4	67	59.3	[20.5, 131]	16	1506	10.6	[6.7,16.1]	9	834	10.8	[5.6,18.8]
Long QT	0	70	0.0	[0.0,42.2]	0	1516	0.0	[0.0, 2.0]	0	838	0.0	[0.0, 3.6]
Narrow angle glaucoma	0	70	0.0	[0.0,42.2]	0	1500	0.0	[0.0, 2.0]	1	830	1.2	[0.1, 5.7]

Note: Run date and time 01NOV2018 11:20:25,

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Table 15-17-3 (Page 6 of 12)
Incidence rates (per 1,000 PY) of events during cohort time by exposure cohorts
AUH - Total analysis population

	LABA				LAMA			
Endpoint	Events	PY	IR	95% CI	Events	PY	IR	95% CI
Atrial fibrillation/flutter	10	315	31.7	[17.3,53.2]	30	613	49.0	[35.5,65.8]
Angina pectoris	6	292	20.5	[9.0,40.1]	6	572	10.5	[4.6,20.6]
AV block	1	375	2.7	[0.1,12.6]	3	741	4.0	[1.1,10.4]
Incident benign prostatic hyperplasia	1	360	2.8	[0.1,13.1]	3	720	4.2	[1.1,10.7]
Hospitalization for acute coronary syndrome	9	378	23.8	[12.5,41.2]	14	754	18.6	[11.3,28.9]
Hospitalization for heart failure	34	375	90.6	[67.4, 119]	113	723	156	[134, 180]
Myocardial infarction	2	382	5.2	[0.9,16.4]	6	757	7.9	[3.5,15.6]
Long QT	0	383	0.0	[0.0, 7.8]	0	757	0.0	[0.0, 3.9]
Narrow angle glaucoma	0	381	0.0	[0.0, 7.8]	0	755	0.0	[0.0, 4.0]

Note: Run date and time 01NOV2018 11:20:25,

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Table 15-17-3 (Page 7 of 12)
Incidence rates (per 1,000 PY) of events during cohort time by exposure cohorts
AUH - Total analysis population

	QVA149				Free LABA+LAMA without ICS				Free LABA+LAMA with ICS			
Endpoint	Events	PY	IR	95% CI	Events	PY	IR	95% CI	Events	PY	IR	95% CI
Other glaucoma	0	1194	0.0	[0.0, 2.5]	1	205	4.9	[0.2,22.9]	0	71	0.0	[0.0,41.2]
Premature depolarization	1	1198	0.8	[0.0, 4.0]	0	210	0.0	[0.0,14.2]	0	69	0.0	[0.0,42.7]
Sick sinus	3	1193	2.5	[0.7, 6.5]	0	208	0.0	[0.0,14.3]	0	71	0.0	[0.0,41.2]
Stroke	14	1208	11.6	[7.0,18.1]	2	212	9.4	[1.7,29.4]	2	71	28.0	[5.0,85.6]
Supraventricular tachycardia	6	1150	5.2	[2.3,10.3]	1	192	5.2	[0.3,24.4]	0	67	0.0	[0.0,43.5]
TIA	6	1209	5.0	[2.2, 9.8]	0	212	0.0	[0.0,14.0]	0	72	0.0	[0.0,40.9]
Torsades de Pointes	0	1213	0.0	[0.0, 2.5]	0	212	0.0	[0.0,14.0]	0	72	0.0	[0.0,40.9]
Unstable angina pectoris	9	1211	7.4	[3.9,12.9]	0	212	0.0	[0.0,14.0]	0	72	0.0	[0.0,40.9]
Urinary retention	4	1209	3.3	[1.1, 7.6]	1	212	4.7	[0.2,22.2]	0	72	0.0	[0.0,40.9]

Note: Run date and time 01NOV2018 11:20:25,

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Table 15-17-3 (Page 8 of 12)
Incidence rates (per 1,000 PY) of events during cohort time by exposure cohorts
AUH - Total analysis population

	Free LABA+ICS				Fixed LABA ICS				Fixed LABA LAMA			
Endpoint	Events	PY	IR	95% CI	Events	PY	IR	95% CI	Events	PY	IR	95% CI
Other glaucoma	0	67	0.0	[0.0,43.6]	2	1487	1.3	[0.2, 4.2]	3	818	3.7	[1.0, 9.5]
Premature depolarization	0	65	0.0	[0.0,45.3]	6	1493	4.0	[1.8, 7.9]	1	824	1.2	[0.1, 5.7]
Sick sinus	0	69	0.0	[0.0,42.3]	5	1490	3.4	[1.3, 7.0]	0	829	0.0	[0.0, 3.6]
Stroke	2	69	29.1	[5.2,88.7]	19	1510	12.6	[8.3,18.4]	18	834	21.6	[14.0,31.8]
Supraventricular tachycardia	0	67	0.0	[0.0,43.7]	3	1442	2.1	[0.6, 5.4]	3	790	3.8	[1.0, 9.8]
TIA	0	70	0.0	[0.0,42.2]	4	1512	2.6	[0.9, 6.0]	1	838	1.2	[0.1, 5.6]
Torsades de Pointes	0	70	0.0	[0.0,42.2]	0	1516	0.0	[0.0, 2.0]	0	838	0.0	[0.0, 3.6]
Unstable angina pectoris	1	68	14.8	[0.8,68.1]	6	1514	4.0	[1.7, 7.8]	3	838	3.6	[1.0, 9.2]
Urinary retention	0	70	0.0	[0.0,42.2]	4	1515	2.6	[0.9, 6.0]	3	838	3.6	[1.0, 9.2]

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Table 15-17-3 (Page 9 of 12)
Incidence rates (per 1,000 PY) of events during cohort time by exposure cohorts
AUH - Total analysis population

	LABA				LAMA			
Endpoint	Events	PY	IR	95% CI	Events	PY	IR	95% CI
Other glaucoma	0	376	0.0	[0.0, 7.9]	3	742	4.0	[1.1,10.4]
Premature depolarization	3	378	7.9	[2.2,20.4]	2	741	2.7	[0.5, 8.5]
Sick sinus	4	376	10.6	[3.6,24.2]	2	747	2.7	[0.5, 8.4]
Stroke	3	383	7.8	[2.1,20.1]	10	755	13.2	[7.2,22.3]
Supraventricular tachycardia	2	363	5.5	[1.0,17.3]	3	721	4.2	[1.1,10.7]
TIA	2	383	5.2	[0.9,16.4]	3	755	4.0	[1.1,10.2]
Torsades de Pointes	0	383	0.0	[0.0, 7.8]	0	757	0.0	[0.0, 3.9]
Unstable angina pectoris	5	379	13.2	[5.2,27.5]	4	756	5.3	[1.8,12.1]
Urinary retention	0	383	0.0	[0.0, 7.8]	5	757	6.6	[2.6,13.8]

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Table 15-17-3 (Page 10 of 12)
Incidence rates (per 1,000 PY) of events during cohort time by exposure cohorts
AUH - Total analysis population

	QVA149				Free LABA+LAMA without ICS				Free LABA+LAMA with ICS			
Endpoint	Events	PY	IR	95% CI	Events	PY	IR	95% CI	Events	PY	IR	95% CI
Ventricular tachycardia	1	1212	0.8	[0.0, 3.9]	0	212	0.0	[0.0,14.0]	0	72	0.0	[0.0,40.9]
Ventricular fibrillation	1	1213	0.8	[0.0, 3.9]	0	212	0.0	[0.0,14.0]	0	72	0.0	[0.0,40.9]
Cardiovascular death	18	1213	14.8	[9.6,21.9]	2	212	9.4	[1.7,29.3]	0	72	0.0	[0.0,40.9]
Respiratory death	31	1213	25.6	[18.6,34.3]	8	212	37.7	[18.9,66.9]	2	72	27.9	[5.0,85.2]
Cardiovascular and respiratory death	0	1213	0.0	[0.0, 2.5]	0	212	0.0	[0.0,14.0]	0	72	0.0	[0.0,40.9]
Cerebrovascular death	0	1213	0.0	[0.0, 2.5]	0	212	0.0	[0.0,14.0]	0	72	0.0	[0.0,40.9]
Cancer death (excluding lungcancer)	7	1213	5.8	[2.7,10.8]	1	212	4.7	[0.2,22.1]	0	72	0.0	[0.0,40.9]
Death due to other causes	26	1213	21.4	[15.1,29.6]	4	212	18.8	[6.5,42.6]	0	72	0.0	[0.0,40.9]
Death with cause unknown	58	1213	47.8	[38.1,59.1]	1	212	4.7	[0.2,22.1]	0	72	0.0	[0.0,40.9]

Note: Run date and time 01NOV2018 11:20:25,

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Table 15-17-3 (Page 11 of 12)
Incidence rates (per 1,000 PY) of events during cohort time by exposure cohorts
AUH - Total analysis population

	Free LABA+ICS				Fixed LABA ICS				Fixed LABA LAMA			
Endpoint	Events	PY	IR	95% CI	Events	PY	IR	95% CI	Events	PY	IR	95% CI
Ventricular tachycardia	0	70	0.0	[0.0,42.2]	0	1516	0.0	[0.0, 2.0]	0	838	0.0	[0.0, 3.6]
Ventricular fibrillation	0	70	0.0	[0.0,42.2]	0	1516	0.0	[0.0, 2.0]	1	838	1.2	[0.1, 5.6]
Cardiovascular death	0	70	0.0	[0.0,42.2]	30	1516	19.8	[14.3,26.8]	2	838	2.4	[0.4, 7.5]
Respiratory death	2	70	28.8	[5.1,87.8]	62	1516	40.9	[32.9,50.3]	2	838	2.4	[0.4, 7.5]
Cardiovascular and respiratory death	0	70	0.0	[0.0,42.2]	0	1516	0.0	[0.0, 2.0]	0	838	0.0	[0.0, 3.6]
Cerebrovascular death	0	70	0.0	[0.0,42.2]	4	1516	2.6	[0.9, 6.0]	2	838	2.4	[0.4, 7.5]
Cancer death (excluding lungcancer)	1	70	14.4	[0.7,66.4]	19	1516	12.5	[8.2,18.3]	2	838	2.4	[0.4, 7.5]
Death due to other causes	1	70	14.4	[0.7,66.4]	58	1516	38.3	[30.5,47.4]	4	838	4.8	[1.6,10.9]
Death with cause unknown	1	70	14.4	[0.7,66.4]	64	1516	42.2	[34.1,51.7]	71	838	84.7	[69.4, 102]

Note: Run date and time 01NOV2018 11:20:25,

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Table 15-17-3 (Page 12 of 12)
Incidence rates (per 1,000 PY) of events during cohort time by exposure cohorts
AUH - Total analysis population

	LABA				LAMA			
Endpoint	Events	PY	IR	95% CI	Events	PY	IR	95% CI
Ventricular tachycardia	0	383	0.0	[0.0, 7.8]	1	757	1.3	[0.1, 6.2]
Ventricular fibrillation	0	383	0.0	[0.0, 7.8]	1	757	1.3	[0.1, 6.2]
Cardiovascular death	2	383	5.2	[0.9,16.3]	14	757	18.5	[11.2,28.7]
Respiratory death	7	383	18.3	[8.6,34.0]	20	757	26.4	[17.6,38.1]
Cardiovascular and respiratory death	0	383	0.0	[0.0, 7.8]	0	757	0.0	[0.0, 3.9]
Cerebrovascular death	1	383	2.6	[0.1,12.3]	6	757	7.9	[3.5,15.6]
Cancer death (excluding lungcancer)	3	383	7.8	[2.1,20.1]	10	757	13.2	[7.2,22.3]
Death due to other causes	6	383	15.7	[6.8,30.7]	15	757	19.8	[12.2,30.3]
Death with cause unknown	9	383	23.5	[12.3,40.6]	22	757	29.0	[19.7,41.2]

Note: Run date and time 01NOV2018 11:20:25,

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Table 15-17-4 (Page 1 of 12)
Incidence rates (per 1,000 PY) of events during cohort time by exposure cohorts
HSD - Total analysis population

	QVA149				Free LABA+LAMA without ICS				Free LABA+LAMA with ICS			
Endpoint	Events	PY	IR	95% CI	Events	PY	IR	95% CI	Events	PY	IR	95% CI
MACE	2	200	10.0	[1.8,31.2]	3	331	9.1	[2.5,23.3]	1	41	24.4	[1.3, 111]
Ischemic heart disease	1	198	5.0	[0.3,23.7]	2	327	6.1	[1.1,19.1]	1	41	24.4	[1.3, 111]
Cardiac arrhythmia	3	200	15.0	[4.1,38.4]	10	327	30.6	[16.7,51.3]	0	41	0.0	[0.0,70.4]
Cerebrovascular disorders	3	198	15.1	[4.1,38.6]	4	331	12.1	[4.1,27.5]	1	41	24.6	[1.3, 111]
Glaucoma	1	200	5.0	[0.3,23.5]	4	330	12.1	[4.1,27.5]	1	41	24.4	[1.2, 111]
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	3	199	15.0	[4.1,38.4]	4	328	12.2	[4.2,27.7]	1	41	24.4	[1.3, 111]
Diabetes mellitus	6	164	36.5	[16.0,70.8]	6	268	22.4	[9.8,43.8]	2	32	61.7	[11.1, 182]
Bronchospasm	0	200	0.0	[0.0,14.9]	0	331	0.0	[0.0, 9.0]	0	41	0.0	[0.0,70.4]
Mortality	3	200	15.0	[4.1,38.3]	3	331	9.1	[2.5,23.3]	1	41	24.4	[1.2, 111]

Note: Run date and time 01NOV2018 11:20:36,

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Table 15-17-4 (Page 2 of 12)
Incidence rates (per 1,000 PY) of events during cohort time by exposure cohorts
HSD - Total analysis population

	Free LABA+ICS				Fixed LABA ICS				Fixed LABA LAMA			
Endpoint	Events	PY	IR	95% CI	Events	PY	IR	95% CI	Events	PY	IR	95% CI
MACE	0	41	0.0	[0.0,70.4]	15	1839	8.2	[5.0,12.5]	2	187	10.7	[1.9,33.3]
Ischemic heart disease	0	41	0.0	[0.0,70.4]	13	1841	7.1	[4.2,11.2]	1	187	5.3	[0.3,25.1]
Cardiac arrhythmia	1	41	24.4	[1.3, 111]	44	1824	24.1	[18.5,30.9]	9	185	48.5	[25.5,83.2]
Cerebrovascular disorders	0	41	0.0	[0.0,70.4]	8	1842	4.3	[2.2, 7.8]	0	187	0.0	[0.0,15.9]
Glaucoma	0	41	0.0	[0.0,70.4]	10	1837	5.4	[3.0, 9.2]	1	186	5.4	[0.3,25.3]
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	0	41	0.0	[0.0,70.4]	21	1838	11.4	[7.7,16.4]	1	187	5.3	[0.3,25.1]
Diabetes mellitus	0	34	0.0	[0.0,84.8]	34	1516	22.4	[16.5,29.8]	4	143	28.1	[9.6,63.0]
Bronchospasm	0	41	0.0	[0.0,70.4]	13	1839	7.1	[4.2,11.2]	1	187	5.3	[0.3,25.1]
Mortality	2	41	48.7	[8.7, 146]	56	1844	30.4	[24.1,37.8]	2	187	10.7	[1.9,33.2]

Note: Run date and time 01NOV2018 11:20:36,

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Table 15-17-4 (Page 3 of 12)
Incidence rates (per 1,000 PY) of events during cohort time by exposure cohorts
HSD - Total analysis population

	LABA				LAMA			
Endpoint	Events	PY	IR	95% CI	Events	PY	IR	95% CI
MACE	2	226	8.9	[1.6,27.6]	15	1214	12.4	[7.6,19.0]
Ischemic heart disease	1	226	4.4	[0.2,20.8]	7	1215	5.8	[2.7,10.8]
Cardiac arrhythmia	3	227	13.2	[3.6,33.9]	26	1209	21.5	[15.1,29.7]
Cerebrovascular disorders	4	226	17.7	[6.1,40.1]	8	1213	6.6	[3.3,11.9]
Glaucoma	0	227	0.0	[0.0,13.1]	8	1212	6.6	[3.3,11.9]
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	4	226	17.7	[6.1,40.0]	14	1211	11.6	[7.0,18.0]
Diabetes mellitus	2	187	10.7	[1.9,33.2]	15	979	15.3	[9.5,23.5]
Bronchospasm	0	227	0.0	[0.0,13.1]	4	1215	3.3	[1.1, 7.5]
Mortality	6	227	26.5	[11.6,51.6]	39	1216	32.1	[24.2,41.7]

Note: Run date and time 01NOV2018 11:20:36,

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Table 15-17-4 (Page 4 of 12)
Incidence rates (per 1,000 PY) of events during cohort time by exposure cohorts
HSD - Total analysis population

	QVA149				Free LABA+LAMA without ICS				Free LABA+LAMA with ICS			
Endpoint	Events	PY	IR	95% CI	Events	PY	IR	95% CI	Events	PY	IR	95% CI
Atrial fibrillation/flutter	3	167	18.0	[4.9,45.8]	10	292	34.3	[18.7,57.4]	0	32	0.0	[0.0,88.1]
Angina pectoris	1	195	5.1	[0.3,24.1]	2	318	6.3	[1.1,19.6]	0	40	0.0	[0.0,72.6]
AV block	1	197	5.1	[0.3,23.9]	1	327	3.1	[0.2,14.4]	0	40	0.0	[0.0,71.4]
Incident benign prostatic hyperplasia	3	145	20.6	[5.6,52.4]	4	266	15.0	[5.1,34.0]	1	33	30.3	[1.6, 136]
Hospitalization for acute coronary syndrome	0	200	0.0	[0.0,14.9]	0	331	0.0	[0.0, 9.0]	1	41	24.4	[1.3, 111]
Hospitalization for heart failure	0	200	0.0	[0.0,14.9]	0	331	0.0	[0.0, 9.0]	0	41	0.0	[0.0,70.4]
Myocardial infarction	0	200	0.0	[0.0,14.9]	0	331	0.0	[0.0, 9.0]	1	41	24.4	[1.3, 111]
Long QT	0	200	0.0	[0.0,14.9]	0	331	0.0	[0.0, 9.0]	0	41	0.0	[0.0,70.4]
Narrow angle glaucoma	0	200	0.0	[0.0,14.9]	0	331	0.0	[0.0, 9.0]	0	41	0.0	[0.0,70.4]

Note: Run date and time 01NOV2018 11:20:36,

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Table 15-17-4 (Page 5 of 12)
Incidence rates (per 1,000 PY) of events during cohort time by exposure cohorts
HSD - Total analysis population

	Free LABA+ICS				Fixed LABA ICS				Fixed LABA LAMA			
Endpoint	Events	PY	IR	95% CI	Events	PY	IR	95% CI	Events	PY	IR	95% CI
Atrial fibrillation/flutter	1	36	27.9	[1.4, 125]	43	1642	26.2	[20.0,33.6]	9	166	54.3	[28.6,92.9]
Angina pectoris	0	40	0.0	[0.0,71.9]	7	1790	3.9	[1.8, 7.3]	0	179	0.0	[0.0,16.6]
AV block	0	41	0.0	[0.0,70.6]	3	1820	1.6	[0.4, 4.3]	0	183	0.0	[0.0,16.2]
Incident benign prostatic hyperplasia	0	34	0.0	[0.0,84.6]	15	1573	9.5	[5.9,14.6]	1	156	6.4	[0.3,30.1]
Hospitalization for acute coronary syndrome	0	41	0.0	[0.0,70.4]	6	1843	3.3	[1.4, 6.4]	1	187	5.3	[0.3,25.1]
Hospitalization for heart failure	0	41	0.0	[0.0,70.4]	2	1841	1.1	[0.2, 3.4]	1	187	5.3	[0.3,25.1]
Myocardial infarction	0	41	0.0	[0.0,70.4]	6	1843	3.3	[1.4, 6.4]	1	187	5.3	[0.3,25.1]
Long QT	0	41	0.0	[0.0,70.4]	0	1844	0.0	[0.0, 1.6]	0	187	0.0	[0.0,15.9]
Narrow angle glaucoma	0	41	0.0	[0.0,70.4]	0	1843	0.0	[0.0, 1.6]	0	187	0.0	[0.0,15.9]

Note: Run date and time 01NOV2018 11:20:36,

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Table 15-17-4 (Page 6 of 12)
Incidence rates (per 1,000 PY) of events during cohort time by exposure cohorts
HSD - Total analysis population

	LABA				LAMA			
Endpoint	Events	PY	IR	95% CI	Events	PY	IR	95% CI
Atrial fibrillation/flutter	3	210	14.3	[3.9,36.5]	25	1036	24.1	[16.8,33.5]
Angina pectoris	0	223	0.0	[0.0,13.4]	2	1172	1.7	[0.3, 5.4]
AV block	0	224	0.0	[0.0,13.3]	1	1195	0.8	[0.0, 4.0]
Incident benign prostatic hyperplasia	3	189	15.9	[4.3,40.5]	6	1024	5.9	[2.6,11.5]
Hospitalization for acute coronary syndrome	1	226	4.4	[0.2,20.8]	5	1215	4.1	[1.6, 8.6]
Hospitalization for heart failure	0	227	0.0	[0.0,13.1]	4	1216	3.3	[1.1, 7.5]
Myocardial infarction	1	226	4.4	[0.2,20.8]	5	1215	4.1	[1.6, 8.6]
Long QT	0	227	0.0	[0.0,13.1]	1	1216	0.8	[0.0, 3.9]
Narrow angle glaucoma	0	227	0.0	[0.0,13.1]	0	1216	0.0	[0.0, 2.5]

Note: Run date and time 01NOV2018 11:20:36,

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Table 15-17-4 (Page 7 of 12)
Incidence rates (per 1,000 PY) of events during cohort time by exposure cohorts
HSD - Total analysis population

	QVA149				Free LABA+LAMA without ICS				Free LABA+LAMA with ICS			
Endpoint	Events	PY	IR	95% CI	Events	PY	IR	95% CI	Events	PY	IR	95% CI
Other glaucoma	1	181	5.5	[0.3,25.9]	4	290	13.8	[4.7,31.3]	1	36	27.6	[1.4, 124]
Premature depolarization	1	185	5.4	[0.3,25.3]	0	309	0.0	[0.0, 9.6]	0	39	0.0	[0.0,73.5]
Sick sinus	1	193	5.2	[0.3,24.4]	0	329	0.0	[0.0, 9.1]	0	41	0.0	[0.0,71.2]
Stroke	2	200	10.0	[1.8,31.2]	3	331	9.1	[2.5,23.3]	0	41	0.0	[0.0,70.4]
Supraventricular tachycardia	0	200	0.0	[0.0,14.9]	0	330	0.0	[0.0, 9.0]	0	40	0.0	[0.0,72.3]
TIA	1	198	5.0	[0.3,23.7]	1	331	3.0	[0.2,14.3]	1	41	24.6	[1.3, 111]
Torsades de Pointes	0	200	0.0	[0.0,14.9]	0	331	0.0	[0.0, 9.0]	0	41	0.0	[0.0,70.4]
Unstable angina pectoris	0	200	0.0	[0.0,14.9]	2	327	6.1	[1.1,19.1]	0	41	0.0	[0.0,70.4]
Urinary retention	0	200	0.0	[0.0,14.9]	0	331	0.0	[0.0, 9.0]	0	41	0.0	[0.0,70.4]

Note: Run date and time 01NOV2018 11:20:36,

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Table 15-17-4 (Page 8 of 12)
Incidence rates (per 1,000 PY) of events during cohort time by exposure cohorts
HSD - Total analysis population

	Free LABA+ICS				Fixed LABA ICS				Fixed LABA LAMA			
Endpoint	Events	PY	IR	95% CI	Events	PY	IR	95% CI	Events	PY	IR	95% CI
Other glaucoma	0	38	0.0	[0.0,76.3]	10	1651	6.1	[3.3,10.3]	1	169	5.9	[0.3,27.7]
Premature depolarization	0	39	0.0	[0.0,74.5]	8	1748	4.6	[2.3, 8.2]	3	177	17.0	[4.6,43.3]
Sick sinus	0	41	0.0	[0.0,70.6]	3	1818	1.7	[0.4, 4.3]	0	185	0.0	[0.0,16.1]
Stroke	0	41	0.0	[0.0,70.4]	7	1843	3.8	[1.8, 7.1]	0	187	0.0	[0.0,15.9]
Supraventricular tachycardia	0	41	0.0	[0.0,70.8]	2	1835	1.1	[0.2, 3.4]	0	186	0.0	[0.0,15.9]
TIA	0	41	0.0	[0.0,70.4]	1	1843	0.5	[0.0, 2.6]	0	187	0.0	[0.0,15.9]
Torsades de Pointes	0	41	0.0	[0.0,70.4]	0	1844	0.0	[0.0, 1.6]	0	187	0.0	[0.0,15.9]
Unstable angina pectoris	0	41	0.0	[0.0,70.4]	2	1844	1.1	[0.2, 3.4]	0	187	0.0	[0.0,15.9]
Urinary retention	0	41	0.0	[0.0,70.4]	6	1843	3.3	[1.4, 6.4]	0	187	0.0	[0.0,15.9]

Note: Run date and time 01NOV2018 11:20:36,

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Table 15-17-4 (Page 9 of 12)
Incidence rates (per 1,000 PY) of events during cohort time by exposure cohorts
HSD - Total analysis population

	LABA				LAMA			
Endpoint	Events	PY	IR	95% CI	Events	PY	IR	95% CI
Other glaucoma	0	200	0.0	[0.0,14.9]	8	1106	7.2	[3.6,13.0]
Premature depolarization	2	214	9.4	[1.7,29.2]	5	1149	4.4	[1.7, 9.1]
Sick sinus	1	222	4.5	[0.2,21.2]	0	1202	0.0	[0.0, 2.5]
Stroke	1	227	4.4	[0.2,20.8]	6	1215	4.9	[2.2, 9.7]
Supraventricular tachycardia	0	224	0.0	[0.0,13.3]	1	1207	0.8	[0.0, 3.9]
TIA	3	226	13.3	[3.6,33.9]	2	1215	1.6	[0.3, 5.2]
Torsades de Pointes	0	227	0.0	[0.0,13.1]	1	1216	0.8	[0.0, 3.9]
Unstable angina pectoris	0	227	0.0	[0.0,13.1]	1	1216	0.8	[0.0, 3.9]
Urinary retention	1	227	4.4	[0.2,20.8]	8	1212	6.6	[3.3,11.9]

Note: Run date and time 01NOV2018 11:20:36,

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Table 15-17-4 (Page 10 of 12)
Incidence rates (per 1,000 PY) of events during cohort time by exposure cohorts
HSD - Total analysis population

	QVA149				Free LABA+LAMA without ICS				Free LABA+LAMA with ICS			
Endpoint	Events	PY	IR	95% CI	Events	PY	IR	95% CI	Events	PY	IR	95% CI
Ventricular tachycardia	0	200	0.0	[0.0,14.9]	0	331	0.0	[0.0, 9.0]	0	41	0.0	[0.0,70.4]
Ventricular fibrillation	0	200	0.0	[0.0,14.9]	0	331	0.0	[0.0, 9.0]	0	41	0.0	[0.0,70.4]
Cardiovascular death	0	200	0.0	[0.0,14.9]	0	331	0.0	[0.0, 9.0]	0	41	0.0	[0.0,70.4]
Respiratory death	0	200	0.0	[0.0,14.9]	0	331	0.0	[0.0, 9.0]	0	41	0.0	[0.0,70.4]
Cardiovascular and respiratory death	0	200	0.0	[0.0,14.9]	0	331	0.0	[0.0, 9.0]	0	41	0.0	[0.0,70.4]
Cerebrovascular death	0	200	0.0	[0.0,14.9]	0	331	0.0	[0.0, 9.0]	0	41	0.0	[0.0,70.4]
Cancer death (excluding lungcancer)	0	200	0.0	[0.0,14.9]	0	331	0.0	[0.0, 9.0]	0	41	0.0	[0.0,70.4]
Death due to other causes	0	200	0.0	[0.0,14.9]	0	331	0.0	[0.0, 9.0]	0	41	0.0	[0.0,70.4]
Death with cause unknown	3	200	15.0	[4.1,38.3]	3	331	9.1	[2.5,23.3]	1	41	24.4	[1.2, 111]

Note: Run date and time 01NOV2018 11:20:36,

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Table 15-17-4 (Page 11 of 12)
Incidence rates (per 1,000 PY) of events during cohort time by exposure cohorts
HSD - Total analysis population

	Free LABA+ICS				Fixed LABA ICS				Fixed LABA LAMA			
Endpoint	Events	PY	IR	95% CI	Events	PY	IR	95% CI	Events	PY	IR	95% CI
Ventricular tachycardia	0	41	0.0	[0.0,70.4]	1	1844	0.5	[0.0, 2.6]	0	187	0.0	[0.0,15.9]
Ventricular fibrillation	0	41	0.0	[0.0,70.4]	0	1844	0.0	[0.0, 1.6]	0	187	0.0	[0.0,15.9]
Cardiovascular death	0	41	0.0	[0.0,70.4]	0	1844	0.0	[0.0, 1.6]	0	187	0.0	[0.0,15.9]
Respiratory death	0	41	0.0	[0.0,70.4]	0	1844	0.0	[0.0, 1.6]	0	187	0.0	[0.0,15.9]
Cardiovascular and respiratory death	0	41	0.0	[0.0,70.4]	0	1844	0.0	[0.0, 1.6]	0	187	0.0	[0.0,15.9]
Cerebrovascular death	0	41	0.0	[0.0,70.4]	0	1844	0.0	[0.0, 1.6]	0	187	0.0	[0.0,15.9]
Cancer death (excluding lungcancer)	0	41	0.0	[0.0,70.4]	0	1844	0.0	[0.0, 1.6]	0	187	0.0	[0.0,15.9]
Death due to other causes	0	41	0.0	[0.0,70.4]	0	1844	0.0	[0.0, 1.6]	0	187	0.0	[0.0,15.9]
Death with cause unknown	2	41	48.7	[8.7, 146]	56	1844	30.4	[24.1,37.8]	2	187	10.7	[1.9,33.2]

Note: Run date and time 01NOV2018 11:20:36,

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Table 15-17-4 (Page 12 of 12)
Incidence rates (per 1,000 PY) of events during cohort time by exposure cohorts
HSD - Total analysis population

	LABA				LAMA			
Endpoint	Events	PY	IR	95% CI	Events	PY	IR	95% CI
Ventricular tachycardia	0	227	0.0	[0.0,13.1]	0	1216	0.0	[0.0, 2.5]
Ventricular fibrillation	0	227	0.0	[0.0,13.1]	0	1216	0.0	[0.0, 2.5]
Cardiovascular death	0	227	0.0	[0.0,13.1]	0	1216	0.0	[0.0, 2.5]
Respiratory death	0	227	0.0	[0.0,13.1]	0	1216	0.0	[0.0, 2.5]
Cardiovascular and respiratory death	0	227	0.0	[0.0,13.1]	0	1216	0.0	[0.0, 2.5]
Cerebrovascular death	0	227	0.0	[0.0,13.1]	0	1216	0.0	[0.0, 2.5]
Cancer death (excluding lungcancer)	0	227	0.0	[0.0,13.1]	0	1216	0.0	[0.0, 2.5]
Death due to other causes	0	227	0.0	[0.0,13.1]	0	1216	0.0	[0.0, 2.5]
Death with cause unknown	6	227	26.5	[11.6,51.6]	39	1216	32.1	[24.2,41.7]

Note: Run date and time 01NOV2018 11:20:36,

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Table 15-17-5 (Page 1 of 12)
Incidence rates (per 1,000 PY) of events during cohort time by exposure cohorts
SIDIAP - Total analysis population

	QVA149				Free LABA+LAMA without ICS				Free LABA+LAMA with ICS			
Endpoint	Events	PY	IR	95% CI	Events	PY	IR	95% CI	Events	PY	IR	95% CI
MACE	116	2528	45.9	[39.2,53.3]	49	1092	44.9	[35.0,56.6]	20	347	57.7	[38.6,82.7]
Ischemic heart disease	16	2555	6.3	[3.9, 9.5]	14	1098	12.8	[7.7,19.9]	5	348	14.3	[5.7,29.9]
Cardiac arrhythmia	40	2545	15.7	[11.9,20.4]	23	1096	21.0	[14.4,29.6]	14	347	40.4	[24.6,62.4]
Cerebrovascular disorders	16	2556	6.3	[3.9, 9.5]	5	1100	4.5	[1.8, 9.5]	6	348	17.2	[7.5,33.7]
Glaucoma	14	2558	5.5	[3.3, 8.5]	9	1099	8.2	[4.3,14.2]	2	349	5.7	[1.0,17.9]
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	64	2539	25.2	[20.3,31.0]	33	1090	30.3	[22.2,40.3]	11	346	31.8	[17.9,52.1]
Diabetes mellitus	54	1941	27.8	[22.0,34.8]	27	838	32.2	[22.8,44.1]	7	270	26.0	[12.2,48.2]
Bronchospasm	5	2560	2.0	[0.8, 4.1]	3	1102	2.7	[0.7, 7.0]	2	348	5.8	[1.0,18.0]
Mortality	80	2562	31.2	[25.8,37.5]	20	1102	18.2	[12.1,26.3]	5	349	14.3	[5.7,29.8]

Note: Run date and time 01NOV2018 11:20:45,

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Table 15-17-5 (Page 2 of 12)
Incidence rates (per 1,000 PY) of events during cohort time by exposure cohorts
SIDIAP - Total analysis population

	Free LABA+ICS				Fixed LABA ICS				Fixed LABA LAMA			
Endpoint	Events	PY	IR	95% CI	Events	PY	IR	95% CI	Events	PY	IR	95% CI
MACE	32	496	64.5	[47.3,85.6]	427	5772	74.0	[68.4,79.9]	22	336	65.6	[44.8,92.3]
Ischemic heart disease	6	500	12.0	[5.2,23.5]	64	5853	10.9	[8.8,13.4]	6	340	17.7	[7.7,34.6]
Cardiac arrhythmia	17	499	34.0	[21.8,50.6]	169	5824	29.0	[25.5,32.9]	5	339	14.7	[5.8,30.7]
Cerebrovascular disorders	8	501	16.0	[8.0,28.6]	61	5859	10.4	[8.3,12.9]	2	340	5.9	[1.0,18.4]
Glaucoma	1	501	2.0	[0.1, 9.4]	42	5859	7.2	[5.5, 9.3]	1	340	2.9	[0.2,13.9]
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	10	500	20.0	[10.9,33.7]	177	5824	30.4	[26.8,34.4]	9	338	26.6	[14.0,46.0]
Diabetes mellitus	9	374	24.1	[12.6,41.6]	181	4460	40.6	[35.8,45.8]	13	249	52.2	[31.1,81.7]
Bronchospasm	6	500	12.0	[5.2,23.5]	39	5863	6.7	[5.0, 8.7]	2	340	5.9	[1.0,18.4]
Mortality	18	501	35.9	[23.3,52.8]	300	5872	51.1	[46.4,56.1]	12	341	35.2	[20.5,56.5]

Note: Run date and time 01NOV2018 11:20:45,

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Table 15-17-5 (Page 3 of 12)
Incidence rates (per 1,000 PY) of events during cohort time by exposure cohorts
SIDIAP - Total analysis population

	LABA				LAMA			
Endpoint	Events	PY	IR	95% CI	Events	PY	IR	95% CI
MACE	61	1569	38.9	[31.2,47.9]	207	3819	54.2	[48.3,60.6]
Ischemic heart disease	8	1579	5.1	[2.5, 9.1]	47	3843	12.2	[9.5,15.6]
Cardiac arrhythmia	25	1576	15.9	[11.1,22.1]	97	3830	25.3	[21.3,29.9]
Cerebrovascular disorders	13	1577	8.2	[4.9,13.1]	33	3847	8.6	[6.3,11.5]
Glaucoma	12	1578	7.6	[4.4,12.3]	34	3847	8.8	[6.5,11.7]
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	53	1567	33.8	[26.6,42.3]	125	3816	32.8	[28.2,37.9]
Diabetes mellitus	35	1227	28.5	[21.2,37.7]	98	2928	33.5	[28.2,39.5]
Bronchospasm	6	1580	3.8	[1.7, 7.5]	9	3855	2.3	[1.2, 4.1]
Mortality	40	1581	25.3	[19.2,32.8]	121	3856	31.4	[26.9,36.4]

Note: Run date and time 01NOV2018 11:20:45,

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Table 15-17-5 (Page 4 of 12)
Incidence rates (per 1,000 PY) of events during cohort time by exposure cohorts
SIDIAP - Total analysis population

	QVA149				Free LABA+LAMA without ICS				Free LABA+LAMA with ICS			
Endpoint	Events	PY	IR	95% CI	Events	PY	IR	95% CI	Events	PY	IR	95% CI
Atrial fibrillation/flutter	38	2266	16.8	[12.6,21.9]	23	989	23.2	[15.9,32.8]	12	306	39.2	[22.8,62.8]
Angina pectoris	6	2473	2.4	[1.1, 4.8]	3	1072	2.8	[0.8, 7.2]	3	337	8.9	[2.4,22.9]
AV block	11	2496	4.4	[2.5, 7.3]	5	1072	4.7	[1.8, 9.8]	0	341	0.0	[0.0, 8.7]
Incident benign prostatic hyperplasia	48	1854	25.9	[20.1,32.8]	22	814	27.0	[18.4,38.4]	7	250	28.0	[13.2,52.0]
Hospitalization for acute coronary syndrome	11	2559	4.3	[2.4, 7.1]	10	1100	9.1	[4.9,15.4]	4	349	11.5	[3.9,26.1]
Hospitalization for heart failure	88	2538	34.7	[28.9,41.3]	32	1097	29.2	[21.3,39.0]	13	348	37.4	[22.2,58.7]
Myocardial infarction	9	2557	3.5	[1.8, 6.1]	10	1098	9.1	[4.9,15.4]	2	349	5.7	[1.0,17.9]
Long QT	2	2561	0.8	[0.1, 2.5]	0	1102	0.0	[0.0, 2.7]	0	349	0.0	[0.0, 8.5]
Narrow angle glaucoma	0	2562	0.0	[0.0, 1.2]	0	1102	0.0	[0.0, 2.7]	0	349	0.0	[0.0, 8.5]

Note: Run date and time 01NOV2018 11:20:45,

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Table 15-17-5 (Page 5 of 12)
Incidence rates (per 1,000 PY) of events during cohort time by exposure cohorts
SIDIAP - Total analysis population

	Free LABA+ICS				Fixed LABA ICS				Fixed LABA LAMA			
Endpoint	Events	PY	IR	95% CI	Events	PY	IR	95% CI	Events	PY	IR	95% CI
Atrial fibrillation/flutter	17	434	39.2	[25.1,58.2]	165	5134	32.1	[28.2,36.5]	5	302	16.5	[6.5,34.5]
Angina pectoris	3	484	6.2	[1.7,16.0]	21	5694	3.7	[2.5, 5.3]	1	334	3.0	[0.2,14.1]
AV block	3	489	6.1	[1.7,15.8]	33	5742	5.7	[4.2, 7.7]	4	330	12.1	[4.1,27.5]
Incident benign prostatic hyperplasia	9	372	24.2	[12.7,41.9]	136	4596	29.6	[25.6,34.0]	8	256	31.3	[15.6,55.7]
Hospitalization for acute coronary syndrome	4	500	8.0	[2.7,18.2]	50	5860	8.5	[6.7,10.8]	2	340	5.9	[1.0,18.4]
Hospitalization for heart failure	21	498	42.2	[28.4,60.1]	328	5795	56.6	[51.7,61.8]	15	337	44.6	[27.7,67.8]
Myocardial infarction	3	501	6.0	[1.6,15.4]	42	5860	7.2	[5.5, 9.3]	4	340	11.8	[4.0,26.7]
Long QT	0	501	0.0	[0.0, 6.0]	1	5872	0.2	[0.0, 0.8]	0	341	0.0	[0.0, 8.8]
Narrow angle glaucoma	0	501	0.0	[0.0, 6.0]	0	5872	0.0	[0.0, 0.5]	0	341	0.0	[0.0, 8.8]

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Table 15-17-5 (Page 6 of 12)
Incidence rates (per 1,000 PY) of events during cohort time by exposure cohorts
SIDIAP - Total analysis population

	LABA				LAMA			
Endpoint	Events	PY	IR	95% CI	Events	PY	IR	95% CI
Atrial fibrillation/flutter	25	1438	17.4	[12.1,24.2]	95	3418	27.8	[23.3,32.9]
Angina pectoris	3	1542	1.9	[0.5, 5.0]	20	3726	5.4	[3.6, 7.8]
AV block	6	1546	3.9	[1.7, 7.6]	21	3764	5.6	[3.7, 8.0]
Incident benign prostatic hyperplasia	42	1225	34.3	[26.2,44.1]	104	2939	35.4	[30.0,41.5]
Hospitalization for acute coronary syndrome	5	1581	3.2	[1.2, 6.6]	29	3852	7.5	[5.4,10.3]
Hospitalization for heart failure	43	1572	27.4	[20.9,35.1]	147	3831	38.4	[33.4,43.9]
Myocardial infarction	5	1580	3.2	[1.2, 6.6]	25	3851	6.5	[4.5, 9.1]
Long QT	0	1581	0.0	[0.0, 1.9]	0	3857	0.0	[0.0, 0.8]
Narrow angle glaucoma	0	1581	0.0	[0.0, 1.9]	0	3856	0.0	[0.0, 0.8]

Note: Run date and time 01NOV2018 11:20:45,

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Table 15-17-5 (Page 7 of 12)
Incidence rates (per 1,000 PY) of events during cohort time by exposure cohorts
SIDIAP - Total analysis population

	QVA149				Free LABA+LAMA without ICS				Free LABA+LAMA with ICS			
Endpoint	Events	PY	IR	95% CI	Events	PY	IR	95% CI	Events	PY	IR	95% CI
Other glaucoma	14	2360	5.9	[3.6, 9.3]	9	1005	9.0	[4.7,15.6]	2	324	6.2	[1.1,19.3]
Premature depolarization	6	2531	2.4	[1.0, 4.7]	3	1088	2.8	[0.8, 7.1]	1	342	2.9	[0.1,13.8]
Sick sinus	0	2562	0.0	[0.0, 1.2]	0	1102	0.0	[0.0, 2.7]	0	349	0.0	[0.0, 8.5]
Stroke	9	2559	3.5	[1.8, 6.1]	2	1101	1.8	[0.3, 5.7]	3	349	8.6	[2.3,22.1]
Supraventricular tachycardia	2	2544	0.8	[0.1, 2.5]	2	1095	1.8	[0.3, 5.7]	0	347	0.0	[0.0, 8.6]
TIA	8	2559	3.1	[1.6, 5.6]	3	1100	2.7	[0.7, 7.0]	3	349	8.6	[2.3,22.1]
Torsades de Pointes	0	2562	0.0	[0.0, 1.2]	0	1102	0.0	[0.0, 2.7]	0	349	0.0	[0.0, 8.5]
Unstable angina pectoris	4	2561	1.6	[0.5, 3.6]	3	1101	2.7	[0.7, 7.0]	1	349	2.9	[0.1,13.5]
Urinary retention	18	2556	7.0	[4.6,10.4]	11	1099	10.0	[5.6,16.5]	5	348	14.4	[5.7,30.0]

Note: Run date and time 01NOV2018 11:20:45,

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Table 15-17-5 (Page 8 of 12)
Incidence rates (per 1,000 PY) of events during cohort time by exposure cohorts
SIDIAP - Total analysis population

	Free LABA+ICS				Fixed LABA ICS				Fixed LABA LAMA			
Endpoint	Events	PY	IR	95% CI	Events	PY	IR	95% CI	Events	PY	IR	95% CI
Other glaucoma	1	457	2.2	[0.1,10.3]	42	5424	7.7	[5.9,10.0]	1	314	3.2	[0.2,15.0]
Premature depolarization	3	494	6.1	[1.7,15.6]	25	5805	4.3	[3.0, 6.0]	1	338	3.0	[0.2,13.9]
Sick sinus	0	501	0.0	[0.0, 6.0]	0	5871	0.0	[0.0, 0.5]	0	341	0.0	[0.0, 8.8]
Stroke	5	501	10.0	[3.9,20.9]	41	5864	7.0	[5.3, 9.1]	2	340	5.9	[1.0,18.4]
Supraventricular tachycardia	0	499	0.0	[0.0, 6.0]	7	5819	1.2	[0.6, 2.3]	1	338	3.0	[0.2,13.9]
TIA	3	501	6.0	[1.6,15.4]	20	5867	3.4	[2.3, 4.9]	0	341	0.0	[0.0, 8.8]
Torsades de Pointes	0	501	0.0	[0.0, 6.0]	0	5872	0.0	[0.0, 0.5]	0	341	0.0	[0.0, 8.8]
Unstable angina pectoris	1	501	2.0	[0.1, 9.4]	9	5871	1.5	[0.8, 2.7]	1	340	2.9	[0.2,13.9]
Urinary retention	1	501	2.0	[0.1, 9.4]	51	5860	8.7	[6.8,11.0]	1	340	2.9	[0.2,13.9]

Note: Run date and time 01NOV2018 11:20:45,

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Table 15-17-5 (Page 9 of 12)
Incidence rates (per 1,000 PY) of events during cohort time by exposure cohorts
SIDIAP - Total analysis population

	LABA				LAMA			
Endpoint	Events	PY	IR	95% CI	Events	PY	IR	95% CI
Other glaucoma	12	1449	8.3	[4.8,13.4]	34	3546	9.6	[7.1,12.7]
Premature depolarization	3	1568	1.9	[0.5, 4.9]	16	3801	4.2	[2.6, 6.4]
Sick sinus	0	1581	0.0	[0.0, 1.9]	1	3856	0.3	[0.0, 1.2]
Stroke	8	1579	5.1	[2.5, 9.1]	21	3851	5.5	[3.7, 7.8]
Supraventricular tachycardia	3	1570	1.9	[0.5, 4.9]	2	3824	0.5	[0.1, 1.6]
TIA	6	1579	3.8	[1.7, 7.5]	12	3852	3.1	[1.8, 5.0]
Torsades de Pointes	0	1581	0.0	[0.0, 1.9]	0	3857	0.0	[0.0, 0.8]
Unstable angina pectoris	2	1581	1.3	[0.2, 4.0]	5	3856	1.3	[0.5, 2.7]
Urinary retention	11	1579	7.0	[3.9,11.5]	22	3849	5.7	[3.9, 8.2]

Note: Run date and time 01NOV2018 11:20:45,

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Table 15-17-5 (Page 10 of 12)
Incidence rates (per 1,000 PY) of events during cohort time by exposure cohorts
SIDIAP - Total analysis population

	QVA149				Free LABA+LAMA without ICS				Free LABA+LAMA with ICS			
Endpoint	Events	PY	IR	95% CI	Events	PY	IR	95% CI	Events	PY	IR	95% CI
Ventricular tachycardia	2	2561	0.8	[0.1, 2.5]	0	1102	0.0	[0.0, 2.7]	2	349	5.7	[1.0,17.9]
Ventricular fibrillation	0	2562	0.0	[0.0, 1.2]	0	1102	0.0	[0.0, 2.7]	0	349	0.0	[0.0, 8.5]
Cardiovascular death	0	2562	0.0	[0.0, 1.2]	0	1102	0.0	[0.0, 2.7]	0	349	0.0	[0.0, 8.5]
Respiratory death	0	2562	0.0	[0.0, 1.2]	0	1102	0.0	[0.0, 2.7]	0	349	0.0	[0.0, 8.5]
Cardiovascular and respiratory death	0	2562	0.0	[0.0, 1.2]	0	1102	0.0	[0.0, 2.7]	0	349	0.0	[0.0, 8.5]
Cerebrovascular death	0	2562	0.0	[0.0, 1.2]	0	1102	0.0	[0.0, 2.7]	0	349	0.0	[0.0, 8.5]
Cancer death (excluding lungcancer)	0	2562	0.0	[0.0, 1.2]	0	1102	0.0	[0.0, 2.7]	0	349	0.0	[0.0, 8.5]
Death due to other causes	0	2562	0.0	[0.0, 1.2]	0	1102	0.0	[0.0, 2.7]	0	349	0.0	[0.0, 8.5]
Death with cause unknown	80	2562	31.2	[25.8,37.5]	20	1102	18.2	[12.1,26.3]	5	349	14.3	[5.7,29.8]

Note: Run date and time 01NOV2018 11:20:45,

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Table 15-17-5 (Page 11 of 12)
Incidence rates (per 1,000 PY) of events during cohort time by exposure cohorts
SIDIAP - Total analysis population

	Free LABA+ICS				Fixed LABA ICS				Fixed LABA LAMA			
Endpoint	Events	PY	IR	95% CI	Events	PY	IR	95% CI	Events	PY	IR	95% CI
Ventricular tachycardia	0	501	0.0	[0.0, 6.0]	4	5871	0.7	[0.2, 1.6]	0	341	0.0	[0.0, 8.8]
Ventricular fibrillation	0	501	0.0	[0.0, 6.0]	0	5872	0.0	[0.0, 0.5]	0	341	0.0	[0.0, 8.8]
Cardiovascular death	0	501	0.0	[0.0, 6.0]	0	5872	0.0	[0.0, 0.5]	0	341	0.0	[0.0, 8.8]
Respiratory death	0	501	0.0	[0.0, 6.0]	0	5872	0.0	[0.0, 0.5]	0	341	0.0	[0.0, 8.8]
Cardiovascular and respiratory death	0	501	0.0	[0.0, 6.0]	0	5872	0.0	[0.0, 0.5]	0	341	0.0	[0.0, 8.8]
Cerebrovascular death	0	501	0.0	[0.0, 6.0]	0	5872	0.0	[0.0, 0.5]	0	341	0.0	[0.0, 8.8]
Cancer death (excluding lungcancer)	0	501	0.0	[0.0, 6.0]	0	5872	0.0	[0.0, 0.5]	0	341	0.0	[0.0, 8.8]
Death due to other causes	0	501	0.0	[0.0, 6.0]	0	5872	0.0	[0.0, 0.5]	0	341	0.0	[0.0, 8.8]
Death with cause unknown	18	501	35.9	[23.3,52.8]	300	5872	51.1	[46.4,56.1]	12	341	35.2	[20.5,56.5]

Note: Run date and time 01NOV2018 11:20:45,

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Table 15-17-5 (Page 12 of 12)
Incidence rates (per 1,000 PY) of events during cohort time by exposure cohorts
SIDIAP - Total analysis population

	LABA				LAMA			
Endpoint	Events	PY	IR	95% CI	Events	PY	IR	95% CI
Ventricular tachycardia	0	1581	0.0	[0.0, 1.9]	1	3856	0.3	[0.0, 1.2]
Ventricular fibrillation	0	1581	0.0	[0.0, 1.9]	1	3856	0.3	[0.0, 1.2]
Cardiovascular death	0	1581	0.0	[0.0, 1.9]	0	3857	0.0	[0.0, 0.8]
Respiratory death	0	1581	0.0	[0.0, 1.9]	0	3857	0.0	[0.0, 0.8]
Cardiovascular and respiratory death	0	1581	0.0	[0.0, 1.9]	0	3857	0.0	[0.0, 0.8]
Cerebrovascular death	0	1581	0.0	[0.0, 1.9]	0	3857	0.0	[0.0, 0.8]
Cancer death (excluding lungcancer)	0	1581	0.0	[0.0, 1.9]	0	3857	0.0	[0.0, 0.8]
Death due to other causes	0	1581	0.0	[0.0, 1.9]	0	3857	0.0	[0.0, 0.8]
Death with cause unknown	40	1581	25.3	[19.2,32.8]	121	3856	31.4	[26.9,36.4]

Note: Run date and time 01NOV2018 11:20:45,

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Table 15-17-6 (Page 1 of 12)
Incidence rates (per 1,000 PY) of events during cohort time by exposure cohorts
POOLED - Total analysis population

	QVA149				Free LABA+LAMA without ICS				Free LABA+LAMA with ICS			
Endpoint	Events	PY	IR	95% CI	Events	PY	IR	95% CI	Events	PY	IR	95% CI
MACE	292	4964	58.8	[53.4,64.6]	126	3093	40.7	[35.1,47.1]	44	718	61.3	[47.2,78.1]
Ischemic heart disease	76	5045	15.1	[12.4,18.2]	46	3106	14.8	[11.4,18.9]	14	722	19.4	[11.8,30.1]
Cardiac arrhythmia	91	5042	18.0	[15.1,21.4]	57	3112	18.3	[14.5,22.8]	23	722	31.8	[21.9,44.8]
Cerebrovascular disorders	60	5059	11.9	[9.5,14.7]	27	3116	8.7	[6.1,11.9]	14	724	19.3	[11.7,30.1]
Glaucoma	19	4795	4.0	[2.6, 5.8]	15	2904	5.2	[3.2, 7.9]	6	685	8.8	[3.8,17.2]
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	94	5046	18.6	[15.6,22.1]	58	3105	18.7	[14.9,23.2]	17	722	23.5	[15.1,35.1]
Diabetes mellitus	82	4117	19.9	[16.5,23.9]	58	2564	22.6	[18.0,28.1]	12	601	20.0	[11.6,32.2]
Bronchospasm	6	5082	1.2	[0.5, 2.3]	3	3127	1.0	[0.3, 2.5]	2	725	2.8	[0.5, 8.7]
Mortality	312	5084	61.4	[55.9,67.2]	96	3127	30.7	[25.8,36.3]	20	727	27.5	[18.3,39.7]

Note: Run date and time 30NOV2018 11:12:17,

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Table 15-17-6 (Page 2 of 12)
Incidence rates (per 1,000 PY) of events during cohort time by exposure cohorts
POOLED - Total analysis population

	Free LABA+ICS				Fixed LABA/ICS				Fixed LABA/LAMA			
Endpoint	Events	PY	IR	95% CI	Events	PY	IR	95% CI	Events	PY	IR	95% CI
MACE	61	935	65.2	[52.4,80.1]	1125	26065	43.2	[41.1,45.3]	206	4241	48.6	[43.3,54.4]
Ischemic heart disease	16	943	17.0	[10.7,25.6]	345	26287	13.1	[12.0,14.3]	56	4284	13.1	[10.4,16.3]
Cardiac arrhythmia	29	943	30.7	[22.1,41.7]	554	26212	21.1	[19.7,22.7]	88	4283	20.5	[17.1,24.5]
Cerebrovascular disorders	17	945	18.0	[11.5,26.9]	334	26303	12.7	[11.6,13.9]	58	4291	13.5	[10.8,16.8]
Glaucoma	1	875	1.1	[0.1, 5.4]	92	24952	3.7	[3.1, 4.4]	10	4115	2.4	[1.3, 4.1]
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	15	946	15.9	[9.8,24.3]	381	26287	14.5	[13.3,15.8]	44	4290	10.3	[7.9,13.2]
Diabetes mellitus	14	751	18.6	[11.3,29.0]	443	22012	20.1	[18.6,21.8]	65	3624	17.9	[14.5,22.0]
Bronchospasm	6	946	6.3	[2.8,12.5]	52	26442	2.0	[1.5, 2.5]	4	4309	0.9	[0.3, 2.1]
Mortality	46	948	48.5	[37.6,61.6]	1588	26455	60.0	[57.6,62.5]	232	4310	53.8	[48.3,59.8]

Note: Run date and time 30NOV2018 11:12:17,

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Table 15-17-6 (Page 3 of 12)
Incidence rates (per 1,000 PY) of events during cohort time by exposure cohorts
POOLED - Total analysis population

	LABA				LAMA			
Endpoint	Events	PY	IR	95% CI	Events	PY	IR	95% CI
MACE	151	3812	39.6	[34.5,45.2]	644	16665	38.6	[36.2,41.2]
Ischemic heart disease	41	3836	10.7	[8.1,13.8]	240	16757	14.3	[12.8,15.9]
Cardiac arrhythmia	58	3830	15.1	[12.0,18.8]	334	16748	19.9	[18.2,21.8]
Cerebrovascular disorders	54	3834	14.1	[11.1,17.6]	228	16767	13.6	[12.2,15.2]
Glaucoma	17	3592	4.7	[3.0, 7.1]	74	15960	4.6	[3.8, 5.6]
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	76	3827	19.9	[16.3,24.0]	267	16761	15.9	[14.4,17.6]
Diabetes mellitus	58	3168	18.3	[14.6,22.7]	256	14027	18.3	[16.4,20.2]
Bronchospasm	6	3850	1.6	[0.7, 3.1]	15	16859	0.9	[0.5, 1.4]
Mortality	159	3851	41.3	[36.1,47.0]	687	16863	40.7	[38.3,43.3]

Note: Run date and time 30NOV2018 11:12:17,

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Table 15-17-6 (Page 4 of 12)
Incidence rates (per 1,000 PY) of events during cohort time by exposure cohorts
POOLED - Total analysis population

	QVA149				Free LABA+LAMA without ICS				Free LABA+LAMA with ICS			
Endpoint	Events	PY	IR	95% CI	Events	PY	IR	95% CI	Events	PY	IR	95% CI
Atrial fibrillation/flutter	86	4360	19.7	[16.4,23.6]	57	2809	20.3	[16.1,25.2]	19	646	29.4	[19.3,42.8]
Angina pectoris	32	4502	7.1	[5.2, 9.5]	16	2809	5.7	[3.6, 8.6]	4	654	6.1	[2.1,13.9]
AV block	18	4987	3.6	[2.3, 5.3]	8	3080	2.6	[1.3, 4.7]	0	716	0.0	[0.0, 4.2]
Incident benign prostatic hyperplasia	59	4142	14.2	[11.4,17.7]	33	2645	12.5	[9.1,16.6]	9	593	15.2	[7.9,26.3]
Hospitalization for acute coronary syndrome	49	5064	9.7	[7.5,12.3]	27	3118	8.7	[6.1,11.9]	11	724	15.2	[8.5,25.0]
Hospitalization for heart failure	203	4998	40.6	[36.1,45.5]	71	3114	22.8	[18.6,27.7]	26	723	35.9	[25.3,49.5]
Myocardial infarction	39	5066	7.7	[5.8,10.0]	25	3119	8.0	[5.6,11.2]	9	724	12.4	[6.5,21.6]
Long QT	2	5084	0.4	[0.1, 1.2]	1	3127	0.3	[0.0, 1.5]	0	727	0.0	[0.0, 4.1]
Narrow angle glaucoma	0	5074	0.0	[0.0, 0.6]	0	3120	0.0	[0.0, 1.0]	0	726	0.0	[0.0, 4.1]

Note: Run date and time 30NOV2018 11:12:17,

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Table 15-17-6 (Page 5 of 12)
Incidence rates (per 1,000 PY) of events during cohort time by exposure cohorts
POOLED - Total analysis population

	Free LABA+ICS				Fixed LABA/ICS				Fixed LABA/LAMA			
Endpoint	Events	PY	IR	95% CI	Events	PY	IR	95% CI	Events	PY	IR	95% CI
Atrial fibrillation/flutter	29	822	35.3	[25.3,47.8]	537	23603	22.8	[21.2,24.4]	84	3790	22.2	[18.4,26.5]
Angina pectoris	5	866	5.8	[2.3,12.1]	150	23379	6.4	[5.6, 7.3]	21	3619	5.8	[3.9, 8.3]
AV block	4	927	4.3	[1.5, 9.8]	52	26213	2.0	[1.6, 2.5]	8	4263	1.9	[0.9, 3.4]
Incident benign prostatic hyperplasia	12	780	15.4	[8.9,24.8]	230	23555	9.8	[8.7,10.9]	25	3886	6.4	[4.5, 9.0]
Hospitalization for acute coronary syndrome	14	944	14.8	[9.0,23.1]	172	26389	6.5	[5.7, 7.4]	27	4301	6.3	[4.4, 8.6]
Hospitalization for heart failure	36	941	38.2	[28.5,50.2]	664	26258	25.3	[23.7,26.9]	137	4263	32.1	[27.8,36.9]
Myocardial infarction	9	945	9.5	[5.0,16.6]	178	26382	6.7	[5.9, 7.6]	27	4298	6.3	[4.4, 8.7]
Long QT	0	948	0.0	[0.0, 3.2]	1	26455	0.0	[0.0, 0.2]	1	4310	0.2	[0.0, 1.1]
Narrow angle glaucoma	0	948	0.0	[0.0, 3.2]	1	26421	0.0	[0.0, 0.2]	1	4294	0.2	[0.0, 1.1]

Note: Run date and time 30NOV2018 11:12:17,

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Table 15-17-6 (Page 6 of 12)
Incidence rates (per 1,000 PY) of events during cohort time by exposure cohorts
POOLED - Total analysis population

	LABA				LAMA			
Endpoint	Events	PY	IR	95% CI	Events	PY	IR	95% CI
Atrial fibrillation/flutter	58	3447	16.8	[13.4,20.9]	318	14970	21.2	[19.3,23.3]
Angina pectoris	19	3491	5.4	[3.6, 8.0]	104	14808	7.0	[5.9, 8.3]
AV block	7	3798	1.8	[0.9, 3.5]	30	16678	1.8	[1.3, 2.4]
Incident benign prostatic hyperplasia	54	3300	16.4	[12.9,20.5]	162	14909	10.9	[9.5,12.4]
Hospitalization for acute coronary syndrome	21	3843	5.5	[3.7, 7.9]	109	16826	6.5	[5.5, 7.6]
Hospitalization for heart failure	92	3829	24.0	[20.1,28.5]	345	16776	20.6	[18.8,22.5]
Myocardial infarction	17	3845	4.4	[2.8, 6.6]	114	16822	6.8	[5.8, 7.9]
Long QT	0	3851	0.0	[0.0, 0.8]	1	16863	0.1	[0.0, 0.3]
Narrow angle glaucoma	0	3846	0.0	[0.0, 0.8]	1	16845	0.1	[0.0, 0.3]

Note: Run date and time 30NOV2018 11:12:17,

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Table 15-17-6 (Page 7 of 12)
Incidence rates (per 1,000 PY) of events during cohort time by exposure cohorts
POOLED - Total analysis population

	QVA149				Free LABA+LAMA without ICS				Free LABA+LAMA with ICS			
Endpoint	Events	PY	IR	95% CI	Events	PY	IR	95% CI	Events	PY	IR	95% CI
Other glaucoma	19	4805	4.0	[2.6, 5.8]	15	2909	5.2	[3.2, 7.9]	6	685	8.8	[3.8,17.2]
Premature depolarization	9	5006	1.8	[0.9, 3.1]	4	3071	1.3	[0.4, 3.0]	2	710	2.8	[0.5, 8.8]
Sick sinus	4	5057	0.8	[0.3, 1.8]	0	3118	0.0	[0.0, 1.0]	0	726	0.0	[0.0, 4.1]
Stroke	37	5072	7.3	[5.4, 9.6]	20	3118	6.4	[4.3, 9.3]	6	725	8.3	[3.6,16.3]
Supraventricular tachycardia	10	4988	2.0	[1.1, 3.4]	6	3084	1.9	[0.8, 3.8]	0	715	0.0	[0.0, 4.2]
TIA	25	5071	4.9	[3.4, 6.9]	8	3124	2.6	[1.3, 4.6]	9	725	12.4	[6.5,21.6]
Torsades de Pointes	0	5084	0.0	[0.0, 0.6]	0	3127	0.0	[0.0, 1.0]	0	727	0.0	[0.0, 4.1]
Unstable angina pectoris	16	5081	3.1	[2.0, 4.8]	9	3121	2.9	[1.5, 5.0]	2	726	2.8	[0.5, 8.6]
Urinary retention	38	5067	7.5	[5.6, 9.8]	26	3119	8.3	[5.8,11.5]	9	723	12.4	[6.5,21.6]

Note: Run date and time 30NOV2018 11:12:17,

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Table 15-17-6 (Page 8 of 12)
Incidence rates (per 1,000 PY) of events during cohort time by exposure cohorts
POOLED - Total analysis population

	Free LABA+ICS				Fixed LABA/ICS				Fixed LABA/LAMA			
Endpoint	Events	PY	IR	95% CI	Events	PY	IR	95% CI	Events	PY	IR	95% CI
Other glaucoma	1	875	1.1	[0.1, 5.4]	91	24976	3.6	[3.0, 4.3]	9	4126	2.2	[1.1, 3.8]
Premature depolarization	3	930	3.2	[0.9, 8.3]	54	26109	2.1	[1.6, 2.6]	5	4264	1.2	[0.5, 2.5]
Sick sinus	0	946	0.0	[0.0, 3.2]	9	26375	0.3	[0.2, 0.6]	0	4295	0.0	[0.0, 0.7]
Stroke	12	946	12.7	[7.3,20.5]	247	26350	9.4	[8.4,10.4]	45	4297	10.5	[8.1,13.4]
Supraventricular tachycardia	1	936	1.1	[0.1, 5.1]	42	26076	1.6	[1.2, 2.1]	5	4223	1.2	[0.5, 2.5]
TIA	7	947	7.4	[3.5,13.8]	100	26403	3.8	[3.2, 4.5]	15	4303	3.5	[2.2, 5.4]
Torsades de Pointes	0	948	0.0	[0.0, 3.2]	0	26455	0.0	[0.0, 0.1]	0	4310	0.0	[0.0, 0.7]
Unstable angina pectoris	5	945	5.3	[2.1,11.1]	54	26439	2.0	[1.6, 2.6]	14	4305	3.3	[2.0, 5.1]
Urinary retention	3	948	3.2	[0.9, 8.2]	166	26379	6.3	[5.5, 7.2]	21	4301	4.9	[3.3, 7.0]

Note: Run date and time 30NOV2018 11:12:17,

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Table 15-17-6 (Page 9 of 12)
Incidence rates (per 1,000 PY) of events during cohort time by exposure cohorts
POOLED - Total analysis population

	LABA				LAMA			
Endpoint	Events	PY	IR	95% CI	Events	PY	IR	95% CI
Other glaucoma	17	3596	4.7	[3.0, 7.1]	73	15970	4.6	[3.7, 5.6]
Premature depolarization	10	3800	2.6	[1.4, 4.5]	30	16597	1.8	[1.3, 2.5]
Sick sinus	5	3839	1.3	[0.5, 2.7]	4	16824	0.2	[0.1, 0.5]
Stroke	32	3842	8.3	[6.1,11.2]	151	16805	9.0	[7.8,10.3]
Supraventricular tachycardia	7	3797	1.8	[0.9, 3.5]	16	16633	1.0	[0.6, 1.5]
TIA	26	3842	6.8	[4.7, 9.4]	88	16820	5.2	[4.4, 6.2]
Torsades de Pointes	0	3851	0.0	[0.0, 0.8]	1	16863	0.1	[0.0, 0.3]
Unstable angina pectoris	11	3845	2.9	[1.6, 4.7]	36	16847	2.1	[1.6, 2.8]
Urinary retention	22	3842	5.7	[3.9, 8.2]	114	16822	6.8	[5.8, 7.9]

Note: Run date and time 30NOV2018 11:12:17,

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Table 15-17-6 (Page 10 of 12)
Incidence rates (per 1,000 PY) of events during cohort time by exposure cohorts
POOLED - Total analysis population

	QVA149				Free LABA+LAMA without ICS				Free LABA+LAMA with ICS			
Endpoint	Events	PY	IR	95% CI	Events	PY	IR	95% CI	Events	PY	IR	95% CI
Ventricular tachycardia	4	5082	0.8	[0.3, 1.8]	0	3127	0.0	[0.0, 1.0]	3	727	4.1	[1.1,10.6]
Ventricular fibrillation	1	5084	0.2	[0.0, 0.9]	0	3127	0.0	[0.0, 1.0]	1	727	1.4	[0.1, 6.5]
Cardiovascular death	21	5084	4.1	[2.8, 5.9]	9	3127	2.9	[1.5, 5.0]	0	727	0.0	[0.0, 4.1]
Respiratory death	38	5084	7.5	[5.6, 9.8]	14	3127	4.5	[2.7, 7.0]	4	727	5.5	[1.9,12.5]
Cardiovascular and respiratory death	2	5084	0.4	[0.1, 1.2]	3	3127	1.0	[0.3, 2.5]	2	727	2.8	[0.5, 8.6]
Cerebrovascular death	0	5084	0.0	[0.0, 0.6]	0	3127	0.0	[0.0, 1.0]	0	727	0.0	[0.0, 4.1]
Cancer death (excluding lungcancer)	10	5084	2.0	[1.1, 3.3]	3	3127	1.0	[0.3, 2.5]	1	727	1.4	[0.1, 6.5]
Death due to other causes	28	5084	5.5	[3.9, 7.5]	7	3127	2.2	[1.1, 4.2]	2	727	2.8	[0.5, 8.6]
Death with cause unknown	215	5084	42.3	[37.7,47.2]	60	3127	19.2	[15.3,23.7]	11	727	15.1	[8.5,24.9]

Note: Run date and time 30NOV2018 11:12:17,

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Table 15-17-6 (Page 11 of 12)
Incidence rates (per 1,000 PY) of events during cohort time by exposure cohorts
POOLED - Total analysis population

	Free LABA+ICS				Fixed LABA/ICS				Fixed LABA/LAMA			
Endpoint	Events	PY	IR	95% CI	Events	PY	IR	95% CI	Events	PY	IR	95% CI
Ventricular tachycardia	0	948	0.0	[0.0, 3.2]	15	26449	0.6	[0.3, 0.9]	2	4309	0.5	[0.1, 1.5]
Ventricular fibrillation	0	948	0.0	[0.0, 3.2]	4	26455	0.2	[0.1, 0.3]	2	4309	0.5	[0.1, 1.5]
Cardiovascular death	1	948	1.1	[0.1, 5.0]	57	26455	2.2	[1.7, 2.7]	4	4310	0.9	[0.3, 2.1]
Respiratory death	8	948	8.4	[4.2,15.2]	134	26455	5.1	[4.4, 5.8]	10	4310	2.3	[1.3, 3.9]
Cardiovascular and respiratory death	0	948	0.0	[0.0, 3.2]	14	26455	0.5	[0.3, 0.8]	1	4310	0.2	[0.0, 1.1]
Cerebrovascular death	1	948	1.1	[0.1, 5.0]	8	26455	0.3	[0.2, 0.5]	3	4310	0.7	[0.2, 1.8]
Cancer death (excluding lungcancer)	2	948	2.1	[0.4, 6.6]	42	26455	1.6	[1.2, 2.1]	2	4310	0.5	[0.1, 1.5]
Death due to other causes	1	948	1.1	[0.1, 5.0]	70	26455	2.6	[2.1, 3.2]	8	4310	1.9	[0.9, 3.3]
Death with cause unknown	33	948	34.8	[25.6,46.3]	1265	26455	47.8	[45.7,50.0]	205	4310	47.6	[42.3,53.2]

Note: Run date and time 30NOV2018 11:12:17,

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Table 15-17-6 (Page 12 of 12)
Incidence rates (per 1,000 PY) of events during cohort time by exposure cohorts
POOLED - Total analysis population

	LABA				LAMA			
Endpoint	Events	PY	IR	95% CI	Events	PY	IR	95% CI
Ventricular tachycardia	0	3851	0.0	[0.0, 0.8]	9	16860	0.5	[0.3, 0.9]
Ventricular fibrillation	0	3851	0.0	[0.0, 0.8]	6	16862	0.4	[0.2, 0.7]
Cardiovascular death	7	3851	1.8	[0.9, 3.4]	28	16863	1.7	[1.2, 2.3]
Respiratory death	18	3851	4.7	[3.0, 6.9]	54	16863	3.2	[2.5, 4.0]
Cardiovascular and respiratory death	0	3851	0.0	[0.0, 0.8]	10	16863	0.6	[0.3, 1.0]
Cerebrovascular death	2	3851	0.5	[0.1, 1.6]	8	16863	0.5	[0.2, 0.9]
Cancer death (excluding lungcancer)	7	3851	1.8	[0.9, 3.4]	30	16863	1.8	[1.3, 2.4]
Death due to other causes	10	3851	2.6	[1.4, 4.4]	23	16863	1.4	[0.9, 1.9]
Death with cause unknown	115	3851	29.9	[25.5,34.8]	536	16863	31.8	[29.6,34.1]

Note: Run date and time 30NOV2018 11:12:17,

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Table 15-18-1 (Page 1 of 4)
Crude hazard ratios for QVA versus comparators (Model 0)
THIN - Total analysis population

	QVA compared to Free LABA+LAMA without ICS			QVA compared to Free LABA+LAMA with ICS		
Endpoint	HR	95% CI	P	HR	95% CI	P
MACE	1.15	[0.63,2.11]	0.6484	.	[. , .]	.
Ischemic heart disease	1.57	[0.76,3.27]	0.2244	.	[. , .]	.
Cardiac arrhythmia	0.86	[0.31,2.38]	0.7773	.	[. , .]	.
Cerebrovascular disorders	1.09	[0.40,2.93]	0.8679	.	[. , .]	.
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	1.03	[0.36,2.90]	0.9579	.	[. , .]	.
Diabetes mellitus	0.65	[0.29,1.50]	0.3171	.	[. , .]	.
Mortality	3.30	[2.10,5.20]	<.0001	.	[. , .]	.

Note: Run date and time 01NOV2018 11:20:04,
If no results, number of events was too low

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Table 15-18-1 (Page 2 of 4)
Crude hazard ratios for QVA versus comparators (Model 0)
THIN - Total analysis population

	QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
Endpoint	HR	95% CI	P	HR	95% CI	P
MACE	.	[. , .]	.	1.28	[0.80,2.04]	0.2987
Ischemic heart disease	.	[. , .]	.	1.62	[0.95,2.75]	0.0761
Cardiac arrhythmia	.	[. , .]	.	0.52	[0.23,1.18]	0.1177
Cerebrovascular disorders	.	[. , .]	.	0.85	[0.40,1.81]	0.6664
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	.	[. , .]	.	1.03	[0.45,2.34]	0.9496
Diabetes mellitus	.	[. , .]	.	0.96	[0.47,1.96]	0.9130
Mortality	1.92	[0.91,4.05]	0.0864	1.59	[1.22,2.07]	0.0006

Note: Run date and time 01NOV2018 11:20:04,
If no results, number of events was too low

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Table 15-18-1 (Page 3 of 4)
Crude hazard ratios for QVA versus comparators (Model 0)
THIN - Total analysis population

	QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint	HR	95% CI	P	HR	95% CI	P
MACE	1.73	[1.00,2.99]	0.0521	1.27	[0.69,2.31]	0.4410
Ischemic heart disease	2.08	[1.10,3.94]	0.0252	1.35	[0.68,2.69]	0.3965
Cardiac arrhythmia	0.77	[0.32,1.87]	0.5632	0.66	[0.25,1.70]	0.3880
Cerebrovascular disorders	0.89	[0.39,2.04]	0.7781	0.81	[0.33,2.00]	0.6480
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	1.47	[0.56,3.81]	0.4339	0.93	[0.34,2.59]	0.8932
Diabetes mellitus	0.99	[0.45,2.17]	0.9820	0.85	[0.36,2.00]	0.7085
Mortality	2.05	[1.49,2.81]	<.0001	2.05	[1.40,3.00]	0.0002

Note: Run date and time 01NOV2018 11:20:04,
If no results, number of events was too low

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Table 15-18-1 (Page 4 of 4)
Crude hazard ratios for QVA versus comparators (Model 0)
THIN - Total analysis population

	QVA compared to LAMA		
Endpoint	HR	95% CI	P
MACE	1.35	[0.84,2.17]	0.2148
Ischemic heart disease	1.69	[0.98,2.90]	0.0591
Cardiac arrhythmia	0.65	[0.29,1.48]	0.3047
Cerebrovascular disorders	0.72	[0.34,1.56]	0.4094
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	1.05	[0.46,2.42]	0.9075
Diabetes mellitus	0.91	[0.44,1.87]	0.7986
Mortality	2.39	[1.81,3.14]	<.0001

Note: Run date and time 01NOV2018 11:20:04,
If no results, number of events was too low

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Table 15-18-2 (Page 1 of 4)
Crude hazard ratios for QVA versus comparators (Model 0)
IPCI - Total analysis population

	QVA compared to Free LABA+LAMA without ICS			QVA compared to Free LABA+LAMA with ICS		
Endpoint	HR	95% CI	P	HR	95% CI	P
MACE	1.01	[0.48,2.11]	0.9752	1.02	[0.38,2.70]	0.9735
Cardiac arrhythmia	1.20	[0.43,3.34]	0.7208	0.58	[0.20,1.68]	0.3147
Cerebrovascular disorders	2.52	[0.87,7.32]	0.0883	.	[. , .]	.
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	2.09	[0.70,6.28]	0.1890	.	[. , .]	.
Diabetes mellitus	.	[. , .]	.	.	[. , .]	.
Mortality	0.74	[0.39,1.44]	0.3790	1.09	[0.42,2.85]	0.8580

Note: Run date and time 01NOV2018 11:20:16,
If no results, number of events was too low

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Table 15-18-2 (Page 2 of 4)
Crude hazard ratios for QVA versus comparators (Model 0)
IPCI - Total analysis population

	QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
Endpoint	HR	95% CI	P	HR	95% CI	P
MACE	0.68	[0.30,1.55]	0.3649	0.85	[0.48,1.51]	0.5889
Cardiac arrhythmia	0.77	[0.26,2.26]	0.6289	1.33	[0.63,2.82]	0.4503
Cerebrovascular disorders	1.11	[0.37,3.32]	0.8565	1.91	[0.98,3.69]	0.0555
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	.	[. , .]	.	1.65	[0.81,3.39]	0.1699
Diabetes mellitus	.	[. , .]	.	1.68	[0.64,4.41]	0.2921
Mortality	0.61	[0.28,1.33]	0.2172	0.77	[0.45,1.31]	0.3316

Note: Run date and time 01NOV2018 11:20:16,
If no results, number of events was too low

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Table 15-18-2 (Page 3 of 4)
Crude hazard ratios for QVA versus comparators (Model 0)
IPCI - Total analysis population

	QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint	HR	95% CI	P	HR	95% CI	P
MACE	1.00	[0.49,2.02]	0.9955	1.11	[0.54,2.29]	0.7782
Cardiac arrhythmia	1.96	[0.68,5.66]	0.2116	.	[. , .]	.
Cerebrovascular disorders	.	[. , .]	.	1.36	[0.59,3.13]	0.4718
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	1.45	[0.57,3.65]	0.4317	2.25	[0.79,6.45]	0.1308
Diabetes mellitus	.	[. , .]	.	.	[. , .]	.
Mortality	1.08	[0.55,2.14]	0.8202	0.72	[0.39,1.35]	0.3128

Note: Run date and time 01NOV2018 11:20:16,
If no results, number of events was too low

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Table 15-18-2 (Page 4 of 4)
Crude hazard ratios for QVA versus comparators (Model 0)
IPCI - Total analysis population

	QVA compared to LAMA		
Endpoint	HR	95% CI	P
MACE	0.92	[0.51,1.66]	0.7915
Cardiac arrhythmia	1.05	[0.50,2.23]	0.8941
Cerebrovascular disorders	1.81	[0.91,3.57]	0.0888
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	1.34	[0.65,2.77]	0.4327
Diabetes mellitus	1.83	[0.67,5.02]	0.2403
Mortality	1.15	[0.66,2.01]	0.6140

Note: Run date and time 01NOV2018 11:20:16,
If no results, number of events was too low

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Table 15-18-3 (Page 1 of 4)
Crude hazard ratios for QVA versus comparators (Model 0)
AUH - Total analysis population

	QVA compared to Free LABA+LAMA without ICS			QVA compared to Free LABA+LAMA with ICS		
Endpoint	HR	95% CI	P	HR	95% CI	P
MACE	1.18	[0.79,1.76]	0.4248	0.88	[0.50,1.53]	0.6388
Ischemic heart disease	.	[. , .]	.	.	[. , .]	.
Cardiac arrhythmia	1.07	[0.43,2.65]	0.8798	.	[. , .]	.
Cerebrovascular disorders	.	[. , .]	.	.	[. , .]	.
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	.	[. , .]	.	.	[. , .]	.
Diabetes mellitus	.	[. , .]	.	.	[. , .]	.
Mortality	1.40	[0.82,2.39]	0.2117	.	[. , .]	.

Note: Run date and time 01NOV2018 11:20:27,
If no results, number of events was too low

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Table 15-18-3 (Page 2 of 4)
Crude hazard ratios for QVA versus comparators (Model 0)
AUH - Total analysis population

	QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
Endpoint	HR	95% CI	P	HR	95% CI	P
MACE	1.13	[0.62,2.05]	0.6914	0.97	[0.78,1.21]	0.7773
Ischemic heart disease	.	[. , .]	.	1.35	[0.85,2.14]	0.2091
Cardiac arrhythmia	.	[. , .]	.	0.79	[0.48,1.30]	0.3519
Cerebrovascular disorders	.	[. , .]	.	1.38	[0.73,2.60]	0.3196
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	.	[. , .]	.	0.93	[0.36,2.43]	0.8899
Diabetes mellitus	.	[. , .]	.	0.68	[0.27,1.67]	0.3980
Mortality	1.55	[0.63,3.82]	0.3448	0.73	[0.57,0.92]	0.0084

Note: Run date and time 01NOV2018 11:20:27,
If no results, number of events was too low

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Table 15-18-3 (Page 3 of 4)
Crude hazard ratios for QVA versus comparators (Model 0)
AUH - Total analysis population

	QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint	HR	95% CI	P	HR	95% CI	P
MACE	0.99	[0.77,1.27]	0.9078	1.48	[1.04,2.11]	0.0301
Ischemic heart disease	2.24	[1.18,4.26]	0.0139	1.37	[0.69,2.72]	0.3759
Cardiac arrhythmia	0.65	[0.38,1.10]	0.1049	1.21	[0.56,2.63]	0.6254
Cerebrovascular disorders	0.87	[0.45,1.67]	0.6765	.	[. , .]	.
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	0.85	[0.30,2.43]	0.7625	.	[. , .]	.
Diabetes mellitus	0.59	[0.22,1.56]	0.2888	.	[. , .]	.
Mortality	1.17	[0.87,1.57]	0.3061	1.59	[1.02,2.47]	0.0399

Note: Run date and time 01NOV2018 11:20:27,
If no results, number of events was too low

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Table 15-18-3 (Page 4 of 4)
Crude hazard ratios for QVA versus comparators (Model 0)
AUH - Total analysis population

	QVA compared to LAMA		
Endpoint	HR	95% CI	P
MACE	0.88	[0.69,1.13]	0.3161
Ischemic heart disease	1.89	[1.02,3.50]	0.0432
Cardiac arrhythmia	0.76	[0.44,1.31]	0.3213
Cerebrovascular disorders	1.16	[0.56,2.39]	0.6853
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	0.82	[0.27,2.48]	0.7280
Diabetes mellitus	0.81	[0.28,2.32]	0.6886
Mortality	0.92	[0.69,1.23]	0.5885

Note: Run date and time 01NOV2018 11:20:27,
If no results, number of events was too low

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Table 15-18-4 (Page 1 of 4)
Crude hazard ratios for QVA versus comparators (Model 0)
HSD - Total analysis population

	QVA compared to Free LABA+LAMA without ICS			QVA compared to Free LABA+LAMA with ICS		
Endpoint	HR	95% CI	P	HR	95% CI	P
Diabetes mellitus	.	[. , .]	.	.	[. , .]	.

Note: Run date and time 01NOV2018 11:20:38,
If no results, number of events was too low

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Table 15-18-4 (Page 2 of 4)
Crude hazard ratios for QVA versus comparators (Model 0)
HSD - Total analysis population

	QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
Endpoint	HR	95% CI	P	HR	95% CI	P
Diabetes mellitus	.	[. , .]	.	1.79	[0.69,4.63]	0.2314

Note: Run date and time 01NOV2018 11:20:38,
If no results, number of events was too low

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Table 15-18-4 (Page 3 of 4)
Crude hazard ratios for QVA versus comparators (Model 0)
HSD - Total analysis population

	QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint	HR	95% CI	P	HR	95% CI	P
Diabetes mellitus	.	[. , .]	.	.	[. , .]	.

Note: Run date and time 01NOV2018 11:20:38,
If no results, number of events was too low

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Table 15-18-4 (Page 4 of 4)
Crude hazard ratios for QVA versus comparators (Model 0)
HSD - Total analysis population

	QVA compared to LAMA		
Endpoint	HR	95% CI	P
Diabetes mellitus	3.04	[1.07,8.60]	0.0362

Note: Run date and time 01NOV2018 11:20:38,
If no results, number of events was too low

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Table 15-18-5 (Page 1 of 4)
Crude hazard ratios for QVA versus comparators (Model 0)
SIDIAP - Total analysis population

	QVA compared to Free LABA+LAMA without ICS			QVA compared to Free LABA+LAMA with ICS		
Endpoint	HR	95% CI	P	HR	95% CI	P
MACE	1.22	[0.87,1.73]	0.2531	1.10	[0.66,1.82]	0.7243
Ischemic heart disease	0.54	[0.25,1.17]	0.1190	.	[. , .]	.
Cardiac arrhythmia	0.99	[0.58,1.70]	0.9778	0.57	[0.30,1.08]	0.0865
Cerebrovascular disorders	1.28	[0.46,3.60]	0.6357	0.35	[0.13,0.93]	0.0362
Glaucoma	0.72	[0.30,1.73]	0.4621	.	[. , .]	.
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	0.91	[0.59,1.42]	0.6928	0.91	[0.47,1.76]	0.7844
Diabetes mellitus	1.05	[0.65,1.70]	0.8387	1.42	[0.64,3.16]	0.3918
Bronchospasm	.	[. , .]	.	.	[. , .]	.
Mortality	1.49	[0.89,2.48]	0.1251	1.81	[0.73,4.51]	0.2032

Note: Run date and time 01NOV2018 11:20:48,
If no results, number of events was too low

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Table 15-18-5 (Page 2 of 4)
Crude hazard ratios for QVA versus comparators (Model 0)
SIDIAP - Total analysis population

	QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
Endpoint	HR	95% CI	P	HR	95% CI	P
MACE	0.98	[0.65,1.47]	0.9098	0.74	[0.60,0.92]	0.0055
Ischemic heart disease	0.60	[0.22,1.66]	0.3270	0.64	[0.35,1.15]	0.1350
Cardiac arrhythmia	0.69	[0.38,1.25]	0.2236	0.67	[0.47,0.96]	0.0278
Cerebrovascular disorders	0.43	[0.17,1.10]	0.0790	0.64	[0.36,1.17]	0.1471
Glaucoma	.	[. , .]	.	0.86	[0.44,1.67]	0.6608
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	1.58	[0.79,3.16]	0.1927	0.88	[0.65,1.19]	0.3921
Diabetes mellitus	1.60	[0.77,3.32]	0.2073	0.84	[0.61,1.15]	0.2736
Bronchospasm	0.24	[0.07,0.84]	0.0250	0.39	[0.15,0.99]	0.0480
Mortality	0.81	[0.47,1.39]	0.4384	0.59	[0.45,0.77]	0.0001

Note: Run date and time 01NOV2018 11:20:48,
If no results, number of events was too low

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Table 15-18-5 (Page 3 of 4)
Crude hazard ratios for QVA versus comparators (Model 0)
SIDIAP - Total analysis population

	QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint	HR	95% CI	P	HR	95% CI	P
MACE	0.77	[0.49,1.22]	0.2697	1.41	[1.03,1.94]	0.0345
Ischemic heart disease	0.36	[0.14,0.95]	0.0387	1.33	[0.55,3.23]	0.5280
Cardiac arrhythmia	.	[. , .]	.	1.28	[0.77,2.14]	0.3377
Cerebrovascular disorders	.	[. , .]	.	0.78	[0.36,1.69]	0.5254
Glaucoma	.	[. , .]	.	0.67	[0.29,1.52]	0.3343
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	1.10	[0.52,2.30]	0.8032	0.85	[0.58,1.25]	0.4133
Diabetes mellitus	0.59	[0.32,1.08]	0.0885	1.21	[0.78,1.88]	0.4027
Bronchospasm	.	[. , .]	.	0.68	[0.21,2.28]	0.5369
Mortality	0.91	[0.48,1.71]	0.7632	1.20	[0.80,1.81]	0.3686

Note: Run date and time 01NOV2018 11:20:48,
If no results, number of events was too low

QVA149A2402

Table 15-18-5 (Page 4 of 4)
Crude hazard ratios for QVA versus comparators (Model 0)
SIDIAP - Total analysis population

	QVA compared to LAMA		
Endpoint	HR	95% CI	P
MACE	1.03	[0.81,1.30]	0.8308
Ischemic heart disease	0.55	[0.30,1.01]	0.0554
Cardiac arrhythmia	0.75	[0.51,1.09]	0.1267
Cerebrovascular disorders	0.70	[0.37,1.32]	0.2671
Glaucoma	0.56	[0.29,1.10]	0.0936
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	0.82	[0.59,1.13]	0.2214
Diabetes mellitus	1.05	[0.74,1.49]	0.7777
Bronchospasm	1.08	[0.36,3.27]	0.8864
Mortality	0.91	[0.67,1.23]	0.5195

Note: Run date and time 01NOV2018 11:20:48,
If no results, number of events was too low

QVA149A2402

Table 15-19-1 (Page 1 of 4)
Adjusted hazard ratios for QVA versus comparators (Model 1)
THIN - Total analysis population

	QVA compared to Free LABA+LAMA without ICS			QVA compared to Free LABA+LAMA with ICS		
Endpoint	HR	95% CI	P	HR	95% CI	P
MACE	1.14	[0.62,2.09]	0.6758	.	[. , .]	.
Ischemic heart disease	1.60	[0.77,3.34]	0.2064	.	[. , .]	.
Cardiac arrhythmia	0.85	[0.31,2.36]	0.7550	.	[. , .]	.
Cerebrovascular disorders	1.05	[0.39,2.84]	0.9279	.	[. , .]	.
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	1.03	[0.36,2.92]	0.9542	.	[. , .]	.
Diabetes mellitus	0.67	[0.29,1.53]	0.3382	.	[. , .]	.
Mortality	3.06	[1.94,4.83]	<.0001	.	[. , .]	.

Note: Run date and time 01NOV2018 11:20:05,
If no results, number of events was too low

QVA149A2402

Table 15-19-1 (Page 2 of 4)
Adjusted hazard ratios for QVA versus comparators (Model 1)
THIN - Total analysis population

	QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
Endpoint	HR	95% CI	P	HR	95% CI	P
MACE	.	[. , .]	.	1.23	[0.77,1.95]	0.3945
Ischemic heart disease	.	[. , .]	.	1.57	[0.93,2.68]	0.0940
Cardiac arrhythmia	.	[. , .]	.	0.50	[0.22,1.12]	0.0931
Cerebrovascular disorders	.	[. , .]	.	0.83	[0.39,1.77]	0.6247
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	.	[. , .]	.	0.95	[0.42,2.17]	0.9037
Diabetes mellitus	.	[. , .]	.	0.96	[0.47,1.96]	0.9126
Mortality	1.69	[0.79,3.63]	0.1757	1.49	[1.15,1.94]	0.0028

Note: Run date and time 01NOV2018 11:20:05,
If no results, number of events was too low

QVA149A2402

Table 15-19-1 (Page 3 of 4)
Adjusted hazard ratios for QVA versus comparators (Model 1)
THIN - Total analysis population

	QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint	HR	95% CI	P	HR	95% CI	P
MACE	1.70	[0.98,2.95]	0.0606	1.10	[0.59,2.05]	0.7596
Ischemic heart disease	2.11	[1.11,4.02]	0.0223	1.35	[0.67,2.74]	0.4058
Cardiac arrhythmia	0.77	[0.32,1.86]	0.5573	0.51	[0.19,1.36]	0.1776
Cerebrovascular disorders	0.89	[0.39,2.06]	0.7930	0.82	[0.33,2.04]	0.6687
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	1.56	[0.60,4.06]	0.3655	0.91	[0.32,2.61]	0.8682
Diabetes mellitus	0.97	[0.44,2.13]	0.9337	0.86	[0.36,2.05]	0.7323
Mortality	1.98	[1.44,2.72]	<.0001	1.76	[1.20,2.60]	0.0042

Note: Run date and time 01NOV2018 11:20:05,
If no results, number of events was too low

QVA149A2402

Table 15-19-1 (Page 4 of 4)
Adjusted hazard ratios for QVA versus comparators (Model 1)
THIN - Total analysis population

	QVA compared to LAMA		
Endpoint	HR	95% CI	P
MACE	1.30	[0.80,2.09]	0.2849
Ischemic heart disease	1.66	[0.96,2.87]	0.0675
Cardiac arrhythmia	0.62	[0.27,1.42]	0.2602
Cerebrovascular disorders	0.70	[0.33,1.52]	0.3707
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	0.97	[0.42,2.25]	0.9503
Diabetes mellitus	0.89	[0.43,1.84]	0.7544
Mortality	2.16	[1.63,2.85]	<.0001

Note: Run date and time 01NOV2018 11:20:05,
If no results, number of events was too low

QVA149A2402

Table 15-19-2 (Page 1 of 4)
Adjusted hazard ratios for QVA versus comparators (Model 1)
IPCI - Total analysis population

	QVA compared to Free LABA+LAMA without ICS			QVA compared to Free LABA+LAMA with ICS		
Endpoint	HR	95% CI	P	HR	95% CI	P
MACE	1.07	[0.51,2.25]	0.8599	0.98	[0.36,2.70]	0.9724
Cardiac arrhythmia	1.23	[0.44,3.44]	0.6916	0.51	[0.17,1.55]	0.2353
Cerebrovascular disorders	2.64	[0.90,7.72]	0.0764	.	[. , .]	.
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	2.35	[0.77,7.23]	0.1345	.	[. , .]	.
Diabetes mellitus	.	[. , .]	.	.	[. , .]	.
Mortality	0.80	[0.41,1.55]	0.5084	1.25	[0.46,3.36]	0.6634

Note: Run date and time 01NOV2018 11:20:17,
If no results, number of events was too low

QVA149A2402

Table 15-19-2 (Page 2 of 4)
Adjusted hazard ratios for QVA versus comparators (Model 1)
IPCI - Total analysis population

	QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
Endpoint	HR	95% CI	P	HR	95% CI	P
MACE	0.77	[0.30,1.95]	0.5754	0.73	[0.41,1.31]	0.2936
Cardiac arrhythmia	0.59	[0.16,2.13]	0.4191	1.37	[0.64,2.95]	0.4231
Cerebrovascular disorders	1.34	[0.40,4.56]	0.6366	1.92	[0.97,3.80]	0.0612
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	.	[. , .]	.	1.50	[0.72,3.12]	0.2761
Diabetes mellitus	.	[. , .]	.	1.38	[0.50,3.80]	0.5282
Mortality	0.50	[0.20,1.22]	0.1285	0.66	[0.39,1.13]	0.1332

Note: Run date and time 01NOV2018 11:20:17,
If no results, number of events was too low

QVA149A2402

Table 15-19-2 (Page 3 of 4)
Adjusted hazard ratios for QVA versus comparators (Model 1)
IPCI - Total analysis population

	QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint	HR	95% CI	P	HR	95% CI	P
MACE	1.00	[0.49,2.04]	0.9960	1.06	[0.50,2.27]	0.8752
Cardiac arrhythmia	1.80	[0.62,5.25]	0.2806	.	[. , .]	.
Cerebrovascular disorders	.	[. , .]	.	1.51	[0.63,3.59]	0.3544
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	1.47	[0.58,3.74]	0.4193	2.40	[0.80,7.24]	0.1205
Diabetes mellitus	.	[. , .]	.	.	[. , .]	.
Mortality	1.20	[0.60,2.37]	0.6082	0.71	[0.36,1.38]	0.3132

Note: Run date and time 01NOV2018 11:20:17,
If no results, number of events was too low

QVA149A2402

Table 15-19-2 (Page 4 of 4)
Adjusted hazard ratios for QVA versus comparators (Model 1)
IPCI - Total analysis population

	QVA compared to LAMA		
Endpoint	HR	95% CI	P
MACE	0.86	[0.47,1.57]	0.6241
Cardiac arrhythmia	1.05	[0.48,2.27]	0.9029
Cerebrovascular disorders	1.87	[0.92,3.77]	0.0823
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	1.26	[0.60,2.65]	0.5442
Diabetes mellitus	1.79	[0.63,5.09]	0.2720
Mortality	1.10	[0.61,1.97]	0.7556

Note: Run date and time 01NOV2018 11:20:17,
If no results, number of events was too low

QVA149A2402

Table 15-19-3 (Page 1 of 4)
Adjusted hazard ratios for QVA versus comparators (Model 1)
AUH - Total analysis population

	QVA compared to Free LABA+LAMA without ICS			QVA compared to Free LABA+LAMA with ICS		
Endpoint	HR	95% CI	P	HR	95% CI	P
MACE	1.16	[0.78,1.74]	0.4629	0.80	[0.46,1.40]	0.4355
Ischemic heart disease	.	[. , .]	.	.	[. , .]	.
Cardiac arrhythmia	1.09	[0.44,2.72]	0.8543	.	[. , .]	.
Cerebrovascular disorders	.	[. , .]	.	.	[. , .]	.
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	.	[. , .]	.	.	[. , .]	.
Diabetes mellitus	.	[. , .]	.	.	[. , .]	.
Mortality	1.40	[0.82,2.40]	0.2176	.	[. , .]	.

Note: Run date and time 01NOV2018 11:20:28,
If no results, number of events was too low

QVA149A2402

Table 15-19-3 (Page 2 of 4)
Adjusted hazard ratios for QVA versus comparators (Model 1)
AUH - Total analysis population

	QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
Endpoint	HR	95% CI	P	HR	95% CI	P
MACE	1.02	[0.56,1.87]	0.9413	0.91	[0.73,1.13]	0.3995
Ischemic heart disease	.	[. , .]	.	1.33	[0.83,2.13]	0.2318
Cardiac arrhythmia	.	[. , .]	.	0.75	[0.45,1.24]	0.2574
Cerebrovascular disorders	.	[. , .]	.	1.43	[0.75,2.71]	0.2780
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	.	[. , .]	.	0.79	[0.30,2.10]	0.6405
Diabetes mellitus	.	[. , .]	.	0.65	[0.26,1.63]	0.3582
Mortality	1.25	[0.50,3.13]	0.6305	0.69	[0.54,0.88]	0.0024

Note: Run date and time 01NOV2018 11:20:28,
If no results, number of events was too low

QVA149A2402

Table 15-19-3 (Page 3 of 4)
Adjusted hazard ratios for QVA versus comparators (Model 1)
AUH - Total analysis population

	QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint	HR	95% CI	P	HR	95% CI	P
MACE	0.96	[0.75,1.24]	0.7600	1.46	[1.01,2.12]	0.0469
Ischemic heart disease	2.20	[1.16,4.20]	0.0162	1.39	[0.68,2.87]	0.3692
Cardiac arrhythmia	0.63	[0.37,1.07]	0.0883	1.29	[0.56,2.96]	0.5560
Cerebrovascular disorders	0.87	[0.45,1.69]	0.6887	.	[. , .]	.
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	0.78	[0.27,2.25]	0.6488	.	[. , .]	.
Diabetes mellitus	0.58	[0.22,1.54]	0.2746	.	[. , .]	.
Mortality	1.12	[0.83,1.51]	0.4491	1.27	[0.80,2.01]	0.3107

Note: Run date and time 01NOV2018 11:20:28,
If no results, number of events was too low

QVA149A2402

Table 15-19-3 (Page 4 of 4)
Adjusted hazard ratios for QVA versus comparators (Model 1)
AUH - Total analysis population

	QVA compared to LAMA		
Endpoint	HR	95% CI	P
MACE	0.82	[0.63,1.06]	0.1268
Ischemic heart disease	1.85	[0.98,3.49]	0.0586
Cardiac arrhythmia	0.77	[0.43,1.38]	0.3779
Cerebrovascular disorders	1.27	[0.61,2.67]	0.5211
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	0.72	[0.23,2.30]	0.5832
Diabetes mellitus	0.76	[0.25,2.34]	0.6355
Mortality	0.81	[0.60,1.10]	0.1855

Note: Run date and time 01NOV2018 11:20:28,
If no results, number of events was too low

QVA149A2402

Table 15-19-4 (Page 1 of 4)
Adjusted hazard ratios for QVA versus comparators (Model 1)
HSD - Total analysis population

	QVA compared to Free LABA+LAMA without ICS			QVA compared to Free LABA+LAMA with ICS		
Endpoint	HR	95% CI	P	HR	95% CI	P
Diabetes mellitus	.	[. , .]	.	.	[. , .]	.

Note: Run date and time 01NOV2018 11:20:39,
If no results, number of events was too low

QVA149A2402

Table 15-19-4 (Page 2 of 4)
Adjusted hazard ratios for QVA versus comparators (Model 1)
HSD - Total analysis population

	QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
Endpoint	HR	95% CI	P	HR	95% CI	P
Diabetes mellitus	.	[. , .]	.	1.67	[0.64,4.33]	0.2944

Note: Run date and time 01NOV2018 11:20:39,
If no results, number of events was too low

QVA149A2402

Table 15-19-4 (Page 3 of 4)
Adjusted hazard ratios for QVA versus comparators (Model 1)
HSD - Total analysis population

	QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint	HR	95% CI	P	HR	95% CI	P
Diabetes mellitus	.	[. , .]	.	.	[. , .]	.

Note: Run date and time 01NOV2018 11:20:39,
If no results, number of events was too low

QVA149A2402

Table 15-19-4 (Page 4 of 4)
Adjusted hazard ratios for QVA versus comparators (Model 1)
HSD - Total analysis population

	QVA compared to LAMA		
Endpoint	HR	95% CI	P
Diabetes mellitus	2.79	[0.97,7.99]	0.0567

Note: Run date and time 01NOV2018 11:20:39,
If no results, number of events was too low

QVA149A2402

Table 15-19-5 (Page 1 of 4)
Adjusted hazard ratios for QVA versus comparators (Model 1)
SIDIAP - Total analysis population

	QVA compared to Free LABA+LAMA without ICS			QVA compared to Free LABA+LAMA with ICS		
Endpoint	HR	95% CI	P	HR	95% CI	P
MACE	1.22	[0.86,1.74]	0.2539	1.23	[0.74,2.04]	0.4270
Ischemic heart disease	0.56	[0.26,1.21]	0.1415	.	[. , .]	.
Cardiac arrhythmia	1.02	[0.60,1.75]	0.9358	0.62	[0.32,1.18]	0.1459
Cerebrovascular disorders	1.28	[0.46,3.61]	0.6368	0.39	[0.14,1.05]	0.0630
Glaucoma	0.72	[0.30,1.73]	0.4576	.	[. , .]	.
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	0.94	[0.60,1.47]	0.7952	0.95	[0.49,1.84]	0.8779
Diabetes mellitus	1.06	[0.65,1.71]	0.8213	1.40	[0.63,3.13]	0.4118
Bronchospasm	.	[. , .]	.	.	[. , .]	.
Mortality	1.47	[0.88,2.45]	0.1414	2.13	[0.85,5.33]	0.1047

Note: Run date and time 01NOV2018 11:20:49,
If no results, number of events was too low

QVA149A2402

Table 15-19-5 (Page 2 of 4)
Adjusted hazard ratios for QVA versus comparators (Model 1)
SIDIAP - Total analysis population

	QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
Endpoint	HR	95% CI	P	HR	95% CI	P
MACE	1.09	[0.72,1.66]	0.6737	0.75	[0.61,0.93]	0.0089
Ischemic heart disease	0.64	[0.23,1.83]	0.4081	0.62	[0.34,1.13]	0.1194
Cardiac arrhythmia	0.73	[0.40,1.34]	0.3071	0.66	[0.46,0.95]	0.0237
Cerebrovascular disorders	0.41	[0.16,1.05]	0.0641	0.61	[0.33,1.10]	0.1012
Glaucoma	.	[. , .]	.	0.91	[0.46,1.79]	0.7863
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	1.40	[0.69,2.81]	0.3484	0.75	[0.55,1.02]	0.0699
Diabetes mellitus	1.53	[0.73,3.24]	0.2621	0.77	[0.56,1.06]	0.1127
Bronchospasm	0.29	[0.08,1.05]	0.0592	0.44	[0.17,1.14]	0.0894
Mortality	0.86	[0.50,1.49]	0.5935	0.60	[0.46,0.79]	0.0002

Note: Run date and time 01NOV2018 11:20:49,
If no results, number of events was too low

QVA149A2402

Table 15-19-5 (Page 3 of 4)
Adjusted hazard ratios for QVA versus comparators (Model 1)
SIDIAP - Total analysis population

	QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint	HR	95% CI	P	HR	95% CI	P
MACE	0.73	[0.46,1.15]	0.1774	1.29	[0.93,1.80]	0.1332
Ischemic heart disease	0.36	[0.14,0.93]	0.0350	1.43	[0.57,3.60]	0.4488
Cardiac arrhythmia	.	[. , .]	.	1.17	[0.69,1.99]	0.5590
Cerebrovascular disorders	.	[. , .]	.	0.67	[0.29,1.51]	0.3311
Glaucoma	.	[. , .]	.	0.73	[0.31,1.71]	0.4659
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	1.07	[0.51,2.25]	0.8555	0.75	[0.50,1.13]	0.1672
Diabetes mellitus	0.59	[0.32,1.09]	0.0912	1.19	[0.74,1.90]	0.4797
Bronchospasm	.	[. , .]	.	0.77	[0.21,2.80]	0.6969
Mortality	0.85	[0.45,1.60]	0.6071	0.98	[0.64,1.48]	0.9072

Note: Run date and time 01NOV2018 11:20:49,
If no results, number of events was too low

QVA149A2402

Table 15-19-5 (Page 4 of 4)
Adjusted hazard ratios for QVA versus comparators (Model 1)
SIDIAP - Total analysis population

	QVA compared to LAMA		
Endpoint	HR	95% CI	P
MACE	0.91	[0.71,1.16]	0.4386
Ischemic heart disease	0.56	[0.30,1.06]	0.0738
Cardiac arrhythmia	0.68	[0.46,1.01]	0.0534
Cerebrovascular disorders	0.63	[0.33,1.22]	0.1701
Glaucoma	0.57	[0.28,1.13]	0.1089
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	0.74	[0.53,1.05]	0.0907
Diabetes mellitus	0.96	[0.67,1.37]	0.8174
Bronchospasm	1.11	[0.36,3.48]	0.8553
Mortality	0.75	[0.55,1.03]	0.0784

Note: Run date and time 01NOV2018 11:20:49,
If no results, number of events was too low

QVA149A2402

Table 15-20-1 (Page 1 of 16)
All hazard ratios in adjusted model (Model 1)
THIN - Total analysis population

			QVA compared to Free LABA+LAMA without ICS			QVA compared to Free LABA+LAMA with ICS		
Endpoint		Level	HR	95% CI	P	HR	95% CI	P
MACE	Cohort	QVA149	1.14	[0.62,2.09]	0.6758	.	[. , .]	.
	Age at start		1.03	[1.00,1.06]	0.0787	.	[. , .]	.
	Sex	Male	3.20	[1.52,6.73]	0.0022	.	[. , .]	.
	Smoking	Current	51E4	[0.00, .]	0.9823	.	[. , .]	.
		Past	57E4	[0.00, .]	0.9822	.	[. , .]	.
	COPD Sev	Moderate	0.75	[0.32,1.79]	0.5241	.	[. , .]	.
		(Very) sev	1.02	[0.40,2.63]	0.9629	.	[. , .]	.
IHD	Cohort	QVA149	1.60	[0.77,3.34]	0.2064	.	[. , .]	.
	Age at start		1.03	[0.99,1.07]	0.1326	.	[. , .]	.
	Sex	Male	2.98	[1.26,7.05]	0.0129	.	[. , .]	.
	Smoking	Current	1.50	[0.19,11.9]	0.7006	.	[. , .]	.
		Past	0.90	[0.12,6.84]	0.9157	.	[. , .]	.
	COPD Sev	Moderate	0.76	[0.29,2.00]	0.5778	.	[. , .]	.
		(Very) sev	0.56	[0.18,1.76]	0.3215	.	[. , .]	.

Note: Run date and time 01NOV2018 11:20:06,
If no results, number of events was too low

QVA149A2402

Table 15-20-1 (Page 2 of 16)
Adjusted hazard ratios for QVA versus comparators (Model 1)
THIN - Total analysis population

			QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
Endpoint		Level	HR	95% CI	P	HR	95% CI	P
MACE	Cohort	QVA149	.	[. , .]	.	1.23	[0.77,1.95]	0.3945
	Age at start		.	[. , .]	.	1.05	[1.04,1.07]	<.0001
	Sex	Male	.	[. , .]	.	1.23	[0.96,1.58]	0.1026
	Smoking	Current	.	[. , .]	.	1.33	[0.80,2.24]	0.2743
		Past	.	[. , .]	.	1.00	[0.61,1.64]	0.9962
	COPD Sev	Moderate	.	[. , .]	.	1.13	[0.75,1.70]	0.5635
		(Very) sev	.	[. , .]	.	1.23	[0.80,1.88]	0.3473
IHD	Cohort	QVA149	.	[. , .]	.	1.57	[0.93,2.68]	0.0940
	Age at start		.	[. , .]	.	1.03	[1.01,1.05]	0.0002
	Sex	Male	.	[. , .]	.	1.70	[1.24,2.34]	0.0011
	Smoking	Current	.	[. , .]	.	1.33	[0.70,2.56]	0.3869
		Past	.	[. , .]	.	0.87	[0.46,1.63]	0.6602
	COPD Sev	Moderate	.	[. , .]	.	0.72	[0.47,1.12]	0.1505
		(Very) sev	.	[. , .]	.	0.74	[0.45,1.21]	0.2313

Note: Run date and time 01NOV2018 11:20:06,
If no results, number of events was too low

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Table 15-20-1 (Page 3 of 16)
Adjusted hazard ratios for QVA versus comparators (Model 1)
THIN - Total analysis population

			QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint		Level	HR	95% CI	P	HR	95% CI	P
MACE	Cohort	QVA149	1.70	[0.98,2.95]	0.0606	1.10	[0.59,2.05]	0.7596
	Age at start		1.03	[1.00,1.06]	0.0530	1.05	[1.02,1.08]	0.0032
	Sex	Male	1.51	[0.87,2.63]	0.1390	1.74	[0.92,3.29]	0.0861
	Smoking	Current	0.67	[0.19,2.34]	0.5257	26E5	[0.00, .]	0.9862
		Past	0.69	[0.21,2.25]	0.5341	13E5	[0.00, .]	0.9869
	COPD Sev	Moderate	0.67	[0.30,1.46]	0.3172	2.17	[0.66,7.07]	0.2052
		(Very) sev	1.02	[0.47,2.18]	0.9695	2.47	[0.53,11.4]	0.2643
IHD	Cohort	QVA149	2.11	[1.11,4.02]	0.0223	1.35	[0.67,2.74]	0.4058
	Age at start		1.00	[0.97,1.04]	0.7708	1.00	[0.96,1.03]	0.7737
	Sex	Male	1.68	[0.87,3.25]	0.1198	3.03	[1.36,6.76]	0.0067
	Smoking	Current	0.81	[0.18,3.62]	0.7806	0.96	[0.21,4.34]	0.9625
		Past	0.51	[0.12,2.19]	0.3634	0.39	[0.09,1.75]	0.2194
	COPD Sev	Moderate	0.75	[0.33,1.71]	0.4993	1.46	[0.51,4.17]	0.4827
		(Very) sev	0.68	[0.26,1.77]	0.4285	1.19	[0.31,4.58]	0.7974

Note: Run date and time 01NOV2018 11:20:06,
If no results, number of events was too low

QVA149A2402

Table 15-20-1 (Page 4 of 16)
Adjusted hazard ratios for QVA versus comparators (Model 1)
THIN - Total analysis population

			QVA compared to LAMA		
Endpoint		Level	HR	95% CI	P
MACE	Cohort	QVA149	1.30	[0.80,2.09]	0.2849
	Age at start		1.06	[1.04,1.07]	<.0001
	Sex	Male	1.42	[1.05,1.93]	0.0240
	Smoking	Current	2.44	[0.97,6.12]	0.0569
		Past	1.97	[0.80,4.87]	0.1396
	COPD Sev	Moderate	1.23	[0.75,2.02]	0.4246
		(Very) sev	1.13	[0.58,2.19]	0.7307
IHD	Cohort	QVA149	1.66	[0.96,2.87]	0.0675
	Age at start		1.01	[0.99,1.03]	0.2027
	Sex	Male	1.32	[0.91,1.92]	0.1420
	Smoking	Current	1.33	[0.47,3.77]	0.5862
		Past	1.46	[0.53,4.04]	0.4608
	COPD Sev	Moderate	0.84	[0.51,1.38]	0.4929
		(Very) sev	0.83	[0.44,1.54]	0.5504

Note: Run date and time 01NOV2018 11:20:06,
If no results, number of events was too low

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Table 15-20-1 (Page 5 of 16)
All hazard ratios in adjusted model (Model 1)
THIN - Total analysis population

			QVA compared to Free LABA+LAMA without ICS			QVA compared to Free LABA+LAMA with ICS		
Endpoint		Level	HR	95% CI	P	HR	95% CI	P
CARD	Cohort	QVA149	0.85	[0.31,2.36]	0.7550	.	[. , .]	.
	Age at start		1.04	[0.99,1.10]	0.1497	.	[. , .]	.
	Sex	Male	1.03	[0.38,2.81]	0.9543	.	[. , .]	.
	Smoking	Current	48E4	[0.00, .]	0.9893	.	[. , .]	.
		Past	58E4	[0.00, .]	0.9891	.	[. , .]	.
	COPD Sev	Moderate	1.48	[0.31,7.03]	0.6233	.	[. , .]	.
		(Very) sev	1.43	[0.25,8.08]	0.6864	.	[. , .]	.
CERE	Cohort	QVA149	1.05	[0.39,2.84]	0.9279	.	[. , .]	.
	Age at start		1.05	[1.00,1.11]	0.0702	.	[. , .]	.
	Sex	Male	0.82	[0.30,2.24]	0.7040	.	[. , .]	.
	Smoking	Current	57E4	[0.00, .]	0.9889	.	[. , .]	.
		Past	66E4	[0.00, .]	0.9888	.	[. , .]	.
	COPD Sev	Moderate	0.69	[0.19,2.50]	0.5679	.	[. , .]	.
		(Very) sev	0.87	[0.20,3.77]	0.8522	.	[. , .]	.

Note: Run date and time 01NOV2018 11:20:06,
If no results, number of events was too low

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Table 15-20-1 (Page 6 of 16)
Adjusted hazard ratios for QVA versus comparators (Model 1)
THIN - Total analysis population

			QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
Endpoint		Level	HR	95% CI	P	HR	95% CI	P
CARD	Cohort	QVA149	.	[. , .]	.	0.50	[0.22,1.12]	0.0931
	Age at start		.	[. , .]	.	1.07	[1.06,1.09]	<.0001
	Sex	Male	.	[. , .]	.	1.56	[1.16,2.09]	0.0031
	Smoking	Current	.	[. , .]	.	1.34	[0.74,2.43]	0.3345
		Past	.	[. , .]	.	1.04	[0.59,1.81]	0.8997
	COPD Sev	Moderate	.	[. , .]	.	1.34	[0.82,2.20]	0.2520
		(Very) sev	.	[. , .]	.	0.94	[0.54,1.64]	0.8304
CERE	Cohort	QVA149	.	[. , .]	.	0.83	[0.39,1.77]	0.6247
	Age at start		.	[. , .]	.	1.04	[1.03,1.06]	<.0001
	Sex	Male	.	[. , .]	.	0.97	[0.69,1.35]	0.8363
	Smoking	Current	.	[. , .]	.	1.04	[0.54,1.99]	0.9023
		Past	.	[. , .]	.	0.83	[0.45,1.54]	0.5596
	COPD Sev	Moderate	.	[. , .]	.	1.10	[0.67,1.78]	0.7135
		(Very) sev	.	[. , .]	.	1.04	[0.60,1.82]	0.8857

Note: Run date and time 01NOV2018 11:20:06,
If no results, number of events was too low

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Table 15-20-1 (Page 7 of 16)
Adjusted hazard ratios for QVA versus comparators (Model 1)
THIN - Total analysis population

			QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint		Level	HR	95% CI	P	HR	95% CI	P
CARD	Cohort	QVA149	0.77	[0.32,1.86]	0.5573	0.51	[0.19,1.36]	0.1776
	Age at start		1.07	[1.03,1.11]	0.0010	1.08	[1.03,1.13]	0.0011
	Sex	Male	1.59	[0.77,3.31]	0.2131	2.22	[0.85,5.78]	0.1032
	Smoking	Current	1.36	[0.17,11.1]	0.7757	49E5	[0.00, .]	0.9914
		Past	1.51	[0.20,11.3]	0.6865	17E5	[0.00, .]	0.9920
	COPD Sev	Moderate	1.11	[0.36,3.42]	0.8567	45.5	[0.00, .]	0.9925
		(Very) sev	0.93	[0.30,2.87]	0.8972	59.5	[0.00, .]	0.9919
CERE	Cohort	QVA149	0.89	[0.39,2.06]	0.7930	0.82	[0.33,2.04]	0.6687
	Age at start		1.05	[1.01,1.09]	0.0154	1.05	[1.00,1.10]	0.0407
	Sex	Male	1.02	[0.51,2.01]	0.9649	1.13	[0.48,2.64]	0.7757
	Smoking	Current	1.05	[0.13,8.69]	0.9654	18E5	[0.00, .]	0.9902
		Past	1.64	[0.22,12.2]	0.6292	18E5	[0.00, .]	0.9902
	COPD Sev	Moderate	1.04	[0.38,2.86]	0.9333	1.07	[0.37,3.08]	0.8953
		(Very) sev	0.67	[0.20,2.26]	0.5179	0.61	[0.13,2.84]	0.5263

Note: Run date and time 01NOV2018 11:20:06,
If no results, number of events was too low

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Table 15-20-1 (Page 8 of 16)
Adjusted hazard ratios for QVA versus comparators (Model 1)
THIN - Total analysis population

			QVA compared to LAMA		
Endpoint		Level	HR	95% CI	P
CARD	Cohort	QVA149	0.62	[0.27,1.42]	0.2602
	Age at start		1.07	[1.05,1.10]	<.0001
	Sex	Male	1.18	[0.81,1.72]	0.3941
	Smoking	Current	1.11	[0.51,2.41]	0.7941
		Past	0.85	[0.40,1.79]	0.6693
	COPD Sev	Moderate	0.97	[0.60,1.59]	0.9180
		(Very) sev	1.00	[0.54,1.88]	0.9903
CERE	Cohort	QVA149	0.70	[0.33,1.52]	0.3707
	Age at start		1.04	[1.02,1.06]	0.0001
	Sex	Male	1.32	[0.91,1.91]	0.1506
	Smoking	Current	1.36	[0.53,3.48]	0.5210
		Past	1.18	[0.47,2.96]	0.7179
	COPD Sev	Moderate	1.75	[0.98,3.11]	0.0585
		(Very) sev	1.47	[0.70,3.12]	0.3150

Note: Run date and time 01NOV2018 11:20:06,
If no results, number of events was too low

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Table 15-20-1 (Page 9 of 16)
All hazard ratios in adjusted model (Model 1)
THIN - Total analysis population

Endpoint		Level	QVA compared to Free LABA+LAMA without ICS HR	95% CI	P	QVA compared to Free LABA+LAMA with ICS HR	95% CI	P
BPHURIN	Cohort	QVA149	1.03	[0.36,2.92]	0.9542	.	[. , .]	.
	Age at start		1.04	[0.99,1.10]	0.1245	.	[. , .]	.
	Sex	Male	12.3	[1.60,94.3]	0.0159	.	[. , .]	.
	Smoking	Current	89E4	[0.00, .]	0.9895	.	[. , .]	.
		Past	38E4	[0.00, .]	0.9902	.	[. , .]	.
	COPD Sev	Moderate	1.78	[0.21,15.1]	0.5976	.	[. , .]	.
		(Very) sev	2.08	[0.23,18.7]	0.5159	.	[. , .]	.
DMVAL	Cohort	QVA149	0.67	[0.29,1.53]	0.3382	.	[. , .]	.
	Age at start		1.01	[0.97,1.05]	0.7610	.	[. , .]	.
	Sex	Male	1.39	[0.63,3.06]	0.4176	.	[. , .]	.
	Smoking	Current	2E5	[0.00, .]	0.9876	.	[. , .]	.
		Past	82E4	[0.00, .]	0.9861	.	[. , .]	.
	COPD Sev	Moderate	1.23	[0.33,4.58]	0.7646	.	[. , .]	.
		(Very) sev	1.16	[0.30,4.48]	0.8293	.	[. , .]	.

Note: Run date and time 01NOV2018 11:20:06,
If no results, number of events was too low

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Table 15-20-1 (Page 10 of 16)
Adjusted hazard ratios for QVA versus comparators (Model 1)
THIN - Total analysis population

			QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
Endpoint		Level	HR	95% CI	P	HR	95% CI	P
BPHURIN	Cohort	QVA149	.	[. , .]	.	0.95	[0.42,2.17]	0.9037
	Age at start		.	[. , .]	.	1.05	[1.03,1.08]	<.0001
	Sex	Male	.	[. , .]	.	31.0	[9.80,97.9]	<.0001
	Smoking	Current	.	[. , .]	.	1.37	[0.47,3.97]	0.5653
		Past	.	[. , .]	.	1.56	[0.57,4.28]	0.3867
	COPD Sev	Moderate	.	[. , .]	.	0.96	[0.53,1.73]	0.8825
		(Very) sev	.	[. , .]	.	0.80	[0.41,1.58]	0.5225
DMVAL	Cohort	QVA149	.	[. , .]	.	0.96	[0.47,1.96]	0.9126
	Age at start		.	[. , .]	.	1.00	[0.99,1.02]	0.7304
	Sex	Male	.	[. , .]	.	1.34	[0.96,1.86]	0.0848
	Smoking	Current	.	[. , .]	.	0.86	[0.43,1.72]	0.6697
		Past	.	[. , .]	.	0.98	[0.50,1.89]	0.9427
	COPD Sev	Moderate	.	[. , .]	.	1.05	[0.68,1.63]	0.8192
		(Very) sev	.	[. , .]	.	0.94	[0.55,1.62]	0.8228

Note: Run date and time 01NOV2018 11:20:06,
If no results, number of events was too low

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Table 15-20-1 (Page 11 of 16)
Adjusted hazard ratios for QVA versus comparators (Model 1)
THIN - Total analysis population

			QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint		Level	HR	95% CI	P	HR	95% CI	P
BPHURIN	Cohort	QVA149	1.56	[0.60,4.06]	0.3655	0.91	[0.32,2.61]	0.8682
	Age at start		1.05	[1.00,1.10]	0.0753	1.02	[0.97,1.07]	0.4068
	Sex	Male	24E6	[0.00, .]	0.9889	14.8	[1.94, 113]	0.0094
	Smoking	Current	97E5	[0.00, .]	0.9968	1.06	[0.12,9.26]	0.9599
		Past	1E7	[0.00, .]	0.9968	0.60	[0.07,4.88]	0.6340
	COPD Sev	Moderate	0.73	[0.23,2.34]	0.5978	0.63	[0.17,2.36]	0.4924
		(Very) sev	0.73	[0.19,2.86]	0.6552	0.67	[0.12,3.68]	0.6491
DMVAL	Cohort	QVA149	0.97	[0.44,2.13]	0.9337	0.86	[0.36,2.05]	0.7323
	Age at start		0.97	[0.93,1.00]	0.0329	1.00	[0.96,1.04]	0.8380
	Sex	Male	0.70	[0.36,1.36]	0.2950	1.05	[0.46,2.36]	0.9109
	Smoking	Current	0.11	[0.03,0.46]	0.0023	0.19	[0.03,1.11]	0.0653
		Past	0.34	[0.10,1.15]	0.0821	0.66	[0.15,2.86]	0.5776
	COPD Sev	Moderate	0.72	[0.24,2.17]	0.5640	74.3	[0.00, .]	0.9908
		(Very) sev	1.06	[0.34,3.34]	0.9192	54.4	[0.00, .]	0.9914

Note: Run date and time 01NOV2018 11:20:06,
If no results, number of events was too low

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Table 15-20-1 (Page 12 of 16)
Adjusted hazard ratios for QVA versus comparators (Model 1)
THIN - Total analysis population

			QVA compared to LAMA		
Endpoint		Level	HR	95% CI	P
BPHURIN	Cohort	QVA149	0.97	[0.42,2.25]	0.9503
	Age at start		1.05	[1.03,1.08]	<.0001
	Sex	Male	30.2	[7.40, 123]	<.0001
	Smoking	Current	1.70	[0.40,7.29]	0.4729
		Past	1.59	[0.38,6.57]	0.5221
	COPD Sev	Moderate	1.93	[0.87,4.27]	0.1046
		(Very) sev	1.98	[0.83,4.73]	0.1239
DMVAL	Cohort	QVA149	0.89	[0.43,1.84]	0.7544
	Age at start		0.99	[0.97,1.01]	0.3801
	Sex	Male	1.63	[1.11,2.41]	0.0130
	Smoking	Current	0.81	[0.28,2.32]	0.6958
		Past	1.43	[0.52,3.95]	0.4843
	COPD Sev	Moderate	1.21	[0.64,2.31]	0.5613
		(Very) sev	1.03	[0.48,2.21]	0.9309

Note: Run date and time 01NOV2018 11:20:06,
If no results, number of events was too low

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Table 15-20-1 (Page 13 of 16)
All hazard ratios in adjusted model (Model 1)
THIN - Total analysis population

			QVA compared to Free LABA+LAMA without ICS			QVA compared to Free LABA+LAMA with ICS		
Endpoint		Level	HR	95% CI	P	HR	95% CI	P
DEATH	Cohort	QVA149	3.06	[1.94,4.83]	<.0001	.	[. , .]	.
	Age at start		1.07	[1.05,1.10]	<.0001	.	[. , .]	.
	Sex	Male	1.44	[0.92,2.24]	0.1117	.	[. , .]	.
	Smoking	Current	1.24	[0.37,4.15]	0.7318	.	[. , .]	.
		Past	1.20	[0.37,3.85]	0.7599	.	[. , .]	.
	COPD Sev	Moderate	0.77	[0.41,1.45]	0.4266	.	[. , .]	.
		(Very) sev	1.56	[0.79,3.08]	0.2011	.	[. , .]	.

Note: Run date and time 01NOV2018 11:20:06,
If no results, number of events was too low

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Table 15-20-1 (Page 14 of 16)
Adjusted hazard ratios for QVA versus comparators (Model 1)
THIN - Total analysis population

			QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
Endpoint		Level	HR	95% CI	P	HR	95% CI	P
DEATH	Cohort	QVA149	1.69	[0.79,3.63]	0.1757	1.49	[1.15,1.94]	0.0028
	Age at start		1.08	[1.05,1.11]	<.0001	1.09	[1.08,1.10]	<.0001
	Sex	Male	1.94	[1.15,3.27]	0.0128	1.09	[0.93,1.26]	0.2955
	Smoking	Current	1.37	[0.39,4.80]	0.6183	1.93	[1.37,2.74]	0.0002
		Past	1.44	[0.44,4.71]	0.5442	1.42	[1.02,1.98]	0.0381
	COPD Sev	Moderate	0.75	[0.38,1.48]	0.4123	1.06	[0.78,1.42]	0.7236
		(Very) sev	1.31	[0.61,2.82]	0.4970	1.70	[1.27,2.27]	0.0011

Note: Run date and time 01NOV2018 11:20:06,
If no results, number of events was too low

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Table 15-20-1 (Page 15 of 16)
Adjusted hazard ratios for QVA versus comparators (Model 1)
THIN - Total analysis population

			QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint		Level	HR	95% CI	P	HR	95% CI	P
DEATH	Cohort	QVA149	1.98	[1.44,2.72]	<.0001	1.76	[1.20,2.60]	0.0042
	Age at start		1.07	[1.05,1.09]	<.0001	1.10	[1.07,1.12]	<.0001
	Sex	Male	1.88	[1.33,2.64]	0.0003	1.56	[1.05,2.34]	0.0290
	Smoking	Current	1.50	[0.59,3.80]	0.3955	1.59	[0.61,4.14]	0.3412
		Past	1.34	[0.54,3.29]	0.5284	1.22	[0.49,3.03]	0.6741
	COPD Sev	Moderate	1.10	[0.66,1.83]	0.7186	1.27	[0.69,2.32]	0.4425
		(Very) sev	1.82	[1.02,3.27]	0.0514	1.92	[0.97,3.79]	0.0667

Note: Run date and time 01NOV2018 11:20:06,
If no results, number of events was too low

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Table 15-20-1 (Page 16 of 16)
Adjusted hazard ratios for QVA versus comparators (Model 1)
THIN - Total analysis population

			QVA compared to LAMA		
Endpoint		Level	HR	95% CI	P
DEATH	Cohort	QVA149	2.16	[1.63,2.85]	<.0001
	Age at start		1.09	[1.08,1.10]	<.0001
	Sex	Male	1.06	[0.86,1.31]	0.5938
	Smoking	Current	1.30	[0.83,2.05]	0.2494
		Past	0.91	[0.58,1.40]	0.6565
	COPD Sev	Moderate	1.29	[0.94,1.77]	0.1182
		(Very) sev	2.17	[1.54,3.05]	<.0001

Note: Run date and time 01NOV2018 11:20:06,
If no results, number of events was too low

QVA149A2402

Table 15-20-2 (Page 1 of 12)
All hazard ratios in adjusted model (Model 1)
IPCI - Total analysis population

			QVA compared to Free LABA+LAMA without ICS			QVA compared to Free LABA+LAMA with ICS		
Endpoint		Level	HR	95% CI	P	HR	95% CI	P
MACE	Cohort	QVA149	1.07	[0.51,2.25]	0.8599	0.98	[0.36,2.70]	0.9724
	Age at start		1.07	[1.03,1.12]	0.0009	1.01	[0.96,1.06]	0.6489
	Sex	Male	1.17	[0.54,2.57]	0.6903	1.20	[0.46,3.10]	0.7107
	Smoking	Current	2.09	[0.26,17.0]	0.4909	4304	[0.00, .]	0.9918
		Past	1.59	[0.20,12.8]	0.6645	5673	[0.00, .]	0.9915
	COPD Sev	Moderate	1.34	[0.24,7.42]	0.7435	1.65	[0.21,13.0]	0.6390
		(Very) sev	1.16	[0.25,5.41]	0.8531	1.54	[0.15,16.4]	0.7226
CARD	Cohort	QVA149	1.23	[0.44,3.44]	0.6916	0.51	[0.17,1.55]	0.2353
	Age at start		1.07	[1.01,1.14]	0.0145	1.07	[1.01,1.13]	0.0305
	Sex	Male	3.77	[0.84,16.9]	0.0821	0.97	[0.33,2.87]	0.9546
	Smoking	Current	16E5	[0.00, .]	0.9926	12E3	[0.00, .]	0.9921
		Past	13E5	[0.00, .]	0.9927	5921	[0.00, .]	0.9927
	COPD Sev	Moderate	0.72	[0.17,3.05]	0.6511	0.58	[0.12,2.70]	0.4902
		(Very) sev	0.93	[0.11,8.08]	0.9452	0.58	[0.10,3.30]	0.5398

Note: Run date and time 01NOV2018 11:20:18,
If no results, number of events was too low

QVA149A2402

Table 15-20-2 (Page 2 of 12)
Adjusted hazard ratios for QVA versus comparators (Model 1)
IPCI - Total analysis population

			QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
Endpoint		Level	HR	95% CI	P	HR	95% CI	P
MACE	Cohort	QVA149	0.77	[0.30,1.95]	0.5754	0.73	[0.41,1.31]	0.2936
	Age at start		1.04	[1.00,1.09]	0.0482	1.07	[1.05,1.08]	<.0001
	Sex	Male	0.94	[0.41,2.18]	0.8857	1.21	[0.86,1.71]	0.2711
	Smoking	Current	0.83	[0.18,3.77]	0.8063	1.00	[0.53,1.90]	0.9921
		Past	0.78	[0.20,3.09]	0.7258	1.09	[0.61,1.94]	0.7733
	COPD Sev	Moderate	0.81	[0.26,2.54]	0.7197	1.46	[0.91,2.34]	0.1254
		(Very) sev	0.90	[0.21,3.97]	0.8932	2.06	[1.02,4.19]	0.0597
CARD	Cohort	QVA149	0.59	[0.16,2.13]	0.4191	1.37	[0.64,2.95]	0.4231
	Age at start		1.10	[1.04,1.17]	0.0018	1.06	[1.04,1.09]	<.0001
	Sex	Male	2.64	[0.76,9.17]	0.1256	1.66	[0.96,2.89]	0.0713
	Smoking	Current	1.44	[0.25,8.24]	0.6797	0.53	[0.23,1.22]	0.1362
		Past	0.33	[0.04,2.70]	0.3032	0.47	[0.23,0.97]	0.0422
	COPD Sev	Moderate	0.78	[0.12,4.96]	0.7988	0.98	[0.43,2.21]	0.9605
		(Very) sev	0.87	[0.07,10.9]	0.9134	0.79	[0.31,2.05]	0.6321

Note: Run date and time 01NOV2018 11:20:18,
If no results, number of events was too low

QVA149A2402

Table 15-20-2 (Page 3 of 12)
Adjusted hazard ratios for QVA versus comparators (Model 1)
IPCI - Total analysis population

			QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint		Level	HR	95% CI	P	HR	95% CI	P
MACE	Cohort	QVA149	1.00	[0.49,2.04]	0.9960	1.06	[0.50,2.27]	0.8752
	Age at start		1.04	[1.00,1.08]	0.0444	1.07	[1.03,1.11]	0.0006
	Sex	Male	1.32	[0.63,2.79]	0.4612	0.89	[0.43,1.83]	0.7427
	Smoking	Current	1.24	[0.13,11.6]	0.8486	4.71	[0.58,38.6]	0.1486
		Past	1.35	[0.15,12.6]	0.7917	2.24	[0.28,18.0]	0.4466
	COPD Sev	Moderate	2.13	[0.24,18.7]	0.5087	1.47	[0.37,5.88]	0.5993
		(Very) sev	2.14	[0.32,14.3]	0.4384	0.69	[0.15,3.16]	0.6328
CARD	Cohort	QVA149	1.80	[0.62,5.25]	0.2806	.	[. , .]	.
	Age at start		1.07	[1.01,1.14]	0.0241	.	[. , .]	.
	Sex	Male	3.75	[0.83,16.9]	0.0850	.	[. , .]	.
	Smoking	Current	15E5	[0.00, .]	0.9926	.	[. , .]	.
		Past	13E5	[0.00, .]	0.9927	.	[. , .]	.
	COPD Sev	Moderate	0.56	[0.09,3.67]	0.5516	.	[. , .]	.
		(Very) sev	1.38	[0.20,9.46]	0.7460	.	[. , .]	.

Note: Run date and time 01NOV2018 11:20:18,
If no results, number of events was too low

QVA149A2402

Table 15-20-2 (Page 4 of 12)
Adjusted hazard ratios for QVA versus comparators (Model 1)
IPCI - Total analysis population

			QVA compared to LAMA		
Endpoint		Level	HR	95% CI	P
MACE	Cohort	QVA149	0.86	[0.47,1.57]	0.6241
	Age at start		1.05	[1.03,1.07]	<.0001
	Sex	Male	1.60	[1.04,2.47]	0.0321
	Smoking	Current	2.44	[0.72,8.24]	0.1541
		Past	1.32	[0.39,4.43]	0.6587
	COPD Sev	Moderate	1.14	[0.65,2.01]	0.6442
		(Very) sev	1.15	[0.48,2.71]	0.7589
CARD	Cohort	QVA149	1.05	[0.48,2.27]	0.9029
	Age at start		1.03	[1.00,1.06]	0.0391
	Sex	Male	2.18	[1.18,4.03]	0.0133
	Smoking	Current	3.20	[0.43,23.7]	0.2577
		Past	2.11	[0.29,15.5]	0.4623
	COPD Sev	Moderate	0.61	[0.30,1.27]	0.1981
		(Very) sev	0.67	[0.24,1.87]	0.4484

Note: Run date and time 01NOV2018 11:20:18,
If no results, number of events was too low

QVA149A2402

Table 15-20-2 (Page 5 of 12)
All hazard ratios in adjusted model (Model 1)
IPCI - Total analysis population

			QVA compared to Free LABA+LAMA without ICS			QVA compared to Free LABA+LAMA with ICS		
Endpoint		Level	HR	95% CI	P	HR	95% CI	P
CERE	Cohort	QVA149	2.64	[0.90,7.72]	0.0764	.	[. , .]	.
	Age at start		1.07	[1.01,1.13]	0.0236	.	[. , .]	.
	Sex	Male	1.36	[0.46,4.02]	0.5806	.	[. , .]	.
	Smoking	Current	0.88	[0.10,7.94]	0.9121	.	[. , .]	.
		Past	0.81	[0.09,7.02]	0.8453	.	[. , .]	.
	COPD Sev	Moderate	2.00	[0.25,16.2]	0.5202	.	[. , .]	.
		(Very) sev	1.40	[0.13,14.8]	0.7824	.	[. , .]	.
BPHURIN	Cohort	QVA149	2.35	[0.77,7.23]	0.1345	.	[. , .]	.
	Age at start		1.10	[1.03,1.18]	0.0030	.	[. , .]	.
	Sex	Male	8.94	[1.10,72.7]	0.0404	.	[. , .]	.
	Smoking	Current	0.28	[0.03,2.90]	0.2851	.	[. , .]	.
		Past	0.62	[0.07,5.27]	0.6639	.	[. , .]	.
	COPD Sev	Moderate	0.95	[0.19,4.81]	0.9485	.	[. , .]	.
		(Very) sev	0.01	[0.00, .]	0.9959	.	[. , .]	.

Note: Run date and time 01NOV2018 11:20:18,
If no results, number of events was too low

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Table 15-20-2 (Page 6 of 12)
Adjusted hazard ratios for QVA versus comparators (Model 1)
IPCI - Total analysis population

			QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
Endpoint		Level	HR	95% CI	P	HR	95% CI	P
CERE	Cohort	QVA149	1.34	[0.40,4.56]	0.6366	1.92	[0.97,3.80]	0.0612
	Age at start		1.04	[0.98,1.09]	0.1766	1.04	[1.02,1.07]	0.0012
	Sex	Male	1.15	[0.40,3.27]	0.7951	1.24	[0.72,2.12]	0.4339
	Smoking	Current	0.43	[0.09,2.05]	0.2865	0.53	[0.21,1.32]	0.1729
		Past	0.36	[0.08,1.54]	0.1687	0.60	[0.27,1.34]	0.2115
	COPD Sev	Moderate	1.42	[0.33,6.05]	0.6381	1.37	[0.61,3.06]	0.4499
		(Very) sev	0.58	[0.06,5.69]	0.6411	0.89	[0.20,4.09]	0.8875
BPHURIN	Cohort	QVA149	.	[. , .]	.	1.50	[0.72,3.12]	0.2761
	Age at start		.	[. , .]	.	1.08	[1.05,1.11]	<.0001
	Sex	Male	.	[. , .]	.	8.54	[3.36,21.7]	<.0001
	Smoking	Current	.	[. , .]	.	0.96	[0.35,2.65]	0.9329
		Past	.	[. , .]	.	0.88	[0.33,2.32]	0.7905
	COPD Sev	Moderate	.	[. , .]	.	1.27	[0.50,3.20]	0.6214
		(Very) sev	.	[. , .]	.	0.58	[0.18,1.84]	0.3581

Note: Run date and time 01NOV2018 11:20:18,
If no results, number of events was too low

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Table 15-20-2 (Page 7 of 12)
Adjusted hazard ratios for QVA versus comparators (Model 1)
IPCI - Total analysis population

			QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint		Level	HR	95% CI	P	HR	95% CI	P
CERE	Cohort	QVA149	.	[. , .]	.	1.51	[0.63,3.59]	0.3544
	Age at start		.	[. , .]	.	1.03	[0.99,1.07]	0.1717
	Sex	Male	.	[. , .]	.	1.06	[0.45,2.47]	0.8998
	Smoking	Current	.	[. , .]	.	0.95	[0.18,4.92]	0.9467
		Past	.	[. , .]	.	0.52	[0.10,2.77]	0.4473
	COPD Sev	Moderate	.	[. , .]	.	1.09	[0.33,3.61]	0.8913
		(Very) sev	.	[. , .]	.	0.02	[0.00, .]	0.9928
BPHURIN	Cohort	QVA149	1.47	[0.58,3.74]	0.4193	2.40	[0.80,7.24]	0.1205
	Age at start		1.05	[1.00,1.11]	0.0749	1.06	[1.00,1.12]	0.0558
	Sex	Male	11.8	[1.55,90.4]	0.0171	21E6	[0.00, .]	0.9903
	Smoking	Current	0.28	[0.03,2.84]	0.2818	0.26	[0.02,3.89]	0.3367
		Past	0.89	[0.11,7.02]	0.9111	0.66	[0.07,6.03]	0.7113
	COPD Sev	Moderate	0.79	[0.21,2.95]	0.7253	1.12	[0.24,5.16]	0.8890
		(Very) sev	0.33	[0.04,2.81]	0.3195	0.02	[0.00, .]	0.9964

Note: Run date and time 01NOV2018 11:20:18,
If no results, number of events was too low

QVA149A2402

Table 15-20-2 (Page 8 of 12)
Adjusted hazard ratios for QVA versus comparators (Model 1)
IPCI - Total analysis population

			QVA compared to LAMA		
Endpoint		Level	HR	95% CI	P
CERE	Cohort	QVA149	1.87	[0.92,3.77]	0.0823
	Age at start		1.04	[1.01,1.07]	0.0066
	Sex	Male	2.00	[1.03,3.91]	0.0416
	Smoking	Current	3.00	[0.38,23.9]	0.3000
		Past	2.42	[0.31,19.1]	0.4015
	COPD Sev	Moderate	0.74	[0.36,1.54]	0.4220
		(Very) sev	0.54	[0.14,2.02]	0.3648
BPHURIN	Cohort	QVA149	1.26	[0.60,2.65]	0.5442
	Age at start		1.06	[1.03,1.10]	0.0001
	Sex	Male	7.68	[2.73,21.6]	0.0001
	Smoking	Current	0.89	[0.20,4.05]	0.8793
		Past	1.15	[0.27,4.82]	0.8500
	COPD Sev	Moderate	1.19	[0.54,2.62]	0.6644
		(Very) sev	1.15	[0.42,3.14]	0.7865

Note: Run date and time 01NOV2018 11:20:18,
If no results, number of events was too low

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Table 15-20-2 (Page 9 of 12)
All hazard ratios in adjusted model (Model 1)
IPCI - Total analysis population

			QVA compared to Free LABA+LAMA without ICS			QVA compared to Free LABA+LAMA with ICS		
Endpoint		Level	HR	95% CI	P	HR	95% CI	P
DMVAL	Cohort	QVA149	.	[. , .]	.	.	[. , .]	.
	Age at start		.	[. , .]	.	.	[. , .]	.
	Sex	Male	.	[. , .]	.	.	[. , .]	.
	Smoking	Current	.	[. , .]	.	.	[. , .]	.
		Past	.	[. , .]	.	.	[. , .]	.
	COPD Sev	Moderate	.	[. , .]	.	.	[. , .]	.
		(Very) sev	.	[. , .]	.	.	[. , .]	.
DEATH	Cohort	QVA149	0.80	[0.41,1.55]	0.5084	1.25	[0.46,3.36]	0.6634
	Age at start		1.08	[1.04,1.13]	<.0001	1.04	[0.99,1.09]	0.0955
	Sex	Male	0.91	[0.47,1.79]	0.7935	0.86	[0.35,2.08]	0.7317
	Smoking	Current	1.10	[0.23,5.22]	0.9013	0.98	[0.11,9.05]	0.9841
		Past	1.11	[0.24,5.11]	0.8899	1.78	[0.22,14.5]	0.5920
	COPD Sev	Moderate	3.23	[0.72,14.5]	0.1313	52.1	[0.00, .]	0.9931
		(Very) sev	2.87	[0.42,19.8]	0.2988	36.7	[0.00, .]	0.9937

Note: Run date and time 01NOV2018 11:20:18,
If no results, number of events was too low

QVA149A2402

Table 15-20-2 (Page 10 of 12)
Adjusted hazard ratios for QVA versus comparators (Model 1)
IPCI - Total analysis population

			QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
Endpoint		Level	HR	95% CI	P	HR	95% CI	P
DMVAL	Cohort	QVA149	.	[. , .]	.	1.38	[0.50,3.80]	0.5282
	Age at start		.	[. , .]	.	0.99	[0.96,1.03]	0.6570
	Sex	Male	.	[. , .]	.	3.63	[1.47,8.98]	0.0053
	Smoking	Current	.	[. , .]	.	0.85	[0.11,6.50]	0.8735
		Past	.	[. , .]	.	1.62	[0.22,12.0]	0.6380
	COPD Sev	Moderate	.	[. , .]	.	1.40	[0.42,4.67]	0.5874
		(Very) sev	.	[. , .]	.	1.81	[0.36,9.14]	0.4825
DEATH	Cohort	QVA149	0.50	[0.20,1.22]	0.1285	0.66	[0.39,1.13]	0.1332
	Age at start		1.08	[1.03,1.12]	0.0007	1.08	[1.07,1.10]	<.0001
	Sex	Male	1.16	[0.53,2.56]	0.7071	1.03	[0.76,1.39]	0.8714
	Smoking	Current	1.29	[0.24,7.05]	0.7692	1.54	[0.80,2.95]	0.2001
		Past	1.13	[0.23,5.57]	0.8844	1.18	[0.67,2.10]	0.5640
	COPD Sev	Moderate	1.96	[0.50,7.79]	0.3442	1.46	[0.96,2.22]	0.0841
		(Very) sev	2.99	[0.56,15.9]	0.2118	1.97	[1.10,3.54]	0.0311

Note: Run date and time 01NOV2018 11:20:18,
If no results, number of events was too low

QVA149A2402

Table 15-20-2 (Page 11 of 12)
Adjusted hazard ratios for QVA versus comparators (Model 1)
IPCI - Total analysis population

			QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint		Level	HR	95% CI	P	HR	95% CI	P
DMVAL	Cohort	QVA149	.	[. , .]	.	.	[. , .]	.
	Age at start		.	[. , .]	.	.	[. , .]	.
	Sex	Male	.	[. , .]	.	.	[. , .]	.
	Smoking	Current	.	[. , .]	.	.	[. , .]	.
		Past	.	[. , .]	.	.	[. , .]	.
	COPD Sev	Moderate	.	[. , .]	.	.	[. , .]	.
		(Very) sev	.	[. , .]	.	.	[. , .]	.
DEATH	Cohort	QVA149	1.20	[0.60,2.37]	0.6082	0.71	[0.36,1.38]	0.3132
	Age at start		1.09	[1.05,1.14]	<.0001	1.08	[1.05,1.11]	<.0001
	Sex	Male	0.62	[0.31,1.25]	0.1818	0.50	[0.27,0.90]	0.0207
	Smoking	Current	0.70	[0.18,2.77]	0.6090	4.34	[0.95,19.8]	0.0579
		Past	1.07	[0.30,3.91]	0.9128	2.50	[0.56,11.1]	0.2276
	COPD Sev	Moderate	46.8	[0.00, .]	0.9918	1.47	[0.57,3.79]	0.4374
		(Very) sev	39.6	[0.00, .]	0.9922	1.34	[0.27,6.51]	0.7273

Note: Run date and time 01NOV2018 11:20:18,
If no results, number of events was too low

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Table 15-20-2 (Page 12 of 12)
Adjusted hazard ratios for QVA versus comparators (Model 1)
IPCI - Total analysis population

			QVA compared to LAMA		
Endpoint		Level	HR	95% CI	P
DMVAL	Cohort	QVA149	1.79	[0.63,5.09]	0.2720
	Age at start		1.02	[0.97,1.06]	0.4895
	Sex	Male	1.54	[0.61,3.88]	0.3649
	Smoking	Current	0.76	[0.10,6.06]	0.7997
		Past	0.83	[0.09,7.43]	0.8656
	COPD Sev	Moderate	1.65	[0.37,7.40]	0.5221
		(Very) sev	1.01	[0.09,11.3]	0.9918
DEATH	Cohort	QVA149	1.10	[0.61,1.97]	0.7556
	Age at start		1.08	[1.06,1.11]	<.0001
	Sex	Male	1.66	[1.05,2.62]	0.0297
	Smoking	Current	1.45	[0.58,3.61]	0.4308
		Past	0.81	[0.30,2.24]	0.6915
	COPD Sev	Moderate	1.30	[0.58,2.95]	0.5353
		(Very) sev	1.37	[0.38,4.95]	0.6482

Note: Run date and time 01NOV2018 11:20:18,
If no results, number of events was too low

QVA149A2402

Table 15-20-3 (Page 1 of 16)
All hazard ratios in adjusted model (Model 1)
AUH - Total analysis population

			QVA compared to Free LABA+LAMA without ICS			QVA compared to Free LABA+LAMA with ICS		
Endpoint		Level	HR	95% CI	P	HR	95% CI	P
MACE	Cohort	QVA149	1.16	[0.78,1.74]	0.4629	0.80	[0.46,1.40]	0.4355
	Age at start		1.03	[1.01,1.05]	0.0006	1.02	[1.00,1.04]	0.0130
	Sex	Male	1.85	[1.33,2.59]	0.0003	1.90	[1.33,2.71]	0.0004
	Smoking	Current	1.50	[0.59,3.78]	0.3913	1.37	[0.46,4.07]	0.5742
		Past	1.35	[0.52,3.46]	0.5379	1.36	[0.46,4.04]	0.5807
	COPD Sev	Moderate	0.98	[0.46,2.08]	0.9615	1.14	[0.39,3.35]	0.8174
		(Very) sev	0.95	[0.46,1.94]	0.8810	1.14	[0.39,3.35]	0.8120
IHD	Cohort	QVA149	.	[. , .]	.	.	[. , .]	.
	Age at start		.	[. , .]	.	.	[. , .]	.
	Sex	Male	.	[. , .]	.	.	[. , .]	.
	Smoking	Current	.	[. , .]	.	.	[. , .]	.
		Past	.	[. , .]	.	.	[. , .]	.
	COPD Sev	Moderate	.	[. , .]	.	.	[. , .]	.
		(Very) sev	.	[. , .]	.	.	[. , .]	.

Note: Run date and time 01NOV2018 11:20:29,
If no results, number of events was too low

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Table 15-20-3 (Page 2 of 16)
Adjusted hazard ratios for QVA versus comparators (Model 1)
AUH - Total analysis population

			QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
Endpoint		Level	HR	95% CI	P	HR	95% CI	P
MACE	Cohort	QVA149	1.02	[0.56,1.87]	0.9413	0.91	[0.73,1.13]	0.3995
	Age at start		1.03	[1.01,1.05]	0.0043	1.04	[1.03,1.05]	<.0001
	Sex	Male	1.92	[1.34,2.76]	0.0004	1.65	[1.33,2.06]	<.0001
	Smoking	Current	1.51	[0.56,4.10]	0.4134	1.34	[0.76,2.36]	0.3188
		Past	1.46	[0.55,3.92]	0.4493	1.24	[0.73,2.10]	0.4374
	COPD Sev	Moderate	1.28	[0.33,4.89]	0.7254	1.54	[0.83,2.84]	0.1759
		(Very) sev	1.33	[0.35,5.05]	0.6795	1.62	[0.84,3.12]	0.1611
IHD	Cohort	QVA149	.	[. , .]	.	1.33	[0.83,2.13]	0.2318
	Age at start		.	[. , .]	.	1.01	[0.99,1.04]	0.2073
	Sex	Male	.	[. , .]	.	2.00	[1.23,3.25]	0.0055
	Smoking	Current	.	[. , .]	.	1.34	[0.38,4.70]	0.6482
		Past	.	[. , .]	.	0.98	[0.27,3.57]	0.9703
	COPD Sev	Moderate	.	[. , .]	.	1.50	[0.26,8.78]	0.6598
		(Very) sev	.	[. , .]	.	0.85	[0.21,3.47]	0.8198

Note: Run date and time 01NOV2018 11:20:29,
If no results, number of events was too low

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Table 15-20-3 (Page 3 of 16)
Adjusted hazard ratios for QVA versus comparators (Model 1)
AUH - Total analysis population

			QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint		Level	HR	95% CI	P	HR	95% CI	P
MACE	Cohort	QVA149	0.96	[0.75,1.24]	0.7600	1.46	[1.01,2.12]	0.0469
	Age at start		1.03	[1.02,1.04]	<.0001	1.03	[1.01,1.05]	0.0004
	Sex	Male	1.86	[1.42,2.43]	<.0001	1.44	[1.06,1.98]	0.0217
	Smoking	Current	1.23	[0.62,2.43]	0.5494	1.02	[0.49,2.10]	0.9608
		Past	1.13	[0.58,2.21]	0.7246	0.97	[0.46,2.04]	0.9415
	COPD Sev	Moderate	1.07	[0.54,2.11]	0.8499	1.13	[0.53,2.40]	0.7566
		(Very) sev	1.20	[0.58,2.46]	0.6279	1.11	[0.54,2.31]	0.7725
IHD	Cohort	QVA149	2.20	[1.16,4.20]	0.0162	1.39	[0.68,2.87]	0.3692
	Age at start		0.99	[0.96,1.02]	0.6596	0.99	[0.96,1.02]	0.5757
	Sex	Male	3.02	[1.53,5.97]	0.0015	2.50	[1.28,4.90]	0.0073
	Smoking	Current	15E5	[0.00, .]	0.9873	14E5	[0.00, .]	0.9872
		Past	13E5	[0.00, .]	0.9874	14E5	[0.00, .]	0.9873
	COPD Sev	Moderate	26.5	[0.00, .]	0.9949	23.9	[0.00, .]	0.9938
		(Very) sev	16.5	[0.00, .]	0.9956	15.9	[0.00, .]	0.9946

Note: Run date and time 01NOV2018 11:20:29,
If no results, number of events was too low

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Table 15-20-3 (Page 4 of 16)
Adjusted hazard ratios for QVA versus comparators (Model 1)
AUH - Total analysis population

			QVA compared to LAMA		
Endpoint		Level	HR	95% CI	P
MACE	Cohort	QVA149	0.82	[0.63,1.06]	0.1268
	Age at start		1.03	[1.02,1.05]	<.0001
	Sex	Male	1.61	[1.25,2.08]	0.0003
	Smoking	Current	1.66	[0.83,3.31]	0.1533
		Past	1.64	[0.83,3.23]	0.1562
	COPD Sev	Moderate	1.34	[0.55,3.28]	0.5338
		(Very) sev	1.51	[0.68,3.33]	0.3283
IHD	Cohort	QVA149	1.85	[0.98,3.49]	0.0586
	Age at start		1.00	[0.98,1.03]	0.7604
	Sex	Male	1.70	[0.94,3.08]	0.0819
	Smoking	Current	87E3	[0.00, .]	0.9852
		Past	85E3	[0.00, .]	0.9852
	COPD Sev	Moderate	0.93	[0.15,5.88]	0.9440
		(Very) sev	0.85	[0.16,4.44]	0.8521

Note: Run date and time 01NOV2018 11:20:29,
If no results, number of events was too low

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Table 15-20-3 (Page 5 of 16)
All hazard ratios in adjusted model (Model 1)
AUH - Total analysis population

Endpoint		Level	QVA compared to Free LABA+LAMA without ICS HR	95% CI	P	QVA compared to Free LABA+LAMA with ICS HR	95% CI	P
CARD	Cohort	QVA149	1.09	[0.44,2.72]	0.8543	.	[. , .]	.
	Age at start		1.05	[1.01,1.10]	0.0132	.	[. , .]	.
	Sex	Male	1.37	[0.65,2.88]	0.4077	.	[. , .]	.
	Smoking	Current	1.07	[0.13,8.59]	0.9473	.	[. , .]	.
		Past	0.90	[0.12,6.66]	0.9202	.	[. , .]	.
	COPD Sev	Moderate	226	[0.00, .]	0.9917	.	[. , .]	.
		(Very) sev	262	[0.00, .]	0.9915	.	[. , .]	.
CERE	Cohort	QVA149	.	[. , .]	.	.	[. , .]	.
	Age at start		.	[. , .]	.	.	[. , .]	.
	Sex	Male	.	[. , .]	.	.	[. , .]	.
	Smoking	Current	.	[. , .]	.	.	[. , .]	.
		Past	.	[. , .]	.	.	[. , .]	.
	COPD Sev	Moderate	.	[. , .]	.	.	[. , .]	.
		(Very) sev	.	[. , .]	.	.	[. , .]	.

Note: Run date and time 01NOV2018 11:20:29,
If no results, number of events was too low

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Table 15-20-3 (Page 6 of 16)
Adjusted hazard ratios for QVA versus comparators (Model 1)
AUH - Total analysis population

			QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
Endpoint		Level	HR	95% CI	P	HR	95% CI	P
CARD	Cohort	QVA149	.	[. , .]	.	0.75	[0.45,1.24]	0.2574
	Age at start		.	[. , .]	.	1.05	[1.02,1.07]	0.0002
	Sex	Male	.	[. , .]	.	1.17	[0.73,1.87]	0.5125
	Smoking	Current	.	[. , .]	.	1.32	[0.29,6.06]	0.7221
		Past	.	[. , .]	.	1.74	[0.35,8.59]	0.5032
	COPD Sev	Moderate	.	[. , .]	.	1.46	[0.39,5.48]	0.5814
		(Very) sev	.	[. , .]	.	1.22	[0.30,4.89]	0.7858
CERE	Cohort	QVA149	.	[. , .]	.	1.43	[0.75,2.71]	0.2780
	Age at start		.	[. , .]	.	1.04	[1.01,1.08]	0.0122
	Sex	Male	.	[. , .]	.	1.00	[0.53,1.90]	0.9965
	Smoking	Current	.	[. , .]	.	1.04	[0.29,3.71]	0.9570
		Past	.	[. , .]	.	0.70	[0.20,2.52]	0.5890
	COPD Sev	Moderate	.	[. , .]	.	1.30	[0.19,8.88]	0.7946
		(Very) sev	.	[. , .]	.	0.78	[0.10,5.89]	0.8163

Note: Run date and time 01NOV2018 11:20:29,
If no results, number of events was too low

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Table 15-20-3 (Page 7 of 16)
Adjusted hazard ratios for QVA versus comparators (Model 1)
AUH - Total analysis population

			QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint		Level	HR	95% CI	P	HR	95% CI	P
CARD	Cohort	QVA149	0.63	[0.37,1.07]	0.0883	1.29	[0.56,2.96]	0.5560
	Age at start		1.05	[1.01,1.08]	0.0034	1.06	[1.02,1.10]	0.0041
	Sex	Male	1.57	[0.91,2.71]	0.1027	1.45	[0.71,2.95]	0.3053
	Smoking	Current	0.67	[0.21,2.15]	0.5039	0.81	[0.19,3.51]	0.7778
		Past	0.76	[0.25,2.33]	0.6337	0.48	[0.11,2.17]	0.3440
	COPD Sev	Moderate	1.05	[0.26,4.30]	0.9426	0.55	[0.15,2.00]	0.3713
		(Very) sev	1.30	[0.29,5.74]	0.7347	0.63	[0.14,2.90]	0.5632
CERE	Cohort	QVA149	0.87	[0.45,1.69]	0.6887	.	[. , .]	.
	Age at start		1.01	[0.97,1.05]	0.5991	.	[. , .]	.
	Sex	Male	1.18	[0.61,2.28]	0.6264	.	[. , .]	.
	Smoking	Current	0.92	[0.20,4.14]	0.9091	.	[. , .]	.
		Past	0.70	[0.15,3.14]	0.6372	.	[. , .]	.
	COPD Sev	Moderate	1.41	[0.20,10.0]	0.7337	.	[. , .]	.
		(Very) sev	1.18	[0.19,7.39]	0.8621	.	[. , .]	.

Note: Run date and time 01NOV2018 11:20:29,
If no results, number of events was too low

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Table 15-20-3 (Page 8 of 16)
Adjusted hazard ratios for QVA versus comparators (Model 1)
AUH - Total analysis population

			QVA compared to LAMA		
Endpoint		Level	HR	95% CI	P
CARD	Cohort	QVA149	0.77	[0.43,1.38]	0.3779
	Age at start		1.04	[1.01,1.07]	0.0116
	Sex	Male	1.48	[0.84,2.60]	0.1720
	Smoking	Current	1.29	[0.25,6.57]	0.7623
		Past	1.12	[0.26,4.74]	0.8787
	COPD Sev	Moderate	0.74	[0.24,2.31]	0.6106
		(Very) sev	0.69	[0.16,2.92]	0.6200
CERE	Cohort	QVA149	1.27	[0.61,2.67]	0.5211
	Age at start		1.01	[0.98,1.05]	0.4303
	Sex	Male	0.91	[0.45,1.85]	0.7943
	Smoking	Current	0.88	[0.19,4.03]	0.8680
		Past	0.61	[0.13,2.76]	0.5174
	COPD Sev	Moderate	1.77	[0.21,15.0]	0.6062
		(Very) sev	1.14	[0.14,9.06]	0.9032

Note: Run date and time 01NOV2018 11:20:29,
If no results, number of events was too low

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Table 15-20-3 (Page 9 of 16)
All hazard ratios in adjusted model (Model 1)
AUH - Total analysis population

			QVA compared to Free LABA+LAMA without ICS			QVA compared to Free LABA+LAMA with ICS		
Endpoint		Level	HR	95% CI	P	HR	95% CI	P
BPHURIN	Cohort	QVA149	.	[. , .]	.	.	[. , .]	.
	Age at start		.	[. , .]	.	.	[. , .]	.
	Sex	Male	.	[. , .]	.	.	[. , .]	.
	Smoking	Current	.	[. , .]	.	.	[. , .]	.
		Past	.	[. , .]	.	.	[. , .]	.
	COPD Sev	Moderate	.	[. , .]	.	.	[. , .]	.
		(Very) sev	.	[. , .]	.	.	[. , .]	.
DMVAL	Cohort	QVA149	.	[. , .]	.	.	[. , .]	.
	Age at start		.	[. , .]	.	.	[. , .]	.
	Sex	Male	.	[. , .]	.	.	[. , .]	.
	Smoking	Current	.	[. , .]	.	.	[. , .]	.
		Past	.	[. , .]	.	.	[. , .]	.
	COPD Sev	Moderate	.	[. , .]	.	.	[. , .]	.
		(Very) sev	.	[. , .]	.	.	[. , .]	.

Note: Run date and time 01NOV2018 11:20:29,
If no results, number of events was too low

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Table 15-20-3 (Page 10 of 16)
Adjusted hazard ratios for QVA versus comparators (Model 1)
AUH - Total analysis population

			QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
Endpoint		Level	HR	95% CI	P	HR	95% CI	P
BPHURIN	Cohort	QVA149	.	[. , .]	.	0.79	[0.30,2.10]	0.6405
	Age at start		.	[. , .]	.	1.04	[0.99,1.10]	0.1305
	Sex	Male	.	[. , .]	.	8.32	[1.87,37.0]	0.0054
	Smoking	Current	.	[. , .]	.	0.47	[0.05,4.65]	0.5165
		Past	.	[. , .]	.	1.06	[0.14,8.12]	0.9585
	COPD Sev	Moderate	.	[. , .]	.	56E3	[0.00, .]	0.9900
		(Very) sev	.	[. , .]	.	47E3	[0.00, .]	0.9901
DMVAL	Cohort	QVA149	.	[. , .]	.	0.65	[0.26,1.63]	0.3582
	Age at start		.	[. , .]	.	1.04	[1.00,1.09]	0.0646
	Sex	Male	.	[. , .]	.	1.63	[0.69,3.87]	0.2693
	Smoking	Current	.	[. , .]	.	0.83	[0.12,5.94]	0.8535
		Past	.	[. , .]	.	0.80	[0.12,5.26]	0.8141
	COPD Sev	Moderate	.	[. , .]	.	0.58	[0.13,2.66]	0.4888
		(Very) sev	.	[. , .]	.	0.56	[0.11,2.87]	0.4873

Note: Run date and time 01NOV2018 11:20:29,
If no results, number of events was too low

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Table 15-20-3 (Page 11 of 16)
Adjusted hazard ratios for QVA versus comparators (Model 1)
AUH - Total analysis population

			QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint		Level	HR	95% CI	P	HR	95% CI	P
BPHURIN	Cohort	QVA149	0.78	[0.27,2.25]	0.6488	.	[. , .]	.
	Age at start		1.05	[0.99,1.12]	0.0973	.	[. , .]	.
	Sex	Male	11.8	[1.54,91.0]	0.0175	.	[. , .]	.
	Smoking	Current	94E3	[0.00, .]	0.9955	.	[. , .]	.
		Past	2E5	[0.00, .]	0.9952	.	[. , .]	.
	COPD Sev	Moderate	6941	[0.00, .]	0.9958	.	[. , .]	.
		(Very) sev	5080	[0.00, .]	0.9960	.	[. , .]	.
DMVAL	Cohort	QVA149	0.58	[0.22,1.54]	0.2746	.	[. , .]	.
	Age at start		1.03	[0.98,1.08]	0.3175	.	[. , .]	.
	Sex	Male	1.94	[0.71,5.28]	0.1967	.	[. , .]	.
	Smoking	Current	24E5	[0.00, .]	0.9913	.	[. , .]	.
		Past	11E5	[0.00, .]	0.9917	.	[. , .]	.
	COPD Sev	Moderate	0.93	[0.10,8.41]	0.9460	.	[. , .]	.
		(Very) sev	0.41	[0.05,3.39]	0.4050	.	[. , .]	.

Note: Run date and time 01NOV2018 11:20:29,
If no results, number of events was too low

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Table 15-20-3 (Page 12 of 16)
Adjusted hazard ratios for QVA versus comparators (Model 1)
AUH - Total analysis population

			QVA compared to LAMA		
Endpoint		Level	HR	95% CI	P
BPHURIN	Cohort	QVA149	0.72	[0.23,2.30]	0.5832
	Age at start		1.09	[1.02,1.16]	0.0139
	Sex	Male	5.51	[1.21,25.1]	0.0273
	Smoking	Current	8204	[0.00, .]	0.9961
		Past	1E4	[0.00, .]	0.9960
	COPD Sev	Moderate	17E4	[0.00, .]	0.9937
		(Very) sev	11E4	[0.00, .]	0.9940
DMVAL	Cohort	QVA149	0.76	[0.25,2.34]	0.6355
	Age at start		1.01	[0.95,1.06]	0.8014
	Sex	Male	1.33	[0.45,3.90]	0.6052
	Smoking	Current	51E3	[0.00, .]	0.9927
		Past	11E4	[0.00, .]	0.9922
	COPD Sev	Moderate	0.66	[0.08,5.29]	0.6959
		(Very) sev	0.53	[0.06,5.16]	0.5918

Note: Run date and time 01NOV2018 11:20:29,
If no results, number of events was too low

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Table 15-20-3 (Page 13 of 16)
All hazard ratios in adjusted model (Model 1)
AUH - Total analysis population

			QVA compared to Free LABA+LAMA without ICS			QVA compared to Free LABA+LAMA with ICS		
Endpoint		Level	HR	95% CI	P	HR	95% CI	P
DEATH	Cohort	QVA149	1.40	[0.82,2.40]	0.2176	.	[. , .]	.
	Age at start		1.08	[1.05,1.10]	<.0001	.	[. , .]	.
	Sex	Male	0.85	[0.59,1.23]	0.3953	.	[. , .]	.
	Smoking	Current	2.06	[0.47,9.11]	0.3461	.	[. , .]	.
		Past	1.88	[0.44,7.96]	0.3981	.	[. , .]	.
	COPD Sev	Moderate	1.40	[0.27,7.30]	0.6966	.	[. , .]	.
		(Very) sev	2.59	[0.53,12.6]	0.2586	.	[. , .]	.

Note: Run date and time 01NOV2018 11:20:29,
If no results, number of events was too low

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Table 15-20-3 (Page 14 of 16)
Adjusted hazard ratios for QVA versus comparators (Model 1)
AUH - Total analysis population

			QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
Endpoint		Level	HR	95% CI	P	HR	95% CI	P
DEATH	Cohort	QVA149	1.25	[0.50,3.13]	0.6305	0.69	[0.54,0.88]	0.0024
	Age at start		1.07	[1.04,1.09]	<.0001	1.09	[1.07,1.10]	<.0001
	Sex	Male	0.97	[0.66,1.42]	0.8615	1.05	[0.84,1.32]	0.6538
	Smoking	Current	3.66	[0.48,27.6]	0.2188	3.30	[1.74,6.26]	0.0003
		Past	2.83	[0.38,20.9]	0.3176	2.07	[1.10,3.92]	0.0252
	COPD Sev	Moderate	1.76	[0.35,8.87]	0.5035	1.58	[0.64,3.92]	0.3446
		(Very) sev	2.87	[0.62,13.2]	0.1888	2.35	[1.03,5.39]	0.0610

Note: Run date and time 01NOV2018 11:20:29,
If no results, number of events was too low

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Table 15-20-3 (Page 15 of 16)
Adjusted hazard ratios for QVA versus comparators (Model 1)
AUH - Total analysis population

			QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint		Level	HR	95% CI	P	HR	95% CI	P
DEATH	Cohort	QVA149	1.12	[0.83,1.51]	0.4491	1.27	[0.80,2.01]	0.3107
	Age at start		1.08	[1.06,1.10]	<.0001	1.09	[1.06,1.11]	<.0001
	Sex	Male	0.83	[0.61,1.11]	0.2105	0.93	[0.66,1.33]	0.6965
	Smoking	Current	1.83	[0.72,4.64]	0.2069	2.84	[0.69,11.6]	0.1550
		Past	1.54	[0.62,3.81]	0.3517	2.11	[0.55,8.09]	0.2828
	COPD Sev	Moderate	1.31	[0.46,3.71]	0.6188	1.68	[0.57,4.98]	0.3504
		(Very) sev	2.47	[0.92,6.68]	0.0792	3.08	[1.06,8.95]	0.0431

Note: Run date and time 01NOV2018 11:20:29,
If no results, number of events was too low

QVA149A2402

Table 15-20-3 (Page 16 of 16)
Adjusted hazard ratios for QVA versus comparators (Model 1)
AUH - Total analysis population

			QVA compared to LAMA		
Endpoint		Level	HR	95% CI	P
DEATH	Cohort	QVA149	0.81	[0.60,1.10]	0.1855
	Age at start		1.07	[1.05,1.09]	<.0001
	Sex	Male	0.94	[0.71,1.26]	0.7016
	Smoking	Current	1.69	[0.75,3.82]	0.2110
		Past	1.56	[0.70,3.51]	0.2831
	COPD Sev	Moderate	1.62	[0.65,4.05]	0.3058
		(Very) sev	3.05	[1.09,8.54]	0.0480

Note: Run date and time 01NOV2018 11:20:29,
If no results, number of events was too low

QVA149A2402

Table 15-20-4 (Page 1 of 4)
All hazard ratios in adjusted model (Model 1)
HSD - Total analysis population

			QVA compared to Free LABA+LAMA without ICS			QVA compared to Free LABA+LAMA with ICS		
Endpoint		Level	HR	95% CI	P	HR	95% CI	P
DMVAL	Cohort	QVA149	.	[. , .]	.	.	[. , .]	.
	Age at start		.	[. , .]	.	.	[. , .]	.
	Sex	Male	.	[. , .]	.	.	[. , .]	.
	Smoking	Current	.	[. , .]	.	.	[. , .]	.
		Past	.	[. , .]	.	.	[. , .]	.
	COPD Sev	Moderate	.	[. , .]	.	.	[. , .]	.
		(Very) sev	.	[. , .]	.	.	[. , .]	.

Note: Run date and time 01NOV2018 11:20:40,
If no results, number of events was too low

QVA149A2402

Table 15-20-4 (Page 2 of 4)
Adjusted hazard ratios for QVA versus comparators (Model 1)
HSD - Total analysis population

			QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
Endpoint		Level	HR	95% CI	P	HR	95% CI	P
DMVAL	Cohort	QVA149	.	[. , .]	.	1.67	[0.64,4.33]	0.2944
	Age at start		.	[. , .]	.	1.00	[0.97,1.03]	0.9983
	Sex	Male	.	[. , .]	.	1.83	[0.87,3.84]	0.1085
	Smoking	Current	.	[. , .]	.	0.64	[0.21,1.98]	0.4438
		Past	.	[. , .]	.	1.10	[0.43,2.83]	0.8367
	COPD Sev	Moderate	.	[. , .]	.	1.06	[0.38,2.90]	0.9166
		(Very) sev	.	[. , .]	.	1.39	[0.39,5.02]	0.6121

Note: Run date and time 01NOV2018 11:20:40,
If no results, number of events was too low

QVA149A2402

Table 15-20-4 (Page 3 of 4)
Adjusted hazard ratios for QVA versus comparators (Model 1)
HSD - Total analysis population

			QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint		Level	HR	95% CI	P	HR	95% CI	P
DMVAL	Cohort	QVA149	.	[. , .]	.	.	[. , .]	.
	Age at start		.	[. , .]	.	.	[. , .]	.
	Sex	Male	.	[. , .]	.	.	[. , .]	.
	Smoking	Current	.	[. , .]	.	.	[. , .]	.
		Past	.	[. , .]	.	.	[. , .]	.
	COPD Sev	Moderate	.	[. , .]	.	.	[. , .]	.
		(Very) sev	.	[. , .]	.	.	[. , .]	.

Note: Run date and time 01NOV2018 11:20:40,
If no results, number of events was too low

QVA149A2402

Table 15-20-4 (Page 4 of 4)
Adjusted hazard ratios for QVA versus comparators (Model 1)
HSD - Total analysis population

			QVA compared to LAMA		
Endpoint		Level	HR	95% CI	P
DMVAL	Cohort	QVA149	2.79	[0.97,7.99]	0.0567
	Age at start		1.01	[0.95,1.06]	0.8312
	Sex	Male	2.32	[0.64,8.39]	0.1985
	Smoking	Current	2.85	[0.28,28.5]	0.3745
		Past	3.76	[0.45,31.7]	0.2233
	COPD Sev	Moderate	1.00	[0.29,3.49]	0.9947
		(Very) sev	0.07	[0.00, .]	0.9952

Note: Run date and time 01NOV2018 11:20:40,
If no results, number of events was too low

QVA149A2402

Table 15-20-5 (Page 1 of 20)
All hazard ratios in adjusted model (Model 1)
SIDIAP - Total analysis population

			QVA compared to Free LABA+LAMA without ICS			QVA compared to Free LABA+LAMA with ICS		
Endpoint		Level	HR	95% CI	P	HR	95% CI	P
MACE	Cohort	QVA149	1.22	[0.86,1.74]	0.2539	1.23	[0.74,2.04]	0.4270
	Age at start		1.06	[1.04,1.08]	<.0001	1.06	[1.04,1.08]	<.0001
	Sex	Male	1.06	[0.66,1.69]	0.8189	0.89	[0.55,1.44]	0.6330
	Smoking	Current	0.93	[0.55,1.55]	0.7718	0.93	[0.53,1.65]	0.8142
		Past	0.99	[0.66,1.48]	0.9458	0.96	[0.62,1.50]	0.8728
	COPD Sev	Moderate	1.30	[0.67,2.53]	0.4421	1.28	[0.60,2.74]	0.5307
		(Very) sev	1.35	[0.65,2.79]	0.4211	1.47	[0.69,3.14]	0.3209
IHD	Cohort	QVA149	0.56	[0.26,1.21]	0.1415	.	[. , .]	.
	Age at start		1.02	[0.98,1.07]	0.2611	.	[. , .]	.
	Sex	Male	1.30	[0.37,4.57]	0.6845	.	[. , .]	.
	Smoking	Current	1.87	[0.42,8.26]	0.4078	.	[. , .]	.
		Past	2.30	[0.64,8.25]	0.2028	.	[. , .]	.
	COPD Sev	Moderate	0.65	[0.17,2.43]	0.5203	.	[. , .]	.
		(Very) sev	0.45	[0.10,2.14]	0.3221	.	[. , .]	.

Note: Run date and time 01NOV2018 11:20:49,
If no results, number of events was too low

QVA149A2402

Table 15-20-5 (Page 2 of 20)
Adjusted hazard ratios for QVA versus comparators (Model 1)
SIDIAP - Total analysis population

			QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
Endpoint		Level	HR	95% CI	P	HR	95% CI	P
MACE	Cohort	QVA149	1.09	[0.72,1.66]	0.6737	0.75	[0.61,0.93]	0.0089
	Age at start		1.06	[1.04,1.08]	<.0001	1.06	[1.05,1.07]	<.0001
	Sex	Male	0.90	[0.57,1.42]	0.6524	1.15	[0.92,1.43]	0.2243
	Smoking	Current	0.91	[0.51,1.62]	0.7423	1.00	[0.76,1.31]	0.9989
		Past	1.15	[0.75,1.76]	0.5276	0.90	[0.72,1.12]	0.3460
	COPD Sev	Moderate	1.22	[0.62,2.41]	0.5659	1.44	[1.03,2.00]	0.0383
		(Very) sev	1.38	[0.70,2.72]	0.3470	1.46	[1.04,2.03]	0.0288
IHD	Cohort	QVA149	0.64	[0.23,1.83]	0.4081	0.62	[0.34,1.13]	0.1194
	Age at start		1.02	[0.98,1.07]	0.3569	1.03	[1.01,1.06]	0.0082
	Sex	Male	1.06	[0.32,3.51]	0.9278	1.41	[0.75,2.62]	0.2838
	Smoking	Current	1.63	[0.37,7.15]	0.5194	1.98	[0.98,4.00]	0.0575
		Past	1.53	[0.43,5.39]	0.5090	1.25	[0.66,2.38]	0.4936
	COPD Sev	Moderate	0.56	[0.15,2.13]	0.3973	1.05	[0.44,2.52]	0.9127
		(Very) sev	0.41	[0.08,2.16]	0.2997	0.90	[0.30,2.71]	0.8567

Note: Run date and time 01NOV2018 11:20:49,
If no results, number of events was too low

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Table 15-20-5 (Page 3 of 20)
Adjusted hazard ratios for QVA versus comparators (Model 1)
SIDIAP - Total analysis population

			QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint		Level	HR	95% CI	P	HR	95% CI	P
MACE	Cohort	QVA149	0.73	[0.46,1.15]	0.1774	1.29	[0.93,1.80]	0.1332
	Age at start		1.05	[1.03,1.08]	<.0001	1.06	[1.04,1.08]	<.0001
	Sex	Male	1.02	[0.62,1.67]	0.9342	0.95	[0.63,1.42]	0.7933
	Smoking	Current	0.79	[0.45,1.39]	0.4134	0.76	[0.46,1.25]	0.2784
		Past	0.91	[0.59,1.41]	0.6716	0.94	[0.64,1.37]	0.7375
	COPD Sev	Moderate	1.16	[0.57,2.37]	0.6855	1.31	[0.75,2.28]	0.3433
		(Very) sev	1.26	[0.58,2.73]	0.5574	1.56	[0.85,2.86]	0.1558
IHD	Cohort	QVA149	0.36	[0.14,0.93]	0.0350	1.43	[0.57,3.60]	0.4488
	Age at start		0.98	[0.93,1.02]	0.3457	1.02	[0.97,1.06]	0.5021
	Sex	Male	2.59	[0.57,11.7]	0.2161	1.76	[0.48,6.40]	0.3935
	Smoking	Current	0.77	[0.20,3.03]	0.7061	0.66	[0.16,2.78]	0.5732
		Past	0.71	[0.21,2.38]	0.5832	1.12	[0.37,3.40]	0.8354
	COPD Sev	Moderate	0.53	[0.15,1.87]	0.3213	0.51	[0.17,1.55]	0.2331
		(Very) sev	0.38	[0.08,1.79]	0.2217	0.34	[0.06,1.85]	0.2234

Note: Run date and time 01NOV2018 11:20:49,
If no results, number of events was too low

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Table 15-20-5 (Page 4 of 20)
Adjusted hazard ratios for QVA versus comparators (Model 1)
SIDIAP - Total analysis population

			QVA compared to LAMA		
Endpoint		Level	HR	95% CI	P
MACE	Cohort	QVA149	0.91	[0.71,1.16]	0.4386
	Age at start		1.06	[1.04,1.07]	<.0001
	Sex	Male	0.97	[0.72,1.32]	0.8500
	Smoking	Current	0.83	[0.57,1.20]	0.3231
		Past	1.01	[0.76,1.35]	0.9323
	COPD Sev	Moderate	1.18	[0.75,1.85]	0.4831
		(Very) sev	1.63	[0.99,2.69]	0.0695
IHD	Cohort	QVA149	0.56	[0.30,1.06]	0.0738
	Age at start		1.02	[0.99,1.04]	0.2690
	Sex	Male	3.07	[1.18,7.95]	0.0211
	Smoking	Current	1.23	[0.54,2.79]	0.6166
		Past	0.97	[0.47,2.03]	0.9413
	COPD Sev	Moderate	0.62	[0.26,1.48]	0.2924
		(Very) sev	0.66	[0.21,2.06]	0.4860

Note: Run date and time 01NOV2018 11:20:49,
If no results, number of events was too low

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Table 15-20-5 (Page 5 of 20)
All hazard ratios in adjusted model (Model 1)
SIDIAP - Total analysis population

			QVA compared to Free LABA+LAMA without ICS			QVA compared to Free LABA+LAMA with ICS		
Endpoint		Level	HR	95% CI	P	HR	95% CI	P
CARD	Cohort	QVA149	1.02	[0.60,1.75]	0.9358	0.62	[0.32,1.18]	0.1459
	Age at start		1.05	[1.02,1.08]	0.0015	1.05	[1.01,1.08]	0.0044
	Sex	Male	2.15	[0.83,5.56]	0.1150	1.26	[0.54,2.93]	0.5969
	Smoking	Current	0.75	[0.32,1.73]	0.4944	0.75	[0.29,1.94]	0.5484
		Past	0.85	[0.45,1.63]	0.6317	1.05	[0.52,2.11]	0.8942
	COPD Sev	Moderate	1.86	[0.39,8.91]	0.4465	2.46	[0.39,15.7]	0.3500
		(Very) sev	1.42	[0.25,8.08]	0.6963	1.78	[0.25,12.5]	0.5665
CERE	Cohort	QVA149	1.28	[0.46,3.61]	0.6368	0.39	[0.14,1.05]	0.0630
	Age at start		1.06	[1.01,1.12]	0.0257	1.05	[1.00,1.11]	0.0440
	Sex	Male	1.19	[0.26,5.52]	0.8271	1.09	[0.29,4.11]	0.8947
	Smoking	Current	3.58	[0.63,20.5]	0.1519	0.99	[0.21,4.57]	0.9902
		Past	2.61	[0.54,12.7]	0.2340	1.07	[0.34,3.40]	0.9071
	COPD Sev	Moderate	0.45	[0.07,2.70]	0.3869	0.54	[0.09,3.30]	0.5074
		(Very) sev	0.84	[0.19,3.71]	0.8138	0.77	[0.15,3.80]	0.7452

Note: Run date and time 01NOV2018 11:20:49,
If no results, number of events was too low

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Table 15-20-5 (Page 6 of 20)
Adjusted hazard ratios for QVA versus comparators (Model 1)
SIDIAP - Total analysis population

			QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
Endpoint		Level	HR	95% CI	P	HR	95% CI	P
CARD	Cohort	QVA149	0.73	[0.40,1.34]	0.3071	0.66	[0.46,0.95]	0.0237
	Age at start		1.04	[1.01,1.07]	0.0084	1.04	[1.03,1.06]	<.0001
	Sex	Male	1.19	[0.56,2.52]	0.6568	1.67	[1.14,2.45]	0.0088
	Smoking	Current	0.68	[0.27,1.74]	0.4226	1.01	[0.66,1.55]	0.9607
		Past	1.05	[0.54,2.05]	0.8871	0.88	[0.62,1.25]	0.4727
	COPD Sev	Moderate	2.27	[0.57,8.99]	0.2493	1.14	[0.67,1.95]	0.6398
		(Very) sev	1.86	[0.38,9.00]	0.4478	1.06	[0.64,1.75]	0.8279
CERE	Cohort	QVA149	0.41	[0.16,1.05]	0.0641	0.61	[0.33,1.10]	0.1012
	Age at start		1.04	[0.99,1.09]	0.1531	1.06	[1.03,1.08]	<.0001
	Sex	Male	1.01	[0.30,3.35]	0.9870	1.97	[0.95,4.10]	0.0681
	Smoking	Current	2.70	[0.46,15.9]	0.2789	1.69	[0.75,3.80]	0.2051
		Past	1.97	[0.44,8.82]	0.3782	1.56	[0.81,2.99]	0.1820
	COPD Sev	Moderate	0.60	[0.12,3.09]	0.5443	0.63	[0.31,1.29]	0.2069
		(Very) sev	1.11	[0.24,5.03]	0.8927	0.91	[0.41,2.01]	0.8148

Note: Run date and time 01NOV2018 11:20:49,
If no results, number of events was too low

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Table 15-20-5 (Page 7 of 20)
Adjusted hazard ratios for QVA versus comparators (Model 1)
SIDIAP - Total analysis population

			QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint		Level	HR	95% CI	P	HR	95% CI	P
CARD	Cohort	QVA149	.	[. , .]	.	1.17	[0.69,1.99]	0.5590
	Age at start		.	[. , .]	.	1.04	[1.01,1.07]	0.0050
	Sex	Male	.	[. , .]	.	2.10	[0.91,4.82]	0.0804
	Smoking	Current	.	[. , .]	.	0.72	[0.32,1.63]	0.4286
		Past	.	[. , .]	.	0.97	[0.52,1.81]	0.9153
	COPD Sev	Moderate	.	[. , .]	.	1.64	[0.39,6.83]	0.5127
		(Very) sev	.	[. , .]	.	1.31	[0.27,6.32]	0.7467
CERE	Cohort	QVA149	.	[. , .]	.	0.67	[0.29,1.51]	0.3311
	Age at start		.	[. , .]	.	1.03	[0.99,1.07]	0.1471
	Sex	Male	.	[. , .]	.	1.22	[0.39,3.76]	0.7318
	Smoking	Current	.	[. , .]	.	2.79	[0.66,11.7]	0.1623
		Past	.	[. , .]	.	2.22	[0.58,8.50]	0.2439
	COPD Sev	Moderate	.	[. , .]	.	0.43	[0.10,1.80]	0.2606
		(Very) sev	.	[. , .]	.	1.14	[0.36,3.59]	0.8180

Note: Run date and time 01NOV2018 11:20:49,
If no results, number of events was too low

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Table 15-20-5 (Page 8 of 20)
Adjusted hazard ratios for QVA versus comparators (Model 1)
SIDIAP - Total analysis population

			QVA compared to LAMA		
Endpoint		Level	HR	95% CI	P
CARD	Cohort	QVA149	0.68	[0.46,1.01]	0.0534
	Age at start		1.05	[1.03,1.07]	<.0001
	Sex	Male	1.35	[0.82,2.24]	0.2398
	Smoking	Current	0.87	[0.50,1.51]	0.6220
		Past	0.99	[0.64,1.56]	0.9803
	COPD Sev	Moderate	1.37	[0.71,2.61]	0.3504
		(Very) sev	1.42	[0.65,3.09]	0.3872
CERE	Cohort	QVA149	0.63	[0.33,1.22]	0.1701
	Age at start		1.05	[1.02,1.09]	0.0026
	Sex	Male	2.08	[0.71,6.08]	0.1794
	Smoking	Current	2.93	[0.97,8.80]	0.0558
		Past	2.65	[0.98,7.19]	0.0558
	COPD Sev	Moderate	0.47	[0.17,1.31]	0.1641
		(Very) sev	0.82	[0.34,2.00]	0.6638

Note: Run date and time 01NOV2018 11:20:49,
If no results, number of events was too low

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Table 15-20-5 (Page 9 of 20)
All hazard ratios in adjusted model (Model 1)
SIDIAP - Total analysis population

Endpoint		Level	QVA compared to Free LABA+LAMA without ICS HR	95% CI	P	QVA compared to Free LABA+LAMA with ICS HR	95% CI	P
GLAUCOME	Cohort	QVA149	0.72	[0.30,1.73]	0.4576	.	[. , .]	.
	Age at start		1.03	[0.98,1.08]	0.2977	.	[. , .]	.
	Sex	Male	0.79	[0.25,2.54]	0.6935	.	[. , .]	.
	Smoking	Current	0.73	[0.17,3.12]	0.6747	.	[. , .]	.
		Past	1.03	[0.33,3.18]	0.9645	.	[. , .]	.
	COPD Sev	Moderate	1.27	[0.16,10.4]	0.8242	.	[. , .]	.
		(Very) sev	1.09	[0.12,9.80]	0.9365	.	[. , .]	.
BPHURIN	Cohort	QVA149	0.94	[0.60,1.47]	0.7952	0.95	[0.49,1.84]	0.8779
	Age at start		1.01	[0.99,1.04]	0.2395	1.01	[0.98,1.03]	0.5634
	Sex	Male	17.5	[2.42, 127]	0.0046	47E5	[0.00, .]	0.9778
	Smoking	Current	1.08	[0.54,2.16]	0.8332	0.88	[0.41,1.86]	0.7312
		Past	0.92	[0.51,1.66]	0.7800	0.68	[0.36,1.28]	0.2350
	COPD Sev	Moderate	0.75	[0.34,1.63]	0.4663	0.80	[0.30,2.15]	0.6583
		(Very) sev	0.92	[0.41,2.08]	0.8487	1.19	[0.45,3.18]	0.7299

Note: Run date and time 01NOV2018 11:20:49,
If no results, number of events was too low

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Table 15-20-5 (Page 10 of 20)
Adjusted hazard ratios for QVA versus comparators (Model 1)
SIDIAP - Total analysis population

			QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
Endpoint		Level	HR	95% CI	P	HR	95% CI	P
GLAUCOME	Cohort	QVA149	.	[. , .]	.	0.91	[0.46,1.79]	0.7863
	Age at start		.	[. , .]	.	1.02	[0.99,1.05]	0.2387
	Sex	Male	.	[. , .]	.	0.73	[0.36,1.47]	0.3759
	Smoking	Current	.	[. , .]	.	1.24	[0.48,3.20]	0.6570
		Past	.	[. , .]	.	1.15	[0.48,2.76]	0.7484
	COPD Sev	Moderate	.	[. , .]	.	1.06	[0.30,3.68]	0.9326
		(Very) sev	.	[. , .]	.	0.87	[0.23,3.28]	0.8392
BPHURIN	Cohort	QVA149	1.40	[0.69,2.81]	0.3484	0.75	[0.55,1.02]	0.0699
	Age at start		1.01	[0.98,1.04]	0.5213	1.03	[1.01,1.04]	<.0001
	Sex	Male	19.6	[2.68, 143]	0.0034	89.0	[12.5, 636]	<.0001
	Smoking	Current	0.88	[0.42,1.87]	0.7460	1.09	[0.74,1.63]	0.6589
		Past	0.67	[0.36,1.26]	0.2117	0.75	[0.53,1.06]	0.0998
	COPD Sev	Moderate	0.52	[0.22,1.23]	0.1403	1.10	[0.66,1.86]	0.7125
		(Very) sev	0.69	[0.31,1.54]	0.3696	1.38	[0.81,2.35]	0.2443

Note: Run date and time 01NOV2018 11:20:49,
If no results, number of events was too low

QVA149A2402

Table 15-20-5 (Page 11 of 20)
Adjusted hazard ratios for QVA versus comparators (Model 1)
SIDIAP - Total analysis population

			QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint		Level	HR	95% CI	P	HR	95% CI	P
GLAUCOME	Cohort	QVA149	.	[. , .]	.	0.73	[0.31,1.71]	0.4659
	Age at start		.	[. , .]	.	1.04	[0.99,1.08]	0.1117
	Sex	Male	.	[. , .]	.	0.65	[0.25,1.65]	0.3621
	Smoking	Current	.	[. , .]	.	0.48	[0.13,1.79]	0.2769
		Past	.	[. , .]	.	0.63	[0.23,1.68]	0.3530
	COPD Sev	Moderate	.	[. , .]	.	0.75	[0.25,2.31]	0.6197
		(Very) sev	.	[. , .]	.	0.72	[0.17,3.01]	0.6563
BPHURIN	Cohort	QVA149	1.07	[0.51,2.25]	0.8555	0.75	[0.50,1.13]	0.1672
	Age at start		1.01	[0.98,1.03]	0.6841	1.01	[0.99,1.03]	0.3136
	Sex	Male	49E5	[0.00, .]	0.9782	48E5	[0.00, .]	0.9696
	Smoking	Current	0.90	[0.42,1.93]	0.7836	1.22	[0.64,2.32]	0.5507
		Past	0.67	[0.34,1.29]	0.2269	1.11	[0.63,1.95]	0.7170
	COPD Sev	Moderate	0.80	[0.29,2.15]	0.6518	0.92	[0.46,1.87]	0.8249
		(Very) sev	1.02	[0.39,2.69]	0.9707	1.05	[0.52,2.11]	0.8915

Note: Run date and time 01NOV2018 11:20:49,
If no results, number of events was too low

QVA149A2402

Table 15-20-5 (Page 12 of 20)
Adjusted hazard ratios for QVA versus comparators (Model 1)
SIDIAP - Total analysis population

			QVA compared to LAMA		
Endpoint		Level	HR	95% CI	P
GLAUCOME	Cohort	QVA149	0.57	[0.28,1.13]	0.1089
	Age at start		1.01	[0.98,1.04]	0.4588
	Sex	Male	0.59	[0.29,1.21]	0.1536
	Smoking	Current	0.84	[0.30,2.31]	0.7307
		Past	1.36	[0.59,3.15]	0.4698
	COPD Sev	Moderate	1.12	[0.41,3.02]	0.8265
		(Very) sev	0.85	[0.23,3.07]	0.8000
BPHURIN	Cohort	QVA149	0.74	[0.53,1.05]	0.0907
	Age at start		1.01	[1.00,1.03]	0.1398
	Sex	Male	5E6	[0.00,****]	0.9616
	Smoking	Current	0.85	[0.53,1.35]	0.4813
		Past	0.70	[0.46,1.05]	0.0853
	COPD Sev	Moderate	1.31	[0.74,2.32]	0.3485
		(Very) sev	1.50	[0.71,3.16]	0.3013

Note: Run date and time 01NOV2018 11:20:49,
If no results, number of events was too low

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Table 15-20-5 (Page 13 of 20)
All hazard ratios in adjusted model (Model 1)
SIDIAP - Total analysis population

			QVA compared to Free LABA+LAMA without ICS			QVA compared to Free LABA+LAMA with ICS		
Endpoint		Level	HR	95% CI	P	HR	95% CI	P
DMVAL	Cohort	QVA149	1.06	[0.65,1.71]	0.8213	1.40	[0.63,3.13]	0.4118
	Age at start		1.00	[0.97,1.02]	0.7694	0.99	[0.96,1.02]	0.3969
	Sex	Male	1.32	[0.68,2.57]	0.4161	1.19	[0.57,2.52]	0.6398
	Smoking	Current	1.11	[0.51,2.41]	0.7846	1.33	[0.50,3.51]	0.5684
		Past	1.23	[0.62,2.43]	0.5530	1.77	[0.75,4.19]	0.1952
	COPD Sev	Moderate	0.61	[0.28,1.33]	0.2185	0.47	[0.18,1.23]	0.1324
		(Very) sev	0.68	[0.31,1.46]	0.3197	0.64	[0.27,1.51]	0.3089
BRONCHOSPASM	Cohort	QVA149	.	[. , .]	.	.	[. , .]	.
	Age at start		.	[. , .]	.	.	[. , .]	.
	Sex	Male	.	[. , .]	.	.	[. , .]	.
	Smoking	Current	.	[. , .]	.	.	[. , .]	.
		Past	.	[. , .]	.	.	[. , .]	.
	COPD Sev	Moderate	.	[. , .]	.	.	[. , .]	.
		(Very) sev	.	[. , .]	.	.	[. , .]	.

Note: Run date and time 01NOV2018 11:20:49,
If no results, number of events was too low

QVA149A2402

Table 15-20-5 (Page 14 of 20)
Adjusted hazard ratios for QVA versus comparators (Model 1)
SIDIAP - Total analysis population

			QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
Endpoint		Level	HR	95% CI	P	HR	95% CI	P
DMVAL	Cohort	QVA149	1.53	[0.73,3.24]	0.2621	0.77	[0.56,1.06]	0.1127
	Age at start		0.99	[0.97,1.02]	0.5435	1.00	[0.98,1.01]	0.6813
	Sex	Male	1.49	[0.71,3.16]	0.2955	1.09	[0.78,1.53]	0.6150
	Smoking	Current	1.23	[0.49,3.04]	0.6607	1.28	[0.83,1.97]	0.2695
		Past	1.38	[0.64,2.99]	0.4147	1.36	[0.92,2.01]	0.1262
	COPD Sev	Moderate	0.48	[0.19,1.20]	0.1263	1.09	[0.62,1.89]	0.7753
		(Very) sev	0.64	[0.26,1.59]	0.3420	1.50	[0.84,2.65]	0.1815
BRONCHOSPASM	Cohort	QVA149	0.29	[0.08,1.05]	0.0592	0.44	[0.17,1.14]	0.0894
	Age at start		1.00	[0.94,1.06]	0.9308	0.96	[0.93,0.98]	0.0019
	Sex	Male	0.19	[0.05,0.74]	0.0165	0.95	[0.49,1.85]	0.8850
	Smoking	Current	0.49	[0.04,5.90]	0.5732	0.60	[0.26,1.39]	0.2301
		Past	2.53	[0.52,12.2]	0.2487	0.61	[0.27,1.34]	0.2172
	COPD Sev	Moderate	1.47	[0.19,11.5]	0.7164	0.68	[0.30,1.53]	0.3569
		(Very) sev	0.99	[0.09,10.6]	0.9954	0.65	[0.24,1.78]	0.4052

Note: Run date and time 01NOV2018 11:20:49,
If no results, number of events was too low

QVA149A2402

Table 15-20-5 (Page 15 of 20)
Adjusted hazard ratios for QVA versus comparators (Model 1)
SIDIAP - Total analysis population

			QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint		Level	HR	95% CI	P	HR	95% CI	P
DMVAL	Cohort	QVA149	0.59	[0.32,1.09]	0.0912	1.19	[0.74,1.90]	0.4797
	Age at start		0.99	[0.97,1.02]	0.5474	0.99	[0.97,1.02]	0.5443
	Sex	Male	1.58	[0.73,3.41]	0.2446	1.02	[0.58,1.80]	0.9363
	Smoking	Current	1.30	[0.53,3.20]	0.5680	1.42	[0.66,3.08]	0.3707
		Past	1.50	[0.67,3.35]	0.3278	1.80	[0.90,3.60]	0.0988
	COPD Sev	Moderate	0.53	[0.21,1.36]	0.1964	0.78	[0.37,1.66]	0.5301
		(Very) sev	0.72	[0.30,1.74]	0.4652	0.87	[0.34,2.26]	0.7831
BRONCHOSPASM	Cohort	QVA149	.	[. , .]	.	0.77	[0.21,2.80]	0.6969
	Age at start		.	[. , .]	.	0.99	[0.93,1.05]	0.6901
	Sex	Male	.	[. , .]	.	0.13	[0.04,0.51]	0.0033
	Smoking	Current	.	[. , .]	.	1.69	[0.24,12.1]	0.5998
		Past	.	[. , .]	.	2.28	[0.37,13.9]	0.3716
	COPD Sev	Moderate	.	[. , .]	.	1.02	[0.07,14.4]	0.9887
		(Very) sev	.	[. , .]	.	1.27	[0.07,23.8]	0.8758

Note: Run date and time 01NOV2018 11:20:49,
If no results, number of events was too low

QVA149A2402

Table 15-20-5 (Page 16 of 20)
Adjusted hazard ratios for QVA versus comparators (Model 1)
SIDIAP - Total analysis population

			QVA compared to LAMA		
Endpoint		Level	HR	95% CI	P
DMVAL	Cohort	QVA149	0.96	[0.67,1.37]	0.8174
	Age at start		1.00	[0.99,1.02]	0.7956
	Sex	Male	1.14	[0.72,1.79]	0.5819
	Smoking	Current	2.18	[1.18,4.05]	0.0136
		Past	1.96	[1.08,3.54]	0.0267
	COPD Sev	Moderate	0.91	[0.52,1.61]	0.7581
		(Very) sev	1.44	[0.80,2.60]	0.2236
BRONCHOSPASM	Cohort	QVA149	1.11	[0.36,3.48]	0.8553
	Age at start		0.98	[0.93,1.04]	0.5365
	Sex	Male	0.14	[0.04,0.46]	0.0011
	Smoking	Current	0.44	[0.08,2.32]	0.3309
		Past	1.00	[0.26,3.88]	0.9979
	COPD Sev	Moderate	1.50	[0.17,13.5]	0.7245
		(Very) sev	1.58	[0.20,12.6]	0.6647

Note: Run date and time 01NOV2018 11:20:49,
If no results, number of events was too low

QVA149A2402

Table 15-20-5 (Page 17 of 20)
All hazard ratios in adjusted model (Model 1)
SIDIAP - Total analysis population

			QVA compared to Free LABA+LAMA without ICS			QVA compared to Free LABA+LAMA with ICS		
Endpoint		Level	HR	95% CI	P	HR	95% CI	P
DEATH	Cohort	QVA149	1.47	[0.88,2.45]	0.1414	2.13	[0.85,5.33]	0.1047
	Age at start		1.07	[1.05,1.10]	<.0001	1.07	[1.04,1.10]	<.0001
	Sex	Male	2.42	[1.03,5.70]	0.0427	4.78	[1.47,15.5]	0.0093
	Smoking	Current	1.03	[0.53,2.00]	0.9326	0.99	[0.49,1.99]	0.9691
		Past	0.80	[0.47,1.36]	0.4105	0.64	[0.37,1.12]	0.1200
	COPD Sev	Moderate	1.33	[0.48,3.69]	0.5899	1.26	[0.30,5.29]	0.7555
		(Very) sev	2.17	[0.80,5.86]	0.1284	2.28	[0.58,8.94]	0.2471

Note: Run date and time 01NOV2018 11:20:49,
If no results, number of events was too low

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Table 15-20-5 (Page 18 of 20)
Adjusted hazard ratios for QVA versus comparators (Model 1)
SIDIAP - Total analysis population

			QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
Endpoint		Level	HR	95% CI	P	HR	95% CI	P
DEATH	Cohort	QVA149	0.86	[0.50,1.49]	0.5935	0.60	[0.46,0.79]	0.0002
	Age at start		1.07	[1.05,1.10]	<.0001	1.09	[1.07,1.10]	<.0001
	Sex	Male	1.81	[0.92,3.57]	0.0860	1.42	[1.06,1.91]	0.0185
	Smoking	Current	0.82	[0.41,1.62]	0.5652	1.39	[1.00,1.94]	0.0524
		Past	0.66	[0.40,1.10]	0.1120	0.79	[0.59,1.04]	0.0934
	COPD Sev	Moderate	1.77	[0.41,7.69]	0.4598	1.33	[0.78,2.26]	0.3109
		(Very) sev	2.88	[0.68,12.3]	0.1685	2.09	[1.33,3.27]	0.0021

Note: Run date and time 01NOV2018 11:20:49,
If no results, number of events was too low

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Table 15-20-5 (Page 19 of 20)
Adjusted hazard ratios for QVA versus comparators (Model 1)
SIDIAP - Total analysis population

			QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint		Level	HR	95% CI	P	HR	95% CI	P
DEATH	Cohort	QVA149	0.85	[0.45,1.60]	0.6071	0.98	[0.64,1.48]	0.9072
	Age at start		1.06	[1.04,1.09]	<.0001	1.09	[1.06,1.11]	<.0001
	Sex	Male	5.05	[1.56,16.4]	0.0069	2.86	[1.40,5.84]	0.0038
	Smoking	Current	0.96	[0.48,1.93]	0.9075	0.96	[0.53,1.75]	0.9035
		Past	0.75	[0.43,1.30]	0.3040	0.71	[0.45,1.14]	0.1535
	COPD Sev	Moderate	1.10	[0.34,3.57]	0.8776	1.13	[0.55,2.32]	0.7345
		(Very) sev	1.91	[0.65,5.59]	0.2404	2.03	[0.98,4.18]	0.0557

Note: Run date and time 01NOV2018 11:20:49,
If no results, number of events was too low

QVA149A2402

Table 15-20-5 (Page 20 of 20)
Adjusted hazard ratios for QVA versus comparators (Model 1)
SIDIAP - Total analysis population

			QVA compared to LAMA		
Endpoint		Level	HR	95% CI	P
DEATH	Cohort	QVA149	0.75	[0.55,1.03]	0.0784
	Age at start		1.08	[1.07,1.10]	<.0001
	Sex	Male	1.78	[1.13,2.81]	0.0134
	Smoking	Current	0.81	[0.52,1.26]	0.3534
		Past	0.61	[0.43,0.87]	0.0059
	COPD Sev	Moderate	1.32	[0.66,2.61]	0.4409
		(Very) sev	2.36	[1.10,5.02]	0.0413

Note: Run date and time 01NOV2018 11:20:49,
If no results, number of events was too low

QVA149A2402

Table 15-20-6 (Page 1 of 20)
All hazard ratios in adjusted model (Model 1)
POOLED - Total analysis population

			QVA compared to Free LABA+LAMA without ICS			QVA compared to Free LABA+LAMA with ICS		
Endpoint		Level	HR	95% CI	P	HR	95% CI	P
MACE	Cohort	QVA149	1.19	[0.94,1.49]	0.1421	0.98	[0.70,1.37]	0.9041
	Age at start		1.04	[1.03,1.06]	<.0001	1.04	[1.03,1.05]	<.0001
	Sex	Male	1.67	[1.31,2.13]	<.0001	1.54	[1.18,2.01]	0.0015
	Smoking	Current	1.03	[0.71,1.49]	0.8685	0.94	[0.63,1.40]	0.7494
		Past	0.95	[0.68,1.33]	0.7695	0.87	[0.60,1.25]	0.4438
	COPD Sev	Moderate	1.10	[0.75,1.63]	0.6140	1.35	[0.80,2.27]	0.2635
		(Very) sev	1.12	[0.74,1.69]	0.5848	1.44	[0.85,2.45]	0.1798
IHD	Cohort	QVA149	1.09	[0.72,1.67]	0.6823	0.74	[0.40,1.38]	0.3492
	Age at start		1.02	[1.00,1.04]	0.1295	1.00	[0.98,1.03]	0.7288
	Sex	Male	2.26	[1.41,3.61]	0.0007	2.35	[1.39,4.00]	0.0016
	Smoking	Current	2.45	[0.84,7.18]	0.1023	0.94	[0.39,2.26]	0.8967
		Past	2.27	[0.81,6.35]	0.1188	0.74	[0.32,1.71]	0.4813
	COPD Sev	Moderate	0.87	[0.47,1.62]	0.6684	0.76	[0.33,1.79]	0.5401
		(Very) sev	0.79	[0.40,1.56]	0.4961	0.73	[0.33,1.60]	0.4297

Note: Run date and time 01NOV2018 11:21:00,
If no results, number of events was too low

QVA149A2402

Table 15-20-6 (Page 2 of 20)
Adjusted hazard ratios for QVA versus comparators (Model 1)
POOLED - Total analysis population

			QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
Endpoint		Level	HR	95% CI	P	HR	95% CI	P
MACE	Cohort	QVA149	0.97	[0.71,1.30]	0.8170	0.85	[0.73,0.97]	0.0201
	Age at start		1.04	[1.03,1.06]	<.0001	1.05	[1.05,1.06]	<.0001
	Sex	Male	1.47	[1.14,1.90]	0.0032	1.32	[1.17,1.49]	<.0001
	Smoking	Current	0.99	[0.68,1.45]	0.9743	1.04	[0.86,1.27]	0.6810
		Past	0.94	[0.67,1.32]	0.7343	0.92	[0.78,1.08]	0.3134
	COPD Sev	Moderate	1.20	[0.71,2.00]	0.5020	1.35	[1.09,1.67]	0.0087
		(Very) sev	1.32	[0.82,2.13]	0.2579	1.44	[1.15,1.81]	0.0030
IHD	Cohort	QVA149	0.93	[0.50,1.73]	0.8114	1.07	[0.81,1.43]	0.6284
	Age at start		1.01	[0.99,1.03]	0.3622	1.02	[1.01,1.03]	<.0001
	Sex	Male	2.10	[1.25,3.51]	0.0047	1.61	[1.28,2.01]	<.0001
	Smoking	Current	1.44	[0.54,3.82]	0.4617	1.54	[1.04,2.28]	0.0313
		Past	1.04	[0.42,2.55]	0.9328	1.10	[0.75,1.61]	0.6352
	COPD Sev	Moderate	0.73	[0.31,1.74]	0.4852	0.91	[0.60,1.38]	0.6701
		(Very) sev	0.69	[0.29,1.62]	0.3957	0.77	[0.52,1.16]	0.2219

Note: Run date and time 01NOV2018 11:21:00,
If no results, number of events was too low

QVA149A2402

Table 15-20-6 (Page 3 of 20)
Adjusted hazard ratios for QVA versus comparators (Model 1)
POOLED - Total analysis population

			QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint		Level	HR	95% CI	P	HR	95% CI	P
MACE	Cohort	QVA149	0.99	[0.81,1.21]	0.9102	1.31	[1.05,1.63]	0.0160
	Age at start		1.04	[1.03,1.05]	<.0001	1.05	[1.04,1.06]	<.0001
	Sex	Male	1.59	[1.29,1.96]	<.0001	1.25	[1.01,1.57]	0.0444
	Smoking	Current	0.87	[0.62,1.23]	0.4394	0.99	[0.71,1.38]	0.9423
		Past	0.84	[0.61,1.16]	0.2938	0.86	[0.63,1.17]	0.3331
	COPD Sev	Moderate	1.05	[0.68,1.64]	0.8139	1.34	[0.92,1.94]	0.1354
		(Very) sev	1.20	[0.81,1.79]	0.3703	1.41	[0.90,2.20]	0.1441
IHD	Cohort	QVA149	1.64	[1.09,2.46]	0.0171	1.46	[0.96,2.23]	0.0760
	Age at start		0.99	[0.98,1.01]	0.5613	1.00	[0.98,1.02]	0.9505
	Sex	Male	2.09	[1.37,3.18]	0.0006	2.69	[1.69,4.27]	<.0001
	Smoking	Current	1.36	[0.56,3.31]	0.4936	1.33	[0.57,3.09]	0.5135
		Past	1.11	[0.47,2.62]	0.8175	1.04	[0.46,2.34]	0.9266
	COPD Sev	Moderate	0.94	[0.49,1.83]	0.8628	1.08	[0.54,2.18]	0.8208
		(Very) sev	0.74	[0.38,1.44]	0.3785	0.80	[0.37,1.76]	0.5883

Note: Run date and time 01NOV2018 11:21:00,
If no results, number of events was too low

QVA149A2402

Table 15-20-6 (Page 4 of 20)
Adjusted hazard ratios for QVA versus comparators (Model 1)
POOLED - Total analysis population

			QVA compared to LAMA		
Endpoint		Level	HR	95% CI	P
MACE	Cohort	QVA149	0.92	[0.79,1.08]	0.3251
	Age at start		1.05	[1.04,1.06]	<.0001
	Sex	Male	1.37	[1.17,1.59]	<.0001
	Smoking	Current	1.16	[0.90,1.49]	0.2568
		Past	1.04	[0.83,1.31]	0.7147
	COPD Sev	Moderate	1.18	[0.94,1.47]	0.1554
		(Very) sev	1.38	[1.01,1.88]	0.0545
IHD	Cohort	QVA149	1.06	[0.77,1.45]	0.7191
	Age at start		1.01	[1.00,1.02]	0.0483
	Sex	Male	1.58	[1.21,2.06]	0.0007
	Smoking	Current	1.73	[0.98,3.04]	0.0571
		Past	1.63	[0.94,2.80]	0.0799
	COPD Sev	Moderate	0.84	[0.60,1.17]	0.3059
		(Very) sev	0.86	[0.59,1.26]	0.4346

Note: Run date and time 01NOV2018 11:21:00,
If no results, number of events was too low

QVA149A2402

Table 15-20-6 (Page 5 of 20)
All hazard ratios in adjusted model (Model 1)
POOLED - Total analysis population

			QVA compared to Free LABA+LAMA without ICS			QVA compared to Free LABA+LAMA with ICS		
Endpoint		Level	HR	95% CI	P	HR	95% CI	P
CARD	Cohort	QVA149	0.96	[0.67,1.39]	0.8459	0.75	[0.45,1.24]	0.2582
	Age at start		1.05	[1.03,1.07]	<.0001	1.05	[1.03,1.07]	<.0001
	Sex	Male	1.93	[1.22,3.03]	0.0046	1.31	[0.81,2.12]	0.2786
	Smoking	Current	0.92	[0.49,1.71]	0.7873	1.03	[0.50,2.09]	0.9436
		Past	0.94	[0.54,1.62]	0.8202	0.94	[0.49,1.79]	0.8539
	COPD Sev	Moderate	1.38	[0.57,3.32]	0.4887	1.57	[0.46,5.31]	0.4807
		(Very) sev	1.32	[0.43,4.11]	0.6382	1.38	[0.34,5.67]	0.6660
CERE	Cohort	QVA149	1.62	[0.97,2.69]	0.0628	0.74	[0.40,1.38]	0.3438
	Age at start		1.05	[1.02,1.07]	0.0004	1.04	[1.01,1.07]	0.0024
	Sex	Male	1.04	[0.64,1.71]	0.8636	1.19	[0.69,2.04]	0.5294
	Smoking	Current	2.12	[0.77,5.81]	0.1447	1.42	[0.57,3.55]	0.4546
		Past	1.69	[0.64,4.42]	0.2870	1.11	[0.47,2.60]	0.8130
	COPD Sev	Moderate	1.14	[0.54,2.43]	0.7279	1.42	[0.56,3.57]	0.4623
		(Very) sev	1.05	[0.46,2.41]	0.9063	0.98	[0.34,2.86]	0.9712

Note: Run date and time 01NOV2018 11:21:00,
If no results, number of events was too low

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Table 15-20-6 (Page 6 of 20)
Adjusted hazard ratios for QVA versus comparators (Model 1)
POOLED - Total analysis population

			QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
Endpoint		Level	HR	95% CI	P	HR	95% CI	P
CARD	Cohort	QVA149	0.76	[0.47,1.22]	0.2575	0.72	[0.56,0.92]	0.0091
	Age at start		1.05	[1.03,1.08]	<.0001	1.06	[1.05,1.07]	<.0001
	Sex	Male	1.55	[0.97,2.48]	0.0663	1.45	[1.21,1.75]	<.0001
	Smoking	Current	0.91	[0.48,1.72]	0.7729	1.04	[0.78,1.39]	0.7690
		Past	0.81	[0.47,1.40]	0.4543	0.95	[0.73,1.22]	0.6777
	COPD Sev	Moderate	1.64	[0.59,4.54]	0.3545	1.17	[0.90,1.51]	0.2473
		(Very) sev	1.63	[0.45,5.87]	0.4744	0.98	[0.73,1.32]	0.9033
CERE	Cohort	QVA149	0.76	[0.42,1.38]	0.3670	1.06	[0.77,1.46]	0.7117
	Age at start		1.04	[1.01,1.06]	0.0039	1.05	[1.04,1.06]	<.0001
	Sex	Male	1.11	[0.66,1.87]	0.6846	1.15	[0.91,1.46]	0.2407
	Smoking	Current	1.71	[0.68,4.34]	0.2564	1.29	[0.85,1.96]	0.2273
		Past	1.16	[0.49,2.74]	0.7406	1.10	[0.75,1.62]	0.6191
	COPD Sev	Moderate	1.09	[0.52,2.33]	0.8141	1.06	[0.72,1.57]	0.7720
		(Very) sev	0.92	[0.38,2.23]	0.8621	1.00	[0.63,1.59]	0.9932

Note: Run date and time 01NOV2018 11:21:00,
If no results, number of events was too low

QVA149A2402

Table 15-20-6 (Page 7 of 20)
Adjusted hazard ratios for QVA versus comparators (Model 1)
POOLED - Total analysis population

			QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint		Level	HR	95% CI	P	HR	95% CI	P
CARD	Cohort	QVA149	0.79	[0.56,1.12]	0.1913	1.16	[0.80,1.69]	0.4246
	Age at start		1.05	[1.03,1.07]	<.0001	1.05	[1.03,1.07]	<.0001
	Sex	Male	1.63	[1.13,2.35]	0.0096	1.78	[1.17,2.70]	0.0072
	Smoking	Current	0.74	[0.41,1.35]	0.3305	1.08	[0.61,1.92]	0.7896
		Past	0.93	[0.55,1.59]	0.7961	0.78	[0.46,1.33]	0.3669
	COPD Sev	Moderate	1.04	[0.57,1.89]	0.9037	1.16	[0.60,2.25]	0.6707
		(Very) sev	1.08	[0.52,2.25]	0.8347	1.17	[0.48,2.84]	0.7317
CERE	Cohort	QVA149	1.22	[0.80,1.87]	0.3542	1.09	[0.71,1.66]	0.7012
	Age at start		1.03	[1.01,1.06]	0.0019	1.03	[1.01,1.05]	0.0023
	Sex	Male	1.20	[0.79,1.81]	0.3890	1.11	[0.72,1.70]	0.6339
	Smoking	Current	1.22	[0.51,2.89]	0.6531	1.63	[0.74,3.59]	0.2257
		Past	1.11	[0.49,2.52]	0.8014	1.15	[0.53,2.47]	0.7273
	COPD Sev	Moderate	1.06	[0.54,2.06]	0.8682	0.93	[0.53,1.63]	0.8062
		(Very) sev	0.93	[0.45,1.91]	0.8465	0.78	[0.40,1.54]	0.4808

Note: Run date and time 01NOV2018 11:21:00,
If no results, number of events was too low

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Table 15-20-6 (Page 8 of 20)
Adjusted hazard ratios for QVA versus comparators (Model 1)
POOLED - Total analysis population

			QVA compared to LAMA		
Endpoint		Level	HR	95% CI	P
CARD	Cohort	QVA149	0.75	[0.57,0.99]	0.0406
	Age at start		1.05	[1.04,1.06]	<.0001
	Sex	Male	1.31	[1.04,1.65]	0.0198
	Smoking	Current	0.99	[0.69,1.42]	0.9587
		Past	0.86	[0.62,1.19]	0.3654
	COPD Sev	Moderate	0.92	[0.68,1.25]	0.6092
		(Very) sev	0.98	[0.67,1.44]	0.9209
CERE	Cohort	QVA149	1.00	[0.71,1.40]	0.9979
	Age at start		1.04	[1.03,1.05]	<.0001
	Sex	Male	1.39	[1.06,1.83]	0.0176
	Smoking	Current	2.12	[1.17,3.86]	0.0138
		Past	1.76	[0.99,3.14]	0.0564
	COPD Sev	Moderate	1.09	[0.70,1.68]	0.7128
		(Very) sev	1.01	[0.62,1.64]	0.9612

Note: Run date and time 01NOV2018 11:21:00,
If no results, number of events was too low

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Table 15-20-6 (Page 9 of 20)
All hazard ratios in adjusted model (Model 1)
POOLED - Total analysis population

			QVA compared to Free LABA+LAMA without ICS			QVA compared to Free LABA+LAMA with ICS		
Endpoint		Level	HR	95% CI	P	HR	95% CI	P
GLAUCOME	Cohort	QVA149	0.69	[0.33,1.46]	0.3352	0.50	[0.19,1.34]	0.1667
	Age at start		1.02	[0.98,1.06]	0.3379	1.03	[0.98,1.08]	0.2824
	Sex	Male	0.82	[0.34,1.99]	0.6618	0.92	[0.32,2.61]	0.8759
	Smoking	Current	0.51	[0.15,1.72]	0.2805	0.71	[0.17,2.96]	0.6340
		Past	0.79	[0.30,2.09]	0.6374	0.76	[0.23,2.54]	0.6557
	COPD Sev	Moderate	1.91	[0.25,14.6]	0.5393	1.20	[0.15,9.34]	0.8624
		(Very) sev	1.39	[0.16,12.4]	0.7725	1.23	[0.16,9.69]	0.8467
BPHURIN	Cohort	QVA149	1.00	[0.69,1.44]	0.9942	0.97	[0.55,1.69]	0.9070
	Age at start		1.03	[1.01,1.05]	0.0085	1.03	[1.01,1.05]	0.0092
	Sex	Male	11.8	[4.32,32.4]	<.0001	18.4	[4.49,75.7]	<.0001
	Smoking	Current	1.19	[0.64,2.21]	0.5876	1.01	[0.52,1.97]	0.9708
		Past	1.05	[0.60,1.84]	0.8603	0.73	[0.41,1.31]	0.2903
	COPD Sev	Moderate	0.97	[0.53,1.79]	0.9215	0.93	[0.41,2.11]	0.8552
		(Very) sev	1.04	[0.52,2.11]	0.9050	1.04	[0.44,2.48]	0.9299

Note: Run date and time 01NOV2018 11:21:00,
If no results, number of events was too low

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Table 15-20-6 (Page 10 of 20)
Adjusted hazard ratios for QVA versus comparators (Model 1)
POOLED - Total analysis population

			QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
Endpoint		Level	HR	95% CI	P	HR	95% CI	P
GLAUCOME	Cohort	QVA149	.	[. , .]	.	0.88	[0.49,1.58]	0.6716
	Age at start		.	[. , .]	.	1.02	[1.00,1.04]	0.0718
	Sex	Male	.	[. , .]	.	0.91	[0.58,1.45]	0.6985
	Smoking	Current	.	[. , .]	.	0.69	[0.35,1.37]	0.2872
		Past	.	[. , .]	.	0.89	[0.49,1.62]	0.7117
	COPD Sev	Moderate	.	[. , .]	.	1.12	[0.54,2.33]	0.7571
		(Very) sev	.	[. , .]	.	0.89	[0.36,2.23]	0.8125
BPHURIN	Cohort	QVA149	1.32	[0.74,2.35]	0.3549	0.83	[0.64,1.07]	0.1506
	Age at start		1.02	[1.00,1.05]	0.0426	1.04	[1.03,1.05]	<.0001
	Sex	Male	13.7	[4.28,44.1]	<.0001	23.5	[12.9,43.1]	<.0001
	Smoking	Current	0.97	[0.49,1.91]	0.9208	1.04	[0.75,1.44]	0.8228
		Past	0.76	[0.42,1.36]	0.3563	0.91	[0.68,1.23]	0.5476
	COPD Sev	Moderate	0.75	[0.39,1.46]	0.4010	1.01	[0.69,1.48]	0.9575
		(Very) sev	0.77	[0.37,1.59]	0.4777	1.04	[0.68,1.58]	0.8668

Note: Run date and time 01NOV2018 11:21:00,
If no results, number of events was too low

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Table 15-20-6 (Page 11 of 20)
Adjusted hazard ratios for QVA versus comparators (Model 1)
POOLED - Total analysis population

			QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint		Level	HR	95% CI	P	HR	95% CI	P
GLAUCOME	Cohort	QVA149	0.92	[0.34,2.53]	0.8745	0.73	[0.35,1.53]	0.4016
	Age at start		1.02	[0.98,1.07]	0.2903	1.01	[0.98,1.05]	0.4985
	Sex	Male	0.57	[0.23,1.40]	0.2203	0.80	[0.36,1.76]	0.5774
	Smoking	Current	1.02	[0.24,4.38]	0.9742	0.36	[0.12,1.14]	0.0825
		Past	0.82	[0.24,2.86]	0.7603	0.58	[0.24,1.39]	0.2233
	COPD Sev	Moderate	0.98	[0.26,3.74]	0.9752	1.31	[0.45,3.85]	0.6243
		(Very) sev	0.91	[0.22,3.84]	0.8970	0.95	[0.26,3.51]	0.9385
BPHURIN	Cohort	QVA149	1.13	[0.72,1.78]	0.5913	0.86	[0.61,1.21]	0.3955
	Age at start		1.02	[1.00,1.04]	0.0279	1.02	[1.00,1.04]	0.0423
	Sex	Male	28.0	[6.88, 114]	<.0001	31.7	[7.81, 129]	<.0001
	Smoking	Current	0.84	[0.43,1.65]	0.6074	1.19	[0.67,2.12]	0.5570
		Past	0.95	[0.52,1.71]	0.8574	1.20	[0.71,2.02]	0.4969
	COPD Sev	Moderate	0.80	[0.42,1.53]	0.5039	0.96	[0.59,1.56]	0.8602
		(Very) sev	0.81	[0.38,1.75]	0.6020	0.94	[0.53,1.69]	0.8387

Note: Run date and time 01NOV2018 11:21:00,
If no results, number of events was too low

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Table 15-20-6 (Page 12 of 20)
Adjusted hazard ratios for QVA versus comparators (Model 1)
POOLED - Total analysis population

			QVA compared to LAMA		
Endpoint		Level	HR	95% CI	P
GLAUCOME	Cohort	QVA149	0.55	[0.30,1.02]	0.0561
	Age at start		1.02	[1.00,1.04]	0.1109
	Sex	Male	0.62	[0.38,1.02]	0.0591
	Smoking	Current	0.74	[0.36,1.52]	0.4115
		Past	0.97	[0.51,1.84]	0.9208
	COPD Sev	Moderate	1.09	[0.51,2.35]	0.8217
		(Very) sev	0.89	[0.33,2.44]	0.8261
BPHURIN	Cohort	QVA149	0.79	[0.60,1.05]	0.1047
	Age at start		1.03	[1.02,1.05]	<.0001
	Sex	Male	19.9	[9.82,40.4]	<.0001
	Smoking	Current	1.02	[0.69,1.51]	0.9093
		Past	0.95	[0.66,1.36]	0.7691
	COPD Sev	Moderate	1.38	[0.98,1.96]	0.0675
		(Very) sev	1.46	[0.89,2.37]	0.1424

Note: Run date and time 01NOV2018 11:21:00,
If no results, number of events was too low

QVA149A2402

Table 15-20-6 (Page 13 of 20)
All hazard ratios in adjusted model (Model 1)
POOLED - Total analysis population

			QVA compared to Free LABA+LAMA without ICS			QVA compared to Free LABA+LAMA with ICS		
Endpoint		Level	HR	95% CI	P	HR	95% CI	P
DMVAL	Cohort	QVA149	1.10	[0.76,1.59]	0.6166	1.37	[0.73,2.57]	0.3206
	Age at start		1.00	[0.98,1.02]	0.9927	1.00	[0.97,1.02]	0.7214
	Sex	Male	1.53	[0.96,2.42]	0.0712	1.27	[0.74,2.20]	0.3829
	Smoking	Current	1.02	[0.50,2.05]	0.9609	1.46	[0.58,3.68]	0.4252
		Past	1.59	[0.86,2.96]	0.1414	2.17	[0.97,4.88]	0.0597
	COPD Sev	Moderate	0.81	[0.47,1.40]	0.4468	0.67	[0.32,1.38]	0.2806
		(Very) sev	0.83	[0.45,1.53]	0.5562	0.77	[0.39,1.53]	0.4606
BRONCHOSPASM	Cohort	QVA149	.	[. , .]	.	.	[. , .]	.
	Age at start		.	[. , .]	.	.	[. , .]	.
	Sex	Male	.	[. , .]	.	.	[. , .]	.
	Smoking	Current	.	[. , .]	.	.	[. , .]	.
		Past	.	[. , .]	.	.	[. , .]	.
	COPD Sev	Moderate	.	[. , .]	.	.	[. , .]	.
		(Very) sev	.	[. , .]	.	.	[. , .]	.

Note: Run date and time 01NOV2018 11:21:00,
If no results, number of events was too low

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Table 15-20-6 (Page 14 of 20)
Adjusted hazard ratios for QVA versus comparators (Model 1)
POOLED - Total analysis population

			QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
Endpoint		Level	HR	95% CI	P	HR	95% CI	P
DMVAL	Cohort	QVA149	1.64	[0.88,3.05]	0.1201	0.85	[0.66,1.11]	0.2337
	Age at start		1.00	[0.98,1.02]	0.8858	1.00	[0.99,1.01]	0.9183
	Sex	Male	1.67	[0.95,2.94]	0.0748	1.37	[1.11,1.69]	0.0038
	Smoking	Current	1.21	[0.48,3.06]	0.6941	1.06	[0.76,1.47]	0.7395
		Past	1.69	[0.81,3.54]	0.1627	1.24	[0.91,1.69]	0.1718
	COPD Sev	Moderate	0.65	[0.33,1.30]	0.2289	1.05	[0.78,1.42]	0.7394
		(Very) sev	0.74	[0.37,1.46]	0.3866	1.22	[0.86,1.73]	0.2797
BRONCHOSPASM	Cohort	QVA149	0.37	[0.11,1.29]	0.1183	0.49	[0.21,1.17]	0.1079
	Age at start		1.00	[0.95,1.07]	0.8858	0.97	[0.94,0.99]	0.0045
	Sex	Male	0.24	[0.07,0.89]	0.0324	0.92	[0.52,1.64]	0.7789
	Smoking	Current	0.45	[0.04,5.32]	0.5267	0.68	[0.32,1.43]	0.3054
		Past	2.36	[0.51,11.0]	0.2742	0.76	[0.38,1.52]	0.4377
	COPD Sev	Moderate	1.57	[0.19,13.0]	0.6757	0.73	[0.38,1.41]	0.3533
		(Very) sev	1.39	[0.16,12.5]	0.7681	0.66	[0.28,1.57]	0.3466

Note: Run date and time 01NOV2018 11:21:00,
If no results, number of events was too low

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Table 15-20-6 (Page 15 of 20)
Adjusted hazard ratios for QVA versus comparators (Model 1)
POOLED - Total analysis population

			QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint		Level	HR	95% CI	P	HR	95% CI	P
DMVAL	Cohort	QVA149	0.80	[0.53,1.21]	0.2948	1.30	[0.89,1.89]	0.1737
	Age at start		0.99	[0.97,1.01]	0.1953	1.00	[0.98,1.01]	0.6736
	Sex	Male	1.20	[0.81,1.79]	0.3691	1.14	[0.75,1.74]	0.5363
	Smoking	Current	1.08	[0.53,2.20]	0.8310	1.24	[0.62,2.51]	0.5413
		Past	1.37	[0.72,2.61]	0.3404	1.76	[0.95,3.26]	0.0728
	COPD Sev	Moderate	0.68	[0.40,1.17]	0.1657	1.12	[0.65,1.95]	0.6801
		(Very) sev	0.83	[0.46,1.50]	0.5389	1.07	[0.56,2.05]	0.8384
BRONCHOSPASM	Cohort	QVA149	.	[. , .]	.	0.94	[0.27,3.23]	0.9160
	Age at start		.	[. , .]	.	0.99	[0.94,1.05]	0.8557
	Sex	Male	.	[. , .]	.	0.17	[0.05,0.60]	0.0061
	Smoking	Current	.	[. , .]	.	1.63	[0.23,11.4]	0.6204
		Past	.	[. , .]	.	2.34	[0.40,13.7]	0.3445
	COPD Sev	Moderate	.	[. , .]	.	1.04	[0.08,13.5]	0.9746
		(Very) sev	.	[. , .]	.	1.53	[0.09,27.4]	0.7761

Note: Run date and time 01NOV2018 11:21:00,
If no results, number of events was too low

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Table 15-20-6 (Page 16 of 20)
Adjusted hazard ratios for QVA versus comparators (Model 1)
POOLED - Total analysis population

			QVA compared to LAMA		
Endpoint		Level	HR	95% CI	P
DMVAL	Cohort	QVA149	1.03	[0.78,1.38]	0.8170
	Age at start		1.00	[0.99,1.01]	0.8736
	Sex	Male	1.46	[1.11,1.90]	0.0060
	Smoking	Current	1.58	[0.97,2.59]	0.0681
		Past	1.97	[1.22,3.17]	0.0055
	COPD Sev	Moderate	1.05	[0.73,1.49]	0.8097
		(Very) sev	1.21	[0.80,1.84]	0.3746
BRONCHOSPASM	Cohort	QVA149	1.19	[0.43,3.33]	0.7377
	Age at start		0.98	[0.94,1.03]	0.4619
	Sex	Male	0.20	[0.07,0.55]	0.0018
	Smoking	Current	0.23	[0.05,1.08]	0.0639
		Past	0.67	[0.21,2.09]	0.4871
	COPD Sev	Moderate	1.12	[0.24,5.14]	0.8899
		(Very) sev	1.46	[0.35,6.16]	0.6045

Note: Run date and time 01NOV2018 11:21:00,
If no results, number of events was too low

QVA149A2402

Table 15-20-6 (Page 17 of 20)
All hazard ratios in adjusted model (Model 1)
POOLED - Total analysis population

			QVA compared to Free LABA+LAMA without ICS			QVA compared to Free LABA+LAMA with ICS		
Endpoint		Level	HR	95% CI	P	HR	95% CI	P
DEATH	Cohort	QVA149	1.71	[1.32,2.22]	<.0001	1.93	[1.18,3.15]	0.0083
	Age at start		1.08	[1.06,1.09]	<.0001	1.07	[1.06,1.09]	<.0001
	Sex	Male	1.15	[0.90,1.46]	0.2558	1.30	[0.99,1.71]	0.0580
	Smoking	Current	1.21	[0.77,1.89]	0.4140	1.18	[0.71,1.97]	0.5143
		Past	1.08	[0.72,1.62]	0.7109	1.04	[0.66,1.64]	0.8751
	COPD Sev	Moderate	1.15	[0.67,1.97]	0.6085	1.18	[0.63,2.22]	0.6164
		(Very) sev	1.96	[1.17,3.29]	0.0163	1.81	[0.98,3.37]	0.0731

Note: Run date and time 01NOV2018 11:21:00,
If no results, number of events was too low

QVA149A2402

Table 15-20-6 (Page 18 of 20)
Adjusted hazard ratios for QVA versus comparators (Model 1)
POOLED - Total analysis population

			QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
Endpoint		Level	HR	95% CI	P	HR	95% CI	P
DEATH	Cohort	QVA149	0.99	[0.71,1.40]	0.9753	0.79	[0.69,0.92]	0.0018
	Age at start		1.07	[1.06,1.09]	<.0001	1.09	[1.08,1.09]	<.0001
	Sex	Male	1.31	[1.01,1.70]	0.0406	1.10	[0.99,1.22]	0.0876
	Smoking	Current	1.13	[0.71,1.81]	0.6098	1.63	[1.36,1.95]	<.0001
		Past	0.97	[0.64,1.46]	0.8672	1.11	[0.94,1.32]	0.2122
	COPD Sev	Moderate	1.22	[0.64,2.31]	0.5580	1.17	[0.96,1.44]	0.1364
		(Very) sev	2.01	[1.06,3.80]	0.0507	1.80	[1.49,2.17]	<.0001

Note: Run date and time 01NOV2018 11:21:00,
If no results, number of events was too low

QVA149A2402

Table 15-20-6 (Page 19 of 20)
Adjusted hazard ratios for QVA versus comparators (Model 1)
POOLED - Total analysis population

			QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint		Level	HR	95% CI	P	HR	95% CI	P
DEATH	Cohort	QVA149	1.35	[1.10,1.66]	0.0043	1.22	[0.98,1.53]	0.0773
	Age at start		1.07	[1.06,1.09]	<.0001	1.09	[1.08,1.10]	<.0001
	Sex	Male	1.23	[1.01,1.50]	0.0436	1.15	[0.92,1.42]	0.2185
	Smoking	Current	1.26	[0.83,1.90]	0.2793	1.39	[0.95,2.04]	0.0941
		Past	1.12	[0.77,1.65]	0.5510	1.00	[0.70,1.41]	0.9912
	COPD Sev	Moderate	1.24	[0.82,1.88]	0.3203	1.23	[0.82,1.86]	0.3237
		(Very) sev	2.11	[1.38,3.22]	0.0013	2.05	[1.29,3.25]	0.0062

Note: Run date and time 01NOV2018 11:21:00,
If no results, number of events was too low

QVA149A2402

Table 15-20-6 (Page 20 of 20)
Adjusted hazard ratios for QVA versus comparators (Model 1)
POOLED - Total analysis population

			QVA compared to LAMA		
Endpoint		Level	HR	95% CI	P
DEATH	Cohort	QVA149	1.09	[0.92,1.29]	0.3396
	Age at start		1.09	[1.08,1.09]	<.0001
	Sex	Male	1.16	[1.00,1.34]	0.0512
	Smoking	Current	1.05	[0.82,1.34]	0.6968
		Past	0.80	[0.64,0.99]	0.0437
	COPD Sev	Moderate	1.23	[0.93,1.64]	0.1632
		(Very) sev	2.09	[1.52,2.85]	0.0003

Note: Run date and time 01NOV2018 11:21:00,
If no results, number of events was too low

QVA149A2402

Table 15-21-1 (Page 1 of 4)
Hazard ratios for QVA versus comparators, IPTW model
THIN - Total analysis population

	QVA compared to Free LABA+LAMA without ICS			QVA compared to Free LABA+LAMA with ICS		
Endpoint	HR	95% CI	P	HR	95% CI	P
MACE	1.33	[0.63,2.80]	0.4547	.	[. , .]	.
Ischemic heart disease	2.23	[0.96,5.20]	0.0626	.	[. , .]	.
Cardiac arrhythmia	3.31	[0.97,11.2]	0.0552	.	[. , .]	.
Cerebrovascular disorders	0.69	[0.23,2.08]	0.5119	.	[. , .]	.
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	0.72	[0.25,2.06]	0.5376	.	[. , .]	.
Diabetes mellitus	0.67	[0.25,1.79]	0.4204	.	[. , .]	.
Mortality	2.64	[1.56,4.47]	0.0003	.	[. , .]	.

Note: Run date and time 01NOV2018 11:20:09,
If no results, number of events was too low

QVA149A2402

Table 15-21-1 (Page 2 of 4)
Hazard ratios for QVA versus comparators, IPTW model
THIN - Total analysis population

	QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
Endpoint	HR	95% CI	P	HR	95% CI	P
MACE	.	[. , .]	.	1.15	[0.59,2.26]	0.6792
Ischemic heart disease	.	[. , .]	.	1.83	[0.92,3.64]	0.0865
Cardiac arrhythmia	.	[. , .]	.	1.47	[0.53,4.09]	0.4641
Cerebrovascular disorders	.	[. , .]	.	0.46	[0.19,1.14]	0.0938
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	.	[. , .]	.	0.39	[0.16,0.98]	0.0447
Diabetes mellitus	.	[. , .]	.	1.00	[0.39,2.57]	0.9943
Mortality	0.87	[0.33,2.31]	0.7834	1.32	[0.87,1.98]	0.1876

Note: Run date and time 01NOV2018 11:20:09,
If no results, number of events was too low

QVA149A2402

Table 15-21-1 (Page 3 of 4)
Hazard ratios for QVA versus comparators, IPTW model
THIN - Total analysis population

	QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint	HR	95% CI	P	HR	95% CI	P
MACE	1.46	[0.83,2.57]	0.1939	0.93	[0.47,1.82]	0.8295
Ischemic heart disease	1.94	[1.00,3.76]	0.0504	1.04	[0.45,2.42]	0.9292
Cardiac arrhythmia	0.71	[0.29,1.72]	0.4422	0.97	[0.34,2.78]	0.9503
Cerebrovascular disorders	0.96	[0.41,2.28]	0.9332	0.64	[0.26,1.61]	0.3476
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	1.32	[0.50,3.53]	0.5756	0.42	[0.14,1.27]	0.1253
Diabetes mellitus	0.98	[0.44,2.20]	0.9565	0.68	[0.27,1.71]	0.4132
Mortality	1.77	[1.28,2.46]	0.0006	1.43	[0.89,2.30]	0.1415

Note: Run date and time 01NOV2018 11:20:09,
If no results, number of events was too low

QVA149A2402

Table 15-21-1 (Page 4 of 4)
Hazard ratios for QVA versus comparators, IPTW model
THIN - Total analysis population

	QVA compared to LAMA		
Endpoint	HR	95% CI	P
MACE	1.06	[0.57,1.98]	0.8541
Ischemic heart disease	1.64	[0.85,3.15]	0.1386
Cardiac arrhythmia	1.08	[0.41,2.87]	0.8729
Cerebrovascular disorders	0.46	[0.20,1.07]	0.0703
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	0.44	[0.17,1.10]	0.0799
Diabetes mellitus	0.71	[0.31,1.60]	0.4038
Mortality	1.77	[1.19,2.61]	0.0044

Note: Run date and time 01NOV2018 11:20:09,
If no results, number of events was too low

QVA149A2402

Table 15-21-2 (Page 1 of 4)
Hazard ratios for QVA versus comparators, IPTW model
IPCI - Total analysis population

	QVA compared to Free LABA+LAMA without ICS			QVA compared to Free LABA+LAMA with ICS		
Endpoint	HR	95% CI	P	HR	95% CI	P
MACE	1.25	[0.59,2.65]	0.5516	1.47	[0.50,4.25]	0.4824
Cardiac arrhythmia	1.37	[0.48,3.93]	0.5612	0.66	[0.22,1.95]	0.4489
Cerebrovascular disorders	2.96	[1.02,8.60]	0.0461	.	[. , .]	.
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	2.66	[0.87,8.15]	0.0857	.	[. , .]	.
Diabetes mellitus	.	[. , .]	.	.	[. , .]	.
Mortality	0.73	[0.37,1.44]	0.3598	1.88	[0.60,5.87]	0.2799

Note: Run date and time 01NOV2018 11:20:21,
If no results, number of events was too low

QVA149A2402

Table 15-21-2 (Page 2 of 4)
Hazard ratios for QVA versus comparators, IPTW model
IPCI - Total analysis population

	QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
Endpoint	HR	95% CI	P	HR	95% CI	P
MACE	0.88	[0.34,2.31]	0.8027	1.19	[0.61,2.30]	0.6150
Cardiac arrhythmia	0.53	[0.15,1.87]	0.3275	1.21	[0.46,3.19]	0.7018
Cerebrovascular disorders	2.16	[0.66,7.08]	0.2030	2.57	[1.14,5.77]	0.0230
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	.	[. , .]	.	2.62	[0.97,7.09]	0.0582
Diabetes mellitus	.	[. , .]	.	1.78	[0.59,5.33]	0.3051
Mortality	0.54	[0.21,1.41]	0.2100	0.75	[0.37,1.52]	0.4192

Note: Run date and time 01NOV2018 11:20:21,
If no results, number of events was too low

QVA149A2402

Table 15-21-2 (Page 3 of 4)
Hazard ratios for QVA versus comparators, IPTW model
IPCI - Total analysis population

	QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint	HR	95% CI	P	HR	95% CI	P
MACE	0.91	[0.39,2.11]	0.8315	1.08	[0.49,2.37]	0.8501
Cardiac arrhythmia	1.60	[0.49,5.17]	0.4352	.	[. , .]	.
Cerebrovascular disorders	.	[. , .]	.	1.37	[0.58,3.23]	0.4733
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	1.28	[0.47,3.50]	0.6355	2.23	[0.74,6.74]	0.1566
Diabetes mellitus	.	[. , .]	.	.	[. , .]	.
Mortality	1.35	[0.62,2.92]	0.4499	0.55	[0.28,1.07]	0.0788

Note: Run date and time 01NOV2018 11:20:21,
If no results, number of events was too low

QVA149A2402

Table 15-21-2 (Page 4 of 4)
Hazard ratios for QVA versus comparators, IPTW model
IPCI - Total analysis population

	QVA compared to LAMA		
Endpoint	HR	95% CI	P
MACE	0.99	[0.51,1.91]	0.9653
Cardiac arrhythmia	0.80	[0.33,1.94]	0.6196
Cerebrovascular disorders	1.77	[0.84,3.70]	0.1308
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	1.38	[0.58,3.28]	0.4607
Diabetes mellitus	1.65	[0.53,5.10]	0.3853
Mortality	0.89	[0.48,1.67]	0.7282

Note: Run date and time 01NOV2018 11:20:21,
If no results, number of events was too low

QVA149A2402

Table 15-21-3 (Page 1 of 4)
Hazard ratios for QVA versus comparators, IPTW model
AUH - Total analysis population

	QVA compared to Free LABA+LAMA without ICS			QVA compared to Free LABA+LAMA with ICS		
Endpoint	HR	95% CI	P	HR	95% CI	P
MACE	1.03	[0.68,1.56]	0.8970	0.52	[0.25,1.09]	0.0823
Ischemic heart disease	.	[. , .]	.	.	[. , .]	.
Cardiac arrhythmia	1.17	[0.45,3.04]	0.7391	.	[. , .]	.
Cerebrovascular disorders	.	[. , .]	.	.	[. , .]	.
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	.	[. , .]	.	.	[. , .]	.
Diabetes mellitus	.	[. , .]	.	.	[. , .]	.
Mortality	1.32	[0.74,2.35]	0.3419	.	[. , .]	.

Note: Run date and time 01NOV2018 11:20:31,
If no results, number of events was too low

QVA149A2402

Table 15-21-3 (Page 2 of 4)
Hazard ratios for QVA versus comparators, IPTW model
AUH - Total analysis population

	QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
Endpoint	HR	95% CI	P	HR	95% CI	P
MACE	0.92	[0.48,1.76]	0.8037	1.04	[0.83,1.31]	0.7180
Ischemic heart disease	.	[. , .]	.	1.41	[0.88,2.27]	0.1543
Cardiac arrhythmia	.	[. , .]	.	0.79	[0.47,1.32]	0.3711
Cerebrovascular disorders	.	[. , .]	.	1.70	[0.87,3.31]	0.1211
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	.	[. , .]	.	0.78	[0.30,2.04]	0.6164
Diabetes mellitus	.	[. , .]	.	0.66	[0.24,1.82]	0.4215
Mortality	1.40	[0.50,3.97]	0.5215	0.72	[0.57,0.92]	0.0083

Note: Run date and time 01NOV2018 11:20:31,
If no results, number of events was too low

QVA149A2402

Table 15-21-3 (Page 3 of 4)
Hazard ratios for QVA versus comparators, IPTW model
AUH - Total analysis population

	QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint	HR	95% CI	P	HR	95% CI	P
MACE	1.04	[0.76,1.42]	0.8064	1.38	[0.93,2.05]	0.1068
Ischemic heart disease	2.73	[1.39,5.34]	0.0034	1.46	[0.69,3.08]	0.3185
Cardiac arrhythmia	0.74	[0.40,1.39]	0.3508	1.35	[0.56,3.28]	0.5057
Cerebrovascular disorders	0.75	[0.31,1.79]	0.5134	.	[. , .]	.
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	1.30	[0.44,3.83]	0.6343	.	[. , .]	.
Diabetes mellitus	0.53	[0.19,1.45]	0.2138	.	[. , .]	.
Mortality	1.37	[0.95,1.97]	0.0923	1.12	[0.68,1.82]	0.6573

Note: Run date and time 01NOV2018 11:20:31,
If no results, number of events was too low

QVA149A2402

Table 15-21-3 (Page 4 of 4)
Hazard ratios for QVA versus comparators, IPTW model
AUH - Total analysis population

	QVA compared to LAMA		
Endpoint	HR	95% CI	P
MACE	0.95	[0.73,1.24]	0.6930
Ischemic heart disease	2.00	[1.05,3.79]	0.0341
Cardiac arrhythmia	0.79	[0.44,1.43]	0.4436
Cerebrovascular disorders	1.45	[0.68,3.08]	0.3398
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	0.67	[0.23,1.94]	0.4561
Diabetes mellitus	0.80	[0.25,2.57]	0.7050
Mortality	0.83	[0.62,1.13]	0.2388

Note: Run date and time 01NOV2018 11:20:31,
If no results, number of events was too low

QVA149A2402

Table 15-21-4 (Page 1 of 4)
Hazard ratios for QVA versus comparators, IPTW model
HSD - Total analysis population

	QVA compared to Free LABA+LAMA without ICS			QVA compared to Free LABA+LAMA with ICS		
Endpoint	HR	95% CI	P	HR	95% CI	P
Diabetes mellitus	.	[. , .]	.	.	[. , .]	.

Note: Run date and time 01NOV2018 11:20:41,
If no results, number of events was too low

QVA149A2402

Table 15-21-4 (Page 2 of 4)
Hazard ratios for QVA versus comparators, IPTW model
HSD - Total analysis population

	QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
Endpoint	HR	95% CI	P	HR	95% CI	P
Diabetes mellitus	.	[. , .]	.	0.65	[0.23,1.82]	0.4085

Note: Run date and time 01NOV2018 11:20:41,
If no results, number of events was too low

QVA149A2402

Table 15-21-4 (Page 3 of 4)
Hazard ratios for QVA versus comparators, IPTW model
HSD - Total analysis population

	QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint	HR	95% CI	P	HR	95% CI	P
Diabetes mellitus	.	[. , .]	.	.	[. , .]	.

Note: Run date and time 01NOV2018 11:20:41,
If no results, number of events was too low

QVA149A2402

Table 15-21-4 (Page 4 of 4)
Hazard ratios for QVA versus comparators, IPTW model
HSD - Total analysis population

	QVA compared to LAMA		
Endpoint	HR	95% CI	P
Diabetes mellitus	1.32	[0.42,4.11]	0.6306

Note: Run date and time 01NOV2018 11:20:41,
If no results, number of events was too low

QVA149A2402

Table 15-21-5 (Page 1 of 4)
Hazard ratios for QVA versus comparators, IPTW model
SIDIAP - Total analysis population

	QVA compared to Free LABA+LAMA without ICS			QVA compared to Free LABA+LAMA with ICS		
Endpoint	HR	95% CI	P	HR	95% CI	P
MACE	1.25	[0.88,1.79]	0.2099	1.42	[0.83,2.42]	0.2031
Ischemic heart disease	0.60	[0.27,1.34]	0.2103	.	[. , .]	.
Cardiac arrhythmia	1.04	[0.61,1.78]	0.8919	0.71	[0.36,1.41]	0.3326
Cerebrovascular disorders	1.24	[0.45,3.40]	0.6749	0.43	[0.16,1.13]	0.0885
Glaucoma	0.72	[0.31,1.70]	0.4594	.	[. , .]	.
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	0.85	[0.54,1.34]	0.4885	1.00	[0.50,2.01]	0.9978
Diabetes mellitus	1.03	[0.64,1.66]	0.9057	1.40	[0.61,3.21]	0.4257
Bronchospasm	.	[. , .]	.	.	[. , .]	.
Mortality	1.40	[0.82,2.39]	0.2177	2.39	[0.93,6.14]	0.0702

Note: Run date and time 01NOV2018 11:20:53,
If no results, number of events was too low

QVA149A2402

Table 15-21-5 (Page 2 of 4)
Hazard ratios for QVA versus comparators, IPTW model
SIDIAP - Total analysis population

	QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
Endpoint	HR	95% CI	P	HR	95% CI	P
MACE	0.94	[0.59,1.49]	0.7921	0.80	[0.63,1.01]	0.0599
Ischemic heart disease	0.83	[0.26,2.66]	0.7503	0.72	[0.38,1.35]	0.3033
Cardiac arrhythmia	0.62	[0.31,1.25]	0.1808	0.63	[0.43,0.94]	0.0251
Cerebrovascular disorders	0.31	[0.12,0.79]	0.0139	0.63	[0.33,1.20]	0.1602
Glaucoma	.	[. , .]	.	1.03	[0.49,2.16]	0.9442
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	1.67	[0.81,3.45]	0.1627	0.76	[0.55,1.04]	0.0861
Diabetes mellitus	1.48	[0.58,3.74]	0.4119	0.83	[0.58,1.18]	0.2893
Bronchospasm	0.26	[0.09,0.77]	0.0151	0.46	[0.18,1.17]	0.1039
Mortality	0.98	[0.55,1.74]	0.9339	0.52	[0.39,0.70]	<.0001

Note: Run date and time 01NOV2018 11:20:53,
If no results, number of events was too low

QVA149A2402

Table 15-21-5 (Page 3 of 4)
Hazard ratios for QVA versus comparators, IPTW model
SIDIAP - Total analysis population

	QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint	HR	95% CI	P	HR	95% CI	P
MACE	0.82	[0.46,1.44]	0.4867	0.91	[0.59,1.39]	0.6512
Ischemic heart disease	0.31	[0.10,0.97]	0.0446	1.45	[0.58,3.66]	0.4266
Cardiac arrhythmia	.	[. , .]	.	1.09	[0.65,1.83]	0.7527
Cerebrovascular disorders	.	[. , .]	.	0.71	[0.33,1.55]	0.3922
Glaucoma	.	[. , .]	.	0.68	[0.27,1.71]	0.4117
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	0.87	[0.36,2.09]	0.7596	0.78	[0.52,1.17]	0.2334
Diabetes mellitus	0.61	[0.29,1.28]	0.1940	1.16	[0.72,1.87]	0.5472
Bronchospasm	.	[. , .]	.	0.69	[0.21,2.25]	0.5337
Mortality	1.05	[0.48,2.29]	0.8966	0.61	[0.35,1.06]	0.0808

Note: Run date and time 01NOV2018 11:20:53,
If no results, number of events was too low

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Table 15-21-5 (Page 4 of 4)
Hazard ratios for QVA versus comparators, IPTW model
SIDIAP - Total analysis population

	QVA compared to LAMA		
Endpoint	HR	95% CI	P
MACE	0.97	[0.75,1.25]	0.7934
Ischemic heart disease	0.66	[0.33,1.32]	0.2443
Cardiac arrhythmia	0.69	[0.45,1.04]	0.0778
Cerebrovascular disorders	0.62	[0.31,1.23]	0.1720
Glaucoma	0.60	[0.28,1.27]	0.1802
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	0.76	[0.54,1.08]	0.1294
Diabetes mellitus	1.01	[0.69,1.46]	0.9654
Bronchospasm	0.90	[0.30,2.67]	0.8468
Mortality	0.64	[0.46,0.91]	0.0133

Note: Run date and time 01NOV2018 11:20:53,
If no results, number of events was too low

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Table 15-22 (Page 1 of 20)
Hazard ratios for QVA versus comparators in stratified analyses, IPTW model
POOLED - Total analysis population

		QVA compared to Free LABA+LAMA without ICS			QVA compared to Free LABA+LAMA with ICS		
Endpoint	Stratum	HR	95% CI	P	HR	95% CI	P
MACE	Males	.	[. , .]	.	1.21	[0.79,1.86]	0.3843
	Females	.	[. , .]	.	0.56	[0.33,0.96]	0.0342
	Age < 70	1.37	[0.87,2.15]	0.1763	.	[. , .]	.
	Age >= 70	1.11	[0.85,1.45]	0.4330	.	[. , .]	.
	COPD sev Mild	.	[. , .]	.	.	[. , .]	.
	COPD sev Moderate	.	[. , .]	.	.	[. , .]	.
	COPD sev (Very) Severe	.	[. , .]	.	.	[. , .]	.
	Probable COPD	.	[. , .]	.	.	[. , .]	.
	Definite COPD	.	[. , .]	.	.	[. , .]	.
	No hist. Card or Cere Dis	.	[. , .]	.	.	[. , .]	.
	Hist. Card or Cere Dis	.	[. , .]	.	.	[. , .]	.
IHD	Age < 70	3.21	[1.43,7.22]	0.0047	2.82	[0.67,11.8]	0.1570
	Age >= 70	0.72	[0.42,1.22]	0.2217	0.69	[0.28,1.74]	0.4377
	No ICS at Cohort Start	1.12	[0.72,1.74]	0.6286	.	[. , .]	.
	ICS at Cohort Start	62E5	[0.00, .]	0.9900	.	[. , .]	.

Note: Stratified models are fitted when P interaction below 0.10 in at least 3 imputed sets
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Table 15-22 (Page 2 of 20)
Hazard ratios for QVA versus comparators in stratified analyses, IPTW model
POOLED - Total analysis population

		QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
Endpoint	Stratum	HR	95% CI	P	HR	95% CI	P
MACE	Males	.	[. , .]	.	.	[. , .]	.
	Females	.	[. , .]	.	.	[. , .]	.
	Age < 70	.	[. , .]	.	1.12	[0.86,1.46]	0.3953
	Age >= 70	.	[. , .]	.	0.87	[0.74,1.03]	0.0977
	COPD sev Mild	0.91	[0.30,2.78]	0.8686	.	[. , .]	.
	COPD sev Moderate	1.24	[0.75,2.05]	0.3951	.	[. , .]	.
	COPD sev (Very) Severe	0.72	[0.40,1.28]	0.2770	.	[. , .]	.
	Probable COPD	.	[. , .]	.	0.80	[0.67,0.97]	0.0223
	Definite COPD	.	[. , .]	.	1.15	[0.93,1.41]	0.1960
	No hist. Card or Cere Dis	.	[. , .]	.	.	[. , .]	.
	Hist. Card or Cere Dis	.	[. , .]	.	.	[. , .]	.
IHD	Age < 70	3.02	[0.73,12.4]	0.1262	1.82	[1.20,2.75]	0.0045
	Age >= 70	0.75	[0.33,1.69]	0.4859	0.90	[0.61,1.31]	0.5741
	No ICS at Cohort Start	.	[. , .]	.	.	[. , .]	.
	ICS at Cohort Start	.	[. , .]	.	.	[. , .]	.

Note: Stratified models are fitted when P interaction below 0.10 in at least 3 imputed sets
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Hazard ratios for QVA versus comparators in stratified analyses, IPTW model
POOLED - Total analysis population

		QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint	Stratum	HR	95% CI	P	HR	95% CI	P
MACE	Males	.	[. , .]	.	1.25	[0.97,1.60]	0.0851
	Females	.	[. , .]	.	0.75	[0.52,1.09]	0.1285
	Age < 70	.	[. , .]	.	1.45	[0.94,2.23]	0.0919
	Age >= 70	.	[. , .]	.	0.96	[0.75,1.22]	0.7149
	COPD sev Mild	.	[. , .]	.	.	[. , .]	.
	COPD sev Moderate	.	[. , .]	.	.	[. , .]	.
	COPD sev (Very) Severe	.	[. , .]	.	.	[. , .]	.
	Probable COPD	.	[. , .]	.	.	[. , .]	.
	Definite COPD	.	[. , .]	.	.	[. , .]	.
	No hist. Card or Cere Dis	.	[. , .]	.	.	[. , .]	.
	Hist. Card or Cere Dis	.	[. , .]	.	.	[. , .]	.
IHD	Age < 70	.	[. , .]	.	.	[. , .]	.
	Age >= 70	.	[. , .]	.	.	[. , .]	.
	No ICS at Cohort Start	.	[. , .]	.	.	[. , .]	.
	ICS at Cohort Start	.	[. , .]	.	.	[. , .]	.

Note: Stratified models are fitted when P interaction below 0.10 in at least 3 imputed sets
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Hazard ratios for QVA versus comparators in stratified analyses, IPTW model
POOLED - Total analysis population

		QVA compared to LAMA		
Endpoint	Stratum	HR	95% CI	P
MACE	Males	.	[. , .]	.
	Females	.	[. , .]	.
	Age < 70	1.00	[0.74,1.34]	0.9822
	Age >= 70	0.95	[0.79,1.14]	0.5615
	COPD sev Mild	.	[. , .]	.
	COPD sev Moderate	.	[. , .]	.
	COPD sev (Very) Severe	.	[. , .]	.
	Probable COPD	.	[. , .]	.
	Definite COPD	.	[. , .]	.
	No hist. Card or Cere Dis	0.92	[0.65,1.29]	0.6199
	Hist. Card or Cere Dis	0.99	[0.83,1.18]	0.8963
IHD	Age < 70	.	[. , .]	.
	Age >= 70	.	[. , .]	.
	No ICS at Cohort Start	.	[. , .]	.
	ICS at Cohort Start	.	[. , .]	.

Note: Stratified models are fitted when P interaction below 0.10 in at least 3 imputed sets
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Hazard ratios for QVA versus comparators in stratified analyses, IPTW model
POOLED - Total analysis population

		QVA compared to Free LABA+LAMA without ICS			QVA compared to Free LABA+LAMA with ICS		
Endpoint	Stratum	HR	95% CI	P	HR	95% CI	P
IHD	Probable COPD	.	[. , .]	.	.	[. , .]	.
	Definite COPD	.	[. , .]	.	.	[. , .]	.
	Start in 2013-2015	.	[. , .]	.	0.98	[0.45,2.13]	0.9648
	Start in 2016-2017	.	[. , .]	.	43E5	[0.00, .]	.
CARD	COPD sev Mild	.	[. , .]	.	.	[. , .]	.
	COPD sev Moderate	.	[. , .]	.	.	[. , .]	.
	COPD sev (Very) Severe	.	[. , .]	.	.	[. , .]	.
	No ICS at Cohort Start	.	[. , .]	.	.	[. , .]	.
	ICS at Cohort Start	.	[. , .]	.	.	[. , .]	.
	No hist. Card or Cere Dis	.	[. , .]	.	1.69	[0.74,3.86]	0.2100
	Hist. Card or Cere Dis	.	[. , .]	.	0.44	[0.21,0.95]	0.0363
CERE	Age < 70	.	[. , .]	.	1.29	[0.32,5.22]	0.7250
	Age >= 70	.	[. , .]	.	0.41	[0.21,0.77]	0.0063
GLAUCOME	No ICS at Cohort Start	.	[. , .]	.	.	[. , .]	.
	ICS at Cohort Start	.	[. , .]	.	.	[. , .]	.

Note: Stratified models are fitted when P interaction below 0.10 in at least 3 imputed sets
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Hazard ratios for QVA versus comparators in stratified analyses, IPTW model
POOLED - Total analysis population

		QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
Endpoint	Stratum	HR	95% CI	P	HR	95% CI	P
IHD	Probable COPD	.	[. , .]	.	0.78	[0.50,1.23]	0.2866
	Definite COPD	.	[. , .]	.	1.71	[1.19,2.44]	0.0034
	Start in 2013-2015	.	[. , .]	.	.	[. , .]	.
	Start in 2016-2017	.	[. , .]	.	.	[. , .]	.
CARD	COPD sev Mild	.	[. , .]	.	.	[. , .]	.
	COPD sev Moderate	.	[. , .]	.	.	[. , .]	.
	COPD sev (Very) Severe	.	[. , .]	.	.	[. , .]	.
	No ICS at Cohort Start	.	[. , .]	.	.	[. , .]	.
	ICS at Cohort Start	.	[. , .]	.	.	[. , .]	.
	No hist. Card or Cere Dis	1.23	[0.63,2.39]	0.5416	.	[. , .]	.
	Hist. Card or Cere Dis	0.36	[0.19,0.68]	0.0019	.	[. , .]	.
CERE	Age < 70	.	[. , .]	.	.	[. , .]	.
	Age >= 70	.	[. , .]	.	.	[. , .]	.
GLAUCOME	No ICS at Cohort Start	.	[. , .]	.	.	[. , .]	.
	ICS at Cohort Start	.	[. , .]	.	.	[. , .]	.

Note: Stratified models are fitted when P interaction below 0.10 in at least 3 imputed sets
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Hazard ratios for QVA versus comparators in stratified analyses, IPTW model
POOLED - Total analysis population

		QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint	Stratum	HR	95% CI	P	HR	95% CI	P
IHD	Probable COPD	.	[. , .]	.	.	[. , .]	.
	Definite COPD	.	[. , .]	.	.	[. , .]	.
	Start in 2013-2015	.	[. , .]	.	.	[. , .]	.
	Start in 2016-2017	.	[. , .]	.	.	[. , .]	.
CARD	COPD sev Mild	0.34	[0.04,3.20]	0.3676	.	[. , .]	.
	COPD sev Moderate	0.97	[0.55,1.70]	0.9095	.	[. , .]	.
	COPD sev (Very) Severe	0.68	[0.37,1.27]	0.2288	.	[. , .]	.
	No ICS at Cohort Start	.	[. , .]	.	.	[. , .]	.
	ICS at Cohort Start	.	[. , .]	.	.	[. , .]	.
	No hist. Card or Cere Dis	.	[. , .]	.	.	[. , .]	.
	Hist. Card or Cere Dis	.	[. , .]	.	.	[. , .]	.
CERE	Age < 70	.	[. , .]	.	.	[. , .]	.
	Age >= 70	.	[. , .]	.	.	[. , .]	.
GLAUCOME	No ICS at Cohort Start	0.64	[0.22,1.85]	0.4148	.	[. , .]	.
	ICS at Cohort Start	2E7	[0.00, .]	0.9927	.	[. , .]	.

Note: Stratified models are fitted when P interaction below 0.10 in at least 3 imputed sets
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Hazard ratios for QVA versus comparators in stratified analyses, IPTW model
POOLED - Total analysis population

		QVA compared to LAMA		
Endpoint	Stratum	HR	95% CI	P
IHD	Probable COPD	0.80	[0.51,1.27]	0.3479
	Definite COPD	1.52	[1.01,2.28]	0.0465
	Start in 2013-2015	.	[. , .]	.
	Start in 2016-2017	.	[. , .]	.
CARD	COPD sev Mild	.	[. , .]	.
	COPD sev Moderate	.	[. , .]	.
	COPD sev (Very) Severe	.	[. , .]	.
	No ICS at Cohort Start	0.90	[0.67,1.21]	0.4940
	ICS at Cohort Start	0.45	[0.23,0.87]	0.0170
	No hist. Card or Cere Dis	0.96	[0.69,1.34]	0.8095
	Hist. Card or Cere Dis	0.56	[0.35,0.90]	0.0165
CERE	Age < 70	.	[. , .]	.
	Age >= 70	.	[. , .]	.
GLAUCOME	No ICS at Cohort Start	.	[. , .]	.
	ICS at Cohort Start	.	[. , .]	.

Note: Stratified models are fitted when P interaction below 0.10 in at least 3 imputed sets
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Hazard ratios for QVA versus comparators in stratified analyses, IPTW model
POOLED - Total analysis population

		QVA compared to Free LABA+LAMA without ICS			QVA compared to Free LABA+LAMA with ICS		
Endpoint	Stratum	HR	95% CI	P	HR	95% CI	P
GLAUCOME	Probable COPD	.	[. , .]	.	0.86	[0.22,3.45]	0.8347
	Definite COPD	.	[. , .]	.	0.05	[0.01,0.28]	0.0008
	Start in 2013-2015	.	[. , .]	.	.	[. , .]	.
	Start in 2016-2017	.	[. , .]	.	.	[. , .]	.
BPHURIN	Age < 70	.	[. , .]	.	.	[. , .]	.
	Age >= 70	.	[. , .]	.	.	[. , .]	.
	COPD sev Mild	.	[. , .]	.	771	[0.00, .]	0.9957
	COPD sev Moderate	.	[. , .]	.	2.41	[0.61,9.49]	0.2376
	COPD sev (Very) Severe	.	[. , .]	.	0.84	[0.32,2.22]	0.7262
	Probable COPD	.	[. , .]	.	0.80	[0.44,1.48]	0.4846
	Definite COPD	.	[. , .]	.	8.54	[2.14,34.1]	0.0024
	No hist. Card or Cere Dis	.	[. , .]	.	3.31	[1.51,7.23]	0.0027
	Hist. Card or Cere Dis	.	[. , .]	.	0.67	[0.30,1.51]	0.3361
	Start in 2013-2015	.	[. , .]	.	.	[. , .]	.
	Start in 2016-2017	.	[. , .]	.	.	[. , .]	.

Note: Stratified models are fitted when P interaction below 0.10 in at least 3 imputed sets
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Hazard ratios for QVA versus comparators in stratified analyses, IPTW model
POOLED - Total analysis population

		QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
Endpoint	Stratum	HR	95% CI	P	HR	95% CI	P
GLAUCOME	Probable COPD	.	[. , .]	.	.	[. , .]	.
	Definite COPD	.	[. , .]	.	.	[. , .]	.
	Start in 2013-2015	.	[. , .]	.	0.69	[0.34,1.36]	0.2818
	Start in 2016-2017	.	[. , .]	.	1.93	[0.66,5.63]	0.2262
BPHURIN	Age < 70	.	[. , .]	.	1.28	[0.80,2.06]	0.3050
	Age >= 70	.	[. , .]	.	0.70	[0.50,0.98]	0.0404
	COPD sev Mild	.	[. , .]	.	.	[. , .]	.
	COPD sev Moderate	.	[. , .]	.	.	[. , .]	.
	COPD sev (Very) Severe	.	[. , .]	.	.	[. , .]	.
	Probable COPD	.	[. , .]	.	.	[. , .]	.
	Definite COPD	.	[. , .]	.	.	[. , .]	.
	No hist. Card or Cere Dis	.	[. , .]	.	.	[. , .]	.
	Hist. Card or Cere Dis	.	[. , .]	.	.	[. , .]	.
	Start in 2013-2015	.	[. , .]	.	.	[. , .]	.
	Start in 2016-2017	.	[. , .]	.	.	[. , .]	.

Note: Stratified models are fitted when P interaction below 0.10 in at least 3 imputed sets
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Hazard ratios for QVA versus comparators in stratified analyses, IPTW model
POOLED - Total analysis population

		QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint	Stratum	HR	95% CI	P	HR	95% CI	P
GLAUCOME	Probable COPD	.	[. , .]	.	.	[. , .]	.
	Definite COPD	.	[. , .]	.	.	[. , .]	.
	Start in 2013-2015	.	[. , .]	.	0.46	[0.20,1.05]	0.0650
	Start in 2016-2017	.	[. , .]	.	3.88	[0.45,33.8]	0.2190
BPHURIN	Age < 70	.	[. , .]	.	.	[. , .]	.
	Age >= 70	.	[. , .]	.	.	[. , .]	.
	COPD sev Mild	.	[. , .]	.	.	[. , .]	.
	COPD sev Moderate	.	[. , .]	.	.	[. , .]	.
	COPD sev (Very) Severe	.	[. , .]	.	.	[. , .]	.
	Probable COPD	.	[. , .]	.	.	[. , .]	.
	Definite COPD	.	[. , .]	.	.	[. , .]	.
	No hist. Card or Cere Dis	.	[. , .]	.	.	[. , .]	.
	Hist. Card or Cere Dis	.	[. , .]	.	.	[. , .]	.
	Start in 2013-2015	0.91	[0.53,1.55]	0.7262	.	[. , .]	.
	Start in 2016-2017	1.50	[0.71,3.21]	0.2902	.	[. , .]	.

Note: Stratified models are fitted when P interaction below 0.10 in at least 3 imputed sets
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Hazard ratios for QVA versus comparators in stratified analyses, IPTW model
POOLED - Total analysis population

		QVA compared to LAMA		
Endpoint	Stratum	HR	95% CI	P
GLAUCOME	Probable COPD	.	[. , .]	.
	Definite COPD	.	[. , .]	.
	Start in 2013-2015	.	[. , .]	.
	Start in 2016-2017	.	[. , .]	.
BPHURIN	Age < 70	.	[. , .]	.
	Age >= 70	.	[. , .]	.
	COPD sev Mild	.	[. , .]	.
	COPD sev Moderate	.	[. , .]	.
	COPD sev (Very) Severe	.	[. , .]	.
	Probable COPD	.	[. , .]	.
	Definite COPD	.	[. , .]	.
	No hist. Card or Cere Dis	.	[. , .]	.
	Hist. Card or Cere Dis	.	[. , .]	.
	Start in 2013-2015	.	[. , .]	.
	Start in 2016-2017	.	[. , .]	.

Note: Stratified models are fitted when P interaction below 0.10 in at least 3 imputed sets
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Hazard ratios for QVA versus comparators in stratified analyses, IPTW model
POOLED - Total analysis population

		QVA compared to Free LABA+LAMA without ICS			QVA compared to Free LABA+LAMA with ICS		
Endpoint	Stratum	HR	95% CI	P	HR	95% CI	P
DMVAL	COPD sev Mild	.	[. , .]	.	.	[. , .]	.
	COPD sev Moderate	.	[. , .]	.	.	[. , .]	.
	COPD sev (Very) Severe	.	[. , .]	.	.	[. , .]	.
	Probable COPD	.	[. , .]	.	1.12	[0.56,2.24]	0.7512
	Definite COPD	.	[. , .]	.	18.2	[0.51, 647]	0.1117
	No hist. Card or Cere Dis	.	[. , .]	.	.	[. , .]	.
	Hist. Card or Cere Dis	.	[. , .]	.	.	[. , .]	.
	Start in 2013-2015	1.17	[0.77,1.78]	0.4652	1.27	[0.65,2.47]	0.4845
	Start in 2016-2017	0.62	[0.26,1.46]	0.2719	63E5	[0.00, .]	0.9901
DEATH	COPD sev Mild	3.14	[1.20,8.25]	0.0206	16E3	[0.00, .]	0.9921
	COPD sev Moderate	1.80	[1.18,2.75]	0.0068	2.82	[1.16,6.85]	0.0230
	COPD sev (Very) Severe	1.15	[0.77,1.72]	0.5017	3.05	[1.18,7.93]	0.0222
	No ICS at Cohort Start	.	[. , .]	.	.	[. , .]	.
	ICS at Cohort Start	.	[. , .]	.	.	[. , .]	.
	Probable COPD	.	[. , .]	.	.	[. , .]	.

Note: Stratified models are fitted when P interaction below 0.10 in at least 3 imputed sets
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Hazard ratios for QVA versus comparators in stratified analyses, IPTW model
POOLED - Total analysis population

		QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
Endpoint	Stratum	HR	95% CI	P	HR	95% CI	P
DMVAL	COPD sev Mild	.	[. , .]	.	.	[. , .]	.
	COPD sev Moderate	.	[. , .]	.	.	[. , .]	.
	COPD sev (Very) Severe	.	[. , .]	.	.	[. , .]	.
	Probable COPD	.	[. , .]	.	.	[. , .]	.
	Definite COPD	.	[. , .]	.	.	[. , .]	.
	No hist. Card or Cere Dis	.	[. , .]	.	.	[. , .]	.
	Hist. Card or Cere Dis	.	[. , .]	.	.	[. , .]	.
	Start in 2013-2015	1.42	[0.74,2.73]	0.2926	.	[. , .]	.
	Start in 2016-2017	19E6	[0.00, .]	0.9934	.	[. , .]	.
DEATH	COPD sev Mild	.	[. , .]	.	.	[. , .]	.
	COPD sev Moderate	.	[. , .]	.	.	[. , .]	.
	COPD sev (Very) Severe	.	[. , .]	.	.	[. , .]	.
	No ICS at Cohort Start	.	[. , .]	.	.	[. , .]	.
	ICS at Cohort Start	.	[. , .]	.	.	[. , .]	.
	Probable COPD	.	[. , .]	.	0.61	[0.48,0.76]	<.0001

Note: Stratified models are fitted when P interaction below 0.10 in at least 3 imputed sets
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Table 15-22 (Page 15 of 20)
Hazard ratios for QVA versus comparators in stratified analyses, IPTW model
POOLED - Total analysis population

		QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint	Stratum	HR	95% CI	P	HR	95% CI	P
DMVAL	COPD sev Mild	.	[. , .]	.	2.21	[0.82,5.95]	0.1170
	COPD sev Moderate	.	[. , .]	.	0.82	[0.47,1.42]	0.4781
	COPD sev (Very) Severe	.	[. , .]	.	2.00	[0.71,5.61]	0.1977
	Probable COPD	.	[. , .]	.	.	[. , .]	.
	Definite COPD	.	[. , .]	.	.	[. , .]	.
	No hist. Card or Cere Dis	0.52	[0.32,0.85]	0.0096	.	[. , .]	.
	Hist. Card or Cere Dis	1.75	[0.83,3.71]	0.1433	.	[. , .]	.
	Start in 2013-2015	.	[. , .]	.	.	[. , .]	.
	Start in 2016-2017	.	[. , .]	.	.	[. , .]	.
DEATH	COPD sev Mild	.	[. , .]	.	.	[. , .]	.
	COPD sev Moderate	.	[. , .]	.	.	[. , .]	.
	COPD sev (Very) Severe	.	[. , .]	.	.	[. , .]	.
	No ICS at Cohort Start	.	[. , .]	.	.	[. , .]	.
	ICS at Cohort Start	.	[. , .]	.	.	[. , .]	.
	Probable COPD	1.19	[0.78,1.82]	0.4257	.	[. , .]	.

Note: Stratified models are fitted when P interaction below 0.10 in at least 3 imputed sets
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Table 15-22 (Page 16 of 20)
Hazard ratios for QVA versus comparators in stratified analyses, IPTW model
POOLED - Total analysis population

		QVA compared to LAMA		
Endpoint	Stratum	HR	95% CI	P
DMVAL	COPD sev Mild	.	[. , .]	.
	COPD sev Moderate	.	[. , .]	.
	COPD sev (Very) Severe	.	[. , .]	.
	Probable COPD	.	[. , .]	.
	Definite COPD	.	[. , .]	.
	No hist. Card or Cere Dis	.	[. , .]	.
	Hist. Card or Cere Dis	.	[. , .]	.
	Start in 2013-2015	.	[. , .]	.
	Start in 2016-2017	.	[. , .]	.
DEATH	COPD sev Mild	.	[. , .]	.
	COPD sev Moderate	.	[. , .]	.
	COPD sev (Very) Severe	.	[. , .]	.
	No ICS at Cohort Start	1.02	[0.84,1.23]	0.8724
	ICS at Cohort Start	0.63	[0.41,0.96]	0.0312
	Probable COPD	0.75	[0.58,0.98]	0.0325

Note: Stratified models are fitted when P interaction below 0.10 in at least 3 imputed sets
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Table 15-22 (Page 17 of 20)
Hazard ratios for QVA versus comparators in stratified analyses, IPTW model
POOLED - Total analysis population

		QVA compared to Free LABA+LAMA without ICS			QVA compared to Free LABA+LAMA with ICS		
Endpoint	Stratum	HR	95% CI	P	HR	95% CI	P
DEATH	Definite COPD	.	[. , .]	.	.	[. , .]	.
	Start in 2013-2015	.	[. , .]	.	.	[. , .]	.
	Start in 2016-2017	.	[. , .]	.	.	[. , .]	.

Note: Stratified models are fitted when P interaction below 0.10 in at least 3 imputed sets
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Hazard ratios for QVA versus comparators in stratified analyses, IPTW model
POOLED - Total analysis population

		QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
Endpoint	Stratum	HR	95% CI	P	HR	95% CI	P
DEATH	Definite COPD	.	[. , .]	.	0.89	[0.73,1.09]	0.2701
	Start in 2013-2015	.	[. , .]	.	.	[. , .]	.
	Start in 2016-2017	.	[. , .]	.	.	[. , .]	.

Note: Stratified models are fitted when P interaction below 0.10 in at least 3 imputed sets
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Table 15-22 (Page 19 of 20)
Hazard ratios for QVA versus comparators in stratified analyses, IPTW model
POOLED - Total analysis population

		QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint	Stratum	HR	95% CI	P	HR	95% CI	P
DEATH	Definite COPD	1.61	[1.27,2.04]	<.0001	.	[. , .]	.
	Start in 2013-2015	.	[. , .]	.	.	[. , .]	.
	Start in 2016-2017	.	[. , .]	.	.	[. , .]	.

Note: Stratified models are fitted when P interaction below 0.10 in at least 3 imputed sets
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Table 15-22 (Page 20 of 20)
Hazard ratios for QVA versus comparators in stratified analyses, IPTW model
POOLED - Total analysis population

		QVA compared to LAMA		
Endpoint	Stratum	HR	95% CI	P
DEATH	Definite COPD	1.15	[0.90,1.46]	0.2737
	Start in 2013-2015	0.86	[0.71,1.05]	0.1359
	Start in 2016-2017	1.29	[0.87,1.91]	0.2113

Note: Stratified models are fitted when P interaction below 0.10 in at least 3 imputed sets
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Table 15-23-1 (Page 1 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
THIN

		QVA compared to Free LABA+LAMA without ICS			QVA compared to Free LABA+LAMA with ICS		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
MACE	Main	1.33	[0.63,2.80]	0.4547	.	[. , .]	.
	Ext 60	1.33	[0.64,2.78]	0.4448	.	[. , .]	.
	Unr drugs	1.29	[0.62,2.69]	0.4954	.	[. , .]	.
	Smoke Never	1.33	[0.63,2.81]	0.4544	.	[. , .]	.
	COPD Severe Mild	1.33	[0.63,2.81]	0.4503	.	[. , .]	.
	COPD Severe VSev	1.32	[0.63,2.78]	0.4648	.	[. , .]	.
Ischemic heart disease	Main	2.23	[0.96,5.20]	0.0626	.	[. , .]	.
	Ext 60	2.19	[0.94,5.12]	0.0690	.	[. , .]	.
	Unr drugs	2.25	[0.98,5.19]	0.0560	.	[. , .]	.
	Smoke Never	2.23	[0.96,5.20]	0.0626	.	[. , .]	.
	COPD Severe Mild	2.24	[0.96,5.20]	0.0617	.	[. , .]	.
	COPD Severe VSev	2.25	[0.97,5.22]	0.0593	.	[. , .]	.

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Table 15-23-1 (Page 2 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
THIN

		QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
MACE	Main	.	[. , .]	.	1.15	[0.59,2.26]	0.6792
	Ext 60	.	[. , .]	.	1.09	[0.56,2.12]	0.7996
	Unr drugs	1.24	[0.39,3.95]	0.7143	1.12	[0.58,2.17]	0.7370
	Smoke Never	.	[. , .]	.	1.15	[0.59,2.27]	0.6785
	COPD Severe Mild	.	[. , .]	.	1.12	[0.58,2.18]	0.7369
	COPD Severe VSev	.	[. , .]	.	1.15	[0.59,2.24]	0.6874
Ischemic heart disease	Main	.	[. , .]	.	1.83	[0.92,3.64]	0.0865
	Ext 60	.	[. , .]	.	1.72	[0.86,3.42]	0.1221
	Unr drugs	.	[. , .]	.	1.77	[0.90,3.48]	0.0966
	Smoke Never	.	[. , .]	.	1.83	[0.92,3.64]	0.0865
	COPD Severe Mild	.	[. , .]	.	1.75	[0.88,3.46]	0.1101
	COPD Severe VSev	.	[. , .]	.	1.77	[0.88,3.53]	0.1076

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Table 15-23-1 (Page 3 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
THIN

		QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
MACE	Main	1.46	[0.83,2.57]	0.1939	0.93	[0.47,1.82]	0.8295
	Ext 60	1.51	[0.86,2.63]	0.1489	0.84	[0.44,1.58]	0.5833
	Unr drugs	1.44	[0.83,2.50]	0.1934	0.82	[0.44,1.54]	0.5402
	Smoke Never	1.46	[0.83,2.57]	0.1936	0.93	[0.47,1.82]	0.8299
	COPD Severe Mild	1.45	[0.82,2.57]	0.1978	0.93	[0.47,1.81]	0.8219
	COPD Severe VSev	1.46	[0.83,2.58]	0.1912	0.96	[0.49,1.86]	0.8930
Ischemic heart disease	Main	1.94	[1.00,3.76]	0.0504	1.04	[0.45,2.42]	0.9292
	Ext 60	1.81	[0.94,3.49]	0.0763	0.96	[0.42,2.16]	0.9132
	Unr drugs	1.80	[0.96,3.38]	0.0683	0.98	[0.45,2.14]	0.9617
	Smoke Never	1.94	[1.00,3.76]	0.0505	1.04	[0.45,2.42]	0.9297
	COPD Severe Mild	1.94	[1.00,3.77]	0.0496	0.98	[0.41,2.36]	0.9719
	COPD Severe VSev	1.95	[1.00,3.77]	0.0487	1.00	[0.42,2.38]	0.9987

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Table 15-23-1 (Page 4 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
THIN

		QVA compared to LAMA		
Endpoint	Analysis	HR	95% CI	P
MACE	Main	1.06	[0.57,1.98]	0.8541
	Ext 60	1.00	[0.54,1.85]	0.9945
	Unr drugs	0.98	[0.53,1.79]	0.9393
	Smoke Never	1.06	[0.57,1.98]	0.8532
	COPD Severe Mild	1.03	[0.56,1.90]	0.9303
	COPD Severe VSev	1.07	[0.58,2.00]	0.8223
Ischemic heart disease	Main	1.64	[0.85,3.15]	0.1386
	Ext 60	1.59	[0.83,3.04]	0.1646
	Unr drugs	1.46	[0.77,2.76]	0.2469
	Smoke Never	1.64	[0.85,3.15]	0.1387
	COPD Severe Mild	1.55	[0.81,2.97]	0.1813
	COPD Severe VSev	1.60	[0.82,3.10]	0.1660

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Table 15-23-1 (Page 5 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
THIN

		QVA compared to Free LABA+LAMA without ICS			QVA compared to Free LABA+LAMA with ICS		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
Cardiac arrhythmia	Main	3.31	[0.97,11.2]	0.0552	.	[. , .]	.
	Ext 60	2.92	[0.87,9.82]	0.0840	.	[. , .]	.
	Unr drugs	4.35	[1.46,13.0]	0.0083	.	[. , .]	.
	Smoke Never	3.31	[0.97,11.3]	0.0551	.	[. , .]	.
	COPD Severe Mild	3.30	[0.98,11.2]	0.0547	.	[. , .]	.
	COPD Severe VSev	3.34	[1.00,11.2]	0.0501	.	[. , .]	.
Cerebrovascular disorders	Main	0.69	[0.23,2.08]	0.5119	.	[. , .]	.
	Ext 60	0.80	[0.29,2.22]	0.6658	.	[. , .]	.
	Unr drugs	0.69	[0.23,2.06]	0.5008	.	[. , .]	.
	Smoke Never	0.69	[0.23,2.08]	0.5125	.	[. , .]	.
	COPD Severe Mild	0.69	[0.23,2.05]	0.5066	.	[. , .]	.
	COPD Severe VSev	0.67	[0.23,1.96]	0.4616	.	[. , .]	.

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Table 15-23-1 (Page 6 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
THIN

		QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
Cardiac arrhythmia	Main	.	[. , .]	.	1.47	[0.53,4.09]	0.4641
	Ext 60	.	[. , .]	.	1.40	[0.50,3.89]	0.5247
	Unr drugs	.	[. , .]	.	1.76	[0.72,4.26]	0.2127
	Smoke Never	.	[. , .]	.	1.47	[0.53,4.10]	0.4634
	COPD Severe Mild	.	[. , .]	.	1.36	[0.49,3.81]	0.5543
	COPD Severe VSev	.	[. , .]	.	1.39	[0.51,3.82]	0.5196
Cerebrovascular disorders	Main	.	[. , .]	.	0.46	[0.19,1.14]	0.0938
	Ext 60	.	[. , .]	.	0.51	[0.23,1.14]	0.0998
	Unr drugs	.	[. , .]	.	0.43	[0.18,1.07]	0.0709
	Smoke Never	.	[. , .]	.	0.46	[0.19,1.14]	0.0938
	COPD Severe Mild	.	[. , .]	.	0.49	[0.19,1.26]	0.1376
	COPD Severe VSev	.	[. , .]	.	0.47	[0.19,1.16]	0.1024

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Table 15-23-1 (Page 7 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
THIN

		QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
Cardiac arrhythmia	Main	0.71	[0.29,1.72]	0.4422	0.97	[0.34,2.78]	0.9503
	Ext 60	0.62	[0.26,1.49]	0.2833	0.80	[0.28,2.29]	0.6774
	Unr drugs	0.91	[0.43,1.91]	0.8043	1.13	[0.45,2.86]	0.7884
	Smoke Never	0.71	[0.29,1.72]	0.4429	0.97	[0.34,2.78]	0.9507
	COPD Severe Mild	0.70	[0.29,1.71]	0.4340	0.92	[0.32,2.65]	0.8777
	COPD Severe VSev	0.71	[0.29,1.73]	0.4542	1.08	[0.37,3.19]	0.8862
Cerebrovascular disorders	Main	0.96	[0.41,2.28]	0.9332	0.64	[0.26,1.61]	0.3476
	Ext 60	1.15	[0.53,2.49]	0.7267	0.64	[0.28,1.45]	0.2840
	Unr drugs	0.97	[0.41,2.29]	0.9387	0.70	[0.28,1.73]	0.4380
	Smoke Never	0.96	[0.41,2.28]	0.9346	0.64	[0.26,1.61]	0.3479
	COPD Severe Mild	0.97	[0.41,2.29]	0.9375	0.66	[0.27,1.67]	0.3831
	COPD Severe VSev	0.95	[0.40,2.25]	0.9055	0.62	[0.25,1.55]	0.3108

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Table 15-23-1 (Page 8 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
THIN

		QVA compared to LAMA		
Endpoint	Analysis	HR	95% CI	P
Cardiac arrhythmia	Main	1.08	[0.41,2.87]	0.8729
	Ext 60	1.00	[0.38,2.64]	0.9970
	Unr drugs	1.36	[0.58,3.16]	0.4762
	Smoke Never	1.08	[0.41,2.87]	0.8729
	COPD Severe Mild	0.99	[0.37,2.61]	0.9776
	COPD Severe VSev	1.12	[0.41,3.11]	0.8231
Cerebrovascular disorders	Main	0.46	[0.20,1.07]	0.0703
	Ext 60	0.50	[0.24,1.07]	0.0735
	Unr drugs	0.45	[0.20,1.03]	0.0580
	Smoke Never	0.46	[0.20,1.07]	0.0702
	COPD Severe Mild	0.49	[0.21,1.14]	0.0966
	COPD Severe VSev	0.46	[0.20,1.05]	0.0638

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Table 15-23-1 (Page 9 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
THIN

		QVA compared to Free LABA+LAMA without ICS			QVA compared to Free LABA+LAMA with ICS		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
Glaucoma	Too few events	.		.	.		.
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	Main	0.72	[0.25,2.06]	0.5376	.	[. , .]	.
	Ext 60	0.81	[0.30,2.22]	0.6861	.	[. , .]	.
	Unr drugs	0.58	[0.20,1.65]	0.3054	.	[. , .]	.
	Smoke Never	0.72	[0.25,2.06]	0.5380	.	[. , .]	.
	COPD Severe Mild	0.71	[0.25,2.03]	0.5201	.	[. , .]	.
	COPD Severe VSev	0.70	[0.25,2.01]	0.5094	.	[. , .]	.

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Table 15-23-1 (Page 10 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
THIN

		QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
Glaucoma	Too few events	.		.	.		.
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	Main	.	[. , .]	.	0.39	[0.16,0.98]	0.0447
	Ext 60	.	[. , .]	.	0.44	[0.19,1.02]	0.0563
	Unr drugs	.	[. , .]	.	0.37	[0.15,0.91]	0.0314
	Smoke Never	.	[. , .]	.	0.39	[0.16,0.98]	0.0448
	COPD Severe Mild	.	[. , .]	.	0.40	[0.16,0.99]	0.0480
	COPD Severe VSev	.	[. , .]	.	0.39	[0.16,0.96]	0.0402

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Hazard ratios for QVA versus comparators, main and sensitivity analyses
THIN

		QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
Glaucoma	Too few events	.		.	.		.
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	Main	1.32	[0.50,3.53]	0.5756	0.42	[0.14,1.27]	0.1253
	Ext 60	1.56	[0.62,3.93]	0.3449	0.56	[0.19,1.59]	0.2747
	Unr drugs	1.17	[0.45,3.08]	0.7459	0.50	[0.17,1.48]	0.2112
	Smoke Never	1.32	[0.50,3.54]	0.5750	0.42	[0.14,1.27]	0.1252
	COPD Severe Mild	1.32	[0.49,3.51]	0.5826	0.44	[0.15,1.31]	0.1398
	COPD Severe VSev	1.29	[0.48,3.42]	0.6124	0.42	[0.14,1.24]	0.1154

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Table 15-23-1 (Page 12 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
THIN

		QVA compared to LAMA		
Endpoint	Analysis	HR	95% CI	P
Glaucoma	Too few events	.		.
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	Main	0.44	[0.17,1.10]	0.0799
	Ext 60	0.52	[0.22,1.22]	0.1356
	Unr drugs	0.36	[0.14,0.91]	0.0306
	Smoke Never	0.44	[0.17,1.10]	0.0799
	COPD Severe Mild	0.46	[0.18,1.20]	0.1115
	COPD Severe VSev	0.44	[0.18,1.12]	0.0861

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Hazard ratios for QVA versus comparators, main and sensitivity analyses
THIN

		QVA compared to Free LABA+LAMA without ICS			QVA compared to Free LABA+LAMA with ICS		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
Diabetes mellitus	Main	0.67	[0.25,1.79]	0.4204	.	[. , .]	.
	Ext 60	0.63	[0.23,1.68]	0.3545	.	[. , .]	.
	Unr drugs	0.66	[0.25,1.78]	0.4141	.	[. , .]	.
	Smoke Never	0.67	[0.25,1.79]	0.4207	.	[. , .]	.
	COPD Severe Mild	0.67	[0.25,1.78]	0.4227	.	[. , .]	.
	COPD Severe VSev	0.67	[0.25,1.82]	0.4333	.	[. , .]	.
Bronchospasm	Too few events	.		.	.		.

Note: Run date and time 01NOV2018 11:20:11,

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Table 15-23-1 (Page 14 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
THIN

		QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
Diabetes mellitus	Main	.	[. , .]	.	1.00	[0.39,2.57]	0.9943
	Ext 60	.	[. , .]	.	0.97	[0.38,2.50]	0.9492
	Unr drugs	.	[. , .]	.	0.94	[0.37,2.43]	0.9019
	Smoke Never	.	[. , .]	.	1.00	[0.39,2.57]	0.9945
	COPD Severe Mild	.	[. , .]	.	0.99	[0.39,2.52]	0.9866
	COPD Severe VSev	.	[. , .]	.	1.13	[0.42,3.03]	0.8110
Bronchospasm	Too few events	.		.	.		.

Note: Run date and time 01NOV2018 11:20:11,

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Table 15-23-1 (Page 15 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
THIN

		QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
Diabetes mellitus	Main	0.98	[0.44,2.20]	0.9565	0.68	[0.27,1.71]	0.4132
	Ext 60	0.92	[0.41,2.05]	0.8297	0.68	[0.27,1.72]	0.4200
	Unr drugs	0.95	[0.42,2.13]	0.9039	0.66	[0.27,1.63]	0.3704
	Smoke Never	0.98	[0.44,2.19]	0.9554	0.68	[0.27,1.71]	0.4126
	COPD Severe Mild	0.98	[0.44,2.20]	0.9598	0.70	[0.28,1.77]	0.4536
	COPD Severe VSev	0.96	[0.43,2.16]	0.9287	0.70	[0.28,1.75]	0.4438
Bronchospasm	Too few events	.		.	.		.

Note: Run date and time 01NOV2018 11:20:11,

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Table 15-23-1 (Page 16 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
THIN

		QVA compared to LAMA		
Endpoint	Analysis	HR	95% CI	P
Diabetes mellitus	Main	0.71	[0.31,1.60]	0.4038
	Ext 60	0.70	[0.31,1.59]	0.3967
	Unr drugs	0.66	[0.29,1.49]	0.3184
	Smoke Never	0.71	[0.31,1.60]	0.4029
	COPD Severe Mild	0.73	[0.32,1.66]	0.4498
	COPD Severe VSev	0.76	[0.33,1.75]	0.5193
Bronchospasm	Too few events	.		.

Note: Run date and time 01NOV2018 11:20:11,

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Table 15-23-1 (Page 17 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
THIN

		QVA compared to Free LABA+LAMA without ICS			QVA compared to Free LABA+LAMA with ICS		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
Mortality	Main	2.64	[1.56,4.47]	0.0003	.	[. , .]	.
	Ext 60	2.52	[1.51,4.20]	0.0004	.	[. , .]	.
	Unr drugs	2.81	[1.69,4.68]	<.0001	.	[. , .]	.
	Naive	4.57	[0.76,27.3]	0.0961	.	[. , .]	.
	Smoke Never	2.64	[1.56,4.47]	0.0003	.	[. , .]	.
	COPD Severe Mild	2.65	[1.57,4.47]	0.0003	.	[. , .]	.
	COPD Severe VSev	2.66	[1.59,4.46]	0.0002	.	[. , .]	.

Note: Run date and time 01NOV2018 11:20:11,

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Table 15-23-1 (Page 18 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
THIN

		QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
Mortality	Main	0.87	[0.33,2.31]	0.7834	1.32	[0.87,1.98]	0.1876
	Ext 60	0.86	[0.36,2.07]	0.7324	1.22	[0.81,1.83]	0.3355
	Unr drugs	0.97	[0.37,2.54]	0.9451	1.43	[0.97,2.12]	0.0745
	Naive	2.78	[0.55,14.0]	0.2153	6.67	[1.75,25.4]	0.0054
	Smoke Never	0.87	[0.33,2.31]	0.7832	1.32	[0.87,1.98]	0.1873
	COPD Severe Mild	0.89	[0.33,2.38]	0.8113	1.36	[0.90,2.06]	0.1401
	COPD Severe VSev	0.90	[0.35,2.32]	0.8255	1.30	[0.87,1.94]	0.1958

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Table 15-23-1 (Page 19 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
THIN

		QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
Mortality	Main	1.77	[1.28,2.46]	0.0006	1.43	[0.89,2.30]	0.1415
	Ext 60	1.67	[1.22,2.29]	0.0013	1.38	[0.88,2.17]	0.1567
	Unr drugs	1.65	[1.20,2.26]	0.0020	1.15	[0.71,1.86]	0.5629
	Naive	1.68	[0.82,3.44]	0.1532	2.51	[0.84,7.43]	0.0978
	Smoke Never	1.77	[1.28,2.46]	0.0006	1.43	[0.89,2.30]	0.1416
	COPD Severe Mild	1.78	[1.28,2.47]	0.0005	1.51	[0.94,2.41]	0.0851
	COPD Severe VSev	1.78	[1.28,2.46]	0.0006	1.39	[0.88,2.19]	0.1563

Note: Run date and time 01NOV2018 11:20:11,

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Table 15-23-1 (Page 20 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
THIN

		QVA compared to LAMA		
Endpoint	Analysis	HR	95% CI	P
Mortality	Main	1.77	[1.19,2.61]	0.0044
	Ext 60	1.60	[1.09,2.35]	0.0159
	Unr drugs	1.63	[1.13,2.37]	0.0099
	Naive	3.38	[1.29,8.88]	0.0134
	Smoke Never	1.77	[1.19,2.61]	0.0044
	COPD Severe Mild	1.86	[1.26,2.74]	0.0018
	COPD Severe VSev	1.75	[1.21,2.54]	0.0032

Note: Run date and time 01NOV2018 11:20:11,

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Table 15-23-2 (Page 1 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
IPCI

		QVA compared to Free LABA+LAMA without ICS			QVA compared to Free LABA+LAMA with ICS		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
MACE	Main	1.25	[0.59,2.65]	0.5516	1.47	[0.50,4.25]	0.4824
	Ext 60	1.19	[0.57,2.48]	0.6457	1.41	[0.49,4.06]	0.5218
	Unr drugs	1.14	[0.55,2.37]	0.7272	1.29	[0.46,3.58]	0.6259
	Naive	1.70	[0.54,5.34]	0.3597	.	[. , .]	.
	Smoke Never	1.27	[0.60,2.68]	0.5275	1.51	[0.52,4.35]	0.4487
	COPD Severe Mild	1.30	[0.61,2.77]	0.4919	1.54	[0.55,4.34]	0.4128
	COPD Severe VSev	1.32	[0.62,2.80]	0.4702	1.54	[0.54,4.38]	0.4205
Ischemic heart disease	Ext 60	1.20	[0.36,3.94]	0.7687	.	[. , .]	.

Note: Run date and time 01NOV2018 11:20:22,

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Table 15-23-2 (Page 2 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
IPCI

		QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
MACE	Main	0.88	[0.34,2.31]	0.8027	1.19	[0.61,2.30]	0.6150
	Ext 60	0.86	[0.34,2.12]	0.7361	1.13	[0.59,2.17]	0.7138
	Unr drugs	0.77	[0.30,1.97]	0.5870	1.10	[0.57,2.14]	0.7709
	Naive	1.41	[0.36,5.51]	0.6215	1.97	[0.62,6.28]	0.2498
	Smoke Never	0.89	[0.34,2.34]	0.8153	1.18	[0.61,2.30]	0.6213
	COPD Severe Mild	0.76	[0.29,1.96]	0.5680	1.21	[0.64,2.29]	0.5497
	COPD Severe VSev	1.10	[0.44,2.71]	0.8410	1.15	[0.61,2.18]	0.6606
Ischemic heart disease	Ext 60	.	[. , .]	.	1.39	[0.48,4.00]	0.5415

Note: Run date and time 01NOV2018 11:20:22,

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Table 15-23-2 (Page 3 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
IPCI

		QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
MACE	Main	0.91	[0.39,2.11]	0.8315	1.08	[0.49,2.37]	0.8501
	Ext 60	0.89	[0.40,1.96]	0.7645	1.09	[0.51,2.33]	0.8288
	Unr drugs	0.91	[0.39,2.10]	0.8182	0.92	[0.43,1.96]	0.8362
	Naive	0.89	[0.24,3.34]	0.8639	1.25	[0.37,4.23]	0.7173
	Smoke Never	0.92	[0.40,2.13]	0.8409	1.08	[0.49,2.38]	0.8412
	COPD Severe Mild	0.93	[0.40,2.15]	0.8581	1.18	[0.53,2.61]	0.6796
	COPD Severe VSev	0.93	[0.40,2.15]	0.8589	1.08	[0.49,2.38]	0.8533
Ischemic heart disease	Ext 60	1.36	[0.38,4.86]	0.6379	.	[. , .]	.

Note: Run date and time 01NOV2018 11:20:22,

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Table 15-23-2 (Page 4 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
IPCI

		QVA compared to LAMA		
Endpoint	Analysis	HR	95% CI	P
MACE	Main	0.99	[0.51,1.91]	0.9653
	Ext 60	1.00	[0.53,1.92]	0.9915
	Unr drugs	0.84	[0.44,1.61]	0.6017
	Naive	1.02	[0.36,2.94]	0.9690
	Smoke Never	0.99	[0.51,1.93]	0.9829
	COPD Severe Mild	1.03	[0.55,1.94]	0.9218
	COPD Severe VSev	0.98	[0.52,1.84]	0.9511
Ischemic heart disease	Ext 60	0.66	[0.24,1.79]	0.4109

Note: Run date and time 01NOV2018 11:20:22,

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Table 15-23-2 (Page 5 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
IPCI

		QVA compared to Free LABA+LAMA without ICS			QVA compared to Free LABA+LAMA with ICS		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
Cardiac arrhythmia	Main	1.37	[0.48,3.93]	0.5612	0.66	[0.22,1.95]	0.4489
	Ext 60	1.22	[0.45,3.28]	0.6980	0.65	[0.22,1.92]	0.4410
	Unr drugs	1.49	[0.54,4.09]	0.4384	0.74	[0.25,2.18]	0.5824
	Smoke Never	1.36	[0.47,3.90]	0.5701	0.67	[0.23,1.99]	0.4757
	COPD Severe Mild	1.29	[0.45,3.69]	0.6311	0.62	[0.21,1.84]	0.3862
	COPD Severe VSev	1.35	[0.47,3.87]	0.5764	0.59	[0.20,1.76]	0.3441
Cerebrovascular disorders	Main	2.96	[1.02,8.60]	0.0461	.	[. , .]	.
	Ext 60	2.72	[0.96,7.75]	0.0608	.	[. , .]	.
	Unr drugs	2.53	[0.92,6.99]	0.0728	1.18	[0.39,3.54]	0.7727
	Naive	.	[. , .]	.	.	[. , .]	.
	Smoke Never	2.99	[1.03,8.68]	0.0439	.	[. , .]	.
	COPD Severe Mild	3.00	[1.02,8.82]	0.0452	.	[. , .]	.
	COPD Severe VSev	3.04	[1.03,8.93]	0.0435	.	[. , .]	.

Note: Run date and time 01NOV2018 11:20:22,

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Table 15-23-2 (Page 6 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
IPCI

		QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
Cardiac arrhythmia	Main	0.53	[0.15,1.87]	0.3275	1.21	[0.46,3.19]	0.7018
	Ext 60	0.53	[0.16,1.79]	0.3091	1.20	[0.48,3.01]	0.7019
	Unr drugs	0.59	[0.17,1.99]	0.3932	1.31	[0.54,3.23]	0.5515
	Smoke Never	0.53	[0.15,1.90]	0.3292	1.26	[0.48,3.31]	0.6381
	COPD Severe Mild	0.43	[0.13,1.43]	0.1709	1.10	[0.46,2.62]	0.8221
	COPD Severe VSev	0.53	[0.16,1.80]	0.3074	1.13	[0.45,2.82]	0.7944
Cerebrovascular disorders	Main	2.16	[0.66,7.08]	0.2030	2.57	[1.14,5.77]	0.0230
	Ext 60	1.76	[0.57,5.46]	0.3281	2.27	[1.01,5.12]	0.0488
	Unr drugs	2.39	[0.73,7.79]	0.1493	2.36	[1.05,5.30]	0.0382
	Naive	.	[. , .]	.	5.73	[1.95,16.8]	0.0016
	Smoke Never	2.14	[0.65,7.05]	0.2104	2.46	[1.11,5.44]	0.0264
	COPD Severe Mild	2.13	[0.65,6.93]	0.2110	2.75	[1.25,6.06]	0.0121
	COPD Severe VSev	2.37	[0.73,7.69]	0.1504	2.57	[1.19,5.54]	0.0162

Note: Run date and time 01NOV2018 11:20:22,

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Table 15-23-2 (Page 7 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
IPCI

		QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
Cardiac arrhythmia	Main	1.60	[0.49,5.17]	0.4352	.	[. , .]	.
	Ext 60	1.70	[0.54,5.31]	0.3635	1.16	[0.38,3.58]	0.7976
	Unr drugs	1.78	[0.57,5.57]	0.3240	1.42	[0.45,4.50]	0.5461
	Smoke Never	1.60	[0.49,5.17]	0.4360	.	[. , .]	.
	COPD Severe Mild	1.65	[0.51,5.33]	0.4005	.	[. , .]	.
	COPD Severe VSev	1.66	[0.52,5.35]	0.3955	.	[. , .]	.
Cerebrovascular disorders	Main	.	[. , .]	.	1.37	[0.58,3.23]	0.4733
	Ext 60	1.99	[0.60,6.62]	0.2627	1.33	[0.57,3.11]	0.5045
	Unr drugs	.	[. , .]	.	1.39	[0.60,3.23]	0.4404
	Naive	.	[. , .]	.	1.63	[0.49,5.44]	0.4274
	Smoke Never	.	[. , .]	.	1.35	[0.57,3.20]	0.4908
	COPD Severe Mild	.	[. , .]	.	1.55	[0.64,3.76]	0.3302
	COPD Severe VSev	.	[. , .]	.	1.46	[0.60,3.53]	0.4055

Note: Run date and time 01NOV2018 11:20:22,

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Hazard ratios for QVA versus comparators, main and sensitivity analyses
IPCI

		QVA compared to LAMA		
Endpoint	Analysis	HR	95% CI	P
Cardiac arrhythmia	Main	0.80	[0.33,1.94]	0.6196
	Ext 60	0.87	[0.38,1.99]	0.7380
	Unr drugs	0.91	[0.40,2.05]	0.8115
	Smoke Never	0.81	[0.33,1.97]	0.6411
	COPD Severe Mild	0.82	[0.34,1.94]	0.6448
	COPD Severe VSev	0.85	[0.36,2.04]	0.7194
Cerebrovascular disorders	Main	1.77	[0.84,3.70]	0.1308
	Ext 60	1.79	[0.86,3.74]	0.1219
	Unr drugs	1.62	[0.78,3.36]	0.1989
	Naive	1.74	[0.57,5.34]	0.3335
	Smoke Never	1.74	[0.84,3.62]	0.1380
	COPD Severe Mild	1.94	[0.94,4.02]	0.0745
	COPD Severe VSev	1.87	[0.90,3.85]	0.0913

Note: Run date and time 01NOV2018 11:20:22,

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Table 15-23-2 (Page 9 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
IPCI

		QVA compared to Free LABA+LAMA without ICS			QVA compared to Free LABA+LAMA with ICS		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
Glaucoma	Too few events	.		.	.		.
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	Main	2.66	[0.87,8.15]	0.0857	.	[. , .]	.
	Ext 60	2.64	[0.88,7.97]	0.0840	.	[. , .]	.
	Unr drugs	2.74	[0.89,8.37]	0.0776	.	[. , .]	.
	Smoke Never	2.69	[0.88,8.19]	0.0817	.	[. , .]	.
	COPD Severe Mild	2.57	[0.84,7.85]	0.0969	.	[. , .]	.
	COPD Severe VSev	2.58	[0.85,7.82]	0.0926	.	[. , .]	.

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Table 15-23-2 (Page 10 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
IPCI

		QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
Glaucoma	Too few events	.		.	.		.
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	Main	.	[. , .]	.	2.62	[0.97,7.09]	0.0582
	Ext 60	.	[. , .]	.	2.54	[0.94,6.87]	0.0679
	Unr drugs	0.60	[0.11,3.24]	0.5500	2.44	[0.90,6.59]	0.0803
	Smoke Never	.	[. , .]	.	2.43	[0.93,6.33]	0.0702
	COPD Severe Mild	.	[. , .]	.	2.64	[1.01,6.91]	0.0475
	COPD Severe VSev	.	[. , .]	.	2.29	[0.92,5.71]	0.0748

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Table 15-23-2 (Page 11 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
IPCI

		QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
Glaucoma	Too few events	.		.	.		.
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	Main	1.28	[0.47,3.50]	0.6355	2.23	[0.74,6.74]	0.1566
	Ext 60	1.34	[0.50,3.63]	0.5607	2.43	[0.81,7.30]	0.1143
	Unr drugs	1.28	[0.47,3.51]	0.6321	1.52	[0.49,4.72]	0.4701
	Smoke Never	1.26	[0.46,3.45]	0.6478	2.26	[0.75,6.83]	0.1499
	COPD Severe Mild	1.28	[0.47,3.48]	0.6307	2.10	[0.73,6.04]	0.1700
	COPD Severe VSev	1.28	[0.47,3.47]	0.6340	1.95	[0.67,5.66]	0.2221

Note: Run date and time 01NOV2018 11:20:22,

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Hazard ratios for QVA versus comparators, main and sensitivity analyses
IPCI

		QVA compared to LAMA		
Endpoint	Analysis	HR	95% CI	P
Glaucoma	Too few events	.		.
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	Main	1.38	[0.58,3.28]	0.4607
	Ext 60	1.33	[0.58,3.04]	0.5016
	Unr drugs	1.29	[0.55,3.03]	0.5557
	Smoke Never	1.39	[0.58,3.29]	0.4607
	COPD Severe Mild	1.25	[0.57,2.73]	0.5720
	COPD Severe VSev	1.27	[0.58,2.77]	0.5507

Note: Run date and time 01NOV2018 11:20:22,

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Table 15-23-2 (Page 13 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
IPCI

		QVA compared to Free LABA+LAMA without ICS			QVA compared to Free LABA+LAMA with ICS		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
Diabetes mellitus	Main	.	[. , .]	.	.	[. , .]	.
	Ext 60	.	[. , .]	.	.	[. , .]	.
	Unr drugs	.	[. , .]	.	.	[. , .]	.
	Smoke Never	.	[. , .]	.	.	[. , .]	.
	COPD Severe Mild	.	[. , .]	.	.	[. , .]	.
	COPD Severe VSev	.	[. , .]	.	.	[. , .]	.
Bronchospasm	Too few events	.		.	.		.

Note: Run date and time 01NOV2018 11:20:22,

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Table 15-23-2 (Page 14 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
IPCI

		QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
Diabetes mellitus	Main	.	[. , .]	.	1.78	[0.59,5.33]	0.3051
	Ext 60	.	[. , .]	.	1.73	[0.57,5.20]	0.3325
	Unr drugs	.	[. , .]	.	1.94	[0.72,5.27]	0.1928
	Smoke Never	.	[. , .]	.	1.89	[0.64,5.54]	0.2480
	COPD Severe Mild	.	[. , .]	.	1.84	[0.63,5.37]	0.2655
	COPD Severe VSev	.	[. , .]	.	1.93	[0.68,5.50]	0.2191
Bronchospasm	Too few events	.		.	.		.

Note: Run date and time 01NOV2018 11:20:22,

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Table 15-23-2 (Page 15 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
IPCI

		QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
Diabetes mellitus	Main	.	[. , .]	.	.	[. , .]	.
	Ext 60	.	[. , .]	.	.	[. , .]	.
	Unr drugs	.	[. , .]	.	.	[. , .]	.
	Smoke Never	.	[. , .]	.	.	[. , .]	.
	COPD Severe Mild	.	[. , .]	.	.	[. , .]	.
	COPD Severe VSev	.	[. , .]	.	.	[. , .]	.
Bronchospasm	Too few events	.		.	.		.

Note: Run date and time 01NOV2018 11:20:22,

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Table 15-23-2 (Page 16 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
IPCI

		QVA compared to LAMA		
Endpoint	Analysis	HR	95% CI	P
Diabetes mellitus	Main	1.65	[0.53,5.10]	0.3853
	Ext 60	1.69	[0.54,5.27]	0.3660
	Unr drugs	1.97	[0.71,5.46]	0.1902
	Smoke Never	1.67	[0.54,5.17]	0.3710
	COPD Severe Mild	1.74	[0.59,5.11]	0.3136
	COPD Severe VSev	1.71	[0.59,4.96]	0.3259
Bronchospasm	Too few events	.		.

Note: Run date and time 01NOV2018 11:20:22,

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Table 15-23-2 (Page 17 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
IPCI

		QVA compared to Free LABA+LAMA without ICS			QVA compared to Free LABA+LAMA with ICS		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
Mortality	Main	0.73	[0.37,1.44]	0.3598	1.88	[0.60,5.87]	0.2799
	Ext 60	0.67	[0.34,1.33]	0.2550	1.81	[0.56,5.82]	0.3190
	Unr drugs	0.64	[0.33,1.27]	0.2026	1.01	[0.28,3.68]	0.9821
	Naive	1.65	[0.56,4.87]	0.3638	.	[. , .]	.
	Smoke Never	0.74	[0.37,1.46]	0.3822	1.87	[0.60,5.86]	0.2846
	COPD Severe Mild	0.77	[0.39,1.53]	0.4493	1.91	[0.62,5.89]	0.2629
	COPD Severe VSev	0.73	[0.37,1.46]	0.3788	1.97	[0.62,6.26]	0.2507

Note: Run date and time 01NOV2018 11:20:22,

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Table 15-23-2 (Page 18 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
IPCI

		QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
Mortality	Main	0.54	[0.21,1.41]	0.2100	0.75	[0.37,1.52]	0.4192
	Ext 60	0.49	[0.20,1.24]	0.1320	0.66	[0.33,1.34]	0.2526
	Unr drugs	0.56	[0.22,1.41]	0.2187	0.70	[0.34,1.43]	0.3331
	Naive	1.04	[0.28,3.93]	0.9541	1.28	[0.37,4.35]	0.6970
	Smoke Never	0.57	[0.23,1.45]	0.2403	0.72	[0.36,1.47]	0.3726
	COPD Severe Mild	0.58	[0.23,1.45]	0.2437	0.83	[0.42,1.61]	0.5726
	COPD Severe VSev	0.67	[0.26,1.71]	0.3970	0.75	[0.37,1.52]	0.4304

Note: Run date and time 01NOV2018 11:20:22,

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Table 15-23-2 (Page 19 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
IPCI

		QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
Mortality	Main	1.35	[0.62,2.92]	0.4499	0.55	[0.28,1.07]	0.0788
	Ext 60	1.18	[0.55,2.53]	0.6716	0.51	[0.26,0.99]	0.0459
	Unr drugs	1.24	[0.58,2.65]	0.5835	0.48	[0.25,0.93]	0.0307
	Naive	2.35	[0.58,9.57]	0.2324	0.77	[0.29,2.02]	0.5895
	Smoke Never	1.36	[0.62,2.94]	0.4418	0.54	[0.28,1.06]	0.0760
	COPD Severe Mild	1.34	[0.62,2.89]	0.4562	0.58	[0.31,1.10]	0.0942
	COPD Severe VSev	1.34	[0.62,2.88]	0.4593	0.54	[0.28,1.04]	0.0663

Note: Run date and time 01NOV2018 11:20:22,

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Table 15-23-2 (Page 20 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
IPCI

		QVA compared to LAMA		
Endpoint	Analysis	HR	95% CI	P
Mortality	Main	0.89	[0.48,1.67]	0.7282
	Ext 60	0.80	[0.43,1.48]	0.4756
	Unr drugs	0.76	[0.41,1.42]	0.3981
	Naive	1.22	[0.51,2.96]	0.6546
	Smoke Never	0.89	[0.48,1.67]	0.7201
	COPD Severe Mild	0.97	[0.54,1.76]	0.9232
	COPD Severe VSev	0.86	[0.47,1.59]	0.6342

Note: Run date and time 01NOV2018 11:20:22,

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Table 15-23-3 (Page 1 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
AUH

		QVA compared to Free LABA+LAMA without ICS			QVA compared to Free LABA+LAMA with ICS		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
MACE	Main	1.03	[0.68,1.56]	0.8970	0.52	[0.25,1.09]	0.0823
	Ext 60	1.03	[0.67,1.56]	0.9069	0.52	[0.25,1.08]	0.0789
	Unr drugs	1.02	[0.68,1.53]	0.9145	0.53	[0.25,1.11]	0.0912
	Naive	1.44	[0.74,2.80]	0.2894	1.59	[0.52,4.86]	0.4193
	Smoke Never	1.04	[0.68,1.57]	0.8652	0.50	[0.23,1.07]	0.0727
	COPD Severe Mild	1.04	[0.68,1.57]	0.8672	0.52	[0.25,1.08]	0.0788
	COPD Severe VSev	1.01	[0.67,1.54]	0.9538	0.52	[0.25,1.09]	0.0848
Ischemic heart disease	Main	.	[. , .]	.	.	[. , .]	.
	Ext 60	.	[. , .]	.	.	[. , .]	.
	Unr drugs	.	[. , .]	.	.	[. , .]	.
	Naive	.	[. , .]	.	.	[. , .]	.
	Smoke Never	.	[. , .]	.	.	[. , .]	.
	COPD Severe Mild	.	[. , .]	.	.	[. , .]	.
	COPD Severe VSev	.	[. , .]	.	.	[. , .]	.

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Table 15-23-3 (Page 2 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
AUH

		QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
MACE	Main	0.92	[0.48,1.76]	0.8037	1.04	[0.83,1.31]	0.7180
	Ext 60	0.96	[0.50,1.83]	0.8998	1.01	[0.81,1.26]	0.9316
	Unr drugs	1.00	[0.52,1.92]	0.9930	1.01	[0.81,1.27]	0.9324
	Naive	1.24	[0.41,3.74]	0.7061	0.92	[0.63,1.36]	0.6898
	Smoke Never	1.03	[0.53,1.98]	0.9345	1.05	[0.83,1.32]	0.7062
	COPD Severe Mild	0.98	[0.49,1.93]	0.9441	1.07	[0.85,1.35]	0.5448
	COPD Severe VSev	0.95	[0.50,1.83]	0.8835	1.04	[0.83,1.30]	0.7321
Ischemic heart disease	Main	.	[. , .]	.	1.41	[0.88,2.27]	0.1543
	Ext 60	.	[. , .]	.	1.32	[0.83,2.07]	0.2375
	Unr drugs	.	[. , .]	.	1.22	[0.76,1.94]	0.4076
	Naive	.	[. , .]	.	1.18	[0.54,2.55]	0.6835
	Smoke Never	.	[. , .]	.	1.46	[0.91,2.36]	0.1194
	COPD Severe Mild	.	[. , .]	.	1.51	[0.94,2.43]	0.0914
	COPD Severe VSev	.	[. , .]	.	1.41	[0.88,2.27]	0.1558

Note: Run date and time 01NOV2018 11:20:33,

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Table 15-23-3 (Page 3 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
AUH

		QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
MACE	Main	1.04	[0.76,1.42]	0.8064	1.38	[0.93,2.05]	0.1068
	Ext 60	1.00	[0.74,1.36]	0.9969	1.28	[0.86,1.90]	0.2249
	Unr drugs	1.05	[0.77,1.43]	0.7495	1.08	[0.74,1.56]	0.7018
	Naive	1.25	[0.79,1.99]	0.3405	1.37	[0.80,2.33]	0.2487
	Smoke Never	1.04	[0.76,1.42]	0.8134	1.41	[0.96,2.08]	0.0832
	COPD Severe Mild	0.94	[0.66,1.34]	0.7235	1.36	[0.92,1.99]	0.1192
	COPD Severe VSev	0.97	[0.70,1.34]	0.8622	1.29	[0.89,1.88]	0.1829
Ischemic heart disease	Main	2.73	[1.39,5.34]	0.0034	1.46	[0.69,3.08]	0.3185
	Ext 60	2.37	[1.25,4.48]	0.0080	1.54	[0.76,3.16]	0.2343
	Unr drugs	2.53	[1.32,4.86]	0.0054	1.57	[0.75,3.28]	0.2337
	Naive	.	[. , .]	.	1.08	[0.40,2.93]	0.8751
	Smoke Never	2.76	[1.41,5.39]	0.0031	1.49	[0.70,3.14]	0.3006
	COPD Severe Mild	2.63	[1.33,5.19]	0.0054	1.50	[0.75,2.99]	0.2472
	COPD Severe VSev	2.78	[1.42,5.43]	0.0029	1.31	[0.66,2.60]	0.4447

Note: Run date and time 01NOV2018 11:20:33,

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Table 15-23-3 (Page 4 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
AUH

		QVA compared to LAMA		
Endpoint	Analysis	HR	95% CI	P
MACE	Main	0.95	[0.73,1.24]	0.6930
	Ext 60	0.96	[0.74,1.25]	0.7679
	Unr drugs	0.92	[0.72,1.18]	0.5235
	Naive	1.00	[0.70,1.43]	0.9988
	Smoke Never	0.94	[0.72,1.23]	0.6755
	COPD Severe Mild	0.96	[0.74,1.25]	0.7585
	COPD Severe VSev	0.94	[0.72,1.21]	0.6240
Ischemic heart disease	Main	2.00	[1.05,3.79]	0.0341
	Ext 60	2.08	[1.12,3.88]	0.0209
	Unr drugs	2.03	[1.12,3.68]	0.0192
	Naive	3.40	[1.33,8.71]	0.0107
	Smoke Never	1.93	[1.01,3.68]	0.0474
	COPD Severe Mild	2.00	[1.05,3.79]	0.0339
	COPD Severe VSev	1.96	[1.04,3.68]	0.0377

Note: Run date and time 01NOV2018 11:20:33,

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Table 15-23-3 (Page 5 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
AUH

		QVA compared to Free LABA+LAMA without ICS			QVA compared to Free LABA+LAMA with ICS		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
Cardiac arrhythmia	Main	1.17	[0.45,3.04]	0.7391	.	[. , .]	.
	Ext 60	1.02	[0.42,2.49]	0.9691	.	[. , .]	.
	Unr drugs	1.18	[0.50,2.79]	0.7074	.	[. , .]	.
	Naive	.	[. , .]	.	.	[. , .]	.
	Smoke Never	1.15	[0.44,2.99]	0.7768	.	[. , .]	.
	COPD Severe Mild	1.19	[0.46,3.07]	0.7237	.	[. , .]	.
	COPD Severe VSev	1.16	[0.45,2.98]	0.7604	.	[. , .]	.
Cerebrovascular disorders	Main	.	[. , .]	.	.	[. , .]	.
	Ext 60	.	[. , .]	.	.	[. , .]	.
	Unr drugs	.	[. , .]	.	.	[. , .]	.
	Smoke Never	.	[. , .]	.	.	[. , .]	.
	COPD Severe Mild	.	[. , .]	.	.	[. , .]	.
	COPD Severe VSev	.	[. , .]	.	.	[. , .]	.

Note: Run date and time 01NOV2018 11:20:33,

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Table 15-23-3 (Page 6 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
AUH

		QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
Cardiac arrhythmia	Main	.	[. , .]	.	0.79	[0.47,1.32]	0.3711
	Ext 60	.	[. , .]	.	0.80	[0.49,1.32]	0.3855
	Unr drugs	.	[. , .]	.	0.93	[0.57,1.50]	0.7516
	Naive	.	[. , .]	.	0.53	[0.20,1.36]	0.1839
	Smoke Never	.	[. , .]	.	0.81	[0.48,1.36]	0.4216
	COPD Severe Mild	.	[. , .]	.	0.83	[0.49,1.39]	0.4773
	COPD Severe VSev	.	[. , .]	.	0.81	[0.48,1.34]	0.4080
Cerebrovascular disorders	Main	.	[. , .]	.	1.70	[0.87,3.31]	0.1211
	Ext 60	.	[. , .]	.	1.50	[0.78,2.86]	0.2216
	Unr drugs	.	[. , .]	.	1.56	[0.80,3.02]	0.1912
	Smoke Never	.	[. , .]	.	1.63	[0.84,3.18]	0.1499
	COPD Severe Mild	.	[. , .]	.	1.71	[0.87,3.33]	0.1170
	COPD Severe VSev	.	[. , .]	.	1.64	[0.84,3.17]	0.1442

Note: Run date and time 01NOV2018 11:20:33,

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Table 15-23-3 (Page 7 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
AUH

		QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
Cardiac arrhythmia	Main	0.74	[0.40,1.39]	0.3508	1.35	[0.56,3.28]	0.5057
	Ext 60	0.79	[0.43,1.45]	0.4519	1.48	[0.62,3.55]	0.3780
	Unr drugs	0.85	[0.48,1.52]	0.5815	1.44	[0.63,3.31]	0.3881
	Naive	0.30	[0.11,0.85]	0.0230	1.27	[0.36,4.55]	0.7123
	Smoke Never	0.74	[0.39,1.38]	0.3399	1.39	[0.57,3.39]	0.4630
	COPD Severe Mild	0.64	[0.32,1.26]	0.1970	1.35	[0.60,3.04]	0.4700
	COPD Severe VSev	0.69	[0.37,1.29]	0.2419	1.21	[0.53,2.77]	0.6527
Cerebrovascular disorders	Main	0.75	[0.31,1.79]	0.5134	.	[. , .]	.
	Ext 60	0.75	[0.31,1.79]	0.5145	2.24	[0.74,6.82]	0.1553
	Unr drugs	0.74	[0.31,1.76]	0.4913	1.34	[0.41,4.42]	0.6278
	Smoke Never	0.74	[0.31,1.79]	0.5096	.	[. , .]	.
	COPD Severe Mild	0.68	[0.26,1.77]	0.4305	.	[. , .]	.
	COPD Severe VSev	0.70	[0.28,1.74]	0.4479	.	[. , .]	.

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Table 15-23-3 (Page 8 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
AUH

		QVA compared to LAMA		
Endpoint	Analysis	HR	95% CI	P
Cardiac arrhythmia	Main	0.79	[0.44,1.43]	0.4436
	Ext 60	0.78	[0.45,1.37]	0.3839
	Unr drugs	0.94	[0.56,1.59]	0.8270
	Naive	0.76	[0.29,2.02]	0.5833
	Smoke Never	0.84	[0.46,1.51]	0.5498
	COPD Severe Mild	0.77	[0.43,1.36]	0.3657
	COPD Severe VSev	0.77	[0.43,1.35]	0.3596
Cerebrovascular disorders	Main	1.45	[0.68,3.08]	0.3398
	Ext 60	1.25	[0.60,2.58]	0.5537
	Unr drugs	1.11	[0.56,2.20]	0.7725
	Smoke Never	1.40	[0.66,2.99]	0.3832
	COPD Severe Mild	1.44	[0.68,3.07]	0.3434
	COPD Severe VSev	1.39	[0.66,2.95]	0.3866

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Table 15-23-3 (Page 9 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
AUH

		QVA compared to Free LABA+LAMA without ICS			QVA compared to Free LABA+LAMA with ICS		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
Glaucoma	Too few events	.		.	.		.
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	Main	.	[. , .]	.	.	[. , .]	.
	Ext 60	.	[. , .]	.	.	[. , .]	.
	Unr drugs	.	[. , .]	.	.	[. , .]	.
	Smoke Never	.	[. , .]	.	.	[. , .]	.
	COPD Severe Mild	.	[. , .]	.	.	[. , .]	.
	COPD Severe VSev	.	[. , .]	.	.	[. , .]	.

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Table 15-23-3 (Page 10 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
AUH

		QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
Glaucoma	Too few events	.		.	.		.
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	Main	.	[. , .]	.	0.78	[0.30,2.04]	0.6164
	Ext 60	.	[. , .]	.	0.89	[0.36,2.18]	0.7921
	Unr drugs	.	[. , .]	.	0.92	[0.38,2.21]	0.8439
	Smoke Never	.	[. , .]	.	0.81	[0.32,2.06]	0.6526
	COPD Severe Mild	.	[. , .]	.	0.85	[0.33,2.19]	0.7348
	COPD Severe VSev	.	[. , .]	.	0.77	[0.30,1.98]	0.5906

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Table 15-23-3 (Page 11 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
AUH

		QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
Glaucoma	Too few events	.		.	.		.
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	Main	1.30	[0.44,3.83]	0.6343	.	[. , .]	.
	Ext 60	1.41	[0.49,4.05]	0.5228	.	[. , .]	.
	Unr drugs	1.27	[0.47,3.41]	0.6332	.	[. , .]	.
	Smoke Never	1.32	[0.45,3.89]	0.6119	.	[. , .]	.
	COPD Severe Mild	1.22	[0.41,3.65]	0.7210	.	[. , .]	.
	COPD Severe VSev	1.35	[0.46,3.98]	0.5894	.	[. , .]	.

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Hazard ratios for QVA versus comparators, main and sensitivity analyses
AUH

		QVA compared to LAMA		
Endpoint	Analysis	HR	95% CI	P
Glaucoma	Too few events	.		.
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	Main	0.67	[0.23,1.94]	0.4561
	Ext 60	0.79	[0.28,2.24]	0.6519
	Unr drugs	0.98	[0.37,2.63]	0.9759
	Smoke Never	0.64	[0.22,1.85]	0.4081
	COPD Severe Mild	0.73	[0.26,2.11]	0.5656
	COPD Severe VSev	0.64	[0.22,1.84]	0.4112

Note: Run date and time 01NOV2018 11:20:33,

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Table 15-23-3 (Page 13 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
AUH

		QVA compared to Free LABA+LAMA without ICS			QVA compared to Free LABA+LAMA with ICS		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
Diabetes mellitus	Main	.	[. , .]	.	.	[. , .]	.
	Ext 60	.	[. , .]	.	.	[. , .]	.
	Unr drugs	.	[. , .]	.	.	[. , .]	.
	Smoke Never	.	[. , .]	.	.	[. , .]	.
	COPD Severe Mild	.	[. , .]	.	.	[. , .]	.
	COPD Severe VSev	.	[. , .]	.	.	[. , .]	.
Bronchospasm	Too few events	.		.	.		.

Note: Run date and time 01NOV2018 11:20:33,

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Table 15-23-3 (Page 14 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
AUH

		QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
Diabetes mellitus	Main	.	[. , .]	.	0.66	[0.24,1.82]	0.4215
	Ext 60	.	[. , .]	.	0.63	[0.24,1.68]	0.3563
	Unr drugs	.	[. , .]	.	0.53	[0.19,1.46]	0.2217
	Smoke Never	.	[. , .]	.	0.68	[0.25,1.87]	0.4548
	COPD Severe Mild	.	[. , .]	.	0.65	[0.24,1.75]	0.3903
	COPD Severe VSev	.	[. , .]	.	0.61	[0.23,1.61]	0.3164
Bronchospasm	Too few events	.		.	.		.

Note: Run date and time 01NOV2018 11:20:33,

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Table 15-23-3 (Page 15 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
AUH

		QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
Diabetes mellitus	Main	0.53	[0.19,1.45]	0.2138	.	[. , .]	.
	Ext 60	0.53	[0.19,1.46]	0.2210	.	[. , .]	.
	Unr drugs	0.52	[0.19,1.43]	0.2049	.	[. , .]	.
	Smoke Never	0.53	[0.19,1.44]	0.2115	.	[. , .]	.
	COPD Severe Mild	0.48	[0.18,1.29]	0.1451	.	[. , .]	.
	COPD Severe VSev	0.52	[0.19,1.42]	0.2018	.	[. , .]	.
Bronchospasm	Too few events	.		.	.		.

Note: Run date and time 01NOV2018 11:20:33,

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Table 15-23-3 (Page 16 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
AUH

		QVA compared to LAMA		
Endpoint	Analysis	HR	95% CI	P
Diabetes mellitus	Main	0.80	[0.25,2.57]	0.7050
	Ext 60	0.85	[0.27,2.66]	0.7818
	Unr drugs	0.78	[0.26,2.35]	0.6655
	Smoke Never	0.83	[0.26,2.70]	0.7617
	COPD Severe Mild	0.80	[0.25,2.53]	0.7054
	COPD Severe VSev	0.71	[0.23,2.17]	0.5424
Bronchospasm	Too few events	.		.

Note: Run date and time 01NOV2018 11:20:33,

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Table 15-23-3 (Page 17 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
AUH

		QVA compared to Free LABA+LAMA without ICS			QVA compared to Free LABA+LAMA with ICS		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
Mortality	Main	1.32	[0.74,2.35]	0.3419	.	[. , .]	.
	Ext 60	1.34	[0.76,2.39]	0.3135	.	[. , .]	.
	Unr drugs	1.24	[0.72,2.14]	0.4298	.	[. , .]	.
	Naive	2.37	[0.90,6.24]	0.0815	.	[. , .]	.
	Smoke Never	1.39	[0.79,2.42]	0.2513	.	[. , .]	.
	COPD Severe Mild	1.31	[0.74,2.32]	0.3614	.	[. , .]	.
	COPD Severe VSev	1.34	[0.76,2.37]	0.3163	.	[. , .]	.

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Table 15-23-3 (Page 18 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
AUH

		QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
Mortality	Main	1.40	[0.50,3.97]	0.5215	0.72	[0.57,0.92]	0.0083
	Ext 60	1.21	[0.46,3.19]	0.7039	0.68	[0.54,0.86]	0.0014
	Unr drugs	1.35	[0.53,3.46]	0.5317	0.71	[0.56,0.90]	0.0044
	Naive	.	[. , .]	.	0.55	[0.34,0.88]	0.0131
	Smoke Never	1.27	[0.44,3.66]	0.6571	0.72	[0.56,0.91]	0.0069
	COPD Severe Mild	1.27	[0.41,3.96]	0.6769	0.73	[0.57,0.93]	0.0097
	COPD Severe VSev	1.54	[0.58,4.07]	0.3873	0.73	[0.58,0.93]	0.0114

Note: Run date and time 01NOV2018 11:20:33,

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Table 15-23-3 (Page 19 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
AUH

		QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
Mortality	Main	1.37	[0.95,1.97]	0.0923	1.12	[0.68,1.82]	0.6573
	Ext 60	1.27	[0.90,1.78]	0.1747	1.08	[0.69,1.70]	0.7452
	Unr drugs	1.31	[0.92,1.86]	0.1334	0.87	[0.57,1.33]	0.5274
	Naive	1.22	[0.66,2.27]	0.5203	1.72	[0.85,3.48]	0.1334
	Smoke Never	1.37	[0.95,1.97]	0.0873	1.10	[0.68,1.79]	0.7016
	COPD Severe Mild	1.31	[0.89,1.92]	0.1739	1.10	[0.66,1.83]	0.7023
	COPD Severe VSev	1.28	[0.88,1.86]	0.2033	1.27	[0.79,2.05]	0.3172

Note: Run date and time 01NOV2018 11:20:33,

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Table 15-23-3 (Page 20 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
AUH

		QVA compared to LAMA		
Endpoint	Analysis	HR	95% CI	P
Mortality	Main	0.83	[0.62,1.13]	0.2388
	Ext 60	0.84	[0.63,1.13]	0.2560
	Unr drugs	0.75	[0.57,0.99]	0.0392
	Naive	0.79	[0.49,1.26]	0.3190
	Smoke Never	0.83	[0.61,1.12]	0.2168
	COPD Severe Mild	0.87	[0.64,1.17]	0.3498
	COPD Severe VSev	0.87	[0.65,1.17]	0.3675

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Table 15-23-4 (Page 1 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
HSD

		QVA compared to Free LABA+LAMA without ICS			QVA compared to Free LABA+LAMA with ICS		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
MACE	Too few events	.		.	.		.
Ischemic heart disease	Too few events	.		.	.		.

Note: Run date and time 01NOV2018 11:20:42,

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Table 15-23-4 (Page 2 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
HSD

		QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
MACE	Too few events	.		.	.		.
Ischemic heart disease	Too few events	.		.	.		.

Note: Run date and time 01NOV2018 11:20:42,

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Table 15-23-4 (Page 3 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
HSD

		QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
MACE	Too few events	.		.	.		.
Ischemic heart disease	Too few events	.		.	.		.

Note: Run date and time 01NOV2018 11:20:42,

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Table 15-23-4 (Page 4 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
HSD

		QVA compared to LAMA		
Endpoint	Analysis	HR	95% CI	P
MACE	Too few events	.		.
Ischemic heart disease	Too few events	.		.

Note: Run date and time 01NOV2018 11:20:42,

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Table 15-23-4 (Page 5 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
HSD

		QVA compared to Free LABA+LAMA without ICS			QVA compared to Free LABA+LAMA with ICS		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
Cardiac arrhythmia	Unr drugs	0.73	[0.22,2.45]	0.6106	.	[. , .]	.
Cerebrovascular disorders	Too few events	.		.	.		.

Note: Run date and time 01NOV2018 11:20:42,

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Table 15-23-4 (Page 6 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
HSD

		QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
Cardiac arrhythmia	Unr drugs	.	[. , .]	.	1.36	[0.38,4.91]	0.6399
Cerebrovascular disorders	Too few events	.		.	.		.

Note: Run date and time 01NOV2018 11:20:42,

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Table 15-23-4 (Page 7 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
HSD

		QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
Cardiac arrhythmia	Unr drugs	0.44	[0.13,1.49]	0.1883	.	[. , .]	.
Cerebrovascular disorders	Too few events	.		.	.		.

Note: Run date and time 01NOV2018 11:20:42,

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Table 15-23-4 (Page 8 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
HSD

		QVA compared to LAMA		
Endpoint	Analysis	HR	95% CI	P
Cardiac arrhythmia	Unr drugs	1.53	[0.44,5.33]	0.5034
Cerebrovascular disorders	Too few events	.		.

Note: Run date and time 01NOV2018 11:20:42,

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Table 15-23-4 (Page 9 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
HSD

		QVA compared to Free LABA+LAMA without ICS			QVA compared to Free LABA+LAMA with ICS		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
Glaucoma	Too few events	.		.	.		.
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	Too few events	.		.	.		.

Note: Run date and time 01NOV2018 11:20:42,

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Table 15-23-4 (Page 10 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
HSD

		QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
Glaucoma	Too few events	.		.	.		.
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	Too few events	.		.	.		.

Note: Run date and time 01NOV2018 11:20:42,

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Table 15-23-4 (Page 11 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
HSD

		QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
Glaucoma	Too few events	.		.	.		.
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	Too few events	.		.	.		.

Note: Run date and time 01NOV2018 11:20:42,

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Table 15-23-4 (Page 12 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
HSD

		QVA compared to LAMA		
Endpoint	Analysis	HR	95% CI	P
Glaucoma	Too few events	.		.
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	Too few events	.		.

Note: Run date and time 01NOV2018 11:20:42,

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Table 15-23-4 (Page 13 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
HSD

		QVA compared to Free LABA+LAMA without ICS			QVA compared to Free LABA+LAMA with ICS		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
Diabetes mellitus	Main	.	[. , .]	.	.	[. , .]	.
	Ext 60	.	[. , .]	.	.	[. , .]	.
	Unr drugs	1.06	[0.25,4.59]	0.9349	.	[. , .]	.
	Smoke Never	.	[. , .]	.	.	[. , .]	.
	COPD Severe Mild	.	[. , .]	.	.	[. , .]	.
	COPD Severe VSev	.	[. , .]	.	.	[. , .]	.
Bronchospasm	Too few events	.		.	.		.

Note: Run date and time 01NOV2018 11:20:42,

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Table 15-23-4 (Page 14 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
HSD

		QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
Diabetes mellitus	Main	.	[. , .]	.	0.65	[0.23,1.82]	0.4085
	Ext 60	.	[. , .]	.	0.60	[0.21,1.66]	0.3215
	Unr drugs	.	[. , .]	.	0.61	[0.22,1.74]	0.3568
	Smoke Never	.	[. , .]	.	0.79	[0.28,2.23]	0.6552
	COPD Severe Mild	.	[. , .]	.	0.72	[0.26,2.01]	0.5265
	COPD Severe VSev	.	[. , .]	.	0.68	[0.24,1.95]	0.4762
Bronchospasm	Too few events	.		.	.		.

Note: Run date and time 01NOV2018 11:20:42,

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Table 15-23-4 (Page 15 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
HSD

		QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
Diabetes mellitus	Main	.	[. , .]	.	.	[. , .]	.
	Ext 60	.	[. , .]	.	.	[. , .]	.
	Unr drugs	.	[. , .]	.	.	[. , .]	.
	Smoke Never	.	[. , .]	.	.	[. , .]	.
	COPD Severe Mild	.	[. , .]	.	.	[. , .]	.
	COPD Severe VSev	.	[. , .]	.	.	[. , .]	.
Bronchospasm	Too few events	.		.	.		.

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Table 15-23-4 (Page 16 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
HSD

		QVA compared to LAMA		
Endpoint	Analysis	HR	95% CI	P
Diabetes mellitus	Main	1.32	[0.42,4.11]	0.6306
	Ext 60	1.27	[0.41,3.91]	0.6817
	Unr drugs	1.10	[0.37,3.24]	0.8685
	Smoke Never	1.47	[0.47,4.61]	0.5095
	COPD Severe Mild	1.44	[0.47,4.42]	0.5252
	COPD Severe VSev	1.36	[0.44,4.20]	0.5950
Bronchospasm	Too few events	.		.

Note: Run date and time 01NOV2018 11:20:42,

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Table 15-23-4 (Page 17 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
HSD

		QVA compared to Free LABA+LAMA without ICS			QVA compared to Free LABA+LAMA with ICS		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
Mortality	Too few events	.		.	.		.

Note: Run date and time 01NOV2018 11:20:42,

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Table 15-23-4 (Page 18 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
HSD

		QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
Mortality	Too few events	.		.	.		.

Note: Run date and time 01NOV2018 11:20:42,

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Table 15-23-4 (Page 19 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
HSD

		QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
Mortality	Too few events	.		.	.		.

Note: Run date and time 01NOV2018 11:20:42,

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Table 15-23-4 (Page 20 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
HSD

		QVA compared to LAMA		
Endpoint	Analysis	HR	95% CI	P
Mortality	Too few events	.		.

Note: Run date and time 01NOV2018 11:20:42,

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Table 15-23-5 (Page 1 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
SIDIAP

		QVA compared to Free LABA+LAMA without ICS			QVA compared to Free LABA+LAMA with ICS		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
MACE	Main	1.25	[0.88,1.79]	0.2099	1.42	[0.83,2.42]	0.2031
	Ext 60	1.27	[0.90,1.78]	0.1799	1.31	[0.79,2.19]	0.2972
	Unr drugs	1.30	[0.92,1.84]	0.1401	1.38	[0.82,2.31]	0.2287
	Naive	1.48	[0.88,2.47]	0.1360	1.92	[0.88,4.20]	0.0999
	Smoke Never	1.25	[0.88,1.78]	0.2124	1.42	[0.83,2.43]	0.1984
	COPD Severe Mild	1.25	[0.88,1.78]	0.2150	1.39	[0.81,2.40]	0.2331
	COPD Severe VSev	1.25	[0.88,1.79]	0.2121	1.38	[0.81,2.36]	0.2410
Ischemic heart disease	Main	0.60	[0.27,1.34]	0.2103	.	[. , .]	.
	Ext 60	0.61	[0.28,1.36]	0.2276	.	[. , .]	.
	Unr drugs	0.57	[0.26,1.24]	0.1548	.	[. , .]	.
	Naive	1.06	[0.33,3.37]	0.9253	.	[. , .]	.
	Smoke Never	0.59	[0.27,1.33]	0.2051	.	[. , .]	.
	COPD Severe Mild	0.59	[0.27,1.33]	0.2045	.	[. , .]	.
	COPD Severe VSev	0.60	[0.27,1.36]	0.2210	.	[. , .]	.

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Table 15-23-5 (Page 2 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
SIDIAP

		QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
MACE	Main	0.94	[0.59,1.49]	0.7921	0.80	[0.63,1.01]	0.0599
	Ext 60	0.94	[0.61,1.45]	0.7898	0.81	[0.65,1.02]	0.0763
	Unr drugs	0.92	[0.60,1.42]	0.7177	0.80	[0.63,1.01]	0.0625
	Naive	1.34	[0.70,2.56]	0.3793	0.99	[0.64,1.55]	0.9758
	Smoke Never	0.94	[0.60,1.49]	0.8054	0.79	[0.63,1.01]	0.0568
	COPD Severe Mild	0.94	[0.60,1.47]	0.7716	0.78	[0.62,0.99]	0.0390
	COPD Severe VSev	0.93	[0.59,1.46]	0.7566	0.79	[0.62,0.99]	0.0409
Ischemic heart disease	Main	0.83	[0.26,2.66]	0.7503	0.72	[0.38,1.35]	0.3033
	Ext 60	0.88	[0.29,2.72]	0.8310	0.70	[0.39,1.27]	0.2401
	Unr drugs	0.86	[0.27,2.69]	0.7887	0.70	[0.37,1.33]	0.2770
	Naive	.	[. , .]	.	0.86	[0.34,2.15]	0.7430
	Smoke Never	0.83	[0.26,2.66]	0.7508	0.72	[0.38,1.34]	0.2980
	COPD Severe Mild	0.82	[0.27,2.51]	0.7251	0.63	[0.34,1.16]	0.1350
	COPD Severe VSev	0.80	[0.26,2.49]	0.6991	0.71	[0.38,1.31]	0.2699

Note: Run date and time 01NOV2018 11:20:54,

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Table 15-23-5 (Page 3 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
SIDIAP

		QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
MACE	Main	0.82	[0.46,1.44]	0.4867	0.91	[0.59,1.39]	0.6512
	Ext 60	0.79	[0.46,1.35]	0.3892	0.99	[0.67,1.46]	0.9572
	Unr drugs	0.79	[0.46,1.35]	0.3848	0.83	[0.56,1.24]	0.3645
	Naive	1.02	[0.34,3.05]	0.9761	1.48	[0.85,2.58]	0.1679
	Smoke Never	0.81	[0.46,1.44]	0.4790	0.90	[0.59,1.39]	0.6365
	COPD Severe Mild	0.82	[0.46,1.45]	0.4887	0.91	[0.61,1.35]	0.6307
	COPD Severe VSev	0.82	[0.47,1.45]	0.4983	0.96	[0.65,1.40]	0.8235
Ischemic heart disease	Main	0.31	[0.10,0.97]	0.0446	1.45	[0.58,3.66]	0.4266
	Ext 60	0.33	[0.11,1.00]	0.0507	0.97	[0.45,2.08]	0.9354
	Unr drugs	0.32	[0.10,0.98]	0.0455	1.21	[0.51,2.84]	0.6671
	Naive	.	[. , .]	.	2.36	[0.70,8.01]	0.1672
	Smoke Never	0.31	[0.10,0.96]	0.0422	1.45	[0.58,3.66]	0.4263
	COPD Severe Mild	0.31	[0.10,0.98]	0.0459	1.36	[0.56,3.32]	0.4934
	COPD Severe VSev	0.32	[0.10,0.98]	0.0467	1.38	[0.56,3.39]	0.4856

Note: Run date and time 01NOV2018 11:20:54,

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Table 15-23-5 (Page 4 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
SIDIAP

		QVA compared to LAMA		
Endpoint	Analysis	HR	95% CI	P
MACE	Main	0.97	[0.75,1.25]	0.7934
	Ext 60	0.98	[0.77,1.25]	0.8865
	Unr drugs	0.94	[0.74,1.21]	0.6490
	Naive	1.36	[0.90,2.06]	0.1418
	Smoke Never	0.97	[0.75,1.25]	0.7931
	COPD Severe Mild	0.97	[0.75,1.24]	0.7852
	COPD Severe VSev	0.96	[0.76,1.23]	0.7753
Ischemic heart disease	Main	0.66	[0.33,1.32]	0.2443
	Ext 60	0.65	[0.34,1.25]	0.1984
	Unr drugs	0.70	[0.36,1.36]	0.2891
	Naive	1.16	[0.45,2.97]	0.7564
	Smoke Never	0.66	[0.33,1.33]	0.2472
	COPD Severe Mild	0.59	[0.31,1.13]	0.1119
	COPD Severe VSev	0.67	[0.35,1.30]	0.2384

Note: Run date and time 01NOV2018 11:20:54,

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Hazard ratios for QVA versus comparators, main and sensitivity analyses
SIDIAP

		QVA compared to Free LABA+LAMA without ICS			QVA compared to Free LABA+LAMA with ICS		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
Cardiac arrhythmia	Main	1.04	[0.61,1.78]	0.8919	0.71	[0.36,1.41]	0.3326
	Ext 60	1.03	[0.61,1.74]	0.9046	0.74	[0.38,1.45]	0.3823
	Unr drugs	0.95	[0.57,1.59]	0.8530	0.72	[0.37,1.43]	0.3519
	Naive	1.15	[0.53,2.48]	0.7307	1.70	[0.55,5.23]	0.3556
	Smoke Never	1.04	[0.61,1.78]	0.8933	0.71	[0.36,1.41]	0.3297
	COPD Severe Mild	1.05	[0.61,1.80]	0.8593	0.75	[0.38,1.48]	0.4022
	COPD Severe VSev	1.05	[0.61,1.80]	0.8596	0.73	[0.37,1.43]	0.3562
Cerebrovascular disorders	Main	1.24	[0.45,3.40]	0.6749	0.43	[0.16,1.13]	0.0885
	Ext 60	1.39	[0.57,3.39]	0.4696	0.52	[0.21,1.28]	0.1559
	Unr drugs	1.37	[0.50,3.70]	0.5406	0.46	[0.18,1.20]	0.1131
	Smoke Never	1.24	[0.45,3.38]	0.6800	0.43	[0.16,1.13]	0.0868
	COPD Severe Mild	1.26	[0.46,3.45]	0.6476	0.45	[0.17,1.17]	0.1021
	COPD Severe VSev	1.27	[0.47,3.48]	0.6363	0.45	[0.17,1.18]	0.1025

Note: Run date and time 01NOV2018 11:20:54,

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Table 15-23-5 (Page 6 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
SIDIAP

		QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
Cardiac arrhythmia	Main	0.62	[0.31,1.25]	0.1808	0.63	[0.43,0.94]	0.0251
	Ext 60	0.58	[0.30,1.12]	0.1041	0.63	[0.43,0.91]	0.0141
	Unr drugs	0.57	[0.30,1.11]	0.0981	0.63	[0.42,0.93]	0.0210
	Naive	0.95	[0.41,2.22]	0.9092	0.90	[0.45,1.80]	0.7562
	Smoke Never	0.62	[0.31,1.25]	0.1780	0.63	[0.42,0.94]	0.0239
	COPD Severe Mild	0.65	[0.34,1.26]	0.2062	0.64	[0.44,0.94]	0.0215
	COPD Severe VSev	0.63	[0.31,1.27]	0.1981	0.61	[0.42,0.89]	0.0101
Cerebrovascular disorders	Main	0.31	[0.12,0.79]	0.0139	0.63	[0.33,1.20]	0.1602
	Ext 60	0.37	[0.16,0.86]	0.0214	0.73	[0.43,1.23]	0.2361
	Unr drugs	0.34	[0.14,0.86]	0.0223	0.65	[0.34,1.21]	0.1732
	Smoke Never	0.32	[0.13,0.81]	0.0166	0.64	[0.33,1.21]	0.1696
	COPD Severe Mild	0.30	[0.12,0.79]	0.0142	0.62	[0.33,1.18]	0.1445
	COPD Severe VSev	0.31	[0.13,0.76]	0.0108	0.65	[0.35,1.20]	0.1655

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Hazard ratios for QVA versus comparators, main and sensitivity analyses
SIDIAP

		QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
Cardiac arrhythmia	Main	.	[. , .]	.	1.09	[0.65,1.83]	0.7527
	Ext 60	.	[. , .]	.	1.08	[0.67,1.75]	0.7578
	Unr drugs	0.72	[0.28,1.80]	0.4770	0.86	[0.48,1.53]	0.6034
	Naive	.	[. , .]	.	1.20	[0.57,2.49]	0.6330
	Smoke Never	.	[. , .]	.	1.09	[0.65,1.83]	0.7554
	COPD Severe Mild	.	[. , .]	.	1.11	[0.66,1.86]	0.6978
	COPD Severe VSev	.	[. , .]	.	1.08	[0.65,1.79]	0.7591
Cerebrovascular disorders	Main	.	[. , .]	.	0.71	[0.33,1.55]	0.3922
	Ext 60	.	[. , .]	.	0.77	[0.39,1.50]	0.4406
	Unr drugs	.	[. , .]	.	0.70	[0.33,1.50]	0.3623
	Smoke Never	.	[. , .]	.	0.71	[0.33,1.55]	0.3937
	COPD Severe Mild	.	[. , .]	.	0.72	[0.33,1.59]	0.4190
	COPD Severe VSev	.	[. , .]	.	0.77	[0.36,1.62]	0.4860

Note: Run date and time 01NOV2018 11:20:54,

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Hazard ratios for QVA versus comparators, main and sensitivity analyses
SIDIAP

		QVA compared to LAMA		
Endpoint	Analysis	HR	95% CI	P
Cardiac arrhythmia	Main	0.69	[0.45,1.04]	0.0778
	Ext 60	0.67	[0.45,0.99]	0.0444
	Unr drugs	0.65	[0.43,0.97]	0.0355
	Naive	1.02	[0.53,1.96]	0.9534
	Smoke Never	0.69	[0.45,1.04]	0.0773
	COPD Severe Mild	0.68	[0.45,1.01]	0.0561
	COPD Severe VSev	0.69	[0.46,1.02]	0.0632
Cerebrovascular disorders	Main	0.62	[0.31,1.23]	0.1720
	Ext 60	0.82	[0.46,1.46]	0.4984
	Unr drugs	0.68	[0.35,1.31]	0.2491
	Smoke Never	0.61	[0.31,1.23]	0.1689
	COPD Severe Mild	0.63	[0.31,1.25]	0.1839
	COPD Severe VSev	0.64	[0.33,1.23]	0.1814

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Hazard ratios for QVA versus comparators, main and sensitivity analyses
SIDIAP

		QVA compared to Free LABA+LAMA without ICS			QVA compared to Free LABA+LAMA with ICS		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
Glaucoma	Main	0.72	[0.31,1.70]	0.4594	.	[. , .]	.
	Ext 60	0.71	[0.32,1.61]	0.4187	.	[. , .]	.
	Unr drugs	0.74	[0.31,1.73]	0.4820	.	[. , .]	.
	Smoke Never	0.73	[0.31,1.71]	0.4628	.	[. , .]	.
	COPD Severe Mild	0.73	[0.31,1.72]	0.4745	.	[. , .]	.
	COPD Severe VSev	0.73	[0.31,1.72]	0.4685	.	[. , .]	.
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	Main	0.85	[0.54,1.34]	0.4885	1.00	[0.50,2.01]	0.9978
	Ext 60	0.85	[0.55,1.31]	0.4691	1.06	[0.53,2.10]	0.8778
	Unr drugs	0.83	[0.53,1.30]	0.4152	1.02	[0.51,2.05]	0.9451
	Naive	1.13	[0.57,2.23]	0.7281	.	[. , .]	.
	Smoke Never	0.85	[0.54,1.35]	0.4964	1.00	[0.49,2.01]	0.9909
	COPD Severe Mild	0.84	[0.53,1.32]	0.4512	1.02	[0.50,2.06]	0.9584
	COPD Severe VSev	0.84	[0.54,1.33]	0.4633	0.99	[0.49,1.98]	0.9741

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Hazard ratios for QVA versus comparators, main and sensitivity analyses
SIDIAP

		QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
Glaucoma	Main	.	[. , .]	.	1.03	[0.49,2.16]	0.9442
	Ext 60	.	[. , .]	.	1.05	[0.54,2.05]	0.8890
	Unr drugs	.	[. , .]	.	1.01	[0.48,2.12]	0.9886
	Smoke Never	.	[. , .]	.	1.02	[0.49,2.14]	0.9540
	COPD Severe Mild	.	[. , .]	.	1.03	[0.50,2.12]	0.9286
	COPD Severe VSev	.	[. , .]	.	0.98	[0.48,2.01]	0.9567
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	Main	1.67	[0.81,3.45]	0.1627	0.76	[0.55,1.04]	0.0861
	Ext 60	1.93	[0.95,3.91]	0.0691	0.84	[0.62,1.13]	0.2434
	Unr drugs	1.77	[0.87,3.62]	0.1170	0.77	[0.56,1.06]	0.1106
	Naive	1.81	[0.68,4.80]	0.2310	0.90	[0.50,1.62]	0.7316
	Smoke Never	1.66	[0.81,3.43]	0.1676	0.76	[0.55,1.04]	0.0866
	COPD Severe Mild	1.54	[0.76,3.13]	0.2344	0.76	[0.55,1.05]	0.0928
	COPD Severe VSev	1.61	[0.78,3.29]	0.1948	0.77	[0.56,1.05]	0.0937

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Hazard ratios for QVA versus comparators, main and sensitivity analyses
SIDIAP

		QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
Glaucoma	Main	.	[. , .]	.	0.68	[0.27,1.71]	0.4117
	Ext 60	.	[. , .]	.	0.79	[0.34,1.83]	0.5781
	Unr drugs	.	[. , .]	.	0.72	[0.31,1.71]	0.4605
	Smoke Never	.	[. , .]	.	0.68	[0.27,1.69]	0.4032
	COPD Severe Mild	.	[. , .]	.	0.69	[0.27,1.72]	0.4213
	COPD Severe VSev	.	[. , .]	.	0.68	[0.27,1.69]	0.4034
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	Main	0.87	[0.36,2.09]	0.7596	0.78	[0.52,1.17]	0.2334
	Ext 60	0.96	[0.40,2.27]	0.9174	0.82	[0.56,1.20]	0.3166
	Unr drugs	0.90	[0.38,2.16]	0.8214	0.69	[0.47,1.02]	0.0613
	Naive	.	[. , .]	.	1.00	[0.53,1.90]	0.9975
	Smoke Never	0.87	[0.37,2.09]	0.7599	0.78	[0.52,1.17]	0.2311
	COPD Severe Mild	0.91	[0.38,2.16]	0.8266	0.78	[0.53,1.16]	0.2262
	COPD Severe VSev	0.89	[0.38,2.13]	0.7987	0.76	[0.52,1.13]	0.1780

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Hazard ratios for QVA versus comparators, main and sensitivity analyses
SIDIAP

		QVA compared to LAMA		
Endpoint	Analysis	HR	95% CI	P
Glaucoma	Main	0.60	[0.28,1.27]	0.1802
	Ext 60	0.65	[0.32,1.29]	0.2190
	Unr drugs	0.58	[0.28,1.20]	0.1443
	Smoke Never	0.60	[0.28,1.27]	0.1785
	COPD Severe Mild	0.61	[0.29,1.29]	0.1984
	COPD Severe VSev	0.58	[0.28,1.22]	0.1544
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	Main	0.76	[0.54,1.08]	0.1294
	Ext 60	0.83	[0.60,1.15]	0.2593
	Unr drugs	0.72	[0.52,1.01]	0.0571
	Naive	0.88	[0.48,1.59]	0.6685
	Smoke Never	0.76	[0.54,1.08]	0.1287
	COPD Severe Mild	0.76	[0.54,1.08]	0.1266
	COPD Severe VSev	0.75	[0.54,1.05]	0.0947

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Hazard ratios for QVA versus comparators, main and sensitivity analyses
SIDIAP

		QVA compared to Free LABA+LAMA without ICS			QVA compared to Free LABA+LAMA with ICS		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
Diabetes mellitus	Main	1.03	[0.64,1.66]	0.9057	1.40	[0.61,3.21]	0.4257
	Ext 60	1.01	[0.63,1.62]	0.9606	1.41	[0.62,3.23]	0.4134
	Unr drugs	1.03	[0.65,1.63]	0.9065	1.48	[0.65,3.38]	0.3514
	Naive	1.51	[0.76,2.98]	0.2354	.	[. , .]	.
	Smoke Never	1.03	[0.64,1.66]	0.9166	1.41	[0.61,3.23]	0.4205
	COPD Severe Mild	1.03	[0.64,1.66]	0.9146	1.44	[0.62,3.33]	0.3922
	COPD Severe VSev	1.04	[0.64,1.67]	0.8806	1.42	[0.63,3.24]	0.4000
Bronchospasm	Main	.	[. , .]	.	.	[. , .]	.
	Ext 60	.	[. , .]	.	.	[. , .]	.
	Unr drugs	.	[. , .]	.	.	[. , .]	.
	Smoke Never	.	[. , .]	.	.	[. , .]	.
	COPD Severe Mild	.	[. , .]	.	.	[. , .]	.
	COPD Severe VSev	.	[. , .]	.	.	[. , .]	.

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Hazard ratios for QVA versus comparators, main and sensitivity analyses
SIDIAP

		QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
Diabetes mellitus	Main	1.48	[0.58,3.74]	0.4119	0.83	[0.58,1.18]	0.2893
	Ext 60	1.12	[0.49,2.53]	0.7911	0.80	[0.57,1.12]	0.2011
	Unr drugs	1.36	[0.58,3.19]	0.4858	0.87	[0.62,1.22]	0.4123
	Naive	2.32	[0.85,6.37]	0.1022	1.26	[0.67,2.40]	0.4750
	Smoke Never	1.50	[0.59,3.78]	0.3950	0.83	[0.59,1.19]	0.3114
	COPD Severe Mild	1.33	[0.50,3.51]	0.5677	0.84	[0.60,1.19]	0.3275
	COPD Severe VSev	1.42	[0.57,3.52]	0.4477	0.84	[0.59,1.18]	0.3112
Bronchospasm	Main	0.26	[0.09,0.77]	0.0151	0.46	[0.18,1.17]	0.1039
	Ext 60	0.35	[0.13,0.98]	0.0462	0.56	[0.26,1.24]	0.1541
	Unr drugs	0.31	[0.11,0.87]	0.0267	0.58	[0.24,1.37]	0.2144
	Smoke Never	0.26	[0.09,0.77]	0.0151	0.46	[0.18,1.17]	0.1035
	COPD Severe Mild	0.26	[0.09,0.77]	0.0155	0.49	[0.20,1.22]	0.1257
	COPD Severe VSev	0.27	[0.09,0.79]	0.0169	0.49	[0.19,1.27]	0.1439

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Hazard ratios for QVA versus comparators, main and sensitivity analyses
SIDIAP

		QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
Diabetes mellitus	Main	0.61	[0.29,1.28]	0.1940	1.16	[0.72,1.87]	0.5472
	Ext 60	0.63	[0.30,1.31]	0.2119	1.16	[0.74,1.83]	0.5141
	Unr drugs	0.67	[0.32,1.39]	0.2772	1.21	[0.77,1.90]	0.4025
	Naive	.	[. , .]	.	1.63	[0.85,3.14]	0.1425
	Smoke Never	0.61	[0.29,1.28]	0.1947	1.16	[0.72,1.87]	0.5420
	COPD Severe Mild	0.61	[0.29,1.27]	0.1869	1.17	[0.74,1.84]	0.5037
	COPD Severe VSev	0.60	[0.28,1.26]	0.1779	1.13	[0.71,1.78]	0.6047
Bronchospasm	Main	.	[. , .]	.	0.69	[0.21,2.25]	0.5337
	Ext 60	.	[. , .]	.	1.02	[0.34,3.07]	0.9649
	Unr drugs	.	[. , .]	.	0.52	[0.16,1.65]	0.2655
	Smoke Never	.	[. , .]	.	0.69	[0.21,2.27]	0.5423
	COPD Severe Mild	.	[. , .]	.	0.71	[0.22,2.29]	0.5688
	COPD Severe VSev	.	[. , .]	.	0.67	[0.21,2.11]	0.4886

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Hazard ratios for QVA versus comparators, main and sensitivity analyses
SIDIAP

		QVA compared to LAMA		
Endpoint	Analysis	HR	95% CI	P
Diabetes mellitus	Main	1.01	[0.69,1.46]	0.9654
	Ext 60	0.96	[0.67,1.37]	0.8078
	Unr drugs	1.07	[0.75,1.54]	0.7109
	Naive	1.25	[0.72,2.17]	0.4381
	Smoke Never	1.01	[0.69,1.46]	0.9700
	COPD Severe Mild	1.03	[0.71,1.49]	0.8780
	COPD Severe VSev	1.01	[0.70,1.45]	0.9543
Bronchospasm	Main	0.90	[0.30,2.67]	0.8468
	Ext 60	1.07	[0.41,2.79]	0.8976
	Unr drugs	0.76	[0.28,2.09]	0.5916
	Smoke Never	0.90	[0.30,2.67]	0.8487
	COPD Severe Mild	0.95	[0.33,2.79]	0.9315
	COPD Severe VSev	0.90	[0.31,2.62]	0.8409

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Hazard ratios for QVA versus comparators, main and sensitivity analyses
SIDIAP

		QVA compared to Free LABA+LAMA without ICS			QVA compared to Free LABA+LAMA with ICS		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
Mortality	Main	1.40	[0.82,2.39]	0.2177	2.39	[0.93,6.14]	0.0702
	Ext 60	1.71	[1.07,2.73]	0.0248	2.30	[1.04,5.07]	0.0398
	Unr drugs	1.56	[0.92,2.63]	0.0981	2.53	[0.99,6.47]	0.0532
	Naive	1.36	[0.59,3.12]	0.4657	.	[. , .]	.
	Smoke Never	1.40	[0.82,2.39]	0.2170	2.40	[0.93,6.16]	0.0692
	COPD Severe Mild	1.37	[0.80,2.34]	0.2471	2.33	[0.91,5.98]	0.0777
	COPD Severe VSev	1.36	[0.80,2.33]	0.2546	2.26	[0.88,5.81]	0.0910

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Hazard ratios for QVA versus comparators, main and sensitivity analyses
SIDIAP

		QVA compared to Free LABA+ICS			QVA compared to Fixed LABA ICS		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
Mortality	Main	0.98	[0.55,1.74]	0.9339	0.52	[0.39,0.70]	<.0001
	Ext 60	0.80	[0.47,1.36]	0.4080	0.63	[0.50,0.80]	0.0002
	Unr drugs	1.04	[0.60,1.80]	0.8973	0.53	[0.40,0.71]	<.0001
	Naive	1.41	[0.53,3.74]	0.4922	0.43	[0.22,0.85]	0.0149
	Smoke Never	0.97	[0.55,1.74]	0.9297	0.52	[0.39,0.70]	<.0001
	COPD Severe Mild	1.02	[0.57,1.81]	0.9542	0.57	[0.42,0.77]	0.0002
	COPD Severe VSev	0.98	[0.56,1.72]	0.9419	0.54	[0.40,0.72]	<.0001

Note: Run date and time 01NOV2018 11:20:54,

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Table 15-23-5 (Page 19 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
SIDIAP

		QVA compared to Fixed LABA LAMA			QVA compared to LABA		
Endpoint	Analysis	HR	95% CI	P	HR	95% CI	P
Mortality	Main	1.05	[0.48,2.29]	0.8966	0.61	[0.35,1.06]	0.0808
	Ext 60	1.04	[0.57,1.90]	0.8868	0.81	[0.52,1.24]	0.3240
	Unr drugs	1.17	[0.54,2.53]	0.6968	0.58	[0.36,0.94]	0.0268
	Naive	.	[. , .]	.	0.48	[0.21,1.11]	0.0883
	Smoke Never	1.06	[0.49,2.30]	0.8829	0.61	[0.35,1.06]	0.0789
	COPD Severe Mild	1.04	[0.48,2.25]	0.9114	0.70	[0.42,1.15]	0.1556
	COPD Severe VSev	1.06	[0.49,2.29]	0.8737	0.63	[0.38,1.04]	0.0689

Note: Run date and time 01NOV2018 11:20:54,

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Table 15-23-5 (Page 20 of 20)
Hazard ratios for QVA versus comparators, main and sensitivity analyses
SIDIAP

		QVA compared to LAMA		
Endpoint	Analysis	HR	95% CI	P
Mortality	Main	0.64	[0.46,0.91]	0.0133
	Ext 60	0.78	[0.60,1.03]	0.0793
	Unr drugs	0.64	[0.46,0.88]	0.0057
	Naive	0.65	[0.34,1.25]	0.2009
	Smoke Never	0.64	[0.45,0.91]	0.0132
	COPD Severe Mild	0.70	[0.50,0.98]	0.0405
	COPD Severe VSev	0.66	[0.47,0.92]	0.0141

Note: Run date and time 01NOV2018 11:20:54,

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Table 15-24-1 (Page 1 of 1)
Hazard ratios for QVA vs Free LABA/LAMA and QVA vs Fixed LABA+LAMA from analyses complete follow-up
THIN - Total analysis population

		QVA compared to Free LABA+LAMA				QVA compared to Fixed LABA+LAMA			
Endpoint	N events during QVA exposure	N events during Free LABA+LAMA exposure	HR	95% CI	P	N events during Fixed LABA+LAMA exposure	HR	95% CI	P
MACE	22	38	1.27	[0.75,2.15]	0.3733	64	1.20	[0.74,1.95]	0.4602
Ischemic heart disease	17	25	1.50	[0.81,2.78]	0.1992	48	1.24	[0.71,2.16]	0.4467
Cardiac arrhythmia	10	21	1.05	[0.49,2.23]	0.9024	40	0.86	[0.43,1.72]	0.6713
Cerebrovascular disorders	8	21	0.82	[0.36,1.86]	0.6430	36	0.76	[0.35,1.65]	0.4924
Glaucoma	3	4	1.65	[0.37,7.39]	0.5149	5	2.04	[0.48,8.55]	0.3313
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	7	19	0.79	[0.33,1.89]	0.5969	23	1.08	[0.46,2.51]	0.8671
Diabetes mellitus	11	41	0.58	[0.30,1.14]	0.1147	38	0.99	[0.51,1.95]	0.9878
Bronchospasm	.	0	.		.	.	.		.
Mortality	69	72	2.12	[1.52,2.95]	0.0000	129	1.84	[1.37,2.46]	0.0000

Note: Total follow-up in years (not censored by events) with exposure to QVA was 1048, to Free LABA+LAMA 2181 and to Fixed LABA+LAMA 3558.
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Table 15-24-2 (Page 1 of 1)
Hazard ratios for QVA vs Free LABA/LAMA and QVA vs Fixed LABA+LAMA from analyses complete follow-up
IPCI - Total analysis population

		QVA compared to Free LABA+LAMA				QVA compared to Fixed LABA+LAMA			
Endpoint	N events during QVA exposure	N events during Free LABA+LAMA exposure	HR	95% CI	P	N events during Fixed LABA+LAMA exposure	HR	95% CI	P
MACE	23	43	1.01	[0.60,1.68]	0.9804	19	1.32	[0.72,2.42]	0.3762
Ischemic heart disease	7	23	0.53	[0.22,1.23]	0.1395	7	1.04	[0.36,2.96]	0.9486
Cardiac arrhythmia	16	19	1.66	[0.85,3.25]	0.1416	8	2.15	[0.92,5.03]	0.0785
Cerebrovascular disorders	16	18	1.56	[0.79,3.07]	0.2025	5	3.49	[1.27,9.54]	0.0150
Glaucoma	2	1	.		.	1	.		.
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	15	17	1.57	[0.78,3.16]	0.2075	11	1.39	[0.63,3.02]	0.4128
Diabetes mellitus	10	10	1.63	[0.67,3.97]	0.2803	8	1.31	[0.51,3.35]	0.5694
Bronchospasm	1	0	.		.	1	.		.
Mortality	23	51	0.84	[0.51,1.39]	0.5015	21	1.18	[0.65,2.13]	0.5838

Note: Total follow-up in years (not censored by events) with exposure to QVA was 656, to Free LABA+LAMA 1031 and to Fixed LABA+LAMA 730.
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Table 15-24-3 (Page 1 of 1)
Hazard ratios for QVA vs Free LABA/LAMA and QVA vs Fixed LABA+LAMA from analyses complete follow-up
AUH - Total analysis population

	QVA compared to Free LABA+LAMA					QVA compared to Fixed LABA+LAMA			
Endpoint	N events during QVA exposure	N events during Free LABA+LAMA exposure	HR	95% CI	P	N events during Fixed LABA+LAMA exposure	HR	95% CI	P
MACE	154	48	1.21	[0.87,1.68]	0.2523	107	1.00	[0.78,1.28]	0.9961
Ischemic heart disease	47	12	1.36	[0.72,2.57]	0.3491	26	1.21	[0.75,1.96]	0.4316
Cardiac arrhythmia	48	16	1.01	[0.57,1.79]	0.9696	37	0.85	[0.55,1.31]	0.4718
Cerebrovascular disorders	30	9	1.08	[0.51,2.29]	0.8367	23	0.84	[0.49,1.45]	0.5288
Glaucoma	2	1	.		.	6	.		.
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	16	4	1.12	[0.37,3.38]	0.8365	10	0.98	[0.44,2.17]	0.9629
Diabetes mellitus	7	1	.		.	14	0.32	[0.13,0.80]	0.0150
Bronchospasm	.	0	.		.	.	.		.
Mortality	179	35	1.65	[1.15,2.38]	0.0068	107	1.07	[0.85,1.37]	0.5566

Note: Total follow-up in years (not censored by events) with exposure to QVA was 1945, to Free LABA+LAMA 574 and to Fixed LABA+LAMA 1273.
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Table 15-24-4 (Page 1 of 1)
Hazard ratios for QVA vs Free LABA/LAMA and QVA vs Fixed LABA+LAMA from analyses complete follow-up
HSD - Total analysis population

		QVA compared to Free LABA+LAMA				QVA compared to Fixed LABA+LAMA			
Endpoint	N events during QVA exposure	N events during Free LABA+LAMA exposure	HR	95% CI	P	N events during Fixed LABA+LAMA exposure	HR	95% CI	P
MACE	2	5	.		.	4	.		.
Ischemic heart disease	1	3	.		.	3	.		.
Cardiac arrhythmia	3	20	0.46	[0.14,1.56]	0.2136	8	0.28	[0.08,1.07]	0.0632
Cerebrovascular disorders	3	7	1.34	[0.34,5.20]	0.6742	.	.		.
Glaucoma	2	3	.		.	1	.		.
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	3	12	0.76	[0.21,2.71]	0.6760	4	0.63	[0.14,2.84]	0.5525
Diabetes mellitus	2	13	.		.	2	.		.
Bronchospasm	.	1	.		.	2	.		.
Mortality	3	11	0.97	[0.27,3.48]	0.9618	.	.		.

Note: Total follow-up in years (not censored by events) with exposure to QVA was 297, to Free LABA+LAMA 849 and to Fixed LABA+LAMA 228.
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Table 15-24-5 (Page 1 of 1)
Hazard ratios for QVA vs Free LABA/LAMA and QVA vs Fixed LABA+LAMA from analyses complete follow-up
SIDIAP - Total analysis population

		QVA compared to Free LABA+LAMA				QVA compared to Fixed LABA+LAMA			
Endpoint	N events during QVA exposure	N events during Free LABA+LAMA exposure	HR	95% CI	P	N events during Fixed LABA+LAMA exposure	HR	95% CI	P
MACE	143	116	1.08	[0.85,1.38]	0.5368	22	0.62	[0.40,0.98]	0.0394
Ischemic heart disease	20	32	0.53	[0.30,0.92]	0.0253	6	0.33	[0.13,0.83]	0.0187
Cardiac arrhythmia	72	70	0.89	[0.64,1.23]	0.4747	10	0.73	[0.37,1.41]	0.3425
Cerebrovascular disorders	35	24	1.21	[0.72,2.04]	0.4652	4	0.85	[0.30,2.40]	0.7596
Glaucoma	22	20	0.88	[0.48,1.61]	0.6683	2	.		.
Bladder outflow obstruction, urinary retention or incident benign prostatic hyperplasia	99	83	0.99	[0.74,1.33]	0.9485	10	1.00	[0.52,1.92]	0.9974
Diabetes mellitus	55	44	1.02	[0.69,1.52]	0.9193	8	0.75	[0.36,1.57]	0.4419
Bronchospasm	17	13	1.06	[0.51,2.18]	0.8778	4	0.44	[0.15,1.30]	0.1358
Mortality	44	40	0.91	[0.59,1.40]	0.6671	4	0.97	[0.35,2.70]	0.9530

Note: Total follow-up in years (not censored by events) with exposure to QVA was 5768, to Free LABA+LAMA 4047 and to Fixed LABA+LAMA 781.
Run date and time 01NOV2018 11:39:25,