16. APPENDICES

Table 15 Subject dispositions from CPRD GOLD – Exposed Female Cohort

Title	n	%
Number of Cervarix vaccinated women in CPRD GOLD	168662	
Number of selected subjects (1)		
Subjects with at least one dose of Cervarix between 01Sep2008 - 31AUG2010	129692	76.89
Subject without an unspecified HPV vaccine or Gardasil at any time before the reference date	129171	76.59
Subjects with age at first dose of Cervarix between 9 – 25 years	128913	76.43
Start in CPRD GOLD for at least 12 months at reference date (first dose of Cervarix)	103486	61.36
Subject flag as Acceptable in CPRD GOLD	103486	61.36
Subject without a diagnostic code of autoimmune disease the year prior to the reference date	103081	61.12
Subjects random selection	65000	38.54

%=100 * n of subjects/ total number of selected subjects

Table 16 Subject dispositions from CPRD GOLD – Historical Female Cohort

Title	n	%
Number of female between 9-25 years old in CPRD GOLD in the period 01SEP2005 - 31AUG2007	1397608	
Number of selected subjects (1)		
Subjects actively registered with the CPRD GOLD practice during the period 01SEP2005 - 31AUG2007	727525	52.06
Subject flag as Acceptable in CPRD GOLD	727525	52.06
Subjects after frequency matching on practice region-birth cohort	**178660**	**12.78**
Subjects with age at reference date between 9 – 25 years	152236	10.89
Start in CPRD GOLD for at least 12 months at reference date	107973	7.73
Subject without an unspecified HPV or Gardasil or Cervarix vaccine at any time before the reference date	107912	7.72
Subject without a diagnostic code of autoimmune disease the year prior to the reference date	107434	7.69
Subjects random selection	65000	4.65

Reference date is a random date between 01SEP2005 and 31AUG2007
%=100 * n of subjects/ total number of selected subjects

Table 17 Subject dispositions from CPRD GOLD – Concurrent Male Cohort

Title	n	%
Number of female between 9-25 years old in CPRD GOLD in the period 01SEP2008 - 31AUG2010	1182814	
Number of selected subjects (1)		
Subjects actively registered with the CPRD GOLD practice during the period 01SEP2008 - 31AUG2010	680169	57.50
Subject flag as Acceptable in CPRD GOLD	680169	57.50
Subjects after frequency matching on practice region-birth cohort	**167198**	**14.14**
Subjects with age at reference date between 9 – 25 years	167198	14.14
Start in CPRD GOLD for at least 12 months at reference date	143248	12.11
Subject without an unspecified HPV or Gardasil or Cervarix vaccine at any time before the reference date	143236	12.11
Subject without a diagnostic code of autoimmune disease the year prior to the reference date	142772	12.07
Subjects random selection	65000	5.50

Reference date is a random date between 01SEP2008 and 31AUG2010
%=100 * n of subjects/ total number of selected subjects

Table 18 Subject dispositions from CPRD GOLD – Historical Male Cohort

Title	n	%
Number of male between 9-25 years old in CPRD GOLD in the period 01SEP2005 - 31AUG2007	1226130	
Number of selected subjects (1)		
Subjects actively registered with the CPRD GOLD practice during the period 01SEP2005 - 31AUG2007	712183	58.08
Subject flag as Acceptable in CPRD GOLD	712183	58.08
Subjects after frequency matching on practice region-birth cohort	**179755**	**14.66**
Subjects with age at reference date between 9 – 25 years	119567	9.75
Start in CPRD GOLD for at least 12 months at reference date	92996	7.58
Subject without an unspecified HPV or Gardasil or Cervarix vaccine at any time before the reference date	92667	7.56
Subject without a diagnostic code of autoimmune disease the year prior to the reference date	92337	7.53
Subjects random selection	65000	5.30

Reference date is a random date between 01SEP2005 and 31AUG2007
%=100 * n of subjects/ total number of selected subjects

Table 19 Number of autoimmune disease cases after patient profile review by exposed/non-exposed status (Total cohort)

		EXP N = 513		NNEXP N = 218		MALE N = 156		HIST N = 165		Total N = 1052	
Characteristics	**Categories**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Identifed autoimmune disease cases after profile review	Yes	254	49.5	96	44.0	65	41.7	51	30.9	466	44.3
	No	259	50.5	122	56.0	91	58.3	114	69.1	586	55.7

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n/% = number / percentage of subjects in a given category
The 1052 subjects represents the number of subjects who were identified with an autoimmune disease through the algorithm

Table 20 Classification of AD , Date of first symptom , Date of diagnosis by exposed/non-exposed status (N=AD) (Total cohort)

		EXP N = 257		NNEXP N = 97		MALE N = 65		HIST N = 52		Total N = 471	
Characteristics	**Categories**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Number of autoimmune diseases after profile review	Yes	257	100	97	100	65	100	52	100	471	100
	No	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
NOAD final classification	Confirmed	149	58.0	54	55.7	47	72.3	34	65.4	284	60.3
	Non-confirmed	108	42.0	43	44.3	18	27.7	18	34.6	187	39.7
Date of 1st symptom*	Confirmed	219	85.2	76	78.4	51	78.5	39	75.0	385	81.7
	Non-confirmed	38	14.8	21	21.6	14	21.5	13	25.0	86	18.3
Date of diagnosis	Confirmed	252	98.1	93	95.9	64	98.5	50	96.2	459	97.5
	Non-confirmed	5	1.9	4	4.1	1	1.5	2	3.8	12	2.5

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = Number of AD cases
n/% = number / percentage of subjects in a given category
Five subjects with simultaneously 2 autoimmune diseases: three subjects with diabetes+thyroiditis, one subject with diabetes+uveitis and one with optic neuritis+uveitis
*In case of missing date of 1st symptom, the date of symptom was always classified as non-confirmed. Among the 385 confirmed dates of symptom, two occur after the date of diagnosis and were later considered as missing
(1 in exposed and 1 in historical male cohort). Two identified dates of symptom were classified as non-confirmed in the exposed cohort

Table 21 Imputation of date of first symptom by exposed/non-exposed status (N=AD) (Total cohort)

		EXP N = 257		NNEXP N = 97		MALE N = 65		HIST N = 52		Total N = 471	
Characteristics	**Categories**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Date of 1st symptom	Date to be imputed	37	14.4	21	21.6	14	21.5	14	26.9	86	18.3
	Known date	220	85.6	76	78.4	51	78.5	38	73.1	385	81.7

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = Number of AD cases
n/% = number / percentage of subjects in a given category
Five subjects with simultaneously 2 autoimmune diseases: three subjects with diabetes+thyroiditis, one subject with diabetes+uveitis and one with optic neuritis+uveitis

Table 22 Classification of date of first symptom among known dates by exposed/non-exposed status (N=AD) (Total cohort)

		EXP N = 220		NNEXP N = 76		MALE N = 51		HIST N = 38		Total N = 385	
Characteristics	**Categories**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Classification of date of 1st symptom	Confirmed	218	99.1	76	100	51	100	38	100	383	99.5
	Non-confirmed	2	0.9	0	0.0	0	0.0	0	0.0	2	0.5

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = Number of AD cases
n/% = number / percentage of subjects in a given category
One subject with two autoimmune diseases in the non-exposed female cohort

Table 23 Details on autoimmune disease cases by exposed/non-exposed status (Total cohort)

		EXP N = 254		NNEXP N = 96		MALE N = 65		HIST N = 51		Total N = 466	
Characteristics	**Categories**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Autoimmune disease cases after profile review	Yes	254	100	96	100	65	100	51	100	466	100
	No	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Confirmation of the autoimmune disease	Confirmed	149	58.7	54	56.3	47	72.3	34	66.7	284	60.9
	Non-Confirmed	105	41.3	42	43.8	18	27.7	17	33.3	182	39.1
A symptom date was identified for the autoimmune disease	Yes	220	86.6	75	78.1	51	78.5	38	74.5	384	82.4
	No	34	13.4	21	21.9	14	21.5	13	25.5	82	17.6
The diagnosis date of autoimmune disease appears within 1 year follow-up period	Yes	93	36.6	95	99.0	65	100	51	100	304	65.2
	No	161	63.4	1	1.0	0	0.0	0	0.0	162	34.8
Time in days between diagnosis date and reference date	within 1 year	93	36.6	95	99.0	65	100	51	100	304	65.2
	between 366 and 900 days	157	61.8	1	1.0	0	0.0	0	0.0	158	33.9
	more than 900 days	4	1.6	0	0.0	0	0.0	0	0.0	4	0.9

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = Number of subjects
n/% = number / percentage of subjects in a given category
Five subjects with simultaneously 2 autoimmune diseases: three subjects with diabetes+thyroiditis, one subject with diabetes+uveitis and one with optic neuritis+uveitis

Table 24 Details on autoimmune disease cases by exposed/non-exposed status for subjects with known date of symptom (Total cohort)

		EXP N = 220		NNEXP N = 75		MALE N = 51		HIST N = 38		Total N = 384	
Characteristics	**Categories**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Time in days between symptom date and reference date	before reference date	40	18.2	26	34.7	20	39.2	17	44.7	103	26.8
	within 1 year	95	43.2	49	65.3	31	60.8	21	55.3	196	51.0
	between 366 and 900 days	84	38.2	0	0.0	0	0.0	0	0.0	84	21.9
	more than 900 days	1	0.5	0	0.0	0	0.0	0	0.0	1	0.3

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = Number of subjects
n/% = number / percentage of subjects in a given category
Five subjects with simultaneously 2 autoimmune diseases: three subjects with diabetes+thyroiditis, one subject with diabetes+uveitis and one with optic neuritis+uveitis

Table 25 Time between date of diagnosis and date of symptom by autoimmune disease (N=AD) (Total cohort)

			EXP N = 220	NNEXP N = 76	MALE N = 51	HIST N = 38	Total N = 385
NOAD	**Characteristics**	**Parameters**	**Value**	**Value**	**Value**	**Value**	**Value**
ACUTE DISSEMINATED ENCEPHALOMYELITIS	Time between diagnosis date and symptom date	N	2	0	0	0	2
		Mean	17.50	-	-	-	17.50
		SD	3.54	-	-	-	3.54
		Median	17.50	-	-	-	17.50
		Minimum	15.00	-	-	-	15.00
		Maximum	20.00	-	-	-	20.00
		Missing	0	0	0	0	0
AI PERIPHERAL NEUROPATHIES AND PLEXOPATHIES	Time between diagnosis date and symptom date	N	0	1	0	0	1
		Mean	-	148.00	-	-	148.00
		SD	-	0.00	-	-	0.00
		Median	-	148.00	-	-	148.00
		Minimum	-	148.00	-	-	148.00
		Maximum	-	148.00	-	-	148.00
		Missing	0	0	0	0	0
AI THYROIDITIS	Time between diagnosis date and symptom date	N	108	31	7	3	149
		Mean	281.13	298.06	288.29	99.67	281.34
		SD	395.57	446.97	247.30	59.72	396.08
		Median	130.00	106.00	195.00	122.00	126.00
		Minimum	0.00	0.00	77.00	32.00	0.00
		Maximum	2178.00	1826.00	773.00	145.00	2178.00
		Missing	0	0	0	0	0
ANKYLOSING SPONDYLITIS	Time between diagnosis date and symptom date	N	1	0	0	2	3
		Mean	2116.00	-	-	163.50	814.33
		SD	0.00	-	-	99.70	1129.48
		Median	2116.00	-	-	163.50	234.00
		Minimum	2116.00	-	-	93.00	93.00
		Maximum	2116.00	-	-	234.00	2116.00
		Missing	0	0	0	0	0
AUTOIMMUNE UVEITIS	Time between diagnosis date and symptom date	N	12	5	3	1	21
		Mean	212.00	15.20	222.33	6.00	156.81
		SD	332.11	21.12	374.72	0.00	288.82

			EXP N = 220	NNEXP N = 76	MALE N = 51	HIST N = 38	Total N = 385
NOAD	**Characteristics**	**Parameters**	**Value**	**Value**	**Value**	**Value**	**Value**
		Median	9.00	3.00	10.00	6.00	8.00
		Minimum	0.00	0.00	2.00	6.00	0.00
		Maximum	899.00	49.00	655.00	6.00	899.00
		Missing	0	0	0	0	0
AUTOIMMUNE HEPATITIS	Time between diagnosis date and symptom date	N	3	0	0	0	3
		Mean	145.33	-	-	-	145.33
		SD	112.51	-	-	-	112.51
		Median	107.00	-	-	-	107.00
		Minimum	57.00	-	-	-	57.00
		Maximum	272.00	-	-	-	272.00
		Missing	0	0	0	0	0
CROHN DISEASES	Time between diagnosis date and symptom date	N	22	9	15	9	55
		Mean	218.05	286.67	372.00	307.11	285.84
		SD	196.93	307.91	311.52	203.40	253.82
		Median	133.50	153.00	374.00	317.00	160.00
		Minimum	5.00	19.00	50.00	21.00	5.00
		Maximum	624.00	853.00	1126.00	569.00	1126.00
		Missing	0	0	0	0	0
GUILLAIN-BARRÉ SYNDROME	Time between diagnosis date and symptom date	N	0	0	1	1	2
		Mean	-	-	2.00	0.00	1.00
		SD	-	-	0.00	0.00	1.41
		Median	-	-	2.00	0.00	1.00
		Minimum	-	-	2.00	0.00	0.00
		Maximum	-	-	2.00	0.00	2.00
		Missing	0	0	0	0	0
IDIOPATHIC THROMBOCYTOPENIC PURPURA (ITP)	Time between diagnosis date and symptom date	N	2	1	0	2	5
		Mean	17.00	36.00	-	8.00	17.20
		SD	15.56	0.00	-	7.07	14.27
		Median	17.00	36.00	-	8.00	13.00
		Minimum	6.00	36.00	-	3.00	3.00
		Maximum	28.00	36.00	-	13.00	36.00
		Missing	0	0	0	0	0

			EXP N = 220	NNEXP N = 76	MALE N = 51	HIST N = 38	Total N = 385
NOAD	**Characteristics**	**Parameters**	**Value**	**Value**	**Value**	**Value**	**Value**
INFLAMMATORY BOWEL	Time between diagnosis date and symptom date	N	6	1	0	3	10
		Mean	861.33	152.00	-	79.00	555.70
		SD	1102.80	0.00	-	18.03	912.06
		Median	441.50	152.00	-	84.00	152.50
		Minimum	104.00	152.00	-	59.00	59.00
		Maximum	3010.00	152.00	-	94.00	3010.00
		Missing	0	0	0	0	0
JUVENILE RHEUMATOID ARTHRITIS (JRA)	Time between diagnosis date and symptom date	N	5	3	1	4	13
		Mean	600.60	268.00	560.00	249.50	412.69
		SD	882.61	210.86	0.00	145.73	550.47
		Median	307.00	320.00	560.00	243.50	307.00
		Minimum	85.00	36.00	560.00	81.00	36.00
		Maximum	2168.00	448.00	560.00	430.00	2168.00
		Missing	0	0	0	0	0
MULTIPLE SCLEROSIS	Time between diagnosis date and symptom date	N	2	1	0	0	3
		Mean	470.50	228.00	-	-	389.67
		SD	432.04	0.00	-	-	336.05
		Median	470.50	228.00	-	-	228.00
		Minimum	165.00	228.00	-	-	165.00
		Maximum	776.00	228.00	-	-	776.00
		Missing	0	0	0	0	0
OPTIC NEURITIS	Time between diagnosis date and symptom date	N	3	1	1	0	5
		Mean	9.67	31.00	442.00	-	100.40
		SD	8.33	0.00	0.00	-	191.27
		Median	7.00	31.00	442.00	-	19.00
		Minimum	3.00	31.00	442.00	-	3.00
		Maximum	19.00	31.00	442.00	-	442.00
		Missing	0	0	0	0	0
OTHER AUTOIMMUNE DISEASES	Time between diagnosis date and symptom date	N	2	3	0	0	5
		Mean	1365.50	327.00	-	-	742.40
		SD	1826.46	16.46	-	-	1075.95
		Median	1365.50	336.00	-	-	336.00
		Minimum	74.00	308.00	-	-	74.00

			EXP N = 220	NNEXP N = 76	MALE N = 51	HIST N = 38	Total N = 385
NOAD	**Characteristics**	**Parameters**	**Value**	**Value**	**Value**	**Value**	**Value**
		Maximum	2657.00	337.00	-	-	2657.00
		Missing	0	0	0	0	0
PSORIATIC ARTHRITIS	Time between diagnosis date and symptom date	N	3	1	0	0	4
		Mean	388.67	281.00	-	-	361.75
		SD	316.50	0.00	-	-	263.97
		Median	285.00	281.00	-	-	283.00
		Minimum	137.00	281.00	-	-	137.00
		Maximum	744.00	281.00	-	-	744.00
		Missing	0	0	0	0	0
RHEUMATOID ARTHRITIS (RA)	Time between diagnosis date and symptom date	N	7	0	1	0	8
		Mean	464.71	-	1092.00	-	543.13
		SD	509.85	-	0.00	-	521.54
		Median	193.00	-	1092.00	-	367.00
		Minimum	126.00	-	1092.00	-	126.00
		Maximum	1540.00	-	1092.00	-	1540.00
		Missing	0	0	0	0	0
SYSTEMIC LUPUS ERYTHEMATOUS	Time between diagnosis date and symptom date	N	1	1	0	0	2
		Mean	86.00	193.00	-	-	139.50
		SD	0.00	0.00	-	-	75.66
		Median	86.00	193.00	-	-	139.50
		Minimum	86.00	193.00	-	-	86.00
		Maximum	86.00	193.00	-	-	193.00
		Missing	0	0	0	0	0
TRANSVERSE MYELITIS	Time between diagnosis date and symptom date	N	1	0	0	0	1
		Mean	1.00	-	-	-	1.00
		SD	0.00	-	-	-	0.00
		Median	1.00	-	-	-	1.00
		Minimum	1.00	-	-	-	1.00
		Maximum	1.00	-	-	-	1.00
		Missing	0	0	0	0	0
TYPE 1 DIABETES MELLITUS	Time between diagnosis date and symptom date	N	24	17	20	9	70
		Mean	58.46	34.35	26.95	44.22	41.77
		SD	128.64	51.13	39.89	90.42	87.65

			EXP N = 220	NNEXP N = 76	MALE N = 51	HIST N = 38	Total N = 385
NOAD	**Characteristics**	**Parameters**	**Value**	**Value**	**Value**	**Value**	**Value**
		Median	14.00	15.00	14.00	14.00	14.00
		Minimum	0.00	0.00	0.00	0.00	0.00
		Maximum	539.00	217.00	151.00	280.00	539.00
		Missing	0	0	0	0	0
ULCERATIVE COLITIS	Time between diagnosis date and symptom date	N	16	1	2	4	23
		Mean	149.69	36.00	24.00	153.75	134.52
		SD	123.53	0.00	19.80	155.70	124.55
		Median	137.00	36.00	24.00	89.00	76.00
		Minimum	11.00	36.00	10.00	52.00	10.00
		Maximum	472.00	36.00	38.00	385.00	472.00
		Missing	0	0	0	0	0

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = Number of AD cases
Value = value of the considered parameter
SD = Standard deviation
In the non-exposed female cohort one subject has simultaneously a date of symptom for diabetes and thyroiditis diseases

Table 26 Number of subjects included in sensitivity analysis - Imputed dates of symptom (Total cohort)

		EXP N = 95		NNEXP N = 49		MALE N = 31		HIST N = 21		Total N = 196	
Characteristics	**Categories**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Number of subjects with a 1st symptom date within 1 year of FU	Included	95	100	49	100	31	100	21	100	196	100

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n = number of subjects in a given category
% = n / Number of subjects with available results x 100
Included = if date of symptom within 1 year of FU

Table 27 Number of subjects included in the main analysis (Total cohort)

		EXP N = 55		NNEXP N = 48		MALE N = 31		HIST N = 21		Total N = 155	
Characteristics	**Categories**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Subjects included in main analysis: known date of symptom and within 1 year of FU	Included	55	100	48	100	31	100	21	100	155	100
Confirmation of the autoimmune disease	Confirmed	38	69.1	28	58.3	27	87.1	16	76.2	109	70.3
	Non-Confirmed	17	30.9	20	41.7	4	12.9	5	23.8	46	29.7
Co-Primary endpoints	Neuroinflammatory/Ophthalmic diseases	4	7.3	7	14.6	3	9.7	2	9.5	16	10.3
	Other autoimmune diseases	51	92.7	41	85.4	28	90.3	19	90.5	139	89.7

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n/% = number / percentage of subjects in a given category
Included = if date of symptom within 1 year of FU

Table 28 Number of subjects included in sensitivity analysis - Onset = date of diagnosis (Total cohort)

		EXP N = 93		NNEXP N = 95		MALE N = 65		HIST N = 51		Total N = 304	
Characteristics	**Categories**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Number of subjects included in the sensitivity analysis - Date of diagnosis within 1 year of FU	Included	93	100	95	100	65	100	51	100	304	100
Confirmation of the autoimmune disease	Confirmed	59	63.4	53	55.8	47	72.3	34	66.7	193	63.5
	Non-Confirmed	34	36.6	42	44.2	18	27.7	17	33.3	111	36.5
Co-Primary endpoints	Neuroinflammatory/Ophthalmic diseases	6	6.5	10	10.5	9	13.8	3	5.9	28	9.2
	Other autoimmune diseases	87	93.5	85	89.5	56	86.2	48	94.1	276	90.8

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n/% = number / percentage of subjects in a given category
Included = if date of symptom within 1 year of FU

Table 29 Number of subjects included in sensitivity analysis - Imputed dates of symptom (Total cohort)

		EXP N = 107		NNEXP N = 62		MALE N = 45		HIST N = 33		Total N = 247	
Characteristics	**Categories**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Number of subjects with a 1st symptom date within 1 year of FU	Included	107	100	62	100	45	100	33	100	247	100

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n/% = number / percentage of subjects in a given category
Included = if date of symptom within 1 year of FU

Table 30 Number of subjects included in sensitivity analysis - Imputed dates of symptom (Total cohort)

		EXP N = 65		NNEXP N = 61		MALE N = 45		HIST N = 33		Total N = 204	
Characteristics	**Categories**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Number of subjects included in the sensitivity analysis after imputation of symptom date	Included	65	100	61	100	45	100	33	100	204	100
Confirmation of the autoimmune disease	Confirmed	42	64.6	34	55.7	35	77.8	20	60.6	131	64.2
	Non-Confirmed	23	35.4	27	44.3	10	22.2	13	39.4	73	35.8
Co-Primary endpoints	Neuroinflammatory/Ophthalmic diseases	5	7.7	9	14.8	7	15.6	4	12.1	25	12.3
	Other autoimmune diseases	60	92.3	52	85.2	38	84.4	29	87.9	179	87.7

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n/% = number / percentage of subjects in a given category
Included = if date of symptom within 1 year of FU

Table 31 Number of subjects included in the SCCS (Total cohort)

		EXP N = 250		Total N = 250	
Characteristics	**Categories**	**n**	**%**	**n**	**%**
Number of subjects included in the SCCS	Included	250	100	250	100

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n/% = number / percentage of subjects in a given category
SCCS = Self Control Case Series
Included = if date of symptom within 1 year of FU

Table 32 Summary of demographic characteristics by exposed/non-exposed status - Overall population - All cases (Total cohort)

		EXP N = 64964		NNEXP N = 64973		MALE N = 64974		HIST N = 64965		Total N = 259876		
Characteristics	**Parameters or Categories**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**P-values**
Age at reference date [years]	Mean	15.33	-	15.42	-	15.27	-	16.00	-	15.51	-	<0.0001
	SD	2.09	-	2.10	-	2.09	-	2.01	-	2.10	-	-
	Median	15.35	-	15.69	-	15.31	-	16.35	-	16.00	-	-
	Minimum	9.44	-	9.35	-	9.27	-	9.19	-	9.19	-	-
	Maximum	24.94	-	24.77	-	24.94	-	24.77	-	24.94	-	-
	Missing	0	-	0	-	0	-	0	-	0	-	-
Age group at reference date [years]	9-13Y	20654	31.8	19783	30.4	21252	32.7	13361	20.6	75050	28.9	-
	14-17Y	38082	58.6	38872	59.8	37990	58.5	42871	66.0	157815	60.7	-
	18-21Y	6199	9.5	6291	9.7	5708	8.8	8689	13.4	26887	10.3	-
	22-25Y	29	0.0	27	0.0	24	0.0	44	0.1	124	0.0	-
Region	North East	25719	39.6	22997	35.4	24389	37.5	21646	33.3	94751	36.5	-
	South East Coast	66	0.1	12	0.0	13	0.0	10	0.0	101	0.0	-
	Northern Ireland	16	0.0	8	0.0	2	0.0	7	0.0	33	0.0	-
	Scotland	46	0.1	15	0.0	17	0.0	11	0.0	89	0.0	-
	Wales	40	0.1	15	0.0	10	0.0	5	0.0	70	0.0	-
	North West	8738	13.5	8424	13.0	9072	14.0	8040	12.4	34274	13.2	-
	Yorkshire & The Humber	2361	3.6	3225	5.0	2445	3.8	3561	5.5	11592	4.5	-
	East Midlands	2954	4.5	3132	4.8	2702	4.2	3270	5.0	12058	4.6	-
	West Midlands	5442	8.4	5424	8.3	5721	8.8	5454	8.4	22041	8.5	-
	East of England	3158	4.9	6078	9.4	4723	7.3	6330	9.7	20289	7.8	-
	South West	5064	7.8	3846	5.9	4114	6.3	4410	6.8	17434	6.7	-
	South Central	8402	12.9	5793	8.9	6247	9.6	6338	9.8	26780	10.3	-
	London	2958	4.6	6004	9.2	5519	8.5	5883	9.1	20364	7.8	-
Region [in category]	North England	36818	56.7	34646	53.3	35906	55.3	33247	51.2	140617	54.1	-
	Midlands	8396	12.9	8556	13.2	8423	13.0	8724	13.4	34099	13.1	-
	South England	19648	30.2	21733	33.4	20616	31.7	22971	35.4	84968	32.7	-
	Ireland Scotland Wales	102	0.2	38	0.1	29	0.0	23	0.0	192	0.1	-

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n/% = number / percentage of subjects in a given category
Value = value of the considered parameter
SD = Standard deviation

Table 33 Data availability by exposed/non-exposed status - Overall population - All cases (Total cohort)

		EXP N = 64964		NNEXP N = 64973		MALE N = 64974		HIST N = 64965		Total N = 259876	
Characteristics	**Parameters or Categories**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**
Number of years in CPRD GOLD at reference date	Mean	9.40	-	7.64	-	9.05	-	7.77	-	8.46	-
	SD	4.25	-	4.26	-	4.30	-	4.40	-	4.38	-
	Median	9.54	-	6.93	-	9.14	-	6.96	-	8.07	-
	Minimum	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-
	Maximum	20.85	-	19.02	-	21.08	-	18.96	-	21.08	-
	Missing	0	-	0	-	0	-	0	-	0	-
Number of years in CPRD GOLD at reference date [in cat]	[0-3[years	5646	8.7	9497	14.6	7062	10.9	9486	14.6	31691	12.2
	[3-6[years	9638	14.8	16923	26.0	10054	15.5	16510	25.4	53125	20.4
	[6-10[years	20456	31.5	20927	32.2	20581	31.7	20924	32.2	82888	31.9
	[10 years	29224	45.0	17626	27.1	27277	42.0	18045	27.8	92172	35.5
HES linkage	Yes	38656	59.5	36148	55.6	37832	58.2	37616	57.9	150252	57.8
	No	26308	40.5	28825	44.4	27142	41.8	27349	42.1	109624	42.2

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n/% = number / percentage of subjects in a given category
Value = value of the considered parameter
SD = Standard deviation

Table 34 Healthcare resources utilization by exposed/non-exposed status - Overall population - All cases (Total cohort)

		EXP N = 64964		NNEXP N = 64973		MALE N = 64974		HIST N = 64965		Total N = 259876	
Characteristics	**Parameters or Categories**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**
Number of GP consultations the year previous reference date	Mean	8.79	-	6.95	-	6.03	-	5.29	-	6.77	-
	SD	10.21	-	9.07	-	8.41	-	7.24	-	8.90	-
	Median	6.00	-	4.00	-	3.00	-	3.00	-	4.00	-
	Minimum	0.00	-	0.00	-	0.00	-	0.00	-	0.00	-
	Maximum	243.00	-	157.00	-	254.00	-	132.00	-	254.00	-
	Missing	0	-	0	-	0	-	0	-	0	-
Number of GP consultations the year previous reference date [in cat]	0 to 1 consultation	12203	18.8	17940	27.6	21057	32.4	22445	34.5	73645	28.3
	2 to 4 consultations	15746	24.2	17056	26.3	17448	26.9	18262	28.1	68512	26.4
	5 to 9 consultations	16113	24.8	14454	22.2	13362	20.6	13186	20.3	57115	22.0
	Equal or more than 10 consultations	20902	32.2	15523	23.9	13107	20.2	11072	17.0	60604	23.3

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n/% = number / percentage of subjects in a given category
Value = value of the considered parameter
SD = Standard deviation

Table 35 Exposure to other vaccines by exposed/non-exposed status - Overall population - All cases (Total cohort)

		EXP N = 64964		NNEXP N = 64973		MALE N = 64974		HIST N = 64965		Total N = 259876	
Characteristics	**Categories**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Any vaccines in the year previous the reference date	Yes	11529	17.7	11008	16.9	9270	14.3	10394	16.0	42201	16.2
	No	53435	82.3	53965	83.1	55704	85.7	54571	84.0	217675	83.8
Any vaccines in the follow-up period	Yes	11596	17.8	7765	12.0	8000	12.3	6253	9.6	33614	12.9
	No	53368	82.2	57208	88.0	56974	87.7	58712	90.4	226262	87.1
Novel adjuvanted vaccines in the year previous the reference date	Yes	311	0.5	0	0.0	325	0.5	0	0.0	636	0.2
	No	64653	99.5	64973	100	64649	99.5	64965	100	259240	99.8
Novel adjuvanted vaccines in the follow-up period	Yes	1679	2.6	0	0.0	1559	2.4	0	0.0	3238	1.2
	No	63285	97.4	64973	100	63415	97.6	64965	100	256638	98.8
Live-attenuated vaccines in the year previous the reference date	Yes	1138	1.8	2986	4.6	861	1.3	2942	4.5	7927	3.1
	No	63826	98.2	61987	95.4	64113	98.7	62023	95.5	251949	96.9
Live-attenuated vaccines in the follow-up period	Yes	1033	1.6	943	1.5	489	0.8	828	1.3	3293	1.3
	No	63931	98.4	64030	98.5	64485	99.2	64137	98.7	256583	98.7
Other vaccines in the year previous the reference date	Yes	10627	16.4	8580	13.2	8507	13.1	7967	12.3	35681	13.7
	No	54337	83.6	56393	86.8	56467	86.9	56998	87.7	224195	86.3
Other vaccines in the follow-up period	Yes	10231	15.7	7062	10.9	7068	10.9	5578	8.6	29939	11.5
	No	54733	84.3	57911	89.1	57906	89.1	59387	91.4	229937	88.5

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n/% = number / percentage of subjects in a given category
P-value: Fisher exact test
Follow-up is 12 months for all the cohorts

Table 36 Exposure to other vaccines in the risk and control follow-up period for Exposed Female Cohort - Overall population - All cases (Total cohort)

		EXP N = 64964	
Characteristics	**Categories**	**n**	**%**
Any vaccines in the risk period [0-12 months]	Yes	11611	17.9
	No	53353	82.1
Any vaccines in the control period [18-30 months]	Yes	11739	18.1
	No	53225	81.9
Novel adjuvanted vaccines in the risk period [0-12 months]	Yes	1682	2.6
	No	63282	97.4
Novel adjuvanted vaccines in the control period [18-30 months]	Yes	56	0.1
	No	64908	99.9
Live-attenuated vaccines in the risk period [0-12 months]	Yes	1038	1.6
	No	63926	98.4
Live-attenuated vaccines in the control period [18-30 months]	Yes	343	0.5
	No	64621	99.5
Other vaccines in the risk period [0-12 months]	Yes	10244	15.8
	No	54720	84.2
Other vaccines in the control period [18-30 months]	Yes	11515	17.7
	No	53449	82.3

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n/% = number / percentage of subjects in a given category
P-value: Fisher exact test

Table 37 Exposure to Cervarix vaccine - Overall population - All cases (Total cohort)

		EXP N = 64964		NNEXP N = 64973		MALE N = 64974		HIST N = 64965		Total N = 259876	
Characteristics	**Parameters or Categories**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**
Subject received a Cervarix dose	Yes	64964	100	2	0.0	3	0.0	0	0.0	64969	25.0
	No	0	0.0	64971	100	64971	100	64965	100	194907	75.0
Number of dose of Cervarix	0 dose	0	0.0	64971	100	64971	100	64965	100	194907	75.0
	1 dose	4781	7.4	2	0.0	0	0.0	0	0.0	4783	1.8
	2 doses	9316	14.3	0	0.0	0	0.0	0	0.0	9316	3.6
	3 doses	50757	78.1	0	0.0	3	0.0	0	0.0	50760	19.5
	4 doses	110	0.2	0	0.0	0	0.0	0	0.0	110	0.0
Cervarix dose and reference date	Cervarix before the reference date	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	Cervarix after or at reference date	64964	100	2	100	3	100	0	0.0	64969	100
	NA	0	0.0	64971	-	64971	-	64965	-	194907	-
Time in days between reference date and last Cervarix dose	Mean	175.28	-	264.25	-	210.67	-	-	-	175.28	-
	SD	96.02	-	88.39	-	23.16	-	-	-	96.02	-
	Median	183.00	-	264.25	-	217.00	-	-	-	183.00	-
	Minimum	0.00	-	201.75	-	185.00	-	-	-	0.00	-
	Maximum	1493.00	-	326.75	-	230.00	-	-	-	1493.00	-
	NA	0	-	64971	-	64971	-	64965	-	194907	-
Time in days between reference date and last Cervarix dose [in category]	within 30 days	6584	10.1	0	0.0	0	0.0	0	0.0	6584	10.1
	between 31 to 60 days	3265	5.0	0	0.0	0	0.0	0	0.0	3265	5.0
	between 61 to 180 days	15381	23.7	0	0.0	0	0.0	0	0.0	15381	23.7
	more than 180 days	39734	61.2	2	100	3	100	0	0.0	39739	61.2
	NA	0	-	64971	-	64971	-	64965	-	194907	-
Year of 1st Cervarix dose	2006	0	0.0	1	50.0	0	0.0	0	0.0	1	0.0
	2007	0	0.0	1	50.0	0	0.0	0	0.0	1	0.0
	2008	14400	22.2	0	0.0	1	33.3	0	0.0	14401	22.2
	2009	44287	68.2	0	0.0	2	66.7	0	0.0	44289	68.2
	2010	6277	9.7	0	0.0	0	0.0	0	0.0	6277	9.7
	2011	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	NA	0	-	64971	-	64971	-	64965	-	194907	-

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort

MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n = number of subjects in a given category
Value = value of the considered parameter
% = n / Number of subjects with available results x 100
SD = Standard deviation

Table 38 Drugs prescription by exposed/non-exposed status - Overall population - All cases (Total cohort)

		EXP N = 64964		NNEXP N = 64973		MALE N = 64974		HIST N = 64965		Total N = 259876	
Characteristics	**Categories**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Prescription of autoimmune disease drugs	Yes	193	87.7	70	93.3	48	94.1	33	86.8	344	89.6
	No	27	12.3	5	6.7	3	5.9	5	13.2	40	10.4
	NA	64744	-	64898	-	64923	-	64927	-	259492	-
Chronic use of autoimmune disease drugs	Yes	176	91.2	63	90.0	43	89.6	31	93.9	313	91.0
	No	17	8.8	7	10.0	5	10.4	2	6.1	31	9.0
	NA	64771	-	64903	-	64926	-	64932	-	259532	-

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n/% = number / percentage of subjects in a given category

Table 39 P-Values comparing exposed female and unexposed female cohorts - Overall population - All cases (Total cohort)

Variable	P value
Age at reference date [years] [in cat]	<.0001
Age at reference date [years]	<.0001
Region	<.0001
Region [in cat]	<.0001
Number of years in CPRD GOLD at reference date	<.0001
Number of years in CPRD GOLD at reference date [in cat]	<.0001
HES linkage	<.0001
Number of GP consultations the year previous reference date	<.0001
Number of GP consultations the year previous reference date [in cat]	<.0001
Any vaccines in the year previous the reference date	0.0001
Any vaccines in the follow-up period	<.0001
Novel adjuvanted vaccines in the year previous the reference date	<.0001
Novel adjuvanted vaccines in the follow-up period	<.0001
Live attenuated vaccines in the year previous the reference date	<.0001
Live attenuated vaccines in the follow-up period	0.0410
Other vaccines in the year previous the reference date	<.0001
Other vaccines in the follow-up period	<.0001
Use of autoimmune disease drugs	0.1776
Chronic use of autoimmune disease drugs	0.7668

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
n/%=number/percentage of subjects in a given category
Chi-square and T-test statistics were computed respectively for categorical and continuous variables

Table 40 P-Values comparing unexposed concurrent male and historical male cohorts - Overall population - All cases (Total cohort)

Variable	P value
Age at reference date [years] [in cat]	<.0001
Age at reference date [years]	<.0001
Region	<.0001
Region [in cat]	<.0001
Number of years in CPRD GOLD at reference date	<.0001
Number of years in CPRD GOLD at reference date [in cat]	<.0001
HES linkage	0.2360
Number of GP consultations the year previous reference date	<.0001
Number of GP consultations the year previous reference date [in cat]	<.0001
Any vaccines in the year previous the reference date	<.0001
Any vaccines in the follow-up period	<.0001
Novel adjuvanted vaccines in the year previous the reference date	<.0001
Novel adjuvanted vaccines in the follow-up period	<.0001
Live attenuated vaccines in the year previous the reference date	<.0001
Live attenuated vaccines in the follow-up period	<.0001
Other vaccines in the year previous the reference date	<.0001
Other vaccines in the follow-up period	<.0001
Use of autoimmune disease drugs	0.2352
Chronic use of autoimmune disease drugs	0.4930

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
n/%=number/percentage of subjects in a given category
Chi-square and T-test statistics were computed respectively for categorical and continuous variables

Table 41 Summary of demographic characteristics by exposed/non-exposed status - Main Analysis - Confirmed cases (Total cohort)

		EXP N = 38		NNEXP N = 28		MALE N = 27		HIST N = 16		Total N = 109		
Characteristics	Parameters or Categories	Value or n	%	Value or n	%	Value or n	%	Value or n	%	Value or n	%	P-values
Age at reference date [years]	Mean	15.92	-	15.37	-	14.75	-	15.70	-	15.46	-	0.3016
	SD	1.96	-	2.48	-	2.41	-	2.15	-	2.26	-	-
	Median	15.95	-	16.33	-	13.86	-	16.43	-	15.72	-	-
	Minimum	12.31	-	12.25	-	12.14	-	12.03	-	12.03	-	-
	Maximum	20.03	-	18.81	-	18.75	-	18.45	-	20.03	-	-
	Missing	0	-	0	-	0	-	0	-	0	-	-
Age group at reference date [years]	9-13Y	6	15.8	11	39.3	15	55.6	3	18.8	35	32.1	-
	14-17Y	27	71.1	13	46.4	9	33.3	10	62.5	59	54.1	-
	18-21Y	5	13.2	4	14.3	3	11.1	3	18.8	15	13.8	-
	22-25Y	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	-
Region	South East Coast	4	10.5	2	7.1	0	0.0	0	0.0	6	5.5	-
	Northern Ireland	1	2.6	5	17.9	0	0.0	1	6.3	7	6.4	-
	Scotland	5	13.2	2	7.1	5	18.5	1	6.3	13	11.9	-
	Wales	3	7.9	1	3.6	3	11.1	0	0.0	7	6.4	-
	North West	3	7.9	4	14.3	7	25.9	1	6.3	15	13.8	-
	Yorkshire & The Humber	1	2.6	1	3.6	3	11.1	1	6.3	6	5.5	-
	East Midlands	4	10.5	1	3.6	2	7.4	2	12.5	9	8.3	-
	West Midlands	4	10.5	0	0.0	1	3.7	3	18.8	8	7.3	-
	East of England	2	5.3	4	14.3	2	7.4	5	31.3	13	11.9	-
	South West	3	7.9	4	14.3	2	7.4	1	6.3	10	9.2	-
	South Central	7	18.4	2	7.1	2	7.4	0	0.0	11	10.1	-
	London	1	2.6	2	7.1	0	0.0	1	6.3	4	3.7	-
Region [in category]	North England	4	10.5	5	17.9	10	37.0	2	12.5	21	19.3	-
	Midlands	8	21.1	1	3.6	3	11.1	5	31.3	17	15.6	-
	South England	17	44.7	14	50.0	6	22.2	7	43.8	44	40.4	-
	Ireland Scotland Wales	9	23.7	8	28.6	8	29.6	2	12.5	27	24.8	-

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n/% = number / percentage of subjects in a given category
Value = value of the considered parameter
SD = Standard deviation

Table 42 Data availability by exposed/non-exposed status - Main Analysis - Confirmed cases (Total cohort)

		EXP N = 38		NNEXP N = 28		MALE N = 27		HIST N = 16		Total N = 109	
Characteristics	**Parameters or Categories**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**
Number of years in CPRD GOLD at reference date	Mean	10.12	-	7.84	-	9.52	-	8.60	-	9.16	-
	SD	4.62	-	5.02	-	3.74	-	4.34	-	4.52	-
	Median	10.44	-	6.09	-	9.93	-	7.86	-	8.53	-
	Minimum	2.25	-	1.08	-	3.22	-	2.08	-	1.08	-
	Maximum	20.27	-	16.75	-	18.26	-	17.02	-	20.27	-
	Missing	0	-	0	-	0	-	0	-	0	-
Number of years in CPRD GOLD at reference date [in cat]	[0-3[years	2	5.3	4	14.3	0	0.0	1	6.3	7	6.4
	[3-6[years	8	21.1	10	35.7	5	18.5	4	25.0	27	24.8
	[6-10[years	8	21.1	6	21.4	11	40.7	5	31.3	30	27.5
	[10 years	20	52.6	8	28.6	11	40.7	6	37.5	45	41.3
HES linkage	Yes	25	65.8	14	50.0	14	51.9	10	62.5	63	57.8
	No	13	34.2	14	50.0	13	48.1	6	37.5	46	42.2

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n/% = number / percentage of subjects in a given category
Value = value of the considered parameter
SD = Standard deviation

Table 43 Healthcare resources utilization by exposed/non-exposed status - Main Analysis - Confirmed cases (Total cohort)

		EXP N = 38		NNEXP N = 28		MALE N = 27		HIST N = 16		Total N = 109	
Characteristics	**Parameters or Categories**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**
Number of GP consultations the year previous reference date	Mean	10.53	-	7.50	-	6.33	-	5.75	-	8.01	-
	SD	10.62	-	6.69	-	6.96	-	4.73	-	8.26	-
	Median	6.50	-	5.50	-	4.00	-	4.00	-	5.00	-
	Minimum	0.00	-	1.00	-	0.00	-	0.00	-	0.00	-
	Maximum	40.00	-	25.00	-	24.00	-	15.00	-	40.00	-
	Missing	0	-	0	-	0	-	0	-	0	-
Number of GP consultations the year previous reference date [in cat]	0 to 1 consultation	5	13.2	3	10.7	5	18.5	2	12.5	15	13.8
	2 to 4 consultations	10	26.3	9	32.1	11	40.7	7	43.8	37	33.9
	5 to 9 consultations	8	21.1	8	28.6	6	22.2	3	18.8	25	22.9
	Equal or more than 10 consultations	15	39.5	8	28.6	5	18.5	4	25.0	32	29.4

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n/% = number / percentage of subjects in a given category
Value = value of the considered parameter
SD = Standard deviation

Table 44 Exposure to other vaccines by exposed/non-exposed status - Main Analysis - Confirmed cases (Total cohort)

		EXP N = 38		NNEXP N = 28		MALE N = 27		HIST N = 16		Total N = 109	
Characteristics	**Categories**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Any vaccines in the year previous the reference date	Yes	10	26.3	3	10.7	0	0.0	5	31.3	18	16.5
	No	28	73.7	25	89.3	27	100	11	68.8	91	83.5
Any vaccines in the follow-up period	Yes	4	10.5	0	0.0	0	0.0	0	0.0	4	3.7
	No	34	89.5	28	100	27	100	16	100	105	96.3
Novel adjuvanted vaccines in the year previous the reference date	Yes	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	No	38	100	28	100	27	100	16	100	109	100
Novel adjuvanted vaccines in the follow-up period	Yes	1	2.6	0	0.0	0	0.0	0	0.0	1	0.9
	No	37	97.4	28	100	27	100	16	100	108	99.1
Live-attenuated vaccines in the year previous the reference date	Yes	2	5.3	1	3.6	0	0.0	2	12.5	5	4.6
	No	36	94.7	27	96.4	27	100	14	87.5	104	95.4
Live-attenuated vaccines in the follow-up period	Yes	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	No	38	100	28	100	27	100	16	100	109	100
Other vaccines in the year previous the reference date	Yes	8	21.1	2	7.1	0	0.0	5	31.3	15	13.8
	No	30	78.9	26	92.9	27	100	11	68.8	94	86.2
Other vaccines in the follow-up period	Yes	3	7.9	0	0.0	0	0.0	0	0.0	3	2.8
	No	35	92.1	28	100	27	100	16	100	106	97.2

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n/% = number / percentage of subjects in a given category
Follow-up is 12 months for all the cohorts

Table 45 Exposure to other vaccines in the risk and control follow-up period for Exposed Female Cohort - Main Analysis - Confirmed cases (Total cohort)

		EXP N = 38	
Characteristics	**Categories**	**n**	**%**
Any vaccines in the risk period [0-12 months]	Yes	14	36.8
	No	24	63.2
Any vaccines in the control period [18-30 months]	Yes	13	34.2
	No	25	65.8
Novel adjuvanted vaccines in the risk period [0-12 months]	Yes	3	7.9
	No	35	92.1
Novel adjuvanted vaccines in the control period [18-30 months]	Yes	0	0.0
	No	38	100
Live-attenuated vaccines in the risk period [0-12 months]	Yes	3	7.9
	No	35	92.1
Live-attenuated vaccines in the control period [18-30 months]	Yes	1	2.6
	No	37	97.4
Other vaccines in the risk period [0-12 months]	Yes	13	34.2
	No	25	65.8
Other vaccines in the control period [18-30 months]	Yes	12	31.6
	No	26	68.4

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n/% = number / percentage of subjects in a given category

Table 46 Exposure to Cervarix vaccine - Main Analysis - Confirmed cases (Total cohort)

		EXP N = 38		NNEXP N = 28		MALE N = 27		HIST N = 16		Total N = 109	
Characteristics	**Parameters or Categories**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**
Subject received a Cervarix dose	Yes	38	100	0	0.0	0	0.0	0	0.0	38	34.9
	No	0	0.0	28	100	27	100	16	100	71	65.1
Number of dose of Cervarix	0 dose	0	0.0	28	100	27	100	16	100	71	65.1
	1 dose	4	10.5	0	0.0	0	0.0	0	0.0	4	3.7
	2 doses	7	18.4	0	0.0	0	0.0	0	0.0	7	6.4
	3 doses	27	71.1	0	0.0	0	0.0	0	0.0	27	24.8
	4 doses	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Cervarix dose and reference date	Cervarix before the reference date	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	Cervarix after or at reference date	38	100	0	0.0	0	0.0	0	0.0	38	100
	NA	0	0.0	28	-	27	-	16	-	71	-
Time in days between reference date and last Cervarix dose	Mean	196.32	-	-	-	-	-	-	-	196.32	-
	SD	122.30	-	-	-	-	-	-	-	122.30	-
	Median	195.50	-	-	-	-	-	-	-	195.50	-
	Minimum	0.00	-	-	-	-	-	-	-	0.00	-
	Maximum	576.00	-	-	-	-	-	-	-	576.00	-
	NA	0	-	28	-	27	-	16	-	71	-
Time in days between reference date and last Cervarix dose [in category]	within 30 days	5	13.2	0	0.0	0	0.0	0	0.0	5	13.2
	between 31 to 60 days	2	5.3	0	0.0	0	0.0	0	0.0	2	5.3
	between 61 to 180 days	3	7.9	0	0.0	0	0.0	0	0.0	3	7.9
	more than 180 days	28	73.7	0	0.0	0	0.0	0	0.0	28	73.7
	NA	0	-	28	-	27	-	16	-	71	-
Year of 1st Cervarix dose	2006	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	2007	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	2008	9	23.7	0	0.0	0	0.0	0	0.0	9	23.7
	2009	22	57.9	0	0.0	0	0.0	0	0.0	22	57.9
	2010	7	18.4	0	0.0	0	0.0	0	0.0	7	18.4
	2011	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	NA	0	-	28	-	27	-	16	-	71	-

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort

MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n = number of subjects in a given category
Value = value of the considered parameter
% = n / Number of subjects with available results x 100
SD = Standard deviation

Table 47 Drugs prescription by exposed/non-exposed status - Main Analysis - Confirmed cases (Total cohort)

		EXP N = 38		NNEXP N = 28		MALE N = 27		HIST N = 16		Total N = 109	
Characteristics	**Categories**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Prescription of autoimmune disease drugs	Yes	38	100	27	96.4	26	96.3	14	87.5	105	96.3
	No	0	0.0	1	3.6	1	3.7	2	12.5	4	3.7
Chronic use of autoimmune disease drugs	Yes	36	94.7	26	96.3	25	96.2	13	92.9	100	95.2
	No	2	5.3	1	3.7	1	3.8	1	7.1	5	4.8
	NA	0	0.0	1	-	1	-	2	-	4	-

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n/% = number / percentage of subjects in a given category

Table 48 P-Values comparing exposed female and unexposed female cohorts - Main Analysis - Confirmed cases (Total cohort)

Variable	P value
Age at reference date [years] [in cat]	0.0787
Age at reference date [years]	0.3170
Region	0.2171
Region [in cat]	0.2129
Number of years in CPRD GOLD at reference date	0.0608
Number of years in CPRD GOLD at reference date [in cat]	0.1781
HES linkage	0.1973
Number of GP consultations the year previous reference date	0.1896
Number of GP consultations the year previous reference date [in cat]	0.7541
Any vaccines in the year previous the reference date	0.1152
Any vaccines in the follow-up period	0.0765
Novel adjuvanted vaccines in the follow-up period	0.3871
Live attenuated vaccines in the year previous the reference date	0.7444
Other vaccines in the year previous the reference date	0.1193
Other vaccines in the follow-up period	0.1281
Use of autoimmune disease drugs	0.2404
Chronic use of autoimmune disease drugs	0.7678

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
n/%=number/percentage of subjects in a given category
Chi-square and T-test statistics were computed respectively for categorical and continuous variables

Table 49 P-Values comparing unexposed concurrent male and historical male cohorts - Main Analysis - Confirmed cases (Total cohort)

Variable	P value
Age at reference date [years] [in cat]	0.0606
Age at reference date [years]	0.1976
Region	0.0991
Region [in cat]	0.0668
Number of years in CPRD GOLD at reference date	0.4676
Number of years in CPRD GOLD at reference date [in cat]	0.5401
HES linkage	0.4967
Number of GP consultations the year previous reference date	0.7682
Number of GP consultations the year previous reference date [in cat]	0.9178
Any vaccines in the year previous the reference date	0.0020
Live attenuated vaccines in the year previous the reference date	0.0599
Other vaccines in the year previous the reference date	0.0020
Use of autoimmune disease drugs	0.2738
Chronic use of autoimmune disease drugs	0.6482

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
n/%=number/percentage of subjects in a given category
Chi-square and T-test statistics were computed respectively for categorical and continuous variables

Table 50 Summary of demographic characteristics by exposed/non-exposed status - Main Analysis - All cases (Total cohort)

		EXP N = 55		NNEXP N = 48		MALE N = 31		HIST N = 21		Total N = 155		
Characteristics	Parameters or Categories	Value or n	%	Value or n	%	Value or n	%	Value or n	%	Value or n	%	P-values
Age at reference date [years]	Mean	15.70	-	15.33	-	14.93	-	16.02	-	15.47	-	0.2973
	SD	2.02	-	2.22	-	2.35	-	2.21	-	2.18	-	-
	Median	15.72	-	15.74	-	15.29	-	16.64	-	15.71	-	-
	Minimum	12.24	-	12.21	-	12.14	-	12.03	-	12.03	-	-
	Maximum	20.03	-	18.81	-	18.75	-	18.68	-	20.03	-	-
	Missing	0	-	0	-	0	-	0	-	0	-	-
Age group at reference date [years]	9-13Y	12	21.8	16	33.3	15	48.4	4	19.0	47	30.3	-
	14-17Y	37	67.3	28	58.3	12	38.7	11	52.4	88	56.8	-
	18-21Y	6	10.9	4	8.3	4	12.9	6	28.6	20	12.9	-
	22-25Y	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	-
Region	South East Coast	5	9.1	3	6.3	2	6.5	2	9.5	12	7.7	-
	Northern Ireland	2	3.6	7	14.6	0	0.0	2	9.5	11	7.1	-
	Scotland	7	12.7	4	8.3	5	16.1	3	14.3	19	12.3	-
	Wales	4	7.3	6	12.5	3	9.7	0	0.0	13	8.4	-
	North West	4	7.3	6	12.5	8	25.8	1	4.8	19	12.3	-
	Yorkshire & The Humber	1	1.8	2	4.2	3	9.7	1	4.8	7	4.5	-
	East Midlands	5	9.1	1	2.1	2	6.5	2	9.5	10	6.5	-
	West Midlands	6	10.9	0	0.0	1	3.2	3	14.3	10	6.5	-
	East of England	2	3.6	5	10.4	2	6.5	5	23.8	14	9.0	-
	South West	8	14.5	6	12.5	2	6.5	1	4.8	17	11.0	-
	South Central	10	18.2	5	10.4	3	9.7	0	0.0	18	11.6	-
	London	1	1.8	3	6.3	0	0.0	1	4.8	5	3.2	-
Region [in category]	North England	5	9.1	8	16.7	11	35.5	2	9.5	26	16.8	-
	Midlands	11	20.0	1	2.1	3	9.7	5	23.8	20	12.9	-
	South England	26	47.3	22	45.8	9	29.0	9	42.9	66	42.6	-
	Ireland Scotland Wales	13	23.6	17	35.4	8	25.8	5	23.8	43	27.7	-

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n/% = number / percentage of subjects in a given category
Value = value of the considered parameter
SD = Standard deviation

Table 51 Data availability by exposed/non-exposed status - Main Analysis - All cases (Total cohort)

		EXP N = 55		NNEXP N = 48		MALE N = 31		HIST N = 21		Total N = 155	
Characteristics	**Parameters or Categories**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**
Number of years in CPRD GOLD at reference date	Mean	9.97	-	7.55	-	10.08	-	8.84	-	9.09	-
	SD	4.42	-	4.83	-	3.92	-	3.98	-	4.50	-
	Median	10.08	-	6.49	-	9.95	-	8.79	-	8.67	-
	Minimum	2.25	-	1.05	-	3.22	-	2.08	-	1.05	-
	Maximum	20.27	-	16.75	-	18.26	-	17.02	-	20.27	-
	Missing	0	-	0	-	0	-	0	-	0	-
Number of years in CPRD GOLD at reference date [in cat]	[0-3[years	2	3.6	9	18.8	0	0.0	1	4.8	12	7.7
	[3-6[years	11	20.0	14	29.2	5	16.1	4	19.0	34	21.9
	[6-10[years	14	25.5	11	22.9	12	38.7	8	38.1	45	29.0
	[10 years	28	50.9	14	29.2	14	45.2	8	38.1	64	41.3
HES linkage	Yes	37	67.3	24	50.0	16	51.6	11	52.4	88	56.8
	No	18	32.7	24	50.0	15	48.4	10	47.6	67	43.2

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n/% = number / percentage of subjects in a given category
Value = value of the considered parameter
SD = Standard deviation

Table 52 Healthcare resources utilization by exposed/non-exposed status - Main Analysis - All cases (Total cohort)

		EXP N = 55		NNEXP N = 48		MALE N = 31		HIST N = 21		Total N = 155	
Characteristics	**Parameters or Categories**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**
Number of GP consultations the year previous reference date	Mean	10.05	-	8.75	-	7.39	-	6.10	-	8.58	-
	SD	10.19	-	8.94	-	8.77	-	6.48	-	9.12	-
	Median	7.00	-	5.50	-	4.00	-	4.00	-	5.00	-
	Minimum	0.00	-	0.00	-	0.00	-	0.00	-	0.00	-
	Maximum	40.00	-	39.00	-	39.00	-	27.00	-	40.00	-
	Missing	0	-	0	-	0	-	0	-	0	-
Number of GP consultations the year previous reference date [in cat]	0 to 1 consultation	8	14.5	5	10.4	5	16.1	4	19.0	22	14.2
	2 to 4 consultations	14	25.5	14	29.2	12	38.7	9	42.9	49	31.6
	5 to 9 consultations	12	21.8	14	29.2	8	25.8	3	14.3	37	23.9
	Equal or more than 10 consultations	21	38.2	15	31.3	6	19.4	5	23.8	47	30.3

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n/% = number / percentage of subjects in a given category
Value = value of the considered parameter
SD = Standard deviation

Table 53 Exposure to other vaccines by exposed/non-exposed status - Main Analysis - All cases (Total cohort)

		EXP N = 55		NNEXP N = 48		MALE N = 31		HIST N = 21		Total N = 155	
Characteristics	**Categories**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Any vaccines in the year previous the reference date	Yes	11	20.0	7	14.6	0	0.0	6	28.6	24	15.5
	No	44	80.0	41	85.4	31	100	15	71.4	131	84.5
Any vaccines in the follow-up period	Yes	5	9.1	1	2.1	0	0.0	0	0.0	6	3.9
	No	50	90.9	47	97.9	31	100	21	100	149	96.1
Novel adjuvanted vaccines in the year previous the reference date	Yes	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	No	55	100	48	100	31	100	21	100	155	100
Novel adjuvanted vaccines in the follow-up period	Yes	1	1.8	0	0.0	0	0.0	0	0.0	1	0.6
	No	54	98.2	48	100	31	100	21	100	154	99.4
Live-attenuated vaccines in the year previous the reference date	Yes	2	3.6	2	4.2	0	0.0	3	14.3	7	4.5
	No	53	96.4	46	95.8	31	100	18	85.7	148	95.5
Live-attenuated vaccines in the follow-up period	Yes	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	No	55	100	48	100	31	100	21	100	155	100
Other vaccines in the year previous the reference date	Yes	9	16.4	5	10.4	0	0.0	6	28.6	20	12.9
	No	46	83.6	43	89.6	31	100	15	71.4	135	87.1
Other vaccines in the follow-up period	Yes	4	7.3	1	2.1	0	0.0	0	0.0	5	3.2
	No	51	92.7	47	97.9	31	100	21	100	150	96.8

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n = number of subjects in a given category
Follow-up is 12 months for all the cohorts

Table 54 Exposure to other vaccines in the risk and control follow-up period for Exposed Female Cohort - Main Analysis - All cases (Total cohort)

		EXP N = 55	
Characteristics	**Categories**	**n**	**%**
Any vaccines in the risk period [0-12 months]	Yes	16	29.1
	No	39	70.9
Any vaccines in the control period [18-30 months]	Yes	16	29.1
	No	39	70.9
Novel adjuvanted vaccines in the risk period [0-12 months]	Yes	3	5.5
	No	52	94.5
Novel adjuvanted vaccines in the control period [18-30 months]	Yes	0	0.0
	No	55	100
Live-attenuated vaccines in the risk period [0-12 months]	Yes	4	7.3
	No	51	92.7
Live-attenuated vaccines in the control period [18-30 months]	Yes	1	1.8
	No	54	98.2
Other vaccines in the risk period [0-12 months]	Yes	14	25.5
	No	41	74.5
Other vaccines in the control period [18-30 months]	Yes	15	27.3
	No	40	72.7

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n/% = number / percentage of subjects in a given category

Table 55 Exposure to Cervarix vaccine - Main Analysis - All cases (Total cohort)

		EXP N = 55		NNEXP N = 48		MALE N = 31		HIST N = 21		Total N = 155	
Characteristics	**Parameters or Categories**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**
Subject received a Cervarix dose	Yes	55	100	0	0.0	0	0.0	0	0.0	55	35.5
	No	0	0.0	48	100	31	100	21	100	100	64.5
Number of dose of Cervarix	0 dose	0	0.0	48	100	31	100	21	100	100	64.5
	1 dose	6	10.9	0	0.0	0	0.0	0	0.0	6	3.9
	2 doses	10	18.2	0	0.0	0	0.0	0	0.0	10	6.5
	3 doses	39	70.9	0	0.0	0	0.0	0	0.0	39	25.2
	4 doses	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Cervarix dose and reference date	Cervarix before the reference date	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	Cervarix after or at reference date	55	100	0	0.0	0	0.0	0	0.0	55	100
	NA	0	0.0	48	-	31	-	21	-	100	-
Time in days between reference date and last Cervarix dose	Mean	182.36	-	-	-	-	-	-	-	182.36	-
	SD	114.37	-	-	-	-	-	-	-	114.37	-
	Median	195.00	-	-	-	-	-	-	-	195.00	-
	Minimum	0.00	-	-	-	-	-	-	-	0.00	-
	Maximum	576.00	-	-	-	-	-	-	-	576.00	-
	NA	0	-	48	-	31	-	21	-	100	-
Time in days between reference date and last Cervarix dose [in category]	within 30 days	9	16.4	0	0.0	0	0.0	0	0.0	9	16.4
	between 31 to 60 days	3	5.5	0	0.0	0	0.0	0	0.0	3	5.5
	between 61 to 180 days	3	5.5	0	0.0	0	0.0	0	0.0	3	5.5
	more than 180 days	40	72.7	0	0.0	0	0.0	0	0.0	40	72.7
	NA	0	-	48	-	31	-	21	-	100	-
Year of 1st Cervarix dose	2006	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	2007	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	2008	11	20.0	0	0.0	0	0.0	0	0.0	11	20.0
	2009	34	61.8	0	0.0	0	0.0	0	0.0	34	61.8
	2010	10	18.2	0	0.0	0	0.0	0	0.0	10	18.2
	2011	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	NA	0	-	48	-	31	-	21	-	100	-

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort

MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n = number of subjects in a given category
Value = value of the considered parameter
% = n / Number of subjects with available results x 100
SD = Standard deviation

Table 56 Drugs prescription by exposed/non-exposed status - Main Analysis - All cases (Total cohort)

		EXP N = 55		NNEXP N = 48		MALE N = 31		HIST N = 21		Total N = 155	
Characteristics	**Categories**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Prescription of autoimmune disease drugs	Yes	48	87.3	44	91.7	30	96.8	18	85.7	140	90.3
	No	7	12.7	4	8.3	1	3.2	3	14.3	15	9.7
Chronic use of autoimmune disease drugs	Yes	46	95.8	40	90.9	27	90.0	16	88.9	129	92.1
	No	2	4.2	4	9.1	3	10.0	2	11.1	11	7.9
	NA	7	-	4	-	1	-	3	-	15	-

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n/% = number / percentage of subjects in a given category

Table 57 P-Values comparing Exposed female and Non-Exposed female cohorts - Main Analysis - All cases (Total cohort)

Variable	P value
Age at reference date [years] [in cat]	0.4169
Age at reference date [years]	0.3744
Region	0.0878
Region [in cat]	0.0238
Number of years in CPRD GOLD at reference date	0.0093
Number of years in CPRD GOLD at reference date [in cat]	0.0243
HES linkage	0.0752
Number of GP consultations the year previous reference date	0.4943
Number of GP consultations the year previous reference date [in cat]	0.7110
Any vaccines in the year previous the reference date	0.4702
Any vaccines in the follow-up period	0.1298
Novel adjuvanted vaccines in the follow-up period	0.3479
Live attenuated vaccines in the year previous the reference date	0.8895
Other vaccines in the year previous the reference date	0.3797
Other vaccines in the follow-up period	0.2215
Use of autoimmune disease drugs	0.4714
Chronic use of autoimmune disease drugs	0.3393

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
n/%=number/percentage of subjects in a given category
Chi-square and T-test statistics were computed respectively for categorical and continuous variables

Table 58 P-Values comparing Non-Exposed concurrent male and historical male cohorts - Main Analysis - All cases (Total cohort)

Variable	P value
Age at reference date [years] [in cat]	0.0790
Age at reference date [years]	0.1012
Region	0.0999
Region [in cat]	0.1265
Number of years in CPRD GOLD at reference date	0.2706
Number of years in CPRD GOLD at reference date [in cat]	0.6399
HES linkage	0.9566
Number of GP consultations the year previous reference date	0.5672
Number of GP consultations the year previous reference date [in cat]	0.7969
Any vaccines in the year previous the reference date	0.0016
Live attenuated vaccines in the year previous the reference date	0.0302
Other vaccines in the year previous the reference date	0.0016
Use of autoimmune disease drugs	0.1420
Chronic use of autoimmune disease drugs	0.9029

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
n/%=number/percentage of subjects in a given category
Chi-square and T-test statistics were computed respectively for categorical and continuous variables

Table 59 Summary of demographic characteristics by exposed/non-exposed status - Imputed date - Confirmed cases (Total cohort)

		EXP N = 42		NNEXP N = 34		MALE N = 35		HIST N = 20		Total N = 131		
Characteristics	Parameters or Categories	Value or n	%	Value or n	%	Value or n	%	Value or n	%	Value or n	%	P-values
Age at reference date [years]	Mean	15.86	-	15.05	-	14.66	-	15.93	-	15.34	-	-
	SD	1.94	-	2.46	-	2.43	-	2.09	-	2.28	-	-
	Median	15.71	-	15.64	-	13.57	-	16.67	-	15.63	-	-
	Minimum	12.31	-	12.24	-	11.76	-	12.03	-	11.76	-	-
	Maximum	20.03	-	18.81	-	18.75	-	18.45	-	20.03	-	-
	Missing	0	-	0	-	0	-	0	-	0	-	-
Age group at reference date [years]	9-13Y	7	16.7	16	47.1	20	57.1	3	15.0	46	35.1	-
	14-17Y	30	71.4	14	41.2	11	31.4	13	65.0	68	51.9	-
	18-21Y	5	11.9	4	11.8	4	11.4	4	20.0	17	13.0	-
	22-25Y	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	-
Region	South East Coast	4	9.5	2	5.9	0	0.0	0	0.0	6	4.6	-
	Northern Ireland	2	4.8	5	14.7	0	0.0	1	5.0	8	6.1	-
	Scotland	5	11.9	3	8.8	7	20.0	1	5.0	16	12.2	-
	Wales	4	9.5	1	2.9	4	11.4	2	10.0	11	8.4	-
	North West	3	7.1	5	14.7	7	20.0	2	10.0	17	13.0	-
	Yorkshire & The Humber	1	2.4	1	2.9	3	8.6	1	5.0	6	4.6	-
	East Midlands	5	11.9	1	2.9	5	14.3	2	10.0	13	9.9	-
	West Midlands	4	9.5	1	2.9	1	2.9	3	15.0	9	6.9	-
	East of England	2	4.8	7	20.6	3	8.6	5	25.0	17	13.0	-
	South West	4	9.5	4	11.8	3	8.6	2	10.0	13	9.9	-
	South Central	7	16.7	2	5.9	2	5.7	0	0.0	11	8.4	-
	London	1	2.4	2	5.9	0	0.0	1	5.0	4	3.1	-
Region [in category]	North England	4	9.5	6	17.6	10	28.6	3	15.0	23	17.6	-
	Midlands	9	21.4	2	5.9	6	17.1	5	25.0	22	16.8	-
	South England	18	42.9	17	50.0	8	22.9	8	40.0	51	38.9	-
	Ireland Scotland Wales	11	26.2	9	26.5	11	31.4	4	20.0	35	26.7	-

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n/% = number / percentage of subjects in a given category
Value = value of the considered parameter
SD = Standard deviation

Table 60 Data availability by exposed/non-exposed status - Imputed date - Confirmed cases (Total cohort)

		EXP N = 42		NNEXP N = 34		MALE N = 35		HIST N = 20		Total N = 131	
Characteristics	**Parameters or Categories**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**
Number of years in CPRD GOLD at reference date	Mean	9.87	-	7.51	-	9.32	-	8.15	-	8.85	-
	SD	4.80	-	4.94	-	3.67	-	4.66	-	4.59	-
	Median	10.44	-	6.09	-	9.93	-	7.22	-	8.51	-
	Minimum	1.57	-	1.02	-	1.28	-	1.23	-	1.02	-
	Maximum	20.27	-	16.75	-	18.26	-	17.02	-	20.27	-
	Missing	0	-	0	-	0	-	0	-	0	-
Number of years in CPRD GOLD at reference date [in cat]	[0-3[years	4	9.5	7	20.6	1	2.9	3	15.0	15	11.5
	[3-6[years	8	19.0	10	29.4	5	14.3	4	20.0	27	20.6
	[6-10[years	8	19.0	8	23.5	14	40.0	6	30.0	36	27.5
	[10 years	22	52.4	9	26.5	15	42.9	7	35.0	53	40.5
HES linkage	Yes	27	64.3	19	55.9	19	54.3	12	60.0	77	58.8
	No	15	35.7	15	44.1	16	45.7	8	40.0	54	41.2

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n/% = number / percentage of subjects in a given category
Value = value of the considered parameter
SD = Standard deviation

Table 61 Healthcare resources utilization by exposed/non-exposed status - Imputed date - Confirmed cases (Total cohort)

		EXP N = 42		NNEXP N = 34		MALE N = 35		HIST N = 20		Total N = 131	
Characteristics	**Parameters or Categories**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**
Number of GP consultations the year previous reference date	Mean	11.05	-	8.03	-	6.91	-	8.65	-	8.79	-
	SD	12.32	-	7.95	-	7.89	-	10.59	-	9.97	-
	Median	6.00	-	5.50	-	4.00	-	5.00	-	5.00	-
	Minimum	0.00	-	1.00	-	0.00	-	0.00	-	0.00	-
	Maximum	54.00	-	34.00	-	33.00	-	42.00	-	54.00	-
	Missing	0	-	0	-	0	-	0	-	0	-
Number of GP consultations the year previous reference date [in cat]	0 to 1 consultation	6	14.3	4	11.8	5	14.3	2	10.0	17	13.0
	2 to 4 consultations	10	23.8	11	32.4	16	45.7	8	40.0	45	34.4
	5 to 9 consultations	10	23.8	9	26.5	7	20.0	4	20.0	30	22.9
	Equal or more than 10 consultations	16	38.1	10	29.4	7	20.0	6	30.0	39	29.8

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n/% = number / percentage of subjects in a given category
Value = value of the considered parameter
SD = Standard deviation

Table 62 Exposure to other vaccines by exposed/non-exposed status - Imputed date - Confirmed cases (Total cohort)

		EXP N = 42		NNEXP N = 34		MALE N = 35		HIST N = 20		Total N = 131	
Characteristics	**Categories**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Any vaccines in the year previous the reference date	Yes	12	28.6	4	11.8	0	0.0	6	30.0	22	16.8
	No	30	71.4	30	88.2	35	100	14	70.0	109	83.2
Any vaccines in the follow-up period	Yes	5	11.9	1	2.9	1	2.9	0	0.0	7	5.3
	No	37	88.1	33	97.1	34	97.1	20	100	124	94.7
Novel adjuvanted vaccines in the year previous the reference date	Yes	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	No	42	100	34	100	35	100	20	100	131	100
Novel adjuvanted vaccines in the follow-up period	Yes	1	2.4	0	0.0	1	2.9	0	0.0	2	1.5
	No	41	97.6	34	100	34	97.1	20	100	129	98.5
Live-attenuated vaccines in the year previous the reference date	Yes	2	4.8	1	2.9	0	0.0	2	10.0	5	3.8
	No	40	95.2	33	97.1	35	100	18	90.0	126	96.2
Live-attenuated vaccines in the follow-up period	Yes	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	No	42	100	34	100	35	100	20	100	131	100
Other vaccines in the year previous the reference date	Yes	10	23.8	3	8.8	0	0.0	6	30.0	19	14.5
	No	32	76.2	31	91.2	35	100	14	70.0	112	85.5
Other vaccines in the follow-up period	Yes	4	9.5	1	2.9	0	0.0	0	0.0	5	3.8
	No	38	90.5	33	97.1	35	100	20	100	126	96.2

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n/% = number / percentage of subjects in a given category
P-value: Fisher exact test
Follow-up is 12 months for all the cohorts

Table 63 Exposure to other vaccines in the risk and control follow-up period for Exposed Female Cohort - Imputed date - Confirmed cases (Total cohort)

		EXP N = 42	
Characteristics	**Categories**	**n**	**%**
Any vaccines in the risk period [0-12 months]	Yes	15	35.7
	No	27	64.3
Any vaccines in the control period [18-30 months]	Yes	15	35.7
	No	27	64.3
Novel adjuvanted vaccines in the risk period [0-12 months]	Yes	3	7.1
	No	39	92.9
Novel adjuvanted vaccines in the control period [18-30 months]	Yes	0	0.0
	No	42	100
Live-attenuated vaccines in the risk period [0-12 months]	Yes	3	7.1
	No	39	92.9
Live-attenuated vaccines in the control period [18-30 months]	Yes	1	2.4
	No	41	97.6
Other vaccines in the risk period [0-12 months]	Yes	14	33.3
	No	28	66.7
Other vaccines in the control period [18-30 months]	Yes	14	33.3
	No	28	66.7

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n/% = number / percentage of subjects in a given category
P-value: Fisher exact test

Table 64 Exposure to Cervarix vaccine - Imputed date - Confirmed cases (Total cohort)

		EXP N = 42		NNEXP N = 34		MALE N = 35		HIST N = 20		Total N = 131	
Characteristics	**Parameters or Categories**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**
Subject received a Cervarix dose	Yes	42	100	0	0.0	0	0.0	0	0.0	42	32.1
	No	0	0.0	34	100	35	100	20	100	89	67.9
Number of dose of Cervarix	0 dose	0	0.0	34	100	35	100	20	100	89	67.9
	1 dose	6	14.3	0	0.0	0	0.0	0	0.0	6	4.6
	2 doses	7	16.7	0	0.0	0	0.0	0	0.0	7	5.3
	3 doses	29	69.0	0	0.0	0	0.0	0	0.0	29	22.1
	4 doses	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Cervarix dose and reference date	Cervarix before the reference date	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	Cervarix after or at reference date	42	100	0	0.0	0	0.0	0	0.0	42	100
	NA	0	0.0	34	-	35	-	20	-	89	-
Time in days between reference date and last Cervarix dose	Mean	188.40	-	-	-	-	-	-	-	188.40	-
	SD	124.09	-	-	-	-	-	-	-	124.09	-
	Median	195.50	-	-	-	-	-	-	-	195.50	-
	Minimum	0.00	-	-	-	-	-	-	-	0.00	-
	Maximum	576.00	-	-	-	-	-	-	-	576.00	-
	NA	0	-	34	-	35	-	20	-	89	-
Time in days between reference date and last Cervarix dose [in category]	within 30 days	7	16.7	0	0.0	0	0.0	0	0.0	7	16.7
	between 31 to 60 days	2	4.8	0	0.0	0	0.0	0	0.0	2	4.8
	between 61 to 180 days	3	7.1	0	0.0	0	0.0	0	0.0	3	7.1
	more than 180 days	30	71.4	0	0.0	0	0.0	0	0.0	30	71.4
	NA	0	-	34	-	35	-	20	-	89	-
Year of 1st Cervarix dose	2006	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	2007	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	2008	9	21.4	0	0.0	0	0.0	0	0.0	9	21.4
	2009	24	57.1	0	0.0	0	0.0	0	0.0	24	57.1
	2010	9	21.4	0	0.0	0	0.0	0	0.0	9	21.4
	2011	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	NA	0	-	34	-	35	-	20	-	89	-

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort

MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n = number of subjects in a given category
Value = value of the considered parameter
% = n / Number of subjects with available results x 100
SD = Standard deviation

Table 65 Drugs prescription by exposed/non-exposed status - Imputed date - Confirmed cases (Total cohort)

		EXP N = 42		NNEXP N = 34		MALE N = 35		HIST N = 20		Total N = 131	
Characteristics	**Categories**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Prescription of autoimmune disease drugs	Yes	42	100	32	94.1	31	88.6	18	90.0	123	93.9
	No	0	0.0	2	5.9	4	11.4	2	10.0	8	6.1
Chronic use of autoimmune disease drugs	Yes	39	92.9	31	96.9	30	96.8	17	94.4	117	95.1
	No	3	7.1	1	3.1	1	3.2	1	5.6	6	4.9
	NA	0	0.0	2	-	4	-	2	-	8	-

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n/% = number / percentage of subjects in a given category

Table 66 P-Values comparing exposed female and unexposed female cohorts - Imputed date - Confirmed cases (Total cohort)

Variable	P value
Age at reference date [years] [in cat]	0.0129
Age at reference date [years]	0.1138
Region	0.2103
Region [in cat]	0.2319
Number of years in CPRD GOLD at reference date	0.0388
Number of years in CPRD GOLD at reference date [in cat]	0.1264
HES linkage	0.4561
Number of GP consultations the year previous reference date	0.2207
Number of GP consultations the year previous reference date [in cat]	0.7881
Any vaccines in the year previous the reference date	0.0739
Any vaccines in the follow-up period	0.1496
Novel adjuvanted vaccines in the follow-up period	0.3651
Live attenuated vaccines in the year previous the reference date	0.6852
Other vaccines in the year previous the reference date	0.0845
Other vaccines in the follow-up period	0.2498
Use of autoimmune disease drugs	0.1112
Chronic use of autoimmune disease drugs	0.4489

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
n/%=number/percentage of subjects in a given category
Chi-square and T-test statistics were computed respectively for categorical and continuous variables

Table 67 P-Values comparing unexposed concurrent male and historical male cohorts - Imputed date - Confirmed cases (Total cohort)

Variable	P value
Age at reference date [years] [in cat]	0.0094
Age at reference date [years]	0.0551
Region	0.2356
Region [in cat]	0.3505
Number of years in CPRD GOLD at reference date	0.3073
Number of years in CPRD GOLD at reference date [in cat]	0.3366
HES linkage	0.6810
Number of GP consultations the year previous reference date	0.4923
Number of GP consultations the year previous reference date [in cat]	0.8453
Any vaccines in the year previous the reference date	0.0006
Any vaccines in the follow-up period	0.4455
Novel adjuvanted vaccines in the follow-up period	0.4455
Live attenuated vaccines in the year previous the reference date	0.0567
Other vaccines in the year previous the reference date	0.0006
Use of autoimmune disease drugs	0.8701
Chronic use of autoimmune disease drugs	0.6911

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
n/%=number/percentage of subjects in a given category
Chi-square and T-test statistics were computed respectively for categorical and continuous variables

Table 68 Summary of demographic characteristics by exposed/non-exposed status - Imputed date - All cases (Total cohort)

		EXP N = 65		NNEXP N = 61		MALE N = 45		HIST N = 33		Total N = 204		
Characteristics	Parameters or Categories	Value or n	%	Value or n	%	Value or n	%	Value or n	%	Value or n	%	P-values
Age at reference date [years]	Mean	15.64	-	15.25	-	14.92	-	16.34	-	15.48	-	0.0332
	SD	1.97	-	2.25	-	2.34	-	2.08	-	2.19	-	-
	Median	15.71	-	15.65	-	15.29	-	17.23	-	15.72	-	-
	Minimum	12.24	-	11.83	-	11.76	-	12.03	-	11.76	-	-
	Maximum	20.03	-	18.81	-	18.75	-	18.68	-	20.03	-	-
	Missing	0	-	0	-	0	-	0	-	0	-	-
Age group at reference date [years]	9-13Y	14	21.5	22	36.1	22	48.9	5	15.2	63	30.9	-
	14-17Y	45	69.2	34	55.7	18	40.0	20	60.6	117	57.4	-
	18-21Y	6	9.2	5	8.2	5	11.1	8	24.2	24	11.8	-
	22-25Y	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	-
Region	South East Coast	5	7.7	4	6.6	4	8.9	2	6.1	15	7.4	-
	Northern Ireland	4	6.2	7	11.5	0	0.0	2	6.1	13	6.4	-
	Scotland	9	13.8	6	9.8	7	15.6	6	18.2	28	13.7	-
	Wales	5	7.7	6	9.8	5	11.1	2	6.1	18	8.8	-
	North West	6	9.2	8	13.1	9	20.0	2	6.1	25	12.3	-
	Yorkshire & The Humber	2	3.1	2	3.3	3	6.7	2	6.1	9	4.4	-
	East Midlands	6	9.2	1	1.6	5	11.1	2	6.1	14	6.9	-
	West Midlands	6	9.2	2	3.3	1	2.2	3	9.1	12	5.9	-
	East of England	2	3.1	10	16.4	3	6.7	7	21.2	22	10.8	-
	South West	9	13.8	6	9.8	3	6.7	3	9.1	21	10.3	-
	South Central	10	15.4	5	8.2	4	8.9	0	0.0	19	9.3	-
	London	1	1.5	4	6.6	1	2.2	2	6.1	8	3.9	-
Region [in category]	North England	8	12.3	10	16.4	12	26.7	4	12.1	34	16.7	-
	Midlands	12	18.5	3	4.9	6	13.3	5	15.2	26	12.7	-
	South England	27	41.5	29	47.5	15	33.3	14	42.4	85	41.7	-
	Ireland Scotland Wales	18	27.7	19	31.1	12	26.7	10	30.3	59	28.9	-

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n/% = number / percentage of subjects in a given category
Value = value of the considered parameter
SD = Standard deviation

Table 69 Data availability by exposed/non-exposed status - Imputed date - All cases (Total cohort)

		EXP N = 65		NNEXP N = 61		MALE N = 45		HIST N = 33		Total N = 204	
Characteristics	**Parameters or Categories**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**
Number of years in CPRD GOLD at reference date	Mean	9.84	-	7.25	-	9.78	-	8.10	-	8.77	-
	SD	4.64	-	4.60	-	4.09	-	4.05	-	4.54	-
	Median	10.22	-	6.72	-	9.95	-	7.51	-	8.52	-
	Minimum	1.57	-	1.02	-	1.28	-	1.23	-	1.02	-
	Maximum	20.27	-	16.75	-	18.26	-	17.02	-	20.27	-
	Missing	0	-	0	-	0	-	0	-	0	-
Number of years in CPRD GOLD at reference date [in cat]	[0-3[years	5	7.7	13	21.3	2	4.4	4	12.1	24	11.8
	[3-6[years	12	18.5	15	24.6	6	13.3	6	18.2	39	19.1
	[6-10[years	14	21.5	18	29.5	16	35.6	13	39.4	61	29.9
	[10 years	34	52.3	15	24.6	21	46.7	10	30.3	80	39.2
HES linkage	Yes	42	64.6	34	55.7	26	57.8	18	54.5	120	58.8
	No	23	35.4	27	44.3	19	42.2	15	45.5	84	41.2

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n/% = number / percentage of subjects in a given category
Value = value of the considered parameter
SD = Standard deviation

Table 70 Healthcare resources utilization by exposed/non-exposed status - Imputed date - All cases (Total cohort)

		EXP N = 65		NNEXP N = 61		MALE N = 45		HIST N = 33		Total N = 204	
Characteristics	**Parameters or Categories**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**
Number of GP consultations the year previous reference date	Mean	10.54	-	10.18	-	8.36	-	8.03	-	9.54	-
	SD	11.39	-	10.48	-	9.20	-	9.98	-	10.42	-
	Median	6.00	-	6.00	-	4.00	-	4.00	-	5.00	-
	Minimum	0.00	-	0.00	-	0.00	-	0.00	-	0.00	-
	Maximum	54.00	-	45.00	-	39.00	-	42.00	-	54.00	-
	Missing	0	-	0	-	0	-	0	-	0	-
Number of GP consultations the year previous reference date [in cat]	0 to 1 consultation	10	15.4	7	11.5	5	11.1	7	21.2	29	14.2
	2 to 4 consultations	16	24.6	16	26.2	19	42.2	12	36.4	63	30.9
	5 to 9 consultations	14	21.5	16	26.2	9	20.0	5	15.2	44	21.6
	Equal or more than 10 consultations	25	38.5	22	36.1	12	26.7	9	27.3	68	33.3

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n/% = number / percentage of subjects in a given category
Value = value of the considered parameter
SD = Standard deviation

Table 71 Exposure to other vaccines by exposed/non-exposed status - Imputed date - All cases (Total cohort)

		EXP N = 65		NNEXP N = 61		MALE N = 45		HIST N = 33		Total N = 204	
Characteristics	**Categories**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Any vaccines in the year previous the reference date	Yes	13	20.0	11	18.0	0	0.0	8	24.2	32	15.7
	No	52	80.0	50	82.0	45	100	25	75.8	172	84.3
Any vaccines in the follow-up period	Yes	7	10.8	2	3.3	1	2.2	1	3.0	11	5.4
	No	58	89.2	59	96.7	44	97.8	32	97.0	193	94.6
Novel adjuvanted vaccines in the year previous the reference date	Yes	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	No	65	100	61	100	45	100	33	100	204	100
Novel adjuvanted vaccines in the follow-up period	Yes	1	1.5	0	0.0	1	2.2	0	0.0	2	1.0
	No	64	98.5	61	100	44	97.8	33	100	202	99.0
Live-attenuated vaccines in the year previous the reference date	Yes	2	3.1	3	4.9	0	0.0	3	9.1	8	3.9
	No	63	96.9	58	95.1	45	100	30	90.9	196	96.1
Live-attenuated vaccines in the follow-up period	Yes	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	No	65	100	61	100	45	100	33	100	204	100
Other vaccines in the year previous the reference date	Yes	11	16.9	9	14.8	0	0.0	8	24.2	28	13.7
	No	54	83.1	52	85.2	45	100	25	75.8	176	86.3
Other vaccines in the follow-up period	Yes	6	9.2	2	3.3	0	0.0	1	3.0	9	4.4
	No	59	90.8	59	96.7	45	100	32	97.0	195	95.6

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n/% = number / percentage of subjects in a given category
P-value: Fisher exact test
Follow-up is 12 months for all the cohorts

Table 72 Exposure to other vaccines in the risk and control follow-up period for Exposed Female Cohort - Imputed date - All cases (Total cohort)

		EXP N = 65	
Characteristics	**Categories**	**n**	**%**
Any vaccines in the risk period [0-12 months]	Yes	19	29.2
	No	46	70.8
Any vaccines in the control period [18-30 months]	Yes	19	29.2
	No	46	70.8
Novel adjuvanted vaccines in the risk period [0-12 months]	Yes	3	4.6
	No	62	95.4
Novel adjuvanted vaccines in the control period [18-30 months]	Yes	0	0.0
	No	65	100
Live-attenuated vaccines in the risk period [0-12 months]	Yes	4	6.2
	No	61	93.8
Live-attenuated vaccines in the control period [18-30 months]	Yes	1	1.5
	No	64	98.5
Other vaccines in the risk period [0-12 months]	Yes	17	26.2
	No	48	73.8
Other vaccines in the control period [18-30 months]	Yes	18	27.7
	No	47	72.3

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n/% = number / percentage of subjects in a given category
P-value: Fisher exact test

Table 73 Exposure to Cervarix vaccine - Imputed date - All cases (Total cohort)

		EXP N = 65		NNEXP N = 61		MALE N = 45		HIST N = 33		Total N = 204	
Characteristics	**Parameters or Categories**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**
Subject received a Cervarix dose	Yes	65	100	0	0.0	0	0.0	0	0.0	65	31.9
	No	0	0.0	61	100	45	100	33	100	139	68.1
Number of dose of Cervarix	0 dose	0	0.0	61	100	45	100	33	100	139	68.1
	1 dose	8	12.3	0	0.0	0	0.0	0	0.0	8	3.9
	2 doses	11	16.9	0	0.0	0	0.0	0	0.0	11	5.4
	3 doses	46	70.8	0	0.0	0	0.0	0	0.0	46	22.5
	4 doses	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Cervarix dose and reference date	Cervarix before the reference date	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	Cervarix after or at reference date	65	100	0	0.0	0	0.0	0	0.0	65	100
	NA	0	0.0	61	-	45	-	33	-	139	-
Time in days between reference date and last Cervarix dose	Mean	180.18	-	-	-	-	-	-	-	180.18	-
	SD	111.33	-	-	-	-	-	-	-	111.33	-
	Median	195.00	-	-	-	-	-	-	-	195.00	-
	Minimum	0.00	-	-	-	-	-	-	-	0.00	-
	Maximum	576.00	-	-	-	-	-	-	-	576.00	-
	NA	0	-	61	-	45	-	33	-	139	-
Time in days between reference date and last Cervarix dose [in category]	within 30 days	11	16.9	0	0.0	0	0.0	0	0.0	11	16.9
	between 31 to 60 days	3	4.6	0	0.0	0	0.0	0	0.0	3	4.6
	between 61 to 180 days	6	9.2	0	0.0	0	0.0	0	0.0	6	9.2
	more than 180 days	45	69.2	0	0.0	0	0.0	0	0.0	45	69.2
	NA	0	-	61	-	45	-	33	-	139	-
Year of 1st Cervarix dose	2006	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	2007	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	2008	12	18.5	0	0.0	0	0.0	0	0.0	12	18.5
	2009	40	61.5	0	0.0	0	0.0	0	0.0	40	61.5
	2010	13	20.0	0	0.0	0	0.0	0	0.0	13	20.0
	2011	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	NA	0	-	61	-	45	-	33	-	139	-

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort

MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n = number of subjects in a given category
Value = value of the considered parameter
% = n / Number of subjects with available results x 100
SD = Standard deviation

Table 74 Drugs prescription by exposed/non-exposed status - Imputed date - All cases (Total cohort)

		EXP N = 65		NNEXP N = 61		MALE N = 45		HIST N = 33		Total N = 204	
Characteristics	**Categories**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Prescription of autoimmune disease drugs	Yes	57	87.7	55	90.2	38	84.4	30	90.9	180	88.2
	No	8	12.3	6	9.8	7	15.6	3	9.1	24	11.8
Chronic use of autoimmune disease drugs	Yes	53	93.0	51	92.7	34	89.5	27	90.0	165	91.7
	No	4	7.0	4	7.3	4	10.5	3	10.0	15	8.3
	NA	8	-	6	-	7	-	3	-	24	-

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n/% = number / percentage of subjects in a given category

Table 75 P-Values comparing exposed female and unexposed female cohorts - Imputed date - All cases (Total cohort)

Variable	P value
Age at reference date [years] [in cat]	0.1943
Age at reference date [years]	0.3084
Region	0.1150
Region [in cat]	0.1328
Number of years in CPRD GOLD at reference date	0.0021
Number of years in CPRD GOLD at reference date [in cat]	0.0087
HES linkage	0.3087
Number of GP consultations the year previous reference date	0.8548
Number of GP consultations the year previous reference date [in cat]	0.8666
Any vaccines in the year previous the reference date	0.7787
Any vaccines in the follow-up period	0.1028
Novel adjuvanted vaccines in the follow-up period	0.3307
Live attenuated vaccines in the year previous the reference date	0.5968
Other vaccines in the year previous the reference date	0.7392
Other vaccines in the follow-up period	0.1709
Use of autoimmune disease drugs	0.6591
Chronic use of autoimmune disease drugs	0.9582

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
n/%=number/percentage of subjects in a given category
Chi-square and T-test statistics were computed respectively for categorical and continuous variables

Table 76 P-Values comparing unexposed concurrent male and historical male cohorts - Imputed date - All cases (Total cohort)

Variable	P value
Age at reference date [years] [in cat]	0.0071
Age at reference date [years]	0.0072
Region	0.1640
Region [in cat]	0.4716
Number of years in CPRD GOLD at reference date	0.0768
Number of years in CPRD GOLD at reference date [in cat]	0.3753
HES linkage	0.7761
Number of GP consultations the year previous reference date	0.8820
Number of GP consultations the year previous reference date [in cat]	0.6416
Any vaccines in the year previous the reference date	0.0005
Any vaccines in the follow-up period	0.8235
Novel adjuvanted vaccines in the follow-up period	0.3887
Live attenuated vaccines in the year previous the reference date	0.0391
Other vaccines in the year previous the reference date	0.0005
Other vaccines in the follow-up period	0.2399
Use of autoimmune disease drugs	0.3988
Chronic use of autoimmune disease drugs	0.9435

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
n/%=number/percentage of subjects in a given category
Chi-square and T-test statistics were computed respectively for categorical and continuous variables

Table 77 Summary of demographic characteristics by exposed/non-exposed status - Diagnosis date - Confirmed cases (Total cohort)

		EXP N = 59		NNEXP N = 53		MALE N = 47		HIST N = 34		Total N = 193		
Characteristics	Parameters or Categories	Value or n	%	Value or n	%	Value or n	%	Value or n	%	Value or n	%	P-values
Age at reference date [years]	Mean	15.88	-	15.22	-	14.96	-	16.07	-	15.51	-	0.0576
	SD	1.96	-	2.26	-	2.32	-	1.97	-	2.17	-	-
	Median	16.19	-	15.63	-	15.25	-	16.67	-	15.80	-	-
	Minimum	12.22	-	12.17	-	11.76	-	12.03	-	11.76	-	-
	Maximum	20.03	-	18.81	-	19.45	-	18.56	-	20.03	-	-
	Missing	0	-	0	-	0	-	0	-	0	-	-
Age group at reference date [years]	9-13Y	11	18.6	19	35.8	22	46.8	5	14.7	57	29.5	-
	14-17Y	40	67.8	28	52.8	20	42.6	23	67.6	111	57.5	-
	18-21Y	8	13.6	6	11.3	5	10.6	6	17.6	25	13.0	-
	22-25Y	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	-
Region	South East Coast	4	6.8	3	5.7	0	0.0	1	2.9	8	4.1	-
	Northern Ireland	3	5.1	5	9.4	0	0.0	2	5.9	10	5.2	-
	Scotland	8	13.6	5	9.4	7	14.9	2	5.9	22	11.4	-
	Wales	9	15.3	3	5.7	5	10.6	3	8.8	20	10.4	-
	North West	4	6.8	9	17.0	12	25.5	4	11.8	29	15.0	-
	Yorkshire & The Humber	1	1.7	1	1.9	3	6.4	1	2.9	6	3.1	-
	East Midlands	6	10.2	1	1.9	5	10.6	2	5.9	14	7.3	-
	West Midlands	6	10.2	2	3.8	3	6.4	5	14.7	16	8.3	-
	East of England	2	3.4	10	18.9	5	10.6	7	20.6	24	12.4	-
	South West	5	8.5	4	7.5	4	8.5	3	8.8	16	8.3	-
	South Central	9	15.3	6	11.3	2	4.3	1	2.9	18	9.3	-
	London	2	3.4	4	7.5	1	2.1	3	8.8	10	5.2	-
Region [in category]	North England	5	8.5	10	18.9	15	31.9	5	14.7	35	18.1	-
	Midlands	12	20.3	3	5.7	8	17.0	7	20.6	30	15.5	-
	South England	22	37.3	27	50.9	12	25.5	15	44.1	76	39.4	-
	Ireland Scotland Wales	20	33.9	13	24.5	12	25.5	7	20.6	52	26.9	-

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n/% = number / percentage of subjects in a given category
Value = value of the considered parameter
SD = Standard deviation

Table 78 Data availability by exposed/non-exposed status - Diagnosis date - Confirmed cases (Total cohort)

		EXP N = 59		NNEXP N = 53		MALE N = 47		HIST N = 34		Total N = 193	
Characteristics	**Parameters or Categories**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**
Number of years in CPRD GOLD at reference date	Mean	9.88	-	7.26	-	9.73	-	8.87	-	8.95	-
	SD	4.65	-	4.45	-	3.78	-	4.30	-	4.44	-
	Median	10.08	-	6.26	-	9.94	-	8.46	-	8.63	-
	Minimum	1.57	-	1.02	-	1.28	-	1.23	-	1.02	-
	Maximum	20.27	-	16.75	-	18.26	-	17.02	-	20.27	-
	Missing	0	-	0	-	0	-	0	-	0	-
Number of years in CPRD GOLD at reference date [in cat]	[0-3[years	6	10.2	8	15.1	1	2.1	3	8.8	18	9.3
	[3-6[years	9	15.3	18	34.0	7	14.9	6	17.6	40	20.7
	[6-10[years	14	23.7	14	26.4	17	36.2	11	32.4	56	29.0
	[10 years	30	50.8	13	24.5	22	46.8	14	41.2	79	40.9
HES linkage	Yes	33	55.9	31	58.5	29	61.7	19	55.9	112	58.0
	No	26	44.1	22	41.5	18	38.3	15	44.1	81	42.0

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n/% = number / percentage of subjects in a given category
Value = value of the considered parameter
SD = Standard deviation

Table 79 Healthcare resources utilization by exposed/non-exposed status - Diagnosis date - Confirmed cases (Total cohort)

		EXP N = 59		NNEXP N = 53		MALE N = 47		HIST N = 34		Total N = 193	
Characteristics	**Parameters or Categories**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**
Number of GP consultations the year previous reference date	Mean	14.08	-	12.11	-	10.49	-	13.15	-	12.50	-
	SD	14.54	-	11.44	-	11.34	-	14.23	-	12.91	-
	Median	9.00	-	9.00	-	6.00	-	9.00	-	8.00	-
	Minimum	0.00	-	1.00	-	0.00	-	0.00	-	0.00	-
	Maximum	75.00	-	50.00	-	47.00	-	52.00	-	75.00	-
	Missing	0	-	0	-	0	-	0	-	0	-
Number of GP consultations the year previous reference date [in cat]	0 to 1 consultation	7	11.9	4	7.5	5	10.6	2	5.9	18	9.3
	2 to 4 consultations	10	16.9	12	22.6	16	34.0	10	29.4	48	24.9
	5 to 9 consultations	13	22.0	12	22.6	8	17.0	5	14.7	38	19.7
	Equal or more than 10 consultations	29	49.2	25	47.2	18	38.3	17	50.0	89	46.1

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n/% = number / percentage of subjects in a given category
Value = value of the considered parameter
SD = Standard deviation

Table 80 Exposure to other vaccines by exposed/non-exposed status - Diagnosis date - Confirmed cases (Total cohort)

		EXP N = 59		NNEXP N = 53		MALE N = 47		HIST N = 34		Total N = 193	
Characteristics	**Categories**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Any vaccines in the year previous the reference date	Yes	16	27.1	10	18.9	4	8.5	9	26.5	39	20.2
	No	43	72.9	43	81.1	43	91.5	25	73.5	154	79.8
Any vaccines in the follow-up period	Yes	9	15.3	3	5.7	1	2.1	1	2.9	14	7.3
	No	50	84.7	50	94.3	46	97.9	33	97.1	179	92.7
Novel adjuvanted vaccines in the year previous the reference date	Yes	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	No	59	100	53	100	47	100	34	100	193	100
Novel adjuvanted vaccines in the follow-up period	Yes	1	1.7	0	0.0	1	2.1	0	0.0	2	1.0
	No	58	98.3	53	100	46	97.9	34	100	191	99.0
Live-attenuated vaccines in the year previous the reference date	Yes	3	5.1	2	3.8	1	2.1	3	8.8	9	4.7
	No	56	94.9	51	96.2	46	97.9	31	91.2	184	95.3
Live-attenuated vaccines in the follow-up period	Yes	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	No	59	100	53	100	47	100	34	100	193	100
Other vaccines in the year previous the reference date	Yes	13	22.0	8	15.1	4	8.5	8	23.5	33	17.1
	No	46	78.0	45	84.9	43	91.5	26	76.5	160	82.9
Other vaccines in the follow-up period	Yes	8	13.6	3	5.7	0	0.0	1	2.9	12	6.2
	No	51	86.4	50	94.3	47	100	33	97.1	181	93.8

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n/% = number / percentage of subjects in a given category
P-value: Fisher exact test
Follow-up is 12 months for all the cohorts

Table 81 Exposure to other vaccines in the risk and control follow-up period for Exposed Female Cohort - Diagnosis date - Confirmed cases (Total cohort)

		EXP N = 59	
Characteristics	**Categories**	**n**	**%**
Any vaccines in the risk period [0-12 months]	Yes	21	35.6
	No	38	64.4
Any vaccines in the control period [18-30 months]	Yes	21	35.6
	No	38	64.4
Novel adjuvanted vaccines in the risk period [0-12 months]	Yes	3	5.1
	No	56	94.9
Novel adjuvanted vaccines in the control period [18-30 months]	Yes	0	0.0
	No	59	100
Live-attenuated vaccines in the risk period [0-12 months]	Yes	4	6.8
	No	55	93.2
Live-attenuated vaccines in the control period [18-30 months]	Yes	1	1.7
	No	58	98.3
Other vaccines in the risk period [0-12 months]	Yes	20	33.9
	No	39	66.1
Other vaccines in the control period [18-30 months]	Yes	20	33.9
	No	39	66.1

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n/% = number / percentage of subjects in a given category
P-value: Fisher exact test

Table 82 Exposure to Cervarix vaccine - Diagnosis date - Confirmed cases (Total cohort)

		EXP N = 59		NNEXP N = 53		MALE N = 47		HIST N = 34		Total N = 193	
Characteristics	**Parameters or Categories**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**
Subject received a Cervarix dose	Yes	59	100	0	0.0	0	0.0	0	0.0	59	30.6
	No	0	0.0	53	100	47	100	34	100	134	69.4
Number of dose of Cervarix	0 dose	0	0.0	53	100	47	100	34	100	134	69.4
	1 dose	9	15.3	0	0.0	0	0.0	0	0.0	9	4.7
	2 doses	10	16.9	0	0.0	0	0.0	0	0.0	10	5.2
	3 doses	40	67.8	0	0.0	0	0.0	0	0.0	40	20.7
	4 doses	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Cervarix dose and reference date	Cervarix before the reference date	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	Cervarix after or at reference date	59	100	0	0.0	0	0.0	0	0.0	59	100
	NA	0	0.0	53	-	47	-	34	-	134	-
Time in days between reference date and last Cervarix dose	Mean	176.25	-	-	-	-	-	-	-	176.25	-
	SD	114.60	-	-	-	-	-	-	-	114.60	-
	Median	187.00	-	-	-	-	-	-	-	187.00	-
	Minimum	0.00	-	-	-	-	-	-	-	0.00	-
	Maximum	576.00	-	-	-	-	-	-	-	576.00	-
	NA	0	-	53	-	47	-	34	-	134	-
Time in days between reference date and last Cervarix dose [in category]	within 30 days	11	18.6	0	0.0	0	0.0	0	0.0	11	18.6
	between 31 to 60 days	2	3.4	0	0.0	0	0.0	0	0.0	2	3.4
	between 61 to 180 days	9	15.3	0	0.0	0	0.0	0	0.0	9	15.3
	more than 180 days	37	62.7	0	0.0	0	0.0	0	0.0	37	62.7
	NA	0	-	53	-	47	-	34	-	134	-
Year of 1st Cervarix dose	2006	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	2007	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	2008	11	18.6	0	0.0	0	0.0	0	0.0	11	18.6
	2009	37	62.7	0	0.0	0	0.0	0	0.0	37	62.7
	2010	11	18.6	0	0.0	0	0.0	0	0.0	11	18.6
	2011	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	NA	0	-	53	-	47	-	34	-	134	-

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort

MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n = number of subjects in a given category
Value = value of the considered parameter
% = n / Number of subjects with available results x 100
SD = Standard deviation

Table 83 Drugs prescription by exposed/non-exposed status - Diagnosis date - Confirmed cases (Total cohort)

		EXP N = 59		NNEXP N = 53		MALE N = 47		HIST N = 34		Total N = 193	
Characteristics	**Categories**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Prescription of autoimmune disease drugs	Yes	59	100	51	96.2	43	91.5	31	91.2	184	95.3
	No	0	0.0	2	3.8	4	8.5	3	8.8	9	4.7
Chronic use of autoimmune disease drugs	Yes	56	94.9	49	96.1	42	97.7	30	96.8	177	96.2
	No	3	5.1	2	3.9	1	2.3	1	3.2	7	3.8
	NA	0	0.0	2	-	4	-	3	-	9	-

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n/% = number / percentage of subjects in a given category

Table 84 P-Values comparing exposed female and unexposed female cohorts - Diagnosis date - Confirmed cases (Total cohort)

Variable	P value
Age at reference date [years] [in cat]	0.1208
Age at reference date [years]	0.0992
Region	0.0755
Region [in cat]	0.0326
Number of years in CPRD GOLD at reference date	0.0030
Number of years in CPRD GOLD at reference date [in cat]	0.0212
HES linkage	0.7847
Number of GP consultations the year previous reference date	0.4304
Number of GP consultations the year previous reference date [in cat]	0.7969
Any vaccines in the year previous the reference date	0.3018
Any vaccines in the follow-up period	0.1012
Novel adjuvanted vaccines in the follow-up period	0.3411
Live attenuated vaccines in the year previous the reference date	0.7373
Other vaccines in the year previous the reference date	0.3475
Other vaccines in the follow-up period	0.1608
Use of autoimmune disease drugs	0.1322
Chronic use of autoimmune disease drugs	0.7702

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
n/%=number/percentage of subjects in a given category
Chi-square and T-test statistics were computed respectively for categorical and continuous variables

Table 85 P-Values comparing unexposed concurrent male and historical male cohorts - Diagnosis date - Confirmed cases (Total cohort)

Variable	P value
Age at reference date [years] [in cat]	0.0103
Age at reference date [years]	0.0264
Region	0.2853
Region [in cat]	0.1909
Number of years in CPRD GOLD at reference date	0.3440
Number of years in CPRD GOLD at reference date [in cat]	0.5502
HES linkage	0.5988
Number of GP consultations the year previous reference date	0.3528
Number of GP consultations the year previous reference date [in cat]	0.7198
Any vaccines in the year previous the reference date	0.0298
Any vaccines in the follow-up period	0.8159
Novel adjuvanted vaccines in the follow-up period	0.3921
Live attenuated vaccines in the year previous the reference date	0.1699
Other vaccines in the year previous the reference date	0.0604
Other vaccines in the follow-up period	0.2368
Use of autoimmune disease drugs	0.9606
Chronic use of autoimmune disease drugs	0.8137

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
n/%=number/percentage of subjects in a given category
Chi-square and T-test statistics were computed respectively for categorical and continuous variables

Table 86 Summary of demographic characteristics by exposed/non-exposed status - Diagnosis date - All cases (Total cohort)

		EXP N = 93		NNEXP N = 95		MALE N = 65		HIST N = 51		Total N = 304		
Characteristics	Parameters or Categories	Value or n	%	Value or n	%	Value or n	%	Value or n	%	Value or n	%	P-values
Age at reference date [years]	Mean	15.69	-	15.48	-	15.21	-	16.41	-	15.64	-	0.0114
	SD	1.95	-	2.16	-	2.17	-	1.95	-	2.09	-	-
	Median	16.19	-	15.83	-	15.35	-	17.23	-	16.19	-	-
	Minimum	12.22	-	11.83	-	11.76	-	12.03	-	11.76	-	-
	Maximum	20.03	-	18.81	-	19.45	-	18.68	-	20.03	-	-
	Missing	0	-	0	-	0	-	0	-	0	-	-
Age group at reference date [years]	9-13Y	21	22.6	28	29.5	25	38.5	7	13.7	81	26.6	-
	14-17Y	63	67.7	56	58.9	34	52.3	33	64.7	186	61.2	-
	18-21Y	9	9.7	11	11.6	6	9.2	11	21.6	37	12.2	-
	22-25Y	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	-
Region	North East	1	1.1	1	1.1	0	0.0	0	0.0	2	0.7	-
	South East Coast	6	6.5	8	8.4	5	7.7	3	5.9	22	7.2	-
	Northern Ireland	6	6.5	7	7.4	1	1.5	3	5.9	17	5.6	-
	Scotland	12	12.9	11	11.6	8	12.3	7	13.7	38	12.5	-
	Wales	12	12.9	9	9.5	7	10.8	3	5.9	31	10.2	-
	North West	7	7.5	12	12.6	16	24.6	5	9.8	40	13.2	-
	Yorkshire & The Humber	4	4.3	3	3.2	3	4.6	3	5.9	13	4.3	-
	East Midlands	7	7.5	1	1.1	5	7.7	2	3.9	15	4.9	-
	West Midlands	9	9.7	5	5.3	3	4.6	6	11.8	23	7.6	-
	East of England	3	3.2	14	14.7	5	7.7	9	17.6	31	10.2	-
	South West	10	10.8	7	7.4	4	6.2	4	7.8	25	8.2	-
	South Central	14	15.1	9	9.5	4	6.2	1	2.0	28	9.2	-
	London	2	2.2	8	8.4	4	6.2	5	9.8	19	6.3	-
Region [in category]	North England	12	12.9	16	16.8	19	29.2	8	15.7	55	18.1	-
	Midlands	16	17.2	6	6.3	8	12.3	8	15.7	38	12.5	-
	South England	35	37.6	46	48.4	22	33.8	22	43.1	125	41.1	-
	Ireland Scotland Wales	30	32.3	27	28.4	16	24.6	13	25.5	86	28.3	-

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n/% = number / percentage of subjects in a given category
Value = value of the considered parameter
SD = Standard deviation

Table 87 Data availability by exposed/non-exposed status - Diagnosis date - All cases (Total cohort)

		EXP N = 93		NNEXP N = 95		MALE N = 65		HIST N = 51		Total N = 304	
Characteristics	**Parameters or Categories**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**
Number of years in CPRD GOLD at reference date	Mean	9.97	-	7.25	-	9.96	-	8.84	-	8.93	-
	SD	4.52	-	4.63	-	4.24	-	4.12	-	4.57	-
	Median	9.61	-	6.26	-	9.95	-	8.13	-	8.73	-
	Minimum	1.57	-	1.02	-	1.02	-	1.23	-	1.02	-
	Maximum	20.27	-	17.10	-	18.26	-	17.02	-	20.27	-
	Missing	0	-	0	-	0	-	0	-	0	-
Number of years in CPRD GOLD at reference date [in cat]	[0-3[years	7	7.5	19	20.0	4	6.2	4	7.8	34	11.2
	[3-6[years	14	15.1	26	27.4	8	12.3	8	15.7	56	18.4
	[6-10[years	26	28.0	26	27.4	22	33.8	20	39.2	94	30.9
	[10 years	46	49.5	24	25.3	31	47.7	19	37.3	120	39.5
HES linkage	Yes	54	58.1	54	56.8	38	58.5	28	54.9	174	57.2
	No	39	41.9	41	43.2	27	41.5	23	45.1	130	42.8

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n/% = number / percentage of subjects in a given category
Value = value of the considered parameter
SD = Standard deviation

Table 88 Healthcare resources utilization by exposed/non-exposed status - Diagnosis date - All cases (Total cohort)

		EXP N = 93		NNEXP N = 95		MALE N = 65		HIST N = 51		Total N = 304	
Characteristics	**Parameters or Categories**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**
Number of GP consultations the year previous reference date	Mean	13.76	-	13.31	-	11.55	-	13.04	-	13.03	-
	SD	13.42	-	13.25	-	11.25	-	13.60	-	12.92	-
	Median	10.00	-	9.00	-	7.00	-	9.00	-	8.50	-
	Minimum	0.00	-	0.00	-	0.00	-	0.00	-	0.00	-
	Maximum	75.00	-	69.00	-	47.00	-	52.00	-	75.00	-
	Missing	0	-	0	-	0	-	0	-	0	-
Number of GP consultations the year previous reference date [in cat]	0 to 1 consultation	11	11.8	8	8.4	6	9.2	7	13.7	32	10.5
	2 to 4 consultations	16	17.2	21	22.1	19	29.2	13	25.5	69	22.7
	5 to 9 consultations	19	20.4	20	21.1	12	18.5	6	11.8	57	18.8
	Equal or more than 10 consultations	47	50.5	46	48.4	28	43.1	25	49.0	146	48.0

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n/% = number / percentage of subjects in a given category
Value = value of the considered parameter
SD = Standard deviation

Table 89 Exposure to other vaccines by exposed/non-exposed status - Diagnosis date - All cases (Total cohort)

		EXP N = 93		NNEXP N = 95		MALE N = 65		HIST N = 51		Total N = 304	
Characteristics	**Categories**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Any vaccines in the year previous the reference date	Yes	18	19.4	20	21.1	4	6.2	13	25.5	55	18.1
	No	75	80.6	75	78.9	61	93.8	38	74.5	249	81.9
Any vaccines in the follow-up period	Yes	11	11.8	4	4.2	1	1.5	1	2.0	17	5.6
	No	82	88.2	91	95.8	64	98.5	50	98.0	287	94.4
Novel adjuvanted vaccines in the year previous the reference date	Yes	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	No	93	100	95	100	65	100	51	100	304	100
Novel adjuvanted vaccines in the follow-up period	Yes	1	1.1	0	0.0	1	1.5	0	0.0	2	0.7
	No	92	98.9	95	100	64	98.5	51	100	302	99.3
Live-attenuated vaccines in the year previous the reference date	Yes	3	3.2	4	4.2	1	1.5	5	9.8	13	4.3
	No	90	96.8	91	95.8	64	98.5	46	90.2	291	95.7
Live-attenuated vaccines in the follow-up period	Yes	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	No	93	100	95	100	65	100	51	100	304	100
Other vaccines in the year previous the reference date	Yes	15	16.1	17	17.9	4	6.2	12	23.5	48	15.8
	No	78	83.9	78	82.1	61	93.8	39	76.5	256	84.2
Other vaccines in the follow-up period	Yes	10	10.8	4	4.2	0	0.0	1	2.0	15	4.9
	No	83	89.2	91	95.8	65	100	50	98.0	289	95.1

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n/% = number / percentage of subjects in a given category
P-value: Fisher exact test
Follow-up is 12 months for all the cohorts

Table 90 Exposure to other vaccines in the risk and control follow-up period for Exposed Female Cohort - Diagnosis date - All cases (Total cohort)

		EXP N = 93	
Characteristics	**Categories**	**n**	**%**
Any vaccines in the risk period [0-12 months]	Yes	27	29.0
	No	66	71.0
Any vaccines in the control period [18-30 months]	Yes	28	30.1
	No	65	69.9
Novel adjuvanted vaccines in the risk period [0-12 months]	Yes	4	4.3
	No	89	95.7
Novel adjuvanted vaccines in the control period [18-30 months]	Yes	0	0.0
	No	93	100
Live-attenuated vaccines in the risk period [0-12 months]	Yes	5	5.4
	No	88	94.6
Live-attenuated vaccines in the control period [18-30 months]	Yes	1	1.1
	No	92	98.9
Other vaccines in the risk period [0-12 months]	Yes	24	25.8
	No	69	74.2
Other vaccines in the control period [18-30 months]	Yes	27	29.0
	No	66	71.0

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n/% = number / percentage of subjects in a given category
P-value: Fisher exact test

Table 91 Exposure to Cervarix vaccine - Diagnosis date - All cases (Total cohort)

		EXP N = 93		NNEXP N = 95		MALE N = 65		HIST N = 51		Total N = 304	
Characteristics	**Parameters or Categories**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**
Subject received a Cervarix dose	Yes	93	100	0	0.0	0	0.0	0	0.0	93	30.6
	No	0	0.0	95	100	65	100	51	100	211	69.4
Number of dose of Cervarix	0 dose	0	0.0	95	100	65	100	51	100	211	69.4
	1 dose	12	12.9	0	0.0	0	0.0	0	0.0	12	3.9
	2 doses	15	16.1	0	0.0	0	0.0	0	0.0	15	4.9
	3 doses	66	71.0	0	0.0	0	0.0	0	0.0	66	21.7
	4 doses	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Cervarix dose and reference date	Cervarix before the reference date	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	Cervarix after or at reference date	93	100	0	0.0	0	0.0	0	0.0	93	100
	NA	0	0.0	95	-	65	-	51	-	211	-
Time in days between reference date and last Cervarix dose	Mean	178.59	-	-	-	-	-	-	-	178.59	-
	SD	121.62	-	-	-	-	-	-	-	121.62	-
	Median	187.00	-	-	-	-	-	-	-	187.00	-
	Minimum	0.00	-	-	-	-	-	-	-	0.00	-
	Maximum	813.00	-	-	-	-	-	-	-	813.00	-
	NA	0	-	95	-	65	-	51	-	211	-
Time in days between reference date and last Cervarix dose [in category]	within 30 days	16	17.2	0	0.0	0	0.0	0	0.0	16	17.2
	between 31 to 60 days	3	3.2	0	0.0	0	0.0	0	0.0	3	3.2
	between 61 to 180 days	17	18.3	0	0.0	0	0.0	0	0.0	17	18.3
	more than 180 days	57	61.3	0	0.0	0	0.0	0	0.0	57	61.3
	NA	0	-	95	-	65	-	51	-	211	-
Year of 1st Cervarix dose	2006	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	2007	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	2008	16	17.2	0	0.0	0	0.0	0	0.0	16	17.2
	2009	60	64.5	0	0.0	0	0.0	0	0.0	60	64.5
	2010	17	18.3	0	0.0	0	0.0	0	0.0	17	18.3
	2011	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	NA	0	-	95	-	65	-	51	-	211	-

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort

MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n = number of subjects in a given category
Value = value of the considered parameter
% = n / Number of subjects with available results x 100
SD = Standard deviation

Table 92 Drugs prescription by exposed/non-exposed status - Diagnosis date - All cases (Total cohort)

		EXP N = 93		NNEXP N = 95		MALE N = 65		HIST N = 51		Total N = 304	
Characteristics	**Categories**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Prescription of autoimmune disease drugs	Yes	83	89.2	88	92.6	56	86.2	45	88.2	272	89.5
	No	10	10.8	7	7.4	9	13.8	6	11.8	32	10.5
Chronic use of autoimmune disease drugs	Yes	77	92.8	81	92.0	50	89.3	42	93.3	250	91.9
	No	6	7.2	7	8.0	6	10.7	3	6.7	22	8.1
	NA	10	-	7	-	9	-	6	-	32	-

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n/% = number / percentage of subjects in a given category

Table 93 P-Values comparing exposed female and unexposed female cohorts - Diagnosis date - All cases (Total cohort)

Variable	P value
Age at reference date [years] [in cat]	0.4514
Age at reference date [years]	0.4712
Region	0.0625
Region [in cat]	0.0804
Number of years in CPRD GOLD at reference date	<.0001
Number of years in CPRD GOLD at reference date [in cat]	0.0011
HES linkage	0.8654
Number of GP consultations the year previous reference date	0.8140
Number of GP consultations the year previous reference date [in cat]	0.7615
Any vaccines in the year previous the reference date	0.7720
Any vaccines in the follow-up period	0.0540
Novel adjuvanted vaccines in the follow-up period	0.3109
Live attenuated vaccines in the year previous the reference date	0.7214
Other vaccines in the year previous the reference date	0.7474
Other vaccines in the follow-up period	0.0876
Use of autoimmune disease drugs	0.4185
Chronic use of autoimmune disease drugs	0.8580

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
n/%=number/percentage of subjects in a given category
Chi-square and T-test statistics were computed respectively for categorical and continuous variables

Table 94 P-Values comparing unexposed concurrent male and historical male cohorts - Diagnosis date - All cases (Total cohort)

Variable	P value
Age at reference date [years] [in cat]	0.0065
Age at reference date [years]	0.0026
Region	0.3090
Region [in cat]	0.3694
Number of years in CPRD GOLD at reference date	0.1535
Number of years in CPRD GOLD at reference date [in cat]	0.7280
HES linkage	0.7008
Number of GP consultations the year previous reference date	0.5210
Number of GP consultations the year previous reference date [in cat]	0.6354
Any vaccines in the year previous the reference date	0.0035
Any vaccines in the follow-up period	0.8623
Novel adjuvanted vaccines in the follow-up period	0.3737
Live attenuated vaccines in the year previous the reference date	0.0460
Other vaccines in the year previous the reference date	0.0071
Other vaccines in the follow-up period	0.2569
Use of autoimmune disease drugs	0.7402
Chronic use of autoimmune disease drugs	0.4779

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
n/%=number/percentage of subjects in a given category
Chi-square and T-test statistics were computed respectively for categorical and continuous variables

Table 95 Frequency of autoimmune diseases during the one year follow-up period by exposed/non-exposed status - Main Analysis - Confirmed and Non-Confirmed cases (Total cohort)

		EXP N = 64964		NNEXP N = 64973		MALE N = 64974		HIST N = 64965		Total N = 259876	
Characteristics	**Categories**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**
Coprimary endpoints within 1 year follow-up period	Neuroinflammatory Ophthalmic autoimmune diseases	4	6.16	7	10.77	3	4.62	2	3.08	16	6.16
	Other autoimmune diseases	51	78.51	41	63.10	28	43.09	19	29.25	139	53.49

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n = number of subjects in a given category
Per 100000 = n/Number of subjects with available results*100000
Neuroinflammatory/Ophthalmic autoimmune diseases included: Multiple Sclerosis, Transverse Myelitis, Optic Neuritis, Guillain Barré Syndrome, Acute disseminated encephalomyelitis, Autoimmune Peripheral neuropathies & plexopathies and Autoimmune Uveitis. Note: that 1 AD was classified as Other AD
Follow-up period 1 year for all the cohorts

Table 96 Frequency of autoimmune diseases during the one year follow-up period by exposed/non-exposed status - Main Analysis - Confirmed cases (Total cohort)

		EXP N = 64964		NNEXP N = 64973		MALE N = 64974		HIST N = 64965		Total N = 259876	
Characteristics	**Categories**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**
Coprimary endpoints within 1 year follow-up period	Neuroinflammatory/Ophthalmic autoimmune diseases	0	0.00	1	1.54	1	1.54	1	1.54	3	1.15
	Other autoimmune diseases	38	58.49	27	41.56	26	40.02	15	23.09	106	40.79

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n = number of subjects in a given category
Per 100000 = n/Number of subjects with available results*100000
Neuroinflammatory/Ophthalmic autoimmune diseases included: Multiple Sclerosis, Transverse Myelitis, Optic Neuritis, Guillain Barré Syndrome, Acute disseminated encephalomyelitis, Autoimmune Peripheral neuropathies & plexopathies and Autoimmune Uveitis. Note: that 1 AD was classified as Other AD
Follow-up period 1 year for all the cohorts

Table 97 Frequency of autoimmune diseases during the one year follow-up period by exposed/non-exposed status - Main Analysis - Confirmed and Non-Confirmed cases (N=AD) (Total cohort)

		EXP N = 64964		NNEXP N = 64974		MALE N = 64974		HIST N = 64965		Total N = 259877	
Characteristics	**Categories**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**
Individual autoimmune diseases within 1 year follow-up period	Acute disseminated encephalomyelitis	1	1.54	0	0.00	0	0.00	0	0.00	1	0.38
	Autoimmune Thyroiditis	26	40.02	18	27.70	2	3.08	3	4.62	49	18.86
	Autoimmune Uveitis	2	3.08	5	7.70	2	3.08	1	1.54	10	3.85
	Crohn diseases	8	12.31	5	7.70	4	6.16	2	3.08	19	7.31
	Guillain-Barre Syndrome	0	0.00	0	0.00	1	1.54	1	1.54	2	0.77
	Idiopathic Thrombocytopenia Purpura	1	1.54	1	1.54	0	0.00	2	3.08	4	1.54
	Inflammatory Bowel Diseases	0	0.00	0	0.00	0	0.00	1	1.54	1	0.38
	Juvenile Rheumatoid Arthritis	1	1.54	0	0.00	0	0.00	1	1.54	2	0.77
	Multiple Sclerosis	0	0.00	1	1.54	0	0.00	0	0.00	1	0.38
	Optic Neuritis	1	1.54	1	1.54	0	0.00	0	0.00	2	0.77
	Other NOAD	1	1.54	0	0.00	0	0.00	0	0.00	1	0.38
	Psoriatic Arthritis	1	1.54	1	1.54	0	0.00	0	0.00	2	0.77
	Rheumatoid Arthritis	1	1.54	0	0.00	0	0.00	0	0.00	1	0.38
	Type 1 Diabetes Mellitus	8	12.31	16	24.63	20	30.78	8	12.31	52	20.01
	Ulcerative Colitis	4	6.16	1	1.54	2	3.08	2	3.08	9	3.46

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n = number of subjects in a given category
Per 100000 = n/Number of subjects with available results*100000
Neuroinflammatory/Ophthalmic autoimmune diseases included: Multiple Sclerosis, Transverse Myelitis, Optic Neuritis, Guillain Barré Syndrome, Acute dissiminated encephalomyelitis, Autoimmune Peripheral neuropathies & plexopathies and Autoimmune Uveitis. Note: that 1 AD was classified as Other AD
Follow-up period 1 year for all the cohorts
One subject has simultaneously diabetes and thyroid diseases

Table 98 Frequency of autoimmune diseases during the one year follow-up period by exposed/non-exposed status - Main Analysis - Confirmed cases (N=AD) (Total cohort)

		EXP N = 64964		NNEXP N = 64974		MALE N = 64974		HIST N = 64965		Total N = 259877	
Characteristics	**Categories**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**
Individual autoimmune diseases within 1 year follow-up period	Autoimmune Thyroiditis	15	23.09	4	6.16	0	0.00	0	0.00	19	7.31
	Crohn diseases	6	9.24	5	7.70	4	6.16	1	1.54	16	6.16
	Guillain-Barre Syndrome	0	0.00	0	0.00	1	1.54	1	1.54	2	0.77
	Idiopathic Thrombocytopenia Purpura	1	1.54	1	1.54	0	0.00	2	3.08	4	1.54
	Inflammatory Bowel Diseases	0	0.00	0	0.00	0	0.00	1	1.54	1	0.38
	Juvenile Rheumatoid Arthritis	1	1.54	0	0.00	0	0.00	1	1.54	2	0.77
	Multiple Sclerosis	0	0.00	1	1.54	0	0.00	0	0.00	1	0.38
	Other AD	1	1.54	0	0.00	0	0.00	0	0.00	1	0.38
	Psoriatic Arthritis	1	1.54	1	1.54	0	0.00	0	0.00	2	0.77
	Rheumatoid Arthritis	1	1.54	0	0.00	0	0.00	0	0.00	1	0.38
	Type 1 Diabetes Mellitus	8	12.31	16	24.63	20	30.78	8	12.31	52	20.01
	Ulcerative Colitis	4	6.16	0	0.00	2	3.08	2	3.08	8	3.08

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n = number of subjects in a given category
Per 100000 = n/Number of subjects with available results*100000
Neuroinflammatory/Ophthalmic autoimmune diseases included: Multiple Sclerosis, Transverse Myelitis, Optic Neuritis, Guillain Barré Syndrome, Acute dissiminated encephalomyelitis, Autoimmune Peripheral neuropathies & plexopathies and Autoimmune Uveitis. Note: that 1 AD was classified as Other AD
Follow-up period 1 year for all the cohorts

Table 99 Frequency of autoimmune disease during the specific time period by exposed/non-exposed status - Main Analysis - Confirmed and Non-Confirmed cases (Total cohort)

		EXP N = 64964		NNEXP N = 64973		MALE N = 64974		HIST N = 64965		Total N = 259876	
Characteristics	**Categories**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**
Individual autoimmune diseases within 2 months of FU period	Guillain-Barre Syndrome	0	0.00	0	0.00	0	0.00	1	1.54	1	0.38

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n = number of subjects in a given category
Per 100000 = n/Number of subjects with available results*100000
Autoimmune diseases within 2 months included: Guillain Barré Syndrome and Autoimmune Haemolytic Anaemia
FU:Specific time disease follow-up period

Table 100 Frequency of autoimmune disease during the specific time period by exposed/non-exposed status - Main Analysis - Confirmed cases (Total cohort)

		EXP N = 64964		NNEXP N = 64973		MALE N = 64974		HIST N = 64965		Total N = 259876	
Characteristics	**Categories**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**
Individual autoimmune diseases within 2 months of FU period	Guillain-Barre Syndrome	0	0.00	0	0.00	0	0.00	1	1.54	1	0.38

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n = number of subjects in a given category
Per 100000 = n/Number of subjects with available results*100000
Autoimmune diseases within 2 months included: Guillain Barré Syndrome and Autoimmune Haemolytic Anaemia
FU:Specific time disease follow-up period

Table 101 Frequency of autoimmune disease during the specific time period by exposed/non-exposed status - Main Analysis - Confirmed and Non-Confirmed cases (Total cohort)

		EXP N = 64964		NNEXP N = 64973		MALE N = 64974		HIST N = 64965		Total N = 259876	
Characteristics	**Categories**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**
Individual autoimmune disease within 6 months of FU period	Idiopathic Thrombocytopenia Purpura	1	1.54	1	1.54	0	0.00	1	1.54	3	1.15

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n = number of subjects in a given category
Per 100000 = n/Number of subjects with available results*100000
Autoimmune diseases within 6 months included: Idiopathic Thrombocytopenia Purpura
FU:Specific time disease follow-up period

Table 102 Frequency of autoimmune disease during the specific time period by exposed/non-exposed status - Main Analysis - Confirmed cases (Total cohort)

		EXP N = 64964		NNEXP N = 64973		MALE N = 64974		HIST N = 64965		Total N = 259876	
Characteristics	**Categories**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**
Individual autoimmune disease within 6 months of FU period	Idiopathic Thrombocytopenia Purpura	1	1.54	1	1.54	0	0.00	1	1.54	3	1.15

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n = number of subjects in a given category
Per 100000 = n/Number of subjects with available results*100000
Autoimmune diseases within 6 months included: Idiopathic Thrombocytopenia Purpura
FU:Specific time disease follow-up period

Table 103 Frequency of autoimmune disease during the specific time period by exposed/non-exposed status - Main Analysis - Confirmed and Non-Confirmed cases (N=AD) (Total cohort)

		EXP N = 64964		NNEXP N = 64974		MALE N = 64974		HIST N = 64965		Total N = 259877	
Characteristics	**Categories**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**
Individual autoimmune diseases within 12 months of FU period	Acute disseminated encephalomyelitis	1	1.54	0	0.00	0	0.00	0	0.00	1	0.38
	Autoimmune Thyroiditis	26	40.02	18	27.70	2	3.08	3	4.62	49	18.86
	Autoimmune Uveitis	2	3.08	5	7.70	2	3.08	1	1.54	10	3.85
	Crohn diseases	8	12.31	5	7.70	4	6.16	2	3.08	19	7.31
	Inflammatory Bowel Diseases	0	0.00	0	0.00	0	0.00	1	1.54	1	0.38
	Juvenile Rheumatoid Arthritis	1	1.54	0	0.00	0	0.00	1	1.54	2	0.77
	Multiple Sclerosis	0	0.00	1	1.54	0	0.00	0	0.00	1	0.38
	Optic Neuritis	1	1.54	1	1.54	0	0.00	0	0.00	2	0.77
	Other AD	1	1.54	0	0.00	0	0.00	0	0.00	1	0.38
	Psoriatic Arthritis	1	1.54	1	1.54	0	0.00	0	0.00	2	0.77
	Rheumatoid Arthritis	1	1.54	0	0.00	0	0.00	0	0.00	1	0.38
	Type 1 Diabetes Mellitus	8	12.31	16	24.63	20	30.78	8	12.31	52	20.01
	Ulcerative Colitis	4	6.16	1	1.54	2	3.08	2	3.08	9	3.46

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n = number of subjects in a given category
Per 100000 = n/Number of subjects with available results*100000
FU:Specific time disease follow-up period
One subject has simultaneously diabetes and thyroid diseases

Table 104 Frequency of autoimmune disease during the specific time period by exposed/non-exposed status - Main Analysis - Confirmed cases (N=AD) (Total cohort)

		EXP N = 64964		NNEXP N = 64974		MALE N = 64974		HIST N = 64965		Total N = 259877	
Characteristics	**Categories**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**
Individual autoimmune diseases within 12 months of FU period	Autoimmune Thyroiditis	15	23.09	4	6.16	0	0.00	0	0.00	19	7.31
	Crohn diseases	6	9.24	5	7.70	4	6.16	1	1.54	16	6.16
	Inflammatory Bowel Diseases	0	0.00	0	0.00	0	0.00	1	1.54	1	0.38
	Juvenile Rheumatoid Arthritis	1	1.54	0	0.00	0	0.00	1	1.54	2	0.77
	Multiple Sclerosis	0	0.00	1	1.54	0	0.00	0	0.00	1	0.38
	Other AD	1	1.54	0	0.00	0	0.00	0	0.00	1	0.38
	Psoriatic Arthritis	1	1.54	1	1.54	0	0.00	0	0.00	2	0.77
	Rheumatoid Arthritis	1	1.54	0	0.00	0	0.00	0	0.00	1	0.38
	Type 1 Diabetes Mellitus	8	12.31	16	24.63	20	30.78	8	12.31	52	20.01
	Ulcerative Colitis	4	6.16	0	0.00	2	3.08	2	3.08	8	3.08

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n = number of subjects in a given category
Per 100000 = n/Number of subjects with available results*100000
FU:Specific time disease follow-up period

Table 105 Incidence rate of Neuroinflammatory/Ophthalmic autoimmune diseases in Female Cohorts - Main Analysis - Confirmed cases (Total cohort)

				95% CI	
Cohort	**Number of cases**	**Person-time (in years)**	**Incidence Rate (per 100,000 PY)**	**LL**	**UL**
Exposed Female	0	64705	0.000	0.000	5.701
Non-Exposed Female	1	64841	1.542	0.039	8.593

LL, UL = 95% Lower and Upper exact confidence limits

Table 106 Incidence rate difference of Neuroinflammatory/Ophthalmic autoimmune diseases in Female Cohorts - Main Analysis - Confirmed cases (Total cohort)

Characteristics	**IRD Calculation**
IRD(exp-unexp OR conc-hist)	-1.542

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 107 Incidence rate of Other autoimmune diseases in Female Cohorts - Main Analysis - Confirmed cases (Total cohort)

				95% CI	
Cohort	**Number of cases**	**Person-time (in years)**	**Incidence Rate (per 100,000 PY)**	**LL**	**UL**
Exposed Female	38	64705	58.728	41.560	80.609
Non-Exposed Female	27	64841	41.640	27.441	60.584

LL, UL = 95% Lower and Upper exact confidence limits

Table 108 Incidence rate ratios of Other autoimmune diseases in Female Cohorts - Main Analysis - Confirmed cases (Total cohort)

	IRR Calculation					
		95%CI of RR			**95%CI of RR**	
Autoimmune diseases	**Crude Incidence Rate Ratio**	**LL**	**UL**	**Adjusted Incidence Rate Ratio**	**LL**	**UL**
Other autoimmune diseases	1.409	0.861	2.308	1.410	0.861	2.309

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted by age group: age group [9-17] and [18-25]

Table 109 Incidence rate difference of Other autoimmune diseases in Female Cohorts - Main Analysis - Confirmed cases (Total cohort)

Characteristics	IRD Calculation
IRD(exp-unexp OR conc-hist)	17.088

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 110 Incidence rate ratios of Other autoimmune diseases in Female Cohorts (covariates adjusted) - Main Analysis - Confirmed cases (Total cohort)

	IRR Calculation		
		95%CI of RR	
Autoimmune diseases	Adjusted Incidence Rate Ratio	LL	UL
Other autoimmune diseases	1.388	0.844	2.283

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted for other covariates: age group [9-17] and [18-25], healthcare resources utilization in quartile, regions (North England, South England, Midlands & Ireland Scotland Wales), any vaccines during the year prior to the reference date

Table 111 Incidence rate of Neuroinflammatory/Ophthalmic autoimmune diseases in Female Cohorts - Main Analysis - All cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Exposed Female	4	64705	6.182	1.684	15.828
Non-Exposed Female	7	64841	10.796	4.340	22.243

LL, UL = 95% Lower and Upper exact confidence limits

Table 112 Incidence rate ratios of Neuroinflammatory/Ophthalmic diseases in Female Cohorts - Main Analysis - All cases (Total cohort)

	IRR Calculation					
		95%CI of RR			95%CI of RR	
Autoimmune diseases	Crude Incidence Rate Ratio	LL	UL	Adjusted Incidence Rate Ratio	LL	UL
Neuroinflammatory/Ophthalmic autoimmune diseases	0.572	0.168	1.955	0.572	0.168	1.955

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted by age group: age group [9-17] and [18-25]

Table 113 Incidence rate difference of Neuroinflammatory/Ophthalmic autoimmune diseases in Female Cohorts - Main Analysis - All cases (Total cohort)

Characteristics	IRD Calculation
IRD(exp-unexp OR conc-hist)	-4.614

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 114 Incidence rate ratios of Neuroinflammatory/Ophthalmic diseases in Female Cohorts (covariates adjusted) - Main Analysis - All cases (Total cohort)

	IRR Calculation		
		95%CI of RR	
Autoimmune diseases	Adjusted Incidence Rate Ratio	LL	UL
Neuroinflammatory/Ophthalmic autoimmune diseases	0.584	0.169	2.023

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted for other covariates: age group [9-17] and [18-25], healthcare resources utilization in quartile, regions (North England, South England, Midlands & Ireland Scotland Wales), any vaccines during the year prior to the reference date

Table 115 Incidence rate of Other autoimmune diseases in Female Cohorts - Main Analysis - All cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 10,000 PY)	LL	UL
Exposed Female	51	64705	7.882	5.869	10.363
Non-Exposed Female	41	64841	6.323	4.538	8.578

LL, UL = 95% Lower and Upper exact confidence limits

Table 116 Incidence rate ratios of Other autoimmune diseases in Female Cohorts - Main Analysis - All cases (Total cohort)

	IRR Calculation					
		95%CI of RR			95%CI of RR	
Autoimmune diseases	Crude Incidence Rate Ratio	LL	UL	Adjusted Incidence Rate Ratio	LL	UL
Other autoimmune diseases	1.246	0.826	1.879	1.246	0.826	1.879

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted by age group: age group [9-17] and [18-25]

Table 117 Incidence rate difference of Other autoimmune diseases in Female Cohorts - Main Analysis - All cases (Total cohort)

Characteristics	IRD Calculation
IRD(exp-unexp OR conc-hist)	1.559

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 118 Incidence rate ratios of Other autoimmune diseases in Female Cohorts (covariates adjusted) - Main Analysis - All cases (Total cohort)

	IRR Calculation		
		95%CI of RR	
Autoimmune diseases	Adjusted Incidence Rate Ratio	LL	UL
Other autoimmune diseases	1.207	0.798	1.826

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted for other covariates: age group [9-17] and [18-25], healthcare resources utilization in quartile, regions (North England, South England, Midlands & Ireland Scotland Wales), any vaccines during the year prior to the reference date

Table 119 Incidence rate of Neuroinflammatory/Ophthalmic autoimmune diseases in Male Cohorts - Main Analysis - Confirmed cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Concurrent Male	1	64859	1.542	0.039	8.590
Historical Male	1	64868	1.542	0.039	8.589

LL, UL = 95% Lower and Upper exact confidence limits

Table 120 Incidence rate ratios of Neuroinflammatory/Ophthalmic diseases in Male Cohorts - Main Analysis - Confirmed cases (Total cohort)

	IRR Calculation					
		95%CI of RR			95%CI of RR	
Autoimmune diseases	Crude Incidence Rate Ratio	LL	UL	Adjusted Incidence Rate Ratio	LL	UL
Neuroinflammatory/Ophthalmic autoimmune diseases	1.000	0.063	15.987	0.949	0.059	15.177

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted by age group: age group [9-17] and [18-25]

Table 121 Incidence rate difference of Neuroinflammatory/Ophthalmic autoimmune diseases in Male Cohorts - Main Analysis - Confirmed cases (Total cohort)

Characteristics	IRD Calculation
IRD(exp-unexp OR conc-hist)	0.000

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 122 Incidence rate of Other autoimmune diseases in Male Cohorts - Main Analysis - Confirmed cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Concurrent Male	26	64859	40.087	26.186	58.737
Historical Male	15	64868	23.124	12.942	38.139

LL, UL = 95% Lower and Upper exact confidence limits

Table 123 Incidence rate ratios of Other autoimmune diseases in Male Cohorts - Main Analysis - Confirmed cases (Total cohort)

	IRR Calculation					
		95%CI of RR			95%CI of RR	
Autoimmune diseases	Crude Incidence Rate Ratio	LL	UL	Adjusted Incidence Rate Ratio	LL	UL
Other autoimmune diseases	1.733	0.918	3.272	1.769	0.935	3.347

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted by age group: age group [9-17] and [18-25]

Table 124 Incidence rate difference of Other autoimmune diseases in Male Cohorts - Main Analysis - Confirmed cases (Total cohort)

Characteristics	IRD Calculation
IRD(exp-unexp OR conc-hist)	16.964

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 125 Incidence rate ratios of Other autoimmune diseases in Male Cohorts (covariates adjusted) - Main Analysis - Confirmed cases (Total cohort)

	IRR Calculation		
		95%CI of RR	
Autoimmune diseases	Adjusted Incidence Rate Ratio	LL	UL
Other autoimmune diseases	1.793	0.947	3.394

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted for other covariates: age group [9-17] and [18-25], healthcare resources utilization in quartile, regions (North England, South England, Midlands & Ireland Scotland Wales), any vaccines during the year prior to the reference date

Table 126 Incidence rate of Neuroinflammatory/Ophthalmic autoimmune diseases in Male Cohorts - Main Analysis - All cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Concurrent Male	3	64859	4.625	0.954	13.518
Historical Male	2	64868	3.083	0.373	11.137

LL, UL = 95% Lower and Upper exact confidence limits

Table 127 Incidence rate ratios of Neuroinflammatory/Ophthalmic diseases in Male Cohorts - Main Analysis - All cases (Total cohort)

	IRR Calculation					
		95%CI of RR			95%CI of RR	
Autoimmune diseases	Crude Incidence Rate Ratio	LL	UL	Adjusted Incidence Rate Ratio	LL	UL
Neuroinflammatory/Ophthalmic autoimmune diseases	1.500	0.251	8.976	1.729	0.286	10.470

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted by age group: age group [9-17] and [18-25]

Table 128 Incidence rate difference of Neuroinflammatory/Ophthalmic autoimmune diseases in Male Cohorts - Main Analysis - All cases (Total cohort)

Characteristics	IRD Calculation
IRD(exp-unexp OR conc-hist)	1.542

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 129 Incidence rate of Other autoimmune diseases in Male Cohorts - Main Analysis - All cases (Total cohort)

				95% CI	
Cohort	**Number of cases**	**Person-time (in years)**	**Incidence Rate (per 100,000 PY)**	**LL**	**UL**
Concurrent Male	28	64859	43.171	28.687	62.394
Historical Male	19	64868	29.290	17.635	45.740

LL, UL = 95% Lower and Upper exact confidence limits

Table 130 Incidence rate ratios of Other autoimmune diseases in Male Cohorts - Main Analysis - All cases (Total cohort)

	IRR Calculation					
		95%CI of RR			95%CI of RR	
Autoimmune diseases	**Crude Incidence Rate Ratio**	**LL**	**UL**	**Adjusted Incidence Rate Ratio**	**LL**	**UL**
Other autoimmune diseases	1.474	0.823	2.639	1.520	0.847	2.727

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted by age group: age group [9-17] and [18-25]

Table 131 Incidence rate difference of Other autoimmune diseases in Male Cohorts - Main Analysis - All cases (Total cohort)

Characteristics	**IRD Calculation**
IRD(exp-unexp OR conc-hist)	13.881

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 132 Incidence rate of Acute Disseminated Encephalomyelitis in Female Cohorts - Main Analysis - All cases (Total cohort)

				95% CI	
Cohort	**Number of cases**	**Person-time (in years)**	**Incidence Rate (per 100,000 PY)**	**LL**	**UL**
Exposed Female	1	64705	1.545	0.039	8.611
Non-Exposed Female	0	64841	0.000	0.000	5.689

LL, UL = 95% Lower and Upper exact confidence limits

Table 133 Incidence rate of Autoimmune Hepatitis in Female Cohorts - Main Analysis - Confirmed cases (Total cohort)

				95% CI	
Cohort	**Number of cases**	**Person-time (in years)**	**Incidence Rate (per 100,000 PY)**	**LL**	**UL**
Exposed Female	0	64705	0.000	0.000	5.701
Non-Exposed Female	0	64841	0.000	0.000	5.689

LL, UL = 95% Lower and Upper exact confidence limits

Table 134 Incidence rate of Autoimmune Hepatitis in Female Cohorts - Main Analysis - All cases (Total cohort)

				95% CI	
Cohort	**Number of cases**	**Person-time (in years)**	**Incidence Rate (per 100,000 PY)**	**LL**	**UL**
Exposed Female	0	64705	0.000	0.000	5.701
Non-Exposed Female	0	64841	0.000	0.000	5.689

LL, UL = 95% Lower and Upper exact confidence limits

Table 135 Incidence rate of Autoimmune Thyroiditis in Female Cohorts - Main Analysis - Confirmed cases (Total cohort)

				95% CI	
Cohort	**Number of cases**	**Person-time (in years)**	**Incidence Rate (per 100,000 PY)**	**LL**	**UL**
Exposed Female	15	64705	23.182	12.975	38.236
Non-Exposed Female	4	64841	6.169	1.681	15.795

LL, UL = 95% Lower and Upper exact confidence limits

Table 136 Incidence rate ratios of Autoimmune Thyroiditis in Female Cohorts - Main Analysis - Confirmed cases (Total cohort)

	IRR Calculation					
		95%CI of RR			95%CI of RR	
Autoimmune diseases	**Crude Incidence Rate Ratio**	**LL**	**UL**	**Adjusted Incidence Rate Ratio**	**LL**	**UL**
Autoimmune Thyroiditis	3.755	1.246	11.315	3.753	1.246	11.307

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted by age group: age group [9-17] and [18-25]

Table 137 Incidence rate difference of Autoimmune Thyroiditis diseases in Female Cohorts - Main Analysis - Confirmed cases (Total cohort)

Characteristics	**IRD Calculation**
IRD(exp-unexp OR conc-hist)	17.013

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 138 Incidence rate ratios of Autoimmune Thyroiditis in Female Cohorts (covariates adjusted) - Main Analysis - Confirmed cases (Total cohort)

	IRR Calculation		
		95%CI of RR	
Autoimmune diseases	Adjusted Incidence Rate Ratio	LL	UL
Autoimmune Thyroiditis	3.535	1.168	10.704

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted for other covariates: age group [9-17] and [18-25], healthcare resources utilization in quartile, regions (North England, South England, Midlands & Ireland Scotland Wales), any vaccines during the year prior to the reference date

Table 139 Incidence rate of Autoimmune Thyroiditis in Female Cohorts - Main Analysis - All cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Exposed Female	26	64705	40.183	26.249	58.877
Non-Exposed Female	18	64841	27.760	16.452	43.873

LL, UL = 95% Lower and Upper exact confidence limits

Table 140 Incidence rate ratios of Autoimmune Thyroiditis in Female Cohorts - Main Analysis - All cases (Total cohort)

	IRR Calculation					
		95%CI of RR			95%CI of RR	
Autoimmune diseases	Crude Incidence Rate Ratio	LL	UL	Adjusted Incidence Rate Ratio	LL	UL
Autoimmune Thyroiditis	1.447	0.793	2.638	1.446	0.793	2.637

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted by age group: age group [9-17] and [18-25]

Table 141 Incidence rate difference of Autoimmune Thyroiditis diseases in Female Cohorts - Main Analysis - All cases (Total cohort)

Characteristics	IRD Calculation
IRD(exp-unexp OR conc-hist)	12.422

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 142 Incidence rate ratios of Autoimmune Thyroiditis in Female Cohorts (covariates adjusted) - Main Analysis - All cases (Total cohort)

	IRR Calculation		
		95%CI of RR	
Autoimmune diseases	Adjusted Incidence Rate Ratio	LL	UL
Autoimmune Thyroiditis	1.356	0.741	2.482

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted for other covariates: age group [9-17] and [18-25], healthcare resources utilization in quartile, regions (North England, South England, Midlands & Ireland Scotland Wales), any vaccines during the year prior to the reference date

Table 143 Incidence rate of Autoimmune Thyroiditis in Male Cohorts - Main Analysis - All cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Concurrent Male	2	64859	3.084	0.373	11.139
Historical Male	3	64868	4.625	0.954	13.515

LL, UL = 95% Lower and Upper exact confidence limits

Table 144 Incidence rate ratios of Autoimmune Thyroiditis in Male Cohorts - Main Analysis - All cases (Total cohort)

	IRR Calculation				
		95%CI of RR			95%CI of RR
Autoimmune diseases	Crude Incidence Rate Ratio	LL	UL	Adjusted Incidence Rate Ratio	LL	UL
Autoimmune Thyroiditis	0.667	0.111	3.990	0.760	0.126	4.602

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted by age group: age group [9-17] and [18-25]

Table 145 Incidence rate difference of Autoimmune Thyroiditis diseases in Male Cohorts - Main Analysis - All cases (Total cohort)

Characteristics	IRD Calculation
IRD(exp-unexp OR conc-hist)	-1.541

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 146 Incidence rate ratios of Autoimmune Thyroiditis in Male Cohorts (covariates adjusted) - Main Analysis - All cases (Total cohort)

	IRR Calculation		
		95%CI of RR	
Autoimmune diseases	Adjusted Incidence Rate Ratio	LL	UL
Autoimmune Thyroiditis	0.761	0.126	4.613

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted for other covariates: age group [9-17] and [18-25], healthcare resources utilization in quartile, regions (North England, South England, Midlands & Ireland Scotland Wales), any vaccines during the year prior to the reference date

Table 147 Incidence rate of Autoimmune Uveitis in Female Cohorts - Main Analysis - All cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Exposed Female	2	64705	3.091	0.374	11.166
Non-Exposed Female	5	64841	7.711	2.504	17.995

LL, UL = 95% Lower and Upper exact confidence limits

Table 148 Incidence rate of Autoimmune Uveitis in Male Cohorts - Main Analysis - All cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Concurrent Male	2	64859	3.084	0.373	11.139
Historical Male	1	64868	1.542	0.039	8.589

LL, UL = 95% Lower and Upper exact confidence limits

Table 149 Incidence rate of Autoimmune Crohn diseases in Female Cohorts - Main Analysis - Confirmed cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Exposed Female	6	64705	9.273	3.403	20.183
Non-Exposed Female	5	64841	7.711	2.504	17.995

LL, UL = 95% Lower and Upper exact confidence limits

Table 150 Incidence rate ratios of Crohn diseases in Female Cohorts - Main Analysis - Confirmed cases (Total cohort)

	IRR Calculation					
		95%CI of RR			95%CI of RR	
Autoimmune diseases	Crude Incidence Rate Ratio	LL	UL	Adjusted Incidence Rate Ratio	LL	UL
Crohn diseases	1.202	0.367	3.938	1.205	0.368	3.949

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted by age group: age group [9-17] and [18-25]

Table 151 Incidence rate difference of Autoimmune Crohn diseases in Female Cohorts - Main Analysis - Confirmed cases (Total cohort)

Characteristics	IRD Calculation
IRD(exp-unexp OR conc-hist)	1.562

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 152 Incidence rate ratios of Crohn diseases in Female Cohorts (covariates adjusted) - Main Analysis - Confirmed cases (Total cohort)

	IRR Calculation		
		95%CI of RR	
Autoimmune diseases	Adjusted Incidence Rate Ratio	LL	UL
Crohn diseases	1.181	0.356	3.921

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted for other covariates: age group [9-17] and [18-25], healthcare resources utilization in quartile, regions (North England, South England, Midlands & Ireland Scotland Wales), any vaccines during the year prior to the reference date

Table 153 Incidence rate of Crohn diseases in Male Cohorts - Main Analysis - Confirmed cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Concurrent Male	4	64859	6.167	1.680	15.791
Historical Male	1	64868	1.542	0.039	8.589

LL, UL = 95% Lower and Upper exact confidence limits

Table 154 Incidence rate ratios of Crohn diseases in Male Cohorts - Main Analysis - Confirmed cases (Total cohort)

	IRR Calculation					
		95%CI of RR			95%CI of RR	
Autoimmune diseases	Crude Incidence Rate Ratio	LL	UL	Adjusted Incidence Rate Ratio	LL	UL
Crohn diseases	4.000	0.447	35.786	4.219	0.468	38.024

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted by age group: age group [9-17] and [18-25]

Table 155 Incidence rate difference of Crohn diseases in Male Cohorts - Main Analysis - Confirmed cases (Total cohort)

Characteristics	IRD Calculation
IRD(exp-unexp OR conc-hist)	4.626

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 156 Incidence rate of Crohn diseases in Female Cohorts - Main Analysis - All cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Exposed Female	8	64705	12.364	5.338	24.362
Non-Exposed Female	5	64841	7.711	2.504	17.995

LL, UL = 95% Lower and Upper exact confidence limits

Table 157 Incidence rate ratios of Crohn diseases in Female Cohorts - Main Analysis - All cases (Total cohort)

	IRR Calculation					
		95%CI of RR			95%CI of RR	
Autoimmune diseases	Crude Incidence Rate Ratio	LL	UL	Adjusted Incidence Rate Ratio	LL	UL
Crohn diseases	1.602	0.524	4.898	1.606	0.525	4.909

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted by age group: age group [9-17] and [18-25]

Table 158 Incidence rate difference of Crohn diseases in Female Cohorts - Main Analysis - All cases (Total cohort)

Characteristics	IRD Calculation
IRD(exp-unexp OR conc-hist)	4.653

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 159 Incidence rate ratios of Crohn diseases in Female Cohorts (covariates adjusted) - Main Analysis - All cases (Total cohort)

	IRR Calculation		
		95%CI of RR	
Autoimmune diseases	Adjusted Incidence Rate Ratio	LL	UL
Crohn diseases	1.550	0.502	4.789

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted for other covariates: age group [9-17] and [18-25], healthcare resources utilization in quartile, regions (North England, South England, Midlands & Ireland Scotland Wales), any vaccines during the year prior to the reference date

Table 160 Incidence rate of Crohn diseases in Male Cohorts - Main Analysis - All cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Concurrent Male	4	64859	6.167	1.680	15.791
Historical Male	2	64868	3.083	0.373	11.137

LL, UL = 95% Lower and Upper exact confidence limits

Table 161 Incidence rate ratios of Crohn diseases in Male Cohorts - Main Analysis - All cases (Total cohort)

	IRR Calculation				
		95%CI of RR			95%CI of RR
Autoimmune diseases	Crude Incidence Rate Ratio	LL	UL	Adjusted Incidence Rate Ratio	LL	UL
Crohn diseases	2.000	0.366	10.919	2.064	0.376	11.340

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted by age group: age group [9-17] and [18-25]

Table 162 Incidence rate difference of Crohn diseases in Male Cohorts - Main Analysis - All cases (Total cohort)

Characteristics	IRD Calculation
IRD(exp-unexp OR conc-hist)	3.084

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 163 Incidence rate of Inflammatory bowel diseases in Male Cohorts - Main Analysis - Confirmed cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Concurrent Male	0	64859	0.000	0.000	5.688
Historical Male	1	64868	1.542	0.039	8.589

LL, UL = 95% Lower and Upper exact confidence limits

Table 164 Incidence rate of Inflammatory bowel diseases in Female Cohorts - Main Analysis - All cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Exposed Female	0	64705	0.000	0.000	5.701
Non-Exposed Female	0	64841	0.000	0.000	5.689

LL, UL = 95% Lower and Upper exact confidence limits

Table 165 Incidence rate of Inflammatory bowel diseases in Male Cohorts - Main Analysis - All cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Concurrent Male	0	64859	0.000	0.000	5.688
Historical Male	1	64868	1.542	0.039	8.589

LL, UL = 95% Lower and Upper exact confidence limits

Table 166 Incidence rate of Juvenile Rheumatoid Arthritis in Female Cohorts - Main Analysis - Confirmed cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Exposed Female	1	64705	1.545	0.039	8.611
Non-Exposed Female	0	64841	0.000	0.000	5.689

LL, UL = 95% Lower and Upper exact confidence limits

Table 167 Incidence rate of Juvenile Rheumatoid Arthritis in Male Cohorts - Main Analysis - Confirmed cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Concurrent Male	0	64859	0.000	0.000	5.688
Historical Male	1	64868	1.542	0.039	8.589

LL, UL = 95% Lower and Upper exact confidence limits

Table 168 Incidence rate of Juvenile Rheumatoid Arthritis in Female Cohorts - Main Analysis - All cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Exposed Female	1	64705	1.545	0.039	8.611
Non-Exposed Female	0	64841	0.000	0.000	5.689

LL, UL = 95% Lower and Upper exact confidence limits

Table 169 Incidence rate of Juvenile Rheumatoid Arthritis in Male Cohorts - Main Analysis - All cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Concurrent Male	0	64859	0.000	0.000	5.688
Historical Male	1	64868	1.542	0.039	8.589

LL, UL = 95% Lower and Upper exact confidence limits

Table 170 Incidence rate of Multiple Sclerosis in Female Cohorts - Main Analysis - Confirmed cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Exposed Female	0	64705	0.000	0.000	5.701
Non-Exposed Female	1	64841	1.542	0.039	8.593

LL, UL = 95% Lower and Upper exact confidence limits

Table 171 Incidence rate of Multiple Sclerosis in Female Cohorts - Main Analysis - All cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Exposed Female	0	64705	0.000	0.000	5.701
Non-Exposed Female	1	64841	1.542	0.039	8.593

LL, UL = 95% Lower and Upper exact confidence limits

Table 172 Incidence rate of Optic Neuritis in Female Cohorts - Main Analysis - All cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Exposed Female	1	64705	1.545	0.039	8.611
Non-Exposed Female	1	64841	1.542	0.039	8.593

LL, UL = 95% Lower and Upper exact confidence limits

Table 173 Incidence rate of Psoriatic Arthritis in Female Cohorts - Main Analysis - Confirmed cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Exposed Female	1	64705	1.545	0.039	8.611
Non-Exposed Female	1	64841	1.542	0.039	8.593

LL, UL = 95% Lower and Upper exact confidence limits

Table 174 Incidence rate of Psoriatic Arthritis in Female Cohorts - Main Analysis - All cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Exposed Female	1	64705	1.545	0.039	8.611
Non-Exposed Female	1	64841	1.542	0.039	8.593

LL, UL = 95% Lower and Upper exact confidence limits

Table 175 Incidence rate of Rheumatoid Arthritis in Female Cohorts - Main Analysis - Confirmed cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Exposed Female	1	64705	1.545	0.039	8.611
Non-Exposed Female	0	64841	0.000	0.000	5.689

LL, UL = 95% Lower and Upper exact confidence limits

Table 176 Incidence rate of Rheumatoid Arthritis in Female Cohorts - Main Analysis - All cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Exposed Female	1	64705	1.545	0.039	8.611
Non-Exposed Female	0	64841	0.000	0.000	5.689

LL, UL = 95% Lower and Upper exact confidence limits

Table 177 Incidence rate of Systemic Lupus Erythematous in Female Cohorts - Main Analysis - Confirmed cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Exposed Female	0	64705	0.000	0.000	5.701
Non-Exposed Female	0	64841	0.000	0.000	5.689

LL, UL = 95% Lower and Upper exact confidence limits

Table 178 Incidence rate of Systemic Lupus Erythematous in Female Cohorts - Main Analysis - All cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Exposed Female	0	64705	0.000	0.000	5.701
Non-Exposed Female	0	64841	0.000	0.000	5.689

LL, UL = 95% Lower and Upper exact confidence limits

Table 179 Incidence rate of Autoimmune Type 1 Diabetes Mellitus in Female Cohorts - Main Analysis - Confirmed cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Exposed Female	8	64705	12.364	5.338	24.362
Non-Exposed Female	16	64841	24.676	14.104	40.072

LL, UL = 95% Lower and Upper exact confidence limits

Table 180 Incidence rate ratios of Type 1 Diabetes Mellitus in Female Cohorts - Main Analysis - Confirmed cases (Total cohort)

	IRR Calculation					
		95%CI of RR			95%CI of RR	
Autoimmune diseases	Crude Incidence Rate Ratio	LL	UL	Adjusted Incidence Rate Ratio	LL	UL
Type 1 Diabetes Mellitus	0.501	0.214	1.170	0.501	0.214	1.171

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted by age group: age group [9-17] and [18-25]

Table 181 Incidence rate difference of Autoimmune Type 1 Diabetes Mellitus in Female Cohorts - Main Analysis - Confirmed cases (Total cohort)

Characteristics	IRD Calculation
IRD(exp-unexp OR conc-hist)	-12.312

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 182 Incidence rate ratios of Type 1 Diabetes Mellitus in Female Cohorts (covariates adjusted) - Main Analysis - Confirmed cases (Total cohort)

	IRR Calculation		
		95%CI of RR	
Autoimmune diseases	Adjusted Incidence Rate Ratio	LL	UL
Type 1 Diabetes Mellitus	0.514	0.219	1.207

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted for other covariates: age group [9-17] and [18-25], healthcare resources utilization in quartile, regions (North England, South England, Midlands & Ireland Scotland Wales), any vaccines during the year prior to the reference date

Table 183 Incidence rate of Type 1 Diabetes Mellitus in Male Cohorts - Main Analysis - Confirmed cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Concurrent Male	20	64859	30.836	18.836	47.624
Historical Male	8	64868	12.333	5.324	24.300

LL, UL = 95% Lower and Upper exact confidence limits

Table 184 Incidence rate ratios of Type 1 Diabetes Mellitus in Male Cohorts - Main Analysis - Main Analysis - Confirmed cases (Total cohort)

	IRR Calculation					
		95%CI of RR			95%CI of RR	
Autoimmune diseases	Crude Incidence Rate Ratio	LL	UL	Adjusted Incidence Rate Ratio	LL	UL
Type 1 Diabetes Mellitus	2.500	1.101	5.675	2.462	1.083	5.597

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted by age group: age group [9-17] and [18-25]

Table 185 Incidence rate difference of Autoimmune Type 1 Diabetes Mellitus in Male Cohorts - Main Analysis - Confirmed cases (Total cohort)

Characteristics	IRD Calculation
IRD(exp-unexp OR conc-hist)	18.504

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 186 Incidence rate of Type 1 Diabetes Mellitus in Female Cohorts - Main Analysis - All cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Exposed Female	8	64705	12.364	5.338	24.362
Non-Exposed Female	16	64841	24.676	14.104	40.072

LL, UL = 95% Lower and Upper exact confidence limits

Table 187 Incidence rate ratios of Type 1 Diabetes Mellitus in Female Cohorts - Main Analysis - All cases (Total cohort)

	IRR Calculation					
		95%CI of RR			95%CI of RR	
Autoimmune diseases	Crude Incidence Rate Ratio	LL	UL	Adjusted Incidence Rate Ratio	LL	UL
Type 1 Diabetes Mellitus	0.501	0.214	1.170	0.501	0.214	1.171

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted by age group: age group [9-17] and [18-25]

Table 188 Incidence rate difference of Autoimmune Type 1 Diabetes Mellitus in Female Cohorts - Main Analysis - All cases (Total cohort)

Characteristics	IRD Calculation
IRD(exp-unexp OR conc-hist)	-12.312

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 189 Incidence rate ratios of Type 1 Diabetes Mellitus in Female Cohorts (covariates adjusted) - Main Analysis - All cases (Total cohort)

	IRR Calculation		
		95%CI of RR	
Autoimmune diseases	Adjusted Incidence Rate Ratio	LL	UL
Type 1 Diabetes Mellitus	0.514	0.219	1.207

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted for other covariates: age group [9-17] and [18-25], healthcare resources utilization in quartile, regions (North England, South England, Midlands & Ireland Scotland Wales), any vaccines during the year prior to the reference date

Table 190 Incidence rate of Type 1 Diabetes Mellitus in Male Cohorts - Main Analysis - All cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Concurrent Male	20	64859	30.836	18.836	47.624
Historical Male	8	64868	12.333	5.324	24.300

LL, UL = 95% Lower and Upper exact confidence limits

Table 191 Incidence rate ratios of Type 1 Diabetes Mellitus in Male Cohorts - Main Analysis - All cases (Total cohort)

	IRR Calculation					
		95%CI of RR			95%CI of RR	
Autoimmune diseases	Crude Incidence Rate Ratio	LL	UL	Adjusted Incidence Rate Ratio	LL	UL
Type 1 Diabetes Mellitus	2.500	1.101	5.675	2.462	1.083	5.597

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted by age group: age group [9-17] and [18-25]

Table 192 Incidence rate difference of Autoimmune Type 1 Diabetes Mellitus in Male Cohorts - Main Analysis - All cases (Total cohort)

Characteristics	IRD Calculation
IRD(exp-unexp OR conc-hist)	18.504

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 193 Incidence rate of Autoimmune Ulcerative Colitis in Female Cohorts - Main Analysis - Confirmed cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Exposed Female	4	64705	6.182	1.684	15.828
Non-Exposed Female	0	64841	0.000	0.000	5.689

LL, UL = 95% Lower and Upper exact confidence limits

Table 194 Incidence rate of Ulcerative Colitis in Male Cohorts - Main Analysis - Confirmed cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Concurrent Male	2	64859	3.084	0.373	11.139
Historical Male	2	64868	3.083	0.373	11.137

LL, UL = 95% Lower and Upper exact confidence limits

Table 195 Incidence rate of Ulcerative Colitis in Female Cohorts - Main Analysis - All cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Exposed Female	4	64705	6.182	1.684	15.828
Non-Exposed Female	1	64841	1.542	0.039	8.593

LL, UL = 95% Lower and Upper exact confidence limits

Table 196 Incidence rate of Ulcerative Colitis in Male Cohorts - Main Analysis - All cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Concurrent Male	2	64859	3.084	0.373	11.139
Historical Male	2	64868	3.083	0.373	11.137

LL, UL = 95% Lower and Upper exact confidence limits

Table 197 Incidence rate of Idiopathic Thrombocytopenia Purpura in Female Cohorts - Main Analysis - Confirmed cases (Total cohort)

				95% CI	
Cohort	**Number of cases**	**Person-time (in years)**	**Incidence Rate (per 100,000 PY)**	**LL**	**UL**
Exposed Female	1	64705	1.545	0.039	8.611
Non-Exposed Female	1	64841	1.542	0.039	8.593

LL, UL = 95% Lower and Upper exact confidence limits

Table 198 Incidence rate of Idiopathic Thrombocytopenia Purpura in Male Cohorts - Main Analysis - Confirmed cases (Total cohort)

				95% CI	
Cohort	**Number of cases**	**Person-time (in years)**	**Incidence Rate (per 100,000 PY)**	**LL**	**UL**
Concurrent Male	0	64859	0.000	0.000	5.688
Historical Male	1	64868	1.542	0.039	8.589

LL, UL = 95% Lower and Upper exact confidence limits

Table 199 Incidence rate of Idiopathic Thrombocytopenia Purpura in Female Cohorts - Main Analysis - All cases (Total cohort)

				95% CI	
Cohort	**Number of cases**	**Person-time (in years)**	**Incidence Rate (per 100,000 PY)**	**LL**	**UL**
Exposed Female	1	64705	1.545	0.039	8.611
Non-Exposed Female	1	64841	1.542	0.039	8.593

LL, UL = 95% Lower and Upper exact confidence limits

Table 200 Incidence rate of Idiopathic Thrombocytopenia Purpura in Male Cohorts - Main Analysis - All cases (Total cohort)

				95% CI	
Cohort	**Number of cases**	**Person-time (in years)**	**Incidence Rate (per 100,000 PY)**	**LL**	**UL**
Concurrent Male	0	64859	0.000	0.000	5.688
Historical Male	1	64868	1.542	0.039	8.589

LL, UL = 95% Lower and Upper exact confidence limits

Table 201 Frequency of autoimmune diseases during the one year follow-up period by exposed/non-exposed status - Sensitivity Analysis - Imputed date - Confirmed and Non-Confirmed cases (Total cohort)

		EXP N = 64998		NNEXP N = 64994		MALE N = 64988		HIST N = 64978		Total N = 259958	
Characteristics	**Categories**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**
Coprimary endpoints within 1 year follow-up period	Neuroinflammatory Ophthalmic autoimmune diseases	5	7.69	9	13.85	7	10.77	4	6.16	25	9.62
	Other autoimmune diseases	60	92.31	52	80.01	38	58.47	29	44.63	179	68.86

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n = number of subjects in a given category
Per 100000 = n/Number of subjects with available results*100000
Neuroinflammatory/Ophthalmic autoimmune diseases included: Multiple Sclerosis, Transverse Myelitis, Optic Neuritis, Guillain Barré Syndrome, Acute disseminated encephalomyelitis, Autoimmune Peripheral neuropathies & plexopathies and Autoimmune Uveitis. Note: that 1 AD was classified as Other AD
Follow-up period 1 year for all the cohorts

Table 202 Frequency of autoimmune diseases during the one year follow-up period by exposed/non-exposed status - Sensitivity Analysis - Imputed date - Confirmed cases (Total cohort)

		EXP N = 64998		NNEXP N = 64994		MALE N = 64988		HIST N = 64978		Total N = 259958	
Characteristics	**Categories**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**
Coprimary endpoints within 1 year follow-up period	Neuroinflammatory/Ophthalmic autoimmune diseases	0	0.00	1	1.54	2	3.08	1	1.54	4	1.54
	Other autoimmune diseases	42	64.62	33	50.77	33	50.78	19	29.24	127	48.85

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n = number of subjects in a given category
Per 100000 = n/Number of subjects with available results*100000
Neuroinflammatory/Ophthalmic autoimmune diseases included: Multiple Sclerosis, Transverse Myelitis, Optic Neuritis, Guillain Barré Syndrome, Acute disseminated encephalomyelitis, Autoimmune Peripheral neuropathies & plexopathies and Autoimmune Uveitis. Note: that 1 AD was classified as Other AD
Follow-up period 1 year for all the cohorts

Table 203 Frequency of autoimmune diseases during the one year follow-up period by exposed/non-exposed status - Sensitivity Analysis - Imputed date - Confirmed and Non-Confirmed cases (N=AD) (Total cohort)

		EXP N = 65001		NNEXP N = 64995		MALE N = 64988		HIST N = 64979		Total N = 259963	
Characteristics	**Categories**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**
Individual autoimmune diseases within 1 year follow-up period	Acute disseminated encephalomyelitis	1	1.54	0	0.00	0	0.00	0	0.00	1	0.38
	Autoimmune Thyroiditis	32	49.23	27	41.54	5	7.69	7	10.77	71	27.31
	Autoimmune Uveitis	3	4.62	7	10.77	5	7.69	3	4.62	18	6.92
	Crohn diseases	9	13.85	5	7.69	5	7.69	2	3.08	21	8.08
	Guillain-Barre Syndrome	0	0.00	0	0.00	1	1.54	1	1.54	2	0.77
	Idiopathic Thrombocytopenia Purpura	1	1.54	1	1.54	1	1.54	2	3.08	5	1.92
	Inflammatory Bowel Diseases	1	1.54	0	0.00	0	0.00	1	1.54	2	0.77
	Juvenile Rheumatoid Arthritis	1	1.54	0	0.00	0	0.00	1	1.54	2	0.77
	Multiple Sclerosis	0	0.00	1	1.54	0	0.00	0	0.00	1	0.38
	Optic Neuritis	1	1.54	1	1.54	1	1.54	0	0.00	3	1.15
	Other AD	1	1.54	0	0.00	0	0.00	0	0.00	1	0.38
	Psoriatic Arthritis	1	1.54	1	1.54	0	0.00	0	0.00	2	0.77
	Rheumatoid Arthritis	1	1.54	0	0.00	0	0.00	0	0.00	1	0.38
	Type 1 Diabetes Mellitus	10	15.38	18	27.69	23	35.39	14	21.55	65	25.00
	Ulcerative Colitis	4	6.15	1	1.54	4	6.15	2	3.08	11	4.23

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n = number of subjects in a given category
Per 100000 = n/Number of subjects with available results*100000
Neuroinflammatory/Ophthalmic autoimmune diseases included: Multiple Sclerosis, Transverse Myelitis, Optic Neuritis, Guillain Barré Syndrome, Acute dissiminated encephalomyelitis, Autoimmune Peripheral neuropathies & plexopathies and Autoimmune Uveitis. Note: that 1 AD was classified as Other AD
Follow-up period 1 year for all the cohorts
Three subjects have simultaneously diabetes and thyroid diseases (2 in exposed cohorts and 1 in non-exposed female cohort)

Table 204 Frequency of autoimmune diseases during the one year follow-up period by exposed/non-exposed status - Sensitivity Analysis - Imputed date - Confirmed cases (N=AD) (Total cohort)

		EXP N = 65001		NNEXP N = 64995		MALE N = 64988		HIST N = 64979		Total N = 259963	
Characteristics	**Categories**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**
Individual autoimmune diseases within 1 year follow-up period	Autoimmune Thyroiditis	16	24.62	8	12.31	1	1.54	0	0.00	25	9.62
	Crohn diseases	7	10.77	5	7.69	5	7.69	1	1.54	18	6.92
	Guillain-Barre Syndrome	0	0.00	0	0.00	1	1.54	1	1.54	2	0.77
	Idiopathic Thrombocytopenia Purpura	1	1.54	1	1.54	0	0.00	2	3.08	4	1.54
	Inflammatory Bowel Diseases	0	0.00	0	0.00	0	0.00	1	1.54	1	0.38
	Juvenile Rheumatoid Arthritis	1	1.54	0	0.00	0	0.00	1	1.54	2	0.77
	Multiple Sclerosis	0	0.00	1	1.54	0	0.00	0	0.00	1	0.38
	Optic Neuritis	0	0.00	0	0.00	1	1.54	0	0.00	1	0.38
	Other AD	1	1.54	0	0.00	0	0.00	0	0.00	1	0.38
	Psoriatic Arthritis	1	1.54	1	1.54	0	0.00	0	0.00	2	0.77
	Rheumatoid Arthritis	1	1.54	0	0.00	0	0.00	0	0.00	1	0.38
	Type 1 Diabetes Mellitus	10	15.38	18	27.69	23	35.39	12	18.47	63	24.23
	Ulcerative Colitis	4	6.15	0	0.00	4	6.15	2	3.08	10	3.85

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n = number of subjects in a given category
Per 100000 = n/Number of subjects with available results*100000
Neuroinflammatory/Ophthalmic autoimmune diseases included: Multiple Sclerosis, Transverse Myelitis, Optic Neuritis, Guillain Barré Syndrome, Acute dissiminated encephalomyelitis, Autoimmune Peripheral neuropathies & plexopathies and Autoimmune Uveitis. Note: that 1 AD was classified as Other AD
Follow-up period 1 year for all the cohorts

Table 205 Frequency of autoimmune disease during the specific time period by exposed/non-exposed status - Imputed date - Confirmed and Non-Confirmed cases (Total cohort)

		EXP N = 64998		NNEXP N = 64994		MALE N = 64988		HIST N = 64978		Total N = 259958	
Characteristics	**Categories**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**
Individual autoimmune diseases within 2 months of FU period	Guillain-Barre Syndrome	0	0.00	0	0.00	0	0.00	1	1.54	1	0.38

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n = number of subjects in a given category
Per 100000 = n/Number of subjects with available results*100000
Autoimmune diseases within 2 months included: Guillain Barré Syndrome and Autoimmune Haemolytic Anaemia
FU:Specific time disease follow-up period

Table 206 Frequency of autoimmune disease during the specific time period by exposed/non-exposed status - Imputed date - Confirmed cases (Total cohort)

		EXP N = 64998		NNEXP N = 64994		MALE N = 64988		HIST N = 64978		Total N = 259958	
Characteristics	**Categories**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**
Individual autoimmune diseases within 2 months of FU period	Guillain-Barre Syndrome	0	0.00	0	0.00	0	0.00	1	1.54	1	0.38

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n = number of subjects in a given category
Per 100000 = n/Number of subjects with available results*100000
Autoimmune diseases within 2 months included: Guillain Barré Syndrome and Autoimmune Haemolytic Anaemia
FU:Specific time disease follow-up period

Table 207 Frequency of autoimmune disease during the specific time period by exposed/non-exposed status - Imputed date - Confirmed and Non-Confirmed cases (Total cohort)

		EXP N = 64998		NNEXP N = 64994		MALE N = 64988		HIST N = 64978		Total N = 259958	
Characteristics	**Categories**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**
Individual autoimmune disease within 6 months of FU period	Idiopathic Thrombocytopenia Purpura	1	1.54	1	1.54	0	0.00	1	1.54	3	1.15

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n = number of subjects in a given category
Per 100000 = n/Number of subjects with available results*100000
Autoimmune diseases within 6 months included: Idiopathic Thrombocytopenia Purpura
FU:Specific time disease follow-up period

Table 208 Frequency of autoimmune disease during the specific time period by exposed/non-exposed status - Imputed date - Confirmed cases (Total cohort)

		EXP N = 64998		NNEXP N = 64994		MALE N = 64988		HIST N = 64978		Total N = 259958	
Characteristics	**Categories**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**
Individual autoimmune disease within 6 months of FU period	Idiopathic Thrombocytopenia Purpura	1	1.54	1	1.54	0	0.00	1	1.54	3	1.15

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n = number of subjects in a given category
Per 100000 = n/Number of subjects with available results*100000
Autoimmune diseases within 6 months included: Idiopathic Thrombocytopenia Purpura
FU:Specific time disease follow-up period

Table 209 Frequency of autoimmune disease during the specific time period by exposed/non-exposed status - Imputed date - Confirmed and Non-Confirmed cases (N=AD) (Total cohort)

		EXP N = 65001		NNEXP N = 64995		MALE N = 64988		HIST N = 64979		Total N = 259963	
Characteristics	**Categories**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**
Individual autoimmune diseases within 12 months of FU period	Acute disseminated encephalomyelitis	1	1.54	0	0.00	0	0.00	0	0.00	1	0.38
	Autoimmune Thyroiditis	32	49.23	27	41.54	5	7.69	7	10.77	71	27.31
	Autoimmune Uveitis	3	4.62	7	10.77	5	7.69	3	4.62	18	6.92
	Crohn diseases	9	13.85	5	7.69	5	7.69	2	3.08	21	8.08
	Inflammatory Bowel Diseases	1	1.54	0	0.00	0	0.00	1	1.54	2	0.77
	Juvenile Rheumatoid Arthritis	1	1.54	0	0.00	0	0.00	1	1.54	2	0.77
	Multiple Sclerosis	0	0.00	1	1.54	0	0.00	0	0.00	1	0.38
	Optic Neuritis	1	1.54	1	1.54	1	1.54	0	0.00	3	1.15
	Other AD	1	1.54	0	0.00	0	0.00	0	0.00	1	0.38
	Psoriatic Arthritis	1	1.54	1	1.54	0	0.00	0	0.00	2	0.77
	Rheumatoid Arthritis	1	1.54	0	0.00	0	0.00	0	0.00	1	0.38
	Type 1 Diabetes Mellitus	10	15.38	18	27.69	23	35.39	14	21.55	65	25.00
	Ulcerative Colitis	4	6.15	1	1.54	4	6.15	2	3.08	11	4.23

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n = number of subjects in a given category
Per 100000 = n/Number of subjects with available results*100000
FU:Specific time disease follow-up period

Table 210 Frequency of autoimmune disease during the specific time period by exposed/non-exposed status - Imputed date - Confirmed cases (N=AD) (Total cohort)

		EXP N = 65001		NNEXP N = 64995		MALE N = 64988		HIST N = 64979		Total N = 259963	
Characteristics	**Categories**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**
Individual autoimmune diseases within 12 months of FU period	Autoimmune Thyroiditis	16	24.62	8	12.31	1	1.54	0	0.00	25	9.62
	Crohn diseases	7	10.77	5	7.69	5	7.69	1	1.54	18	6.92
	Inflammatory Bowel Diseases	0	0.00	0	0.00	0	0.00	1	1.54	1	0.38
	Juvenile Rheumatoid Arthritis	1	1.54	0	0.00	0	0.00	1	1.54	2	0.77
	Multiple Sclerosis	0	0.00	1	1.54	0	0.00	0	0.00	1	0.38
	Optic Neuritis	0	0.00	0	0.00	1	1.54	0	0.00	1	0.38
	Other AD	1	1.54	0	0.00	0	0.00	0	0.00	1	0.38
	Psoriatic Arthritis	1	1.54	1	1.54	0	0.00	0	0.00	2	0.77
	Rheumatoid Arthritis	1	1.54	0	0.00	0	0.00	0	0.00	1	0.38
	Type 1 Diabetes Mellitus	10	15.38	18	27.69	23	35.39	12	18.47	63	24.23
	Ulcerative Colitis	4	6.15	0	0.00	4	6.15	2	3.08	10	3.85

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n = number of subjects in a given category
Per 100000 = n/Number of subjects with available results*100000
FU:Specific time disease follow-up period

Table 211 Incidence rate of Neuroinflammatory/Ophthalmic autoimmune diseases in Female Cohorts - Imputed date - Confirmed cases (Total cohort)

				95% CI	
Cohort	**Number of cases**	**Person-time (in years)**	**Incidence Rate (per 100,000 PY)**	**LL**	**UL**
Exposed Female	0	64730	0.000	0.000	5.699
Non-Exposed Female	1	64844	1.542	0.039	8.592

LL, UL = 95% Lower and Upper exact confidence limits

Table 212 Incidence rate ratios of Neuroinflammatory/Ophthalmic diseases in Female Cohorts - Imputed date - Confirmed cases (Total cohort)

	IRR Calculation					
		95%CI of RR			95%CI of RR	
Autoimmune diseases	**Crude Incidence Rate Ratio**	**LL**	**UL**	**Adjusted Incidence Rate Ratio**	**LL**	**UL**
Neuroinflammatory/Ophthalmic autoimmune diseases	1.002	0.063	16.019	1.006	0.063	16.082

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted by age group: age group [9-17] and [18-25]

Table 213 Incidence rate difference of Neuroinflammatory/Ophthalmic autoimmune diseases in Female Cohorts - Imputed date - Confirmed cases (Total cohort)

Characteristics	**IRD Calculation**
IRD(exp-unexp OR conc-hist)	-1.542

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 214 Incidence rate ratios of Neuroinflammatory/Ophthalmic diseases in Female Cohorts (covariates adjusted) - Imputed date - Confirmed cases (Total cohort)

	IRR Calculation		
		95%CI of RR	
Autoimmune diseases	**Adjusted Incidence Rate Ratio**	**LL**	**UL**
Neuroinflammatory/Ophthalmic autoimmune diseases	0.319	0.014	7.300

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted for other covariates: age group [9-17] and [18-25], healthcare resources utilization in quartile regions (North England, South England, Midlands & Ireland Scotland Wales), live attenuated & adjuvanted & other vaccines in the follow-up period

Table 215 Incidence rate of Other autoimmune diseases in Female Cohorts - Imputed date - Confirmed cases (Total cohort)

				95% CI	
Cohort	**Number of cases**	**Person-time (in years)**	**Incidence Rate (per 100,000 PY)**	**LL**	**UL**
Exposed Female	42	64730	64.885	46.764	87.706
Non-Exposed Female	33	64844	50.891	35.031	71.470

LL, UL = 95% Lower and Upper exact confidence limits

Table 216 Incidence rate ratios of Other autoimmune diseases in Female Cohorts - Imputed date - Confirmed cases (Total cohort)

	IRR Calculation					
		95%CI of RR			95%CI of RR	
Autoimmune diseases	**Crude Incidence Rate Ratio**	**LL**	**UL**	**Adjusted Incidence Rate Ratio**	**LL**	**UL**
Other autoimmune diseases	1.274	0.808	2.010	1.274	0.808	2.010

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted by age group: age group [9-17] and [18-25]

Table 217 Incidence rate difference of Other autoimmune diseases in Female Cohorts - Imputed date - Confirmed cases (Total cohort)

Characteristics	**IRD Calculation**
IRD(exp-unexp OR conc-hist)	13.994

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 218 Incidence rate ratios of Other autoimmune diseases in Female Cohorts (covariates adjusted) - Imputed date - Confirmed cases (Total cohort)

	IRR Calculation		
		95%CI of RR	
Autoimmune diseases	**Adjusted Incidence Rate Ratio**	**LL**	**UL**
Other autoimmune diseases	1.258	0.794	1.992

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted for other covariates: age group [9-17] and [18-25], healthcare resources utilization in quartile, regions (North England, South England, Midlands & Ireland Scotland Wales), any vaccines during the year prior to the reference date

Table 219 Incidence rate of Neuroinflammatory/Ophthalmic autoimmune diseases in Female Cohorts - Imputed date - All cases (Total cohort)

				95% CI	
Cohort	**Number of cases**	**Person-time (in years)**	**Incidence Rate (per 100,000 PY)**	**LL**	**UL**
Exposed Female	5	64730	7.724	2.508	18.026
Non-Exposed Female	9	64844	13.879	6.347	26.347

LL, UL = 95% Lower and Upper exact confidence limits

Table 220 Incidence rate ratios of Neuroinflammatory/Ophthalmic diseases in Female Cohorts - Imputed date - All cases (Total cohort)

	IRR Calculation					
		95%CI of RR			95%CI of RR	
Autoimmune diseases	**Crude Incidence Rate Ratio**	**LL**	**UL**	**Adjusted Incidence Rate Ratio**	**LL**	**UL**
Neuroinflammatory/Ophthalmic autoimmune diseases	0.556	0.186	1.660	0.556	0.186	1.659

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted by age group: age group [9-17] and [18-25]

Table 221 Incidence rate difference of Neuroinflammatory/Ophthalmic autoimmune diseases in Female Cohorts - Imputed date - All cases (Total cohort)

Characteristics	**IRD Calculation**
IRD(exp-unexp OR conc-hist)	-6.155

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 222 Incidence rate ratios of Neuroinflammatory/Ophthalmic diseases in Female Cohorts (covariates adjusted) - Imputed date - All cases (Total cohort)

	IRR Calculation		
		95%CI of RR	
Autoimmune diseases	**Adjusted Incidence Rate Ratio**	**LL**	**UL**
Neuroinflammatory/Ophthalmic autoimmune diseases	0.557	0.184	1.683

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted for other covariates: age group [9-17] and [18-25], healthcare resources utilization in quartile, regions (North England, South England, Midlands & Ireland Scotland Wales), any vaccines during the year prior to the reference date

Table 223 Incidence rate of Other autoimmune diseases in Female Cohorts - Imputed date - All cases (Total cohort)

				95% CI	
Cohort	**Number of cases**	**Person-time (in years)**	**Incidence Rate (per 10,000 PY)**	**LL**	**UL**
Exposed Female	60	64730	9.269	7.073	11.931
Non-Exposed Female	52	64844	8.019	5.989	10.516

LL, UL = 95% Lower and Upper exact confidence limits

Table 224 Incidence rate ratios of Other autoimmune diseases in Female Cohorts - Imputed date - All cases (Total cohort)

	IRR Calculation					
		95%CI of RR			95%CI of RR	
Autoimmune diseases	**Crude Incidence Rate Ratio**	**LL**	**UL**	**Adjusted Incidence Rate Ratio**	**LL**	**UL**
Other autoimmune diseases	1.155	0.797	1.675	1.155	0.797	1.674

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted by age group: age group [9-17] and [18-25]

Table 225 Incidence rate difference of Other autoimmune diseases in Female Cohorts - Imputed date - All cases (Total cohort)

Characteristics	**IRD Calculation**
IRD(exp-unexp OR conc-hist)	1.250

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 226 Incidence rate ratios of Other autoimmune diseases in Female Cohorts (covariates adjusted) - Imputed date - All cases (Total cohort)

	IRR Calculation		
		95%CI of RR	
Autoimmune diseases	**Adjusted Incidence Rate Ratio**	**LL**	**UL**
Other autoimmune diseases	1.114	0.766	1.619

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted for other covariates: age group [9-17] and [18-25], healthcare resources utilization in quartile, regions (North England, South England, Midlands & Ireland Scotland Wales), any vaccines during the year prior to the reference date

Table 227 Incidence rate of Neuroinflammatory/Ophthalmic autoimmune diseases in Male Cohorts - Imputed date - Confirmed cases (Total cohort)

				95% CI	
Cohort	**Number of cases**	**Person-time (in years)**	**Incidence Rate (per 100,000 PY)**	**LL**	**UL**
Concurrent Male	2	64865	3.083	0.373	11.138
Historical Male	1	64874	1.541	0.039	8.588

LL, UL = 95% Lower and Upper exact confidence limits

Table 228 Incidence rate ratios of Neuroinflammatory/Ophthalmic diseases in Male Cohorts - Imputed date - Confirmed cases (Total cohort)

	IRR Calculation					
		95%CI of RR			95%CI of RR	
Autoimmune diseases	**Crude Incidence Rate Ratio**	**LL**	**UL**	**Adjusted Incidence Rate Ratio**	**LL**	**UL**
Neuroinflammatory/Ophthalmic autoimmune diseases	2.000	0.181	22.055	1.899	0.172	20.938

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted by age group: age group [9-17] and [18-25]

Table 229 Incidence rate difference of Neuroinflammatory/Ophthalmic autoimmune diseases in Male Cohorts - Imputed date - Confirmed cases (Total cohort)

Characteristics	**IRD Calculation**
IRD(exp-unexp OR conc-hist)	1.542

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 230 Incidence rate of Other autoimmune diseases in Male Cohorts - Imputed date - Confirmed cases (Total cohort)

				95% CI	
Cohort	**Number of cases**	**Person-time (in years)**	**Incidence Rate (per 100,000 PY)**	**LL**	**UL**
Concurrent Male	33	64865	50.875	35.020	71.447
Historical Male	19	64874	29.288	17.633	45.736

LL, UL = 95% Lower and Upper exact confidence limits

Table 231 Incidence rate ratios of Other autoimmune diseases in Male Cohorts - Imputed date - Confirmed cases (Total cohort)

	IRR Calculation					
		95%CI of RR			95%CI of RR	
Autoimmune diseases	Crude Incidence Rate Ratio	LL	UL	Adjusted Incidence Rate Ratio	LL	UL
Other autoimmune diseases	1.737	0.988	3.054	1.779	1.010	3.135

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted by age group: age group [9-17] and [18-25]

Table 232 Incidence rate difference of Other autoimmune diseases in Male Cohorts - Imputed date - Confirmed cases (Total cohort)

Characteristics	IRD Calculation
IRD(exp-unexp OR conc-hist)	21.587

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 233 Incidence rate ratios of Other autoimmune diseases in Male Cohorts (covariates adjusted) - Imputed date - Confirmed cases (Total cohort)

	IRR Calculation		
		95%CI of RR	
Autoimmune diseases	Adjusted Incidence Rate Ratio	LL	UL
Other autoimmune diseases	1.793	1.017	3.160

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted for other covariates: age group [9-17] and [18-25], healthcare resources utilization in quartile, regions (North England, South England, Midlands & Ireland Scotland Wales), any vaccines during the year prior to the reference date

Table 234 Incidence rate of Neuroinflammatory/Ophthalmic autoimmune diseases in Male Cohorts - Imputed date - All cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Concurrent Male	7	64865	10.792	4.339	22.235
Historical Male	4	64874	6.166	1.680	15.787

LL, UL = 95% Lower and Upper exact confidence limits

Table 235 Incidence rate ratios of Neuroinflammatory/Ophthalmic diseases in Male Cohorts - Imputed date - All cases (Total cohort)

	IRR Calculation					
		95%CI of RR			95%CI of RR	
Autoimmune diseases	Crude Incidence Rate Ratio	LL	UL	Adjusted Incidence Rate Ratio	LL	UL
Neuroinflammatory/Ophthalmic autoimmune diseases	1.750	0.512	5.978	1.817	0.529	6.240

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted by age group: age group [9-17] and [18-25]

Table 236 Incidence rate difference of Neuroinflammatory/Ophthalmic autoimmune diseases in Male Cohorts - Imputed date - All cases (Total cohort)

Characteristics	IRD Calculation
IRD(exp-unexp OR conc-hist)	4.626

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 237 Incidence rate ratios of Neuroinflammatory/Ophthalmic diseases in Male Cohorts (covariates adjusted) - Imputed date - All cases (Total cohort)

	IRR Calculation		
		95%CI of RR	
Autoimmune diseases	Adjusted Incidence Rate Ratio	LL	UL
Neuroinflammatory/Ophthalmic autoimmune diseases	1.802	0.524	6.190

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted for other covariates: age group [9-17] and [18-25], healthcare resources utilization in quartile, regions (North England, South England, Midlands & Ireland Scotland Wales), any vaccines during the year prior to the reference date

Table 238 Incidence rate of Other autoimmune diseases in Male Cohorts - Imputed date - All cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Concurrent Male	38	64865	58.583	41.457	80.410
Historical Male	29	64874	44.702	29.938	64.200

LL, UL = 95% Lower and Upper exact confidence limits

Table 239 Incidence rate ratios of Other autoimmune diseases in Male Cohorts - Imputed date - All cases (Total cohort)

	IRR Calculation					
		95%CI of RR			95%CI of RR	
Autoimmune diseases	Crude Incidence Rate Ratio	LL	UL	Adjusted Incidence Rate Ratio	LL	UL
Other autoimmune diseases	1.310	0.808	2.124	1.346	0.829	2.187

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted by age group: age group [9-17] and [18-25]

Table 240 Incidence rate difference of Other autoimmune diseases in Male Cohorts - Imputed date - All cases (Total cohort)

Characteristics	IRD Calculation
IRD(exp-unexp OR conc-hist)	13.881

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 241 Incidence rate ratios of Other autoimmune diseases in Male Cohorts (covariates adjusted) - Imputed date - All cases (Total cohort)

	IRR Calculation		
		95%CI of RR	
Autoimmune diseases	Adjusted Incidence Rate Ratio	LL	UL
Other autoimmune diseases	1.360	0.837	2.210

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted for other covariates: age group [9-17] and [18-25], healthcare resources utilization in quartile, regions (North England, South England, Midlands & Ireland Scotland Wales), any vaccines during the year prior to the reference date

Table 242 Incidence rate of Acute Disseminated Encephalomyelitis in Female Cohorts - Imputed date - All cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Exposed Female	1	64730	1.545	0.039	8.608
Non-Exposed Female	0	64844	0.000	0.000	5.689

LL, UL = 95% Lower and Upper exact confidence limits

Table 243 Incidence rate of Autoimmune Hepatitis in Female Cohorts - Imputed date - Confirmed cases (Total cohort)

				95% CI	
Cohort	**Number of cases**	**Person-time (in years)**	**Incidence Rate (per 100,000 PY)**	**LL**	**UL**
Exposed Female	0	64730	0.000	0.000	5.699
Non-Exposed Female	0	64844	0.000	0.000	5.689

LL, UL = 95% Lower and Upper exact confidence limits

Table 244 Incidence rate of Autoimmune Hepatitis in Female Cohorts - Imputed date - All cases (Total cohort)

				95% CI	
Cohort	**Number of cases**	**Person-time (in years)**	**Incidence Rate (per 100,000 PY)**	**LL**	**UL**
Exposed Female	0	64730	0.000	0.000	5.699
Non-Exposed Female	0	64844	0.000	0.000	5.689

LL, UL = 95% Lower and Upper exact confidence limits

Table 245 Incidence rate of Autoimmune Thyroiditis in Female Cohorts - Imputed date - Confirmed cases (Total cohort)

				95% CI	
Cohort	**Number of cases**	**Person-time (in years)**	**Incidence Rate (per 100,000 PY)**	**LL**	**UL**
Exposed Female	16	64730	24.718	14.129	40.141
Non-Exposed Female	8	64844	12.337	5.326	24.309

LL, UL = 95% Lower and Upper exact confidence limits

Table 246 Incidence rate ratios of Autoimmune Thyroiditis in Female Cohorts - Imputed date - Confirmed cases (Total cohort)

	IRR Calculation					
		95%CI of RR			95%CI of RR	
Autoimmune diseases	**Crude Incidence Rate Ratio**	**LL**	**UL**	**Adjusted Incidence Rate Ratio**	**LL**	**UL**
Autoimmune Thyroiditis	2.002	0.857	4.678	2.000	0.856	4.674

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted by age group: age group [9-17] and [18-25]

Table 247 Incidence rate difference of Autoimmune Thyroiditis diseases in Female Cohorts - Imputed date - Confirmed cases (Total cohort)

Characteristics	**IRD Calculation**
IRD(exp-unexp OR conc-hist)	12.381

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 248 Incidence rate ratios of Autoimmune Thyroiditis in Female Cohorts (covariates adjusted) - Imputed date - Confirmed cases (Total cohort)

	IRR Calculation		
		95%CI of RR	
Autoimmune diseases	Adjusted Incidence Rate Ratio	LL	UL
Autoimmune Thyroiditis	1.842	0.785	4.323

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted for other covariates: age group [9-17] and [18-25], healthcare resources utilization in quartile, regions (North England, South England, Midlands & Ireland Scotland Wales), any vaccines during the year prior to the reference date

Table 249 Incidence rate of Autoimmune Thyroiditis in Male Cohorts - Imputed date - Confirmed cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Concurrent Male	1	64865	1.542	0.039	8.590
Historical Male	0	64874	0.000	0.000	5.686

LL, UL = 95% Lower and Upper exact confidence limits

Table 250 Incidence rate difference of Autoimmune Thyroiditis diseases in Male Cohorts - Imputed date - Confirmed cases (Total cohort)

Characteristics	IRD Calculation
IRD(exp-unexp OR conc-hist)	1.542

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 251 Incidence rate of Autoimmune Thyroiditis in Female Cohorts - Imputed date - All cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Exposed Female	32	64730	49.436	33.814	69.789
Non-Exposed Female	27	64844	41.638	27.440	60.581

LL, UL = 95% Lower and Upper exact confidence limits

Table 252 Incidence rate ratios of Autoimmune Thyroiditis in Female Cohorts - Imputed date - All cases (Total cohort)

	IRR Calculation					
		95%CI of RR			95%CI of RR	
Autoimmune diseases	Crude Incidence Rate Ratio	LL	UL	Adjusted Incidence Rate Ratio	LL	UL
Autoimmune Thyroiditis	1.187	0.711	1.980	1.186	0.711	1.979

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted by age group: age group [9-17] and [18-25]

Table 253 Incidence rate difference of Autoimmune Thyroiditis diseases in Female Cohorts - Imputed date - All cases (Total cohort)

Characteristics	IRD Calculation
IRD(exp-unexp OR conc-hist)	7.798

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 254 Incidence rate ratios of Autoimmune Thyroiditis in Female Cohorts (covariates adjusted) - Imputed date - All cases (Total cohort)

	IRR Calculation		
		95%CI of RR	
Autoimmune diseases	Adjusted Incidence Rate Ratio	LL	UL
Autoimmune Thyroiditis	1.096	0.654	1.834

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted for other covariates: age group [9-17] and [18-25], healthcare resources utilization in quartile, regions (North England, South England, Midlands & Ireland Scotland Wales), any vaccines during the year prior to the reference date

Table 255 Incidence rate of Autoimmune Thyroiditis in Male Cohorts - Imputed date - All cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Concurrent Male	5	64865	7.708	2.503	17.989
Historical Male	7	64874	10.790	4.338	22.232

LL, UL = 95% Lower and Upper exact confidence limits

Table 256 Incidence rate ratios of Autoimmune Thyroiditis in Male Cohorts - Imputed date - All cases (Total cohort)

	IRR Calculation					
		95%CI of RR			95%CI of RR	
Autoimmune diseases	Crude Incidence Rate Ratio	LL	UL	Adjusted Incidence Rate Ratio	LL	UL
Autoimmune Thyroiditis	0.714	0.227	2.250	0.731	0.231	2.313

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted by age group: age group [9-17] and [18-25]

Table 257 Incidence rate difference of Autoimmune Thyroiditis diseases in Male Cohorts - Imputed date - All cases (Total cohort)

Characteristics	IRD Calculation
IRD(exp-unexp OR conc-hist)	-3.082

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 258 Incidence rate ratios of Autoimmune Thyroiditis in Male Cohorts (covariates adjusted) - Imputed date - All cases (Total cohort)

	IRR Calculation		
		95%CI of RR	
Autoimmune diseases	Adjusted Incidence Rate Ratio	LL	UL
Autoimmune Thyroiditis	0.219	0.059	0.816

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted for other covariates: age group [9-17] and [18-25], healthcare resources utilization in quartile regions (North England, South England, Midlands & Ireland Scotland Wales), live attenuated & adjuvanted & other vaccines in the follow-up period

Table 259 Incidence rate of Autoimmune Uveitis in Female Cohorts - Imputed date - All cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Exposed Female	3	64730	4.635	0.956	13.544
Non-Exposed Female	7	64844	10.795	4.340	22.242

LL, UL = 95% Lower and Upper exact confidence limits

Table 260 Incidence rate ratios of Autoimmune Uveitis in Female Cohorts - Imputed date - All cases (Total cohort)

	IRR Calculation					
		95%CI of RR			95%CI of RR	
Autoimmune diseases	Crude Incidence Rate Ratio	LL	UL	Adjusted Incidence Rate Ratio	LL	UL
Autoimmune Uveitis	0.429	0.111	1.659	0.428	0.111	1.657

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted by age group: age group [9-17] and [18-25]

Table 261 Incidence rate difference of Autoimmune Uveitis in Female Cohorts - Imputed date - All cases (Total cohort)

Characteristics	IRD Calculation
IRD(exp-unexp OR conc-hist)	-6.160

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 262 Incidence rate ratios of Autoimmune Uveitis in Female Cohorts (covariates adjusted) - Imputed date - All cases (Total cohort)

	IRR Calculation		
		95%CI of RR	
Autoimmune diseases	Adjusted Incidence Rate Ratio	LL	UL
Autoimmune Uveitis	0.453	0.116	1.777

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted for other covariates: age group [9-17] and [18-25], healthcare resources utilization in quartile, regions (North England, South England, Midlands & Ireland Scotland Wales), any vaccines during the year prior to the reference date

Table 263 Incidence rate of Autoimmune Uveitis in Male Cohorts - Imputed date - All cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Concurrent Male	5	64865	7.708	2.503	17.989
Historical Male	3	64874	4.624	0.954	13.514

LL, UL = 95% Lower and Upper exact confidence limits

Table 264 Incidence rate ratios of Autoimmune Uveitis in Male Cohorts - Imputed date - All cases (Total cohort)

	IRR Calculation					
		95%CI of RR			95%CI of RR	
Autoimmune diseases	Crude Incidence Rate Ratio	LL	UL	Adjusted Incidence Rate Ratio	LL	UL
Autoimmune Uveitis	1.667	0.398	6.973	1.789	0.424	7.541

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted by age group: age group [9-17] and [18-25]

Table 265 Incidence rate difference of Autoimmune Uveitis in Male Cohorts - Imputed date - All cases (Total cohort)

Characteristics	IRD Calculation
IRD(exp-unexp OR conc-hist)	3.084

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 266 Incidence rate ratios of Autoimmune Uveitis in Male Cohorts (covariates adjusted) - Imputed date - All cases (Total cohort)

	IRR Calculation		
		95%CI of RR	
Autoimmune diseases	Adjusted Incidence Rate Ratio	LL	UL
Autoimmune Uveitis	1.795	0.426	7.561

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted for other covariates: age group [9-17] and [18-25], healthcare resources utilization in quartile, regions (North England, South England, Midlands & Ireland Scotland Wales), any vaccines during the year prior to the reference date

Table 267 Incidence rate of Autoimmune Crohn diseases in Female Cohorts - Imputed date - Confirmed cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Exposed Female	7	64730	10.814	4.348	22.281
Non-Exposed Female	5	64844	7.711	2.504	17.994

LL, UL = 95% Lower and Upper exact confidence limits

Table 268 Incidence rate ratios of Crohn diseases in Female Cohorts - Imputed date - Confirmed cases (Total cohort)

	IRR Calculation					
		95%CI of RR			95%CI of RR	
Autoimmune diseases	Crude Incidence Rate Ratio	LL	UL	Adjusted Incidence Rate Ratio	LL	UL
Crohn diseases	1.402	0.445	4.416	1.405	0.446	4.427

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted by age group: age group [9-17] and [18-25]

Table 269 Incidence rate difference of Autoimmune Crohn diseases in Female Cohorts - Imputed date - Confirmed cases (Total cohort)

Characteristics	IRD Calculation
IRD(exp-unexp OR conc-hist)	3.103

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 270 Incidence rate ratios of Crohn diseases in Female Cohorts (covariates adjusted) - Imputed date - Confirmed cases (Total cohort)

	IRR Calculation		
		95%CI of RR	
Autoimmune diseases	Adjusted Incidence Rate Ratio	LL	UL
Crohn diseases	1.380	0.433	4.399

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted for other covariates: age group [9-17] and [18-25], healthcare resources utilization in quartile, regions (North England, South England, Midlands & Ireland Scotland Wales), any vaccines during the year prior to the reference date

Table 271 Incidence rate of Crohn diseases in Male Cohorts - Imputed date - Confirmed cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Concurrent Male	5	64865	7.708	2.503	17.989
Historical Male	1	64874	1.541	0.039	8.588

LL, UL = 95% Lower and Upper exact confidence limits

Table 272 Incidence rate ratios of Crohn diseases in Male Cohorts - Imputed date - Confirmed cases (Total cohort)

	IRR Calculation					
		95%CI of RR			95%CI of RR	
Autoimmune diseases	Crude Incidence Rate Ratio	LL	UL	Adjusted Incidence Rate Ratio	LL	UL
Crohn diseases	5.000	0.584	42.794	5.190	0.603	44.676

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted by age group: age group [9-17] and [18-25]

Table 273 Incidence rate difference of Crohn diseases in Male Cohorts - Imputed date - Confirmed cases (Total cohort)

Characteristics	IRD Calculation
IRD(exp-unexp OR conc-hist)	6.167

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 274 Incidence rate of Crohn diseases in Female Cohorts - Imputed date - All cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Exposed Female	9	64730	13.904	6.358	26.394
Non-Exposed Female	5	64844	7.711	2.504	17.994

LL, UL = 95% Lower and Upper exact confidence limits

Table 275 Incidence rate ratios of Crohn diseases in Female Cohorts - Imputed date - All cases (Total cohort)

	IRR Calculation					
		95%CI of RR			95%CI of RR	
Autoimmune diseases	Crude Incidence Rate Ratio	LL	UL	Adjusted Incidence Rate Ratio	LL	UL
Crohn diseases	1.802	0.604	5.377	1.805	0.605	5.387

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted by age group: age group [9-17] and [18-25]

Table 276 Incidence rate difference of Crohn diseases in Female Cohorts - Imputed date - All cases (Total cohort)

Characteristics	IRD Calculation
IRD(exp-unexp OR conc-hist)	6.193

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 277 Incidence rate ratios of Crohn diseases in Female Cohorts (covariates adjusted) - Imputed date - All cases (Total cohort)

	IRR Calculation		
		95%CI of RR	
Autoimmune diseases	Adjusted Incidence Rate Ratio	LL	UL
Crohn diseases	1.750	0.581	5.270

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted for other covariates: age group [9-17] and [18-25], healthcare resources utilization in quartile, regions (North England, South England, Midlands & Ireland Scotland Wales), any vaccines during the year prior to the reference date

Table 278 Incidence rate of Crohn diseases in Male Cohorts - Imputed date - All cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Concurrent Male	5	64865	7.708	2.503	17.989
Historical Male	2	64874	3.083	0.373	11.136

LL, UL = 95% Lower and Upper exact confidence limits

Table 279 Incidence rate ratios of Crohn diseases in Male Cohorts - Imputed date - All cases (Total cohort)

	IRR Calculation					
		95%CI of RR			95%CI of RR	
Autoimmune diseases	Crude Incidence Rate Ratio	LL	UL	Adjusted Incidence Rate Ratio	LL	UL
Crohn diseases	2.500	0.485	12.885	2.553	0.493	13.227

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted by age group: age group [9-17] and [18-25]

Table 280 Incidence rate difference of Crohn diseases in Male Cohorts - Imputed date - All cases (Total cohort)

Characteristics	IRD Calculation
IRD(exp-unexp OR conc-hist)	4.625

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 281 Incidence rate of Inflammatory bowel diseases in Male Cohorts - Imputed date - Confirmed cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Concurrent Male	0	64865	0.000	0.000	5.687
Historical Male	1	64874	1.541	0.039	8.588

LL, UL = 95% Lower and Upper exact confidence limits

Table 282 Incidence rate of Inflammatory bowel diseases in Female Cohorts - Imputed date - All cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Exposed Female	1	64730	1.545	0.039	8.608
Non-Exposed Female	0	64844	0.000	0.000	5.689

LL, UL = 95% Lower and Upper exact confidence limits

Table 283 Incidence rate of Inflammatory bowel diseases in Male Cohorts - Imputed date - All cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Concurrent Male	0	64865	0.000	0.000	5.687
Historical Male	1	64874	1.541	0.039	8.588

LL, UL = 95% Lower and Upper exact confidence limits

Table 284 Incidence rate of Juvenile Rheumatoid Arthritis in Female Cohorts - Imputed date - Confirmed cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Exposed Female	1	64730	1.545	0.039	8.608
Non-Exposed Female	0	64844	0.000	0.000	5.689

LL, UL = 95% Lower and Upper exact confidence limits

Table 285 Incidence rate of Juvenile Rheumatoid Arthritis in Male Cohorts - Imputed date - Confirmed cases (Total cohort)

				95% CI	
Cohort	**Number of cases**	**Person-time (in years)**	**Incidence Rate (per 100,000 PY)**	**LL**	**UL**
Concurrent Male	0	64865	0.000	0.000	5.687
Historical Male	1	64874	1.541	0.039	8.588

LL, UL = 95% Lower and Upper exact confidence limits

Table 286 Incidence rate of Juvenile Rheumatoid Arthritis in Female Cohorts - Imputed date - All cases (Total cohort)

				95% CI	
Cohort	**Number of cases**	**Person-time (in years)**	**Incidence Rate (per 100,000 PY)**	**LL**	**UL**
Exposed Female	1	64730	1.545	0.039	8.608
Non-Exposed Female	0	64844	0.000	0.000	5.689

LL, UL = 95% Lower and Upper exact confidence limits

Table 287 Incidence rate of Juvenile Rheumatoid Arthritis in Male Cohorts - Imputed date - All cases (Total cohort)

				95% CI	
Cohort	**Number of cases**	**Person-time (in years)**	**Incidence Rate (per 100,000 PY)**	**LL**	**UL**
Concurrent Male	0	64865	0.000	0.000	5.687
Historical Male	1	64874	1.541	0.039	8.588

LL, UL = 95% Lower and Upper exact confidence limits

Table 288 Incidence rate of Multiple Sclerosis in Female Cohorts - Imputed date - Confirmed cases (Total cohort)

				95% CI	
Cohort	**Number of cases**	**Person-time (in years)**	**Incidence Rate (per 100,000 PY)**	**LL**	**UL**
Exposed Female	0	64730	0.000	0.000	5.699
Non-Exposed Female	1	64844	1.542	0.039	8.592

LL, UL = 95% Lower and Upper exact confidence limits

Table 289 Incidence rate ratios of Multiple Sclerosis in Female Cohorts - Imputed date - Confirmed cases (Total cohort)

	IRR Calculation					
		95%CI of RR			95%CI of RR	
Autoimmune diseases	**Crude Incidence Rate Ratio**	**LL**	**UL**	**Adjusted Incidence Rate Ratio**	**LL**	**UL**
Multiple Sclerosis	1.002	0.063	16.017	1.006	0.063	16.079

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted by age group: age group [9-17] and [18-25]

Table 290 Incidence rate of Multiple Sclerosis in Female Cohorts - Imputed date - All cases (Total cohort)

				95% CI	
Cohort	**Number of cases**	**Person-time (in years)**	**Incidence Rate (per 100,000 PY)**	**LL**	**UL**
Exposed Female	0	64730	0.000	0.000	5.699
Non-Exposed Female	1	64844	1.542	0.039	8.592

LL, UL = 95% Lower and Upper exact confidence limits

Table 291 Incidence rate ratios of Multiple Sclerosis in Female Cohorts - Imputed date - All cases (Total cohort)

	IRR Calculation					
		95%CI of RR			95%CI of RR	
Autoimmune diseases	**Crude Incidence Rate Ratio**	**LL**	**UL**	**Adjusted Incidence Rate Ratio**	**LL**	**UL**
Multiple Sclerosis	1.001	0.063	16.003	1.005	0.063	16.068

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted by age group: age group [9-17] and [18-25]

Table 292 Incidence rate of Optic Neuritis in Male Cohorts - Imputed date - Confirmed cases (Total cohort)

				95% CI	
Cohort	**Number of cases**	**Person-time (in years)**	**Incidence Rate (per 100,000 PY)**	**LL**	**UL**
Concurrent Male	1	64865	1.542	0.039	8.590
Historical Male	0	64874	0.000	0.000	5.686

LL, UL = 95% Lower and Upper exact confidence limits

Table 293 Incidence rate of Optic Neuritis in Female Cohorts - Imputed date - All cases (Total cohort)

				95% CI	
Cohort	**Number of cases**	**Person-time (in years)**	**Incidence Rate (per 100,000 PY)**	**LL**	**UL**
Exposed Female	1	64730	1.545	0.039	8.608
Non-Exposed Female	1	64844	1.542	0.039	8.592

LL, UL = 95% Lower and Upper exact confidence limits

Table 294 Incidence rate ratios of Optic Neuritis in Female Cohorts - Imputed date - All cases (Total cohort)

	IRR Calculation					
		95%CI of RR			95%CI of RR	
Autoimmune diseases	**Crude Incidence Rate Ratio**	**LL**	**UL**	**Adjusted Incidence Rate Ratio**	**LL**	**UL**
Optic Neuritis	1.001	0.063	16.005	1.000	0.063	15.980

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted by age group: age group [9-17] and [18-25]

Table 295 Incidence rate of Optic Neuritis in Male Cohorts - Imputed date - All cases (Total cohort)

				95% CI	
Cohort	**Number of cases**	**Person-time (in years)**	**Incidence Rate (per 100,000 PY)**	**LL**	**UL**
Concurrent Male	1	64865	1.542	0.039	8.590
Historical Male	0	64874	0.000	0.000	5.686

LL, UL = 95% Lower and Upper exact confidence limits

Table 296 Incidence rate of Psoriatic Arthritis in Female Cohorts - Imputed date - Confirmed cases (Total cohort)

				95% CI	
Cohort	**Number of cases**	**Person-time (in years)**	**Incidence Rate (per 100,000 PY)**	**LL**	**UL**
Exposed Female	1	64730	1.545	0.039	8.608
Non-Exposed Female	1	64844	1.542	0.039	8.592

LL, UL = 95% Lower and Upper exact confidence limits

Table 297 Incidence rate ratios of Psoriatic Arthritis in Female Cohorts - Imputed date - Confirmed cases (Total cohort)

	IRR Calculation					
		95%CI of RR			95%CI of RR	
Autoimmune diseases	**Crude Incidence Rate Ratio**	**LL**	**UL**	**Adjusted Incidence Rate Ratio**	**LL**	**UL**
Psoriatic Arthritis	1.001	0.063	16.005	1.000	0.063	15.980

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted by age group: age group [9-17] and [18-25]

Table 298 Incidence rate of Psoriatic Arthritis in Female Cohorts - Imputed date - All cases (Total cohort)

				95% CI	
Cohort	**Number of cases**	**Person-time (in years)**	**Incidence Rate (per 100,000 PY)**	**LL**	**UL**
Exposed Female	1	64730	1.545	0.039	8.608
Non-Exposed Female	1	64844	1.542	0.039	8.592

LL, UL = 95% Lower and Upper exact confidence limits

Table 299 Incidence rate ratios of Psoriatic Arthritis in Female Cohorts - Imputed date - All cases (Total cohort)

	IRR Calculation					
		95%CI of RR			95%CI of RR	
Autoimmune diseases	**Crude Incidence Rate Ratio**	**LL**	**UL**	**Adjusted Incidence Rate Ratio**	**LL**	**UL**
Psoriatic Arthritis	1.001	0.063	16.005	1.000	0.063	15.980

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted by age group: age group [9-17] and [18-25]

Table 300 Incidence rate of Rheumatoid Arthritis in Female Cohorts - Imputed date - Confirmed cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Exposed Female	1	64730	1.545	0.039	8.608
Non-Exposed Female	0	64844	0.000	0.000	5.689

LL, UL = 95% Lower and Upper exact confidence limits

Table 301 Incidence rate of Rheumatoid Arthritis in Female Cohorts - Imputed date - All cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Exposed Female	1	64730	1.545	0.039	8.608
Non-Exposed Female	0	64844	0.000	0.000	5.689

LL, UL = 95% Lower and Upper exact confidence limits

Table 302 Incidence rate of Systemic Lupus Erythematous in Female Cohorts - Imputed date - Confirmed cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Exposed Female	0	64797	0.000	0.000	5.693
Non-Exposed Female	1	64919	1.540	0.039	8.583

LL, UL = 95% Lower and Upper exact confidence limits

Table 303 Incidence rate of Systemic Lupus Erythematous in Female Cohorts - Imputed date - All cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Exposed Female	0	64882	0.000	0.000	5.686
Non-Exposed Female	1	64945	1.540	0.039	8.579

LL, UL = 95% Lower and Upper exact confidence limits

Table 304 Incidence rate of Autoimmune Type 1 Diabetes Mellitus in Female Cohorts - Imputed date - Confirmed cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Exposed Female	10	64730	15.449	7.408	28.411
Non-Exposed Female	18	64844	27.759	16.452	43.871

LL, UL = 95% Lower and Upper exact confidence limits

Table 305 Incidence rate ratios of Type 1 Diabetes Mellitus in Female Cohorts - Imputed date - Confirmed cases (Total cohort)

	IRR Calculation					
		95%CI of RR			95%CI of RR	
Autoimmune diseases	Crude Incidence Rate Ratio	LL	UL	Adjusted Incidence Rate Ratio	LL	UL
Type 1 Diabetes Mellitus	0.556	0.257	1.205	0.556	0.257	1.205

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted by age group: age group [9-17] and [18-25]

Table 306 Incidence rate difference of Autoimmune Type 1 Diabetes Mellitus in Female Cohorts - Imputed date - Confirmed cases (Total cohort)

Characteristics	IRD Calculation
IRD(exp-unexp OR conc-hist)	-12.310

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 307 Incidence rate ratios of Type 1 Diabetes Mellitus in Female Cohorts (covariates adjusted) - Imputed date - Confirmed cases (Total cohort)

	IRR Calculation		
		95%CI of RR	
Autoimmune diseases	Adjusted Incidence Rate Ratio	LL	UL
Type 1 Diabetes Mellitus	0.586	0.269	1.275

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted for other covariates: age group [9-17] and [18-25], healthcare resources utilization in quartile, regions (North England, South England, Midlands & Ireland Scotland Wales), any vaccines during the year prior to the reference date

Table 308 Incidence rate of Type 1 Diabetes Mellitus in Male Cohorts - Imputed date - Confirmed cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Concurrent Male	23	64865	35.458	22.478	53.205
Historical Male	12	64874	18.497	9.558	32.311

LL, UL = 95% Lower and Upper exact confidence limits

Table 309 Incidence rate ratios of Type 1 Diabetes Mellitus in Male Cohorts - Imputed date - Confirmed cases (Total cohort)

	IRR Calculation					
		95%CI of RR			95%CI of RR	
Autoimmune diseases	Crude Incidence Rate Ratio	LL	UL	Adjusted Incidence Rate Ratio	LL	UL
Type 1 Diabetes Mellitus	1.917	0.954	3.852	1.899	0.944	3.822

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted by age group: age group [9-17] and [18-25]

Table 310 Incidence rate difference of Autoimmune Type 1 Diabetes Mellitus in Male Cohorts - Imputed date - Confirmed cases (Total cohort)

Characteristics	IRD Calculation
IRD(exp-unexp OR conc-hist)	16.961

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 311 Incidence rate ratios of Type 1 Diabetes Mellitus in Male Cohorts (covariates adjusted) - Imputed date - Confirmed cases (Total cohort)

	IRR Calculation		
		95%CI of RR	
Autoimmune diseases	Adjusted Incidence Rate Ratio	LL	UL
Type 1 Diabetes Mellitus	1.887	0.937	3.802

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted for other covariates: age group [9-17] and [18-25], healthcare resources utilization in quartile, regions (North England, South England, Midlands & Ireland Scotland Wales), any vaccines during the year prior to the reference date

Table 312 Incidence rate of Type 1 Diabetes Mellitus in Female Cohorts - Imputed date - All cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Exposed Female	10	64730	15.449	7.408	28.411
Non-Exposed Female	18	64844	27.759	16.452	43.871

LL, UL = 95% Lower and Upper exact confidence limits

Table 313 Incidence rate ratios of Type 1 Diabetes Mellitus in Female Cohorts - Imputed date -All cases (Total cohort)

	IRR Calculation					
		95%CI of RR			95%CI of RR	
Autoimmune diseases	Crude Incidence Rate Ratio	LL	UL	Adjusted Incidence Rate Ratio	LL	UL
Type 1 Diabetes Mellitus	0.556	0.257	1.205	0.556	0.257	1.205

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted by age group: age group [9-17] and [18-25]

Table 314 Incidence rate difference of Autoimmune Type 1 Diabetes Mellitus in Female Cohorts - Imputed date - All cases (Total cohort)

Characteristics	IRD Calculation
IRD(exp-unexp OR conc-hist)	-12.310

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 315 Incidence rate ratios of Type 1 Diabetes Mellitus in Female Cohorts (covariates adjusted) - Imputed date - All cases (Total cohort)

	IRR Calculation		
		95%CI of RR	
Autoimmune diseases	Adjusted Incidence Rate Ratio	LL	UL
Type 1 Diabetes Mellitus	0.586	0.269	1.275

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted for other covariates: age group [9-17] and [18-25], healthcare resources utilization in quartile, regions (North England, South England, Midlands & Ireland Scotland Wales), any vaccines during the year prior to the reference date

Table 316 Incidence rate of Type 1 Diabetes Mellitus in Male Cohorts - Imputed date - All cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Concurrent Male	23	64865	35.46	22.48	53.20
Historical Male	14	64874	21.58	11.80	36.21

LL, UL = 95% Lower and Upper exact confidence limits

Table 317 Incidence rate ratios of Type 1 Diabetes Mellitus in Male Cohorts - Imputed date - All cases (Total cohort)

	IRR Calculation					
		95%CI of RR			95%CI of RR	
Autoimmune diseases	Crude Incidence Rate Ratio	LL	UL	Adjusted Incidence Rate Ratio	LL	UL
Type 1 Diabetes Mellitus	1.643	0.845	3.192	1.645	0.845	3.202

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted by age group: age group [9-17] and [18-25]

Table 318 Incidence rate difference of Autoimmune Type 1 Diabetes Mellitus in Male Cohorts - Imputed date - All cases (Total cohort)

Characteristics	IRD Calculation
IRD(exp-unexp OR conc-hist)	13.878

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 319 Incidence rate ratios of Type 1 Diabetes Mellitus in Male Cohorts (covariates adjusted) - Imputed date - All cases (Total cohort)

	IRR Calculation		
		95%CI of RR	
Autoimmune diseases	Adjusted Incidence Rate Ratio	LL	UL
Type 1 Diabetes Mellitus	1.640	0.842	3.195

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted for other covariates: age group [9-17] and [18-25], healthcare resources utilization in quartile, regions (North England, South England, Midlands & Ireland Scotland Wales), any vaccines during the year prior to the reference date

Table 320 Incidence rate of Autoimmune Ulcerative Colitis in Female Cohorts - Imputed date - Confirmed cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Exposed Female	4	64730	6.180	1.684	15.822
Non-Exposed Female	0	64844	0.000	0.000	5.689

LL, UL = 95% Lower and Upper exact confidence limits

Table 321 Incidence rate of Ulcerative Colitis in Male Cohorts - Imputed date - Confirmed cases (Total cohort)

				95% CI	
Cohort	**Number of cases**	**Person-time (in years)**	**Incidence Rate (per 100,000 PY)**	**LL**	**UL**
Concurrent Male	4	64865	6.167	1.680	15.789
Historical Male	2	64874	3.083	0.373	11.136

LL, UL = 95% Lower and Upper exact confidence limits

Table 322 Incidence rate ratios of Ulcerative Colitis in Male Cohorts - Imputed date - Confirmed cases (Total cohort)

	IRR Calculation					
		95%CI of RR			95%CI of RR	
Autoimmune diseases	**Crude Incidence Rate Ratio**	**LL**	**UL**	**Adjusted Incidence Rate Ratio**	**LL**	**UL**
Ulcerative Colitis	2.000	0.366	10.919	2.064	0.376	11.339

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted by age group: age group [9-17] and [18-25]

Table 323 Incidence rate of Ulcerative Colitis in Female Cohorts - Imputed date - All cases (Total cohort)

				95% CI	
Cohort	**Number of cases**	**Person-time (in years)**	**Incidence Rate (per 100,000 PY)**	**LL**	**UL**
Exposed Female	4	64730	6.180	1.684	15.822
Non-Exposed Female	1	64844	1.542	0.039	8.592

LL, UL = 95% Lower and Upper exact confidence limits

Table 324 Incidence rate ratios of Ulcerative Colitis in Female Cohorts - Imputed date - All cases (Total cohort)

	IRR Calculation					
		95%CI of RR			95%CI of RR	
Autoimmune diseases	**Crude Incidence Rate Ratio**	**LL**	**UL**	**Adjusted Incidence Rate Ratio**	**LL**	**UL**
Ulcerative Colitis	4.004	0.448	35.828	3.998	0.447	35.771

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted by age group: age group [9-17] and [18-25]

Table 325 Incidence rate of Ulcerative Colitis in Male Cohorts - Imputed date - All cases (Total cohort)

				95% CI	
Cohort	**Number of cases**	**Person-time (in years)**	**Incidence Rate (per 100,000 PY)**	**LL**	**UL**
Concurrent Male	4	64865	6.167	1.680	15.789
Historical Male	2	64874	3.083	0.373	11.136

LL, UL = 95% Lower and Upper exact confidence limits

Table 326 Incidence rate ratios of Ulcerative Colitis in Male Cohorts - Imputed date - All cases (Total cohort)

	IRR Calculation					
		95%CI of RR			95%CI of RR	
Autoimmune diseases	Crude Incidence Rate Ratio	LL	UL	Adjusted Incidence Rate Ratio	LL	UL
Ulcerative Colitis	2.000	0.366	10.919	2.064	0.376	11.339

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted by age group: age group [9-17] and [18-25]

Table 327 Incidence rate of Idiopathic Thrombocytopenia Purpura in Female Cohorts - Imputed date - Confirmed cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Exposed Female	1	64730	1.545	0.039	8.608
Non-Exposed Female	1	64844	1.542	0.039	8.592

LL, UL = 95% Lower and Upper exact confidence limits

Table 328 Incidence rate ratios of Idiopathic Thrombocytopenia Purpura in Female Cohorts - Imputed date - Confirmed cases (Total cohort)

	IRR Calculation					
		95%CI of RR			95%CI of RR	
Autoimmune diseases	Crude Incidence Rate Ratio	LL	UL	Adjusted Incidence Rate Ratio	LL	UL
Idiopathic Thrombocytopenia Purpura	1.001	0.063	16.006	1.000	0.063	15.980

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted by age group: age group [9-17] and [18-25]

Table 329 Incidence rate of Idiopathic Thrombocytopenia Purpura in Male Cohorts - Imputed date - Confirmed cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Concurrent Male	0	64865	0.000	0.000	5.687
Historical Male	1	64874	1.541	0.039	8.588

LL, UL = 95% Lower and Upper exact confidence limits

Table 330 Incidence rate of Idiopathic Thrombocytopenia Purpura in Female Cohorts - Imputed date - All cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Exposed Female	1	64730	1.545	0.039	8.608
Non-Exposed Female	1	64844	1.542	0.039	8.592

LL, UL = 95% Lower and Upper exact confidence limits

Table 331 Incidence rate ratios of Idiopathic Thrombocytopenia Purpura in Female Cohorts - Imputed date - All cases (Total cohort)

	IRR Calculation					
		95%CI of RR			95%CI of RR	
Autoimmune diseases	**Crude Incidence Rate Ratio**	**LL**	**UL**	**Adjusted Incidence Rate Ratio**	**LL**	**UL**
Idiopathic Thrombocytopenia Purpura	1.001	0.063	16.006	1.000	0.063	15.980

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted by age group: age group [9-17] and [18-25]

Table 332 Incidence rate of Idiopathic Thrombocytopenia Purpura in Male Cohorts - Imputed date - All cases (Total cohort)

				95% CI	
Cohort	**Number of cases**	**Person-time (in years)**	**Incidence Rate (per 100,000 PY)**	**LL**	**UL**
Concurrent Male	0	64865	0.000	0.000	5.687
Historical Male	1	64874	1.541	0.039	8.588

LL, UL = 95% Lower and Upper exact confidence limits

Table 333 Frequency of autoimmune diseases during the one year follow-up period by exposed/non-exposed status - Sensitivity Analysis - Onset diagnosis - Confirmed and Non-Confirmed cases (Total cohort)

		EXP N = 64998		NNEXP N = 64994		MALE N = 64988		HIST N = 64978		Total N = 259958	
Characteristics	**Categories**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**
Coprimary endpoints within 1 year follow-up period	Neuroinflammatory Ophthalmic autoimmune diseases	6	9.23	10	15.39	9	13.85	3	4.62	28	10.77
	Other autoimmune diseases	87	133.85	85	130.78	56	86.17	48	73.87	276	106.17

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n = number of subjects in a given category
Per 100000 = n/Number of subjects with available results*100000
Neuroinflammatory/Ophthalmic autoimmune diseases included: Multiple Sclerosis, Transverse Myelitis, Optic Neuritis, Guillain Barré Syndrome, Acute dissiminated encephalomyelitis, Autoimmune Peripheral neuropathies & plexopathies and Autoimmune Uveitis. Note: that 1 AD was classified as Other AD
Follow-up period 1 year for all the cohorts

Table 334 Frequency of autoimmune diseases during the one year follow-up period by exposed/non-exposed status - Sensitivity Analysis - Onset diagnosis - Confirmed cases (Total cohort)

		EXP N = 64998		NNEXP N = 64994		MALE N = 64988		HIST N = 64978		Total N = 259958	
Characteristics	**Categories**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**
Coprimary endpoints within 1 year follow-up period	Neuroinflammatory/Ophthalmic autoimmune diseases	1	1.54	1	1.54	2	3.08	1	1.54	5	1.92
	Other autoimmune diseases	58	89.23	52	80.01	45	69.24	33	50.79	188	72.32

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n = number of subjects in a given category
Per 100000 = n/Number of subjects with available results*100000
Neuroinflammatory/Ophthalmic autoimmune diseases included: Multiple Sclerosis, Transverse Myelitis, Optic Neuritis, Guillain Barré Syndrome, Acute dissiminated encephalomyelitis, Autoimmune Peripheral neuropathies & plexopathies and Autoimmune Uveitis. Note: that 1 AD was classified as Other AD
Follow-up period 1 year for all the cohorts

Table 335 Frequency of autoimmune diseases during the one year follow-up period by exposed/non-exposed status - Sensitivity Analysis - Onset diagnosis - Confirmed and Non-Confirmed cases (N=AD) (Total cohort)

		EXP N = 65001		NNEXP N = 64995		MALE N = 64988		HIST N = 64979		Total N = 259963	
Characteristics	**Categories**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**
Individual autoimmune diseases within 1 year follow-up period	Acute disseminated encephalomyelitis	1	1.54	0	0.00	0	0.00	0	0.00	1	0.38
	Ankylosing Spondylitis	1	1.54	0	0.00	0	0.00	2	3.08	3	1.15
	Autoimmune Peripheral Neuropathies and Plexopathie	0	0.00	1	1.54	0	0.00	0	0.00	1	0.38
	Autoimmune Thyroiditis	48	73.85	46	70.77	10	15.39	8	12.31	112	43.08
	Autoimmune Uveitis	3	4.62	7	10.77	6	9.23	3	4.62	19	7.31
	Crohn diseases	13	20.00	9	13.85	16	24.62	10	15.39	48	18.46
	Guillain-Barre Syndrome	0	0.00	0	0.00	1	1.54	1	1.54	2	0.77
	Idiopathic Thrombocytopenia Purpura	1	1.54	1	1.54	1	1.54	2	3.08	5	1.92
	Inflammatory Bowel Diseases	2	3.08	1	1.54	0	0.00	3	4.62	6	2.31
	Juvenile Rheumatoid Arthritis	1	1.54	3	4.62	1	1.54	4	6.16	9	3.46
	Multiple Sclerosis	1	1.54	1	1.54	0	0.00	0	0.00	2	0.77
	Optic Neuritis	1	1.54	1	1.54	2	3.08	0	0.00	4	1.54
	Other AD	1	1.54	3	4.62	0	0.00	0	0.00	4	1.54
	Psoriatic Arthritis	2	3.08	1	1.54	0	0.00	0	0.00	3	1.15
	Rheumatoid Arthritis	2	3.08	1	1.54	1	1.54	0	0.00	4	1.54
	Type 1 Diabetes Mellitus	11	16.92	20	30.77	23	35.39	15	23.08	69	26.54
	Ulcerative Colitis	6	9.23	1	1.54	4	6.15	4	6.16	15	5.77

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n = number of subjects in a given category
Per 100000 = n/Number of subjects with available results*100000
Neuroinflammatory/Ophthalmic autoimmune diseases included: Multiple Sclerosis, Transverse Myelitis, Optic Neuritis, Guillain Barré Syndrome, Acute disseminated encephalomyelitis, Autoimmune Peripheral neuropathies & plexopathies and Autoimmune Uveitis. Note: that 1 AD was classified as Other AD
Follow-up period 1 year for all the cohorts
Two subjects have simultaneously diabetes and thyroid diseases (exposed & non-exposed female cohorts), one subject has simultaneously diabetes and uveitis (hist male cohort)

Table 336 Frequency of autoimmune diseases during the one year follow-up period by exposed/non-exposed status - Sensitivity Analysis - Onset diagnosis - Confirmed cases (N=AD) (Total cohort)

		EXP N = 65001		NNEXP N = 64995		MALE N = 64988		HIST N = 64979		Total N = 259963	
Characteristics	**Categories**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**
Individual autoimmune diseases within 1 year follow-up period	Ankylosing Spondylitis	0	0.00	0	0.00	0	0.00	1	1.54	1	0.38
	Autoimmune Thyroiditis	23	35.38	15	23.08	2	3.08	0	0.00	40	15.39
	Crohn diseases	11	16.92	9	13.85	15	23.08	8	12.31	43	16.54
	Guillain-Barre Syndrome	0	0.00	0	0.00	1	1.54	1	1.54	2	0.77
	Idiopathic Thrombocytopenia Purpura	1	1.54	1	1.54	0	0.00	2	3.08	4	1.54
	Inflammatory Bowel Diseases	1	1.54	0	0.00	0	0.00	2	3.08	3	1.15
	Juvenile Rheumatoid Arthritis	1	1.54	3	4.62	1	1.54	3	4.62	8	3.08
	Multiple Sclerosis	1	1.54	1	1.54	0	0.00	0	0.00	2	0.77
	Optic Neuritis	0	0.00	0	0.00	1	1.54	0	0.00	1	0.38
	Other AD	1	1.54	3	4.62	0	0.00	0	0.00	4	1.54
	Psoriatic Arthritis	1	1.54	1	1.54	0	0.00	0	0.00	2	0.77
	Rheumatoid Arthritis	2	3.08	0	0.00	0	0.00	0	0.00	2	0.77
	Type 1 Diabetes Mellitus	11	16.92	20	30.77	23	35.39	13	20.01	67	25.77
	Ulcerative Colitis	6	9.23	0	0.00	4	6.15	4	6.16	14	5.39

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n = number of subjects in a given category
Per 100000 = n/Number of subjects with available results*100000
Neuroinflammatory/Ophthalmic autoimmune diseases included: Multiple Sclerosis, Transverse Myelitis, Optic Neuritis, Guillain Barré Syndrome, Acute disseminated encephalomyelitis, Autoimmune Peripheral neuropathies & plexopathies and Autoimmune Uveitis. Note: that 1 AD was classified as Other AD
Follow-up period 1 year for all the cohorts

Table 337 Frequency of autoimmune disease during the specific time period by exposed/non-exposed status - Sensitivity Analysis - Onset diagnosis - Confirmed and Non-Confirmed cases (Total cohort)

		EXP N = 64998		NNEXP N = 64994		MALE N = 64988		HIST N = 64978		Total N = 259958	
Characteristics	**Categories**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**
Individual autoimmune diseases within 2 months of FU period	Guillain-Barre Syndrome	0	0.00	0	0.00	0	0.00	1	1.54	1	0.38

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n = number of subjects in a given category
Per 100000 = n/Number of subjects with available results*100000
Autoimmune diseases within 2 months included: Guillain Barré Syndrome and Autoimmune Haemolytic Anaemia
FU:Specific time disease follow-up period

Table 338 Frequency of autoimmune disease during the specific time period by exposed/non-exposed status - Sensitivity Analysis - Onset diagnosis - Confirmed cases (Total cohort)

		EXP N = 64998		NNEXP N = 64994		MALE N = 64988		HIST N = 64978		Total N = 259958	
Characteristics	**Categories**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**
Individual autoimmune diseases within 2 months of FU period	Guillain-Barre Syndrome	0	0.00	0	0.00	0	0.00	1	1.54	1	0.38

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n = number of subjects in a given category
Per 100000 = n/Number of subjects with available results*100000
Autoimmune diseases within 2 months included: Guillain Barré Syndrome and Autoimmune Haemolytic Anaemia
FU:Specific time disease follow-up period

Table 339 Frequency of autoimmune disease during the specific time period by exposed/non-exposed status - Sensitivity Analysis - Onset diagnosis - Confirmed and Non-Confirmed cases (Total cohort)

		EXP N = 64998		NNEXP N = 64994		MALE N = 64988		HIST N = 64978		Total N = 259958	
Characteristics	**Categories**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**
Individual autoimmune disease within 6 months of FU period	Idiopathic Thrombocytopenia Purpura	1	1.54	1	1.54	0	0.00	1	1.54	3	1.15

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n = number of subjects in a given category
Per 100000 = n/Number of subjects with available results*100000
Autoimmune diseases within 6 months included: Idiopathic Thrombocytopenia Purpura
FU:Specific time disease follow-up period

Table 340 Frequency of autoimmune disease during the specific time period by exposed/non-exposed status - Sensitivity Analysis - Onset diagnosis - Confirmed cases (Total cohort)

		EXP N = 64998		NNEXP N = 64994		MALE N = 64988		HIST N = 64978		Total N = 259958	
Characteristics	**Categories**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**
Individual autoimmune disease within 6 months of FU period	Idiopathic Thrombocytopenia Purpura	1	1.54	1	1.54	0	0.00	1	1.54	3	1.15

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n = number of subjects in a given category
Per 100000 = n/Number of subjects with available results*100000
Autoimmune diseases within 6 months included: Idiopathic Thrombocytopenia Purpura
FU:Specific time disease follow-up period

Table 341 Frequency of autoimmune disease during the specific time period by exposed/non-exposed status - Onset Analysis - Confirmed and Non-Confirmed cases (N=AD) (Total cohort)

		EXP N = 65001		NNEXP N = 64995		MALE N = 64988		HIST N = 64979		Total N = 259963	
Characteristics	**Categories**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**
Individual autoimmune diseases within 12 months of FU period	Acute disseminated encephalomyelitis	1	1.54	0	0.00	0	0.00	0	0.00	1	0.38
	Ankylosing Spondylitis	1	1.54	0	0.00	0	0.00	2	3.08	3	1.15
	Autoimmune Peripheral Neuropathies and Plexopathie	0	0.00	1	1.54	0	0.00	0	0.00	1	0.38
	Autoimmune Thyroiditis	48	73.85	46	70.77	10	15.39	8	12.31	112	43.08
	Autoimmune Uveitis	3	4.62	7	10.77	6	9.23	3	4.62	19	7.31
	Crohn diseases	13	20.00	9	13.85	16	24.62	10	15.39	48	18.46
	Inflammatory Bowel Diseases	2	3.08	1	1.54	0	0.00	3	4.62	6	2.31
	Juvenile Rheumatoid Arthritis	1	1.54	3	4.62	1	1.54	4	6.16	9	3.46
	Multiple Sclerosis	1	1.54	1	1.54	0	0.00	0	0.00	2	0.77
	Optic Neuritis	1	1.54	1	1.54	2	3.08	0	0.00	4	1.54
	Other AD	1	1.54	3	4.62	0	0.00	0	0.00	4	1.54
	Psoriatic Arthritis	2	3.08	1	1.54	0	0.00	0	0.00	3	1.15
	Rheumatoid Arthritis	2	3.08	1	1.54	1	1.54	0	0.00	4	1.54
	Type 1 Diabetes Mellitus	11	16.92	20	30.77	23	35.39	15	23.08	69	26.54
	Ulcerative Colitis	6	9.23	1	1.54	4	6.15	4	6.16	15	5.77

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n = number of subjects in a given category
Per 100000 = n/Number of subjects with available results*100000
FU:Specific time disease follow-up period

Table 342 Frequency of autoimmune disease during the specific time period by exposed/non-exposed status - Onset Analysis - Confirmed cases (N=AD) (Total cohort)

		EXP N = 65001		NNEXP N = 64995		MALE N = 64988		HIST N = 64979		Total N = 259963	
Characteristics	**Categories**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**
Individual autoimmune diseases within 12 months of FU period	Ankylosing Spondylitis	0	0.00	0	0.00	0	0.00	1	1.54	1	0.38
	Autoimmune Thyroiditis	23	35.38	15	23.08	2	3.08	0	0.00	40	15.39
	Crohn diseases	11	16.92	9	13.85	15	23.08	8	12.31	43	16.54
	Inflammatory Bowel Diseases	1	1.54	0	0.00	0	0.00	2	3.08	3	1.15
	Juvenile Rheumatoid Arthritis	1	1.54	3	4.62	1	1.54	3	4.62	8	3.08
	Multiple Sclerosis	1	1.54	1	1.54	0	0.00	0	0.00	2	0.77
	Optic Neuritis	0	0.00	0	0.00	1	1.54	0	0.00	1	0.38
	Other AD	1	1.54	3	4.62	0	0.00	0	0.00	4	1.54
	Psoriatic Arthritis	1	1.54	1	1.54	0	0.00	0	0.00	2	0.77
	Rheumatoid Arthritis	2	3.08	0	0.00	0	0.00	0	0.00	2	0.77
	Type 1 Diabetes Mellitus	11	16.92	20	30.77	23	35.39	13	20.01	67	25.77
	Ulcerative Colitis	6	9.23	0	0.00	4	6.15	4	6.16	14	5.39

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n = number of subjects in a given category
Per 100000 = n/Number of subjects with available results*100000
FU:Specific time disease follow-up period

Table 343 Incidence rate of Neuroinflammatory/Ophthalmic autoimmune diseases in Female Cohorts - Onset Diagnosis - Confirmed cases (Total cohort)

				95% CI	
Cohort	**Number of cases**	**Person-time (in years)**	**Incidence Rate (per 100,000 PY)**	**LL**	**UL**
Exposed Female	1	64852	1.542	0.039	8.591
Non-Exposed Female	1	64893	1.541	0.039	8.586

LL, UL = 95% Lower and Upper exact confidence limits

Table 344 Incidence rate ratios of Neuroinflammatory/Ophthalmic diseases in Female Cohorts - Onset Diagnosis - Confirmed cases (Total cohort)

	IRR Calculation					
		95%CI of RR			95%CI of RR	
Autoimmune diseases	**Crude Incidence Rate Ratio**	**LL**	**UL**	**Adjusted Incidence Rate Ratio**	**LL**	**UL**
Neuroinflammatory/Ophthalmic autoimmune diseases	1.001	0.063	15.998	1.007	0.063	16.104

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted by age group: age group [9-17] and [18-25]

Table 345 Incidence rate difference of Neuroinflammatory/Ophthalmic autoimmune diseases in Female Cohorts - Onset Diagnosis - Confirmed cases (Total cohort)

Characteristics	**IRD Calculation**
IRD(exp-unexp OR conc-hist)	0.001

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 346 Incidence rate of Other autoimmune diseases in Female Cohorts - Onset Diagnosis - Confirmed cases (Total cohort)

				95% CI	
Cohort	**Number of cases**	**Person-time (in years)**	**Incidence Rate (per 100,000 PY)**	**LL**	**UL**
Exposed Female	58	64852	89.435	67.912	115.615
Non-Exposed Female	52	64893	80.132	59.847	105.083

LL, UL = 95% Lower and Upper exact confidence limits

Table 347 Incidence rate ratios of Other autoimmune diseases in Female Cohorts - Onset Diagnosis - Confirmed cases (Total cohort)

	IRR Calculation					
		95%CI of RR			95%CI of RR	
Autoimmune diseases	Crude Incidence Rate Ratio	LL	UL	Adjusted Incidence Rate Ratio	LL	UL
Other autoimmune diseases	1.116	0.768	1.623	1.116	0.768	1.623

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted by age group: age group [9-17] and [18-25]

Table 348 Incidence rate difference of Other autoimmune diseases in Female Cohorts - Onset Diagnosis - Confirmed cases (Total cohort)

Characteristics	IRD Calculation
IRD(exp-unexp OR conc-hist)	9.302

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 349 Incidence rate ratios of Other autoimmune diseases in Female Cohorts (covariates adjusted) - Onset Diagnosis - Confirmed cases (Total cohort)

	IRR Calculation		
		95%CI of RR	
Autoimmune diseases	Adjusted Incidence Rate Ratio	LL	UL
Other autoimmune diseases	1.027	0.705	1.497

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted for other covariates: age group [9-17] and [18-25], healthcare resources utilization in quartile, regions (North England, South England, Midlands & Ireland Scotland Wales), any vaccines during the year prior to the reference date

Table 350 Incidence rate of Neuroinflammatory/Ophthalmic autoimmune diseases in Female Cohorts - Onset Diagnosis - All cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Exposed Female	6	64852	9.252	3.395	20.137
Non-Exposed Female	10	64893	15.410	7.390	28.340

LL, UL = 95% Lower and Upper exact confidence limits

Table 351 Incidence rate ratios of Neuroinflammatory/Ophthalmic diseases in Female Cohorts - Onset Diagnosis - All cases (Total cohort)

	IRR Calculation					
		95%CI of RR			95%CI of RR	
Autoimmune diseases	Crude Incidence Rate Ratio	LL	UL	Adjusted Incidence Rate Ratio	LL	UL
Neuroinflammatory/Ophthalmic autoimmune diseases	0.600	0.218	1.652	0.600	0.218	1.651

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted by age group: age group [9-17] and [18-25]

Table 352 Incidence rate difference of Neuroinflammatory/Ophthalmic autoimmune diseases in Female Cohorts - Onset Diagnosis - All cases (Total cohort)

Characteristics	IRD Calculation
IRD(exp-unexp OR conc-hist)	-6.158

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 353 Incidence rate ratios of Neuroinflammatory/Ophthalmic diseases in Female Cohorts (covariates adjusted) - Onset Diagnosis - All cases (Total cohort)

	IRR Calculation		
		95%CI of RR	
Autoimmune diseases	Adjusted Incidence Rate Ratio	LL	UL
Neuroinflammatory/Ophthalmic autoimmune diseases	0.609	0.219	1.696

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted for other covariates: age group [9-17] and [18-25], healthcare resources utilization in quartile, regions (North England, South England, Midlands & Ireland Scotland Wales), any vaccines during the year prior to the reference date

Table 354 Incidence rate of Other autoimmune diseases in Female Cohorts - Onset Diagnosis - All cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 10,000 PY)	LL	UL
Exposed Female	87	64852	13.415	10.745	16.548
Non-Exposed Female	85	64893	13.099	10.463	16.197

LL, UL = 95% Lower and Upper exact confidence limits

Table 355 Incidence rate ratios of Other autoimmune diseases in Female Cohorts - Onset Diagnosis - All cases (Total cohort)

	IRR Calculation					
		95%CI of RR			95%CI of RR	
Autoimmune diseases	Crude Incidence Rate Ratio	LL	UL	Adjusted Incidence Rate Ratio	LL	UL
Other autoimmune diseases	1.024	0.760	1.381	1.024	0.760	1.381

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted by age group: age group [9-17] and [18-25]

Table 356 Incidence rate difference of Other autoimmune diseases in Female Cohorts - Onset Diagnosis - All cases (Total cohort)

Characteristics	IRD Calculation
IRD(exp-unexp OR conc-hist)	0.317

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 357 Incidence rate ratios of Other autoimmune diseases in Female Cohorts (covariates adjusted) - Onset Diagnosis - All cases (Total cohort)

	IRR Calculation		
		95%CI of RR	
Autoimmune diseases	Adjusted Incidence Rate Ratio	LL	UL
Other autoimmune diseases	0.931	0.689	1.258

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted for other covariates: age group [9-17] and [18-25], healthcare resources utilization in quartile, regions (North England, South England, Midlands & Ireland Scotland Wales), any vaccines during the year prior to the reference date

Table 358 Incidence rate of Neuroinflammatory/Ophthalmic autoimmune diseases in Male Cohorts - Onset Diagnosis - Confirmed cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Concurrent Male	2	64897	3.082	0.373	11.133
Historical Male	1	64891	1.541	0.039	8.586

LL, UL = 95% Lower and Upper exact confidence limits

Table 359 Incidence rate ratios of Neuroinflammatory/Ophthalmic diseases in Male Cohorts - Onset Diagnosis - Confirmed cases (Total cohort)

	IRR Calculation					
		95%CI of RR			95%CI of RR	
Autoimmune diseases	Crude Incidence Rate Ratio	LL	UL	Adjusted Incidence Rate Ratio	LL	UL
Neuroinflammatory/Ophthalmic autoimmune diseases	2.000	0.181	22.054	1.899	0.172	20.938

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted by age group: age group [9-17] and [18-25]

Table 360 Incidence rate difference of Neuroinflammatory/Ophthalmic autoimmune diseases in Male Cohorts - Onset Diagnosis - Confirmed cases (Total cohort)

Characteristics	IRD Calculation
IRD(exp-unexp OR conc-hist)	1.541

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 361 Incidence rate of Other autoimmune diseases in Male Cohorts - Onset Diagnosis - Confirmed cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Concurrent Male	45	64897	69.341	50.578	92.783
Historical Male	33	64891	50.854	35.006	71.418

LL, UL = 95% Lower and Upper exact confidence limits

Table 362 Incidence rate ratios of Other autoimmune diseases in Male Cohorts - Onset Diagnosis - Confirmed cases (Total cohort)

	IRR Calculation					
		95%CI of RR			95%CI of RR	
Autoimmune diseases	Crude Incidence Rate Ratio	LL	UL	Adjusted Incidence Rate Ratio	LL	UL
Other autoimmune diseases	1.364	0.870	2.137	1.386	0.883	2.175

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted by age group: age group [9-17] and [18-25]

Table 363 Incidence rate difference of Other autoimmune diseases in Male Cohorts - Onset Diagnosis - Confirmed cases (Total cohort)

Characteristics	IRD Calculation
IRD(exp-unexp OR conc-hist)	18.486

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 364 Incidence rate ratios of Other autoimmune diseases in Male Cohorts (covariates adjusted) - Onset Diagnosis - Confirmed cases (Total cohort)

	IRR Calculation		
		95%CI of RR	
Autoimmune diseases	Adjusted Incidence Rate Ratio	LL	UL
Other autoimmune diseases	1.361	0.867	2.138

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted for other covariates: age group [9-17] and [18-25], healthcare resources utilization in quartile, regions (North England, South England, Midlands & Ireland Scotland Wales), any vaccines during the year prior to the reference date

Table 365 Incidence rate of Neuroinflammatory/Ophthalmic autoimmune diseases in Male Cohorts - Onset Diagnosis - All cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Concurrent Male	9	64897	13.868	6.341	26.326
Historical Male	3	64891	4.623	0.953	13.511

LL, UL = 95% Lower and Upper exact confidence limits

Table 366 Incidence rate ratios of Neuroinflammatory/Ophthalmic diseases in Male Cohorts - Onset Diagnosis - All cases (Total cohort)

	IRR Calculation					
		95%CI of RR			95%CI of RR	
Autoimmune diseases	Crude Incidence Rate Ratio	LL	UL	Adjusted Incidence Rate Ratio	LL	UL
Neuroinflammatory/Ophthalmic autoimmune diseases	3.000	0.812	11.080	3.105	0.837	11.518

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted by age group: age group [9-17] and [18-25]

Table 367 Incidence rate difference of Neuroinflammatory/Ophthalmic autoimmune diseases in Male Cohorts - Onset Diagnosis - All cases (Total cohort)

Characteristics	IRD Calculation
IRD(exp-unexp OR conc-hist)	9.245

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 368 Incidence rate ratios of Neuroinflammatory/Ophthalmic diseases in Male Cohorts (covariates adjusted) - Onset Diagnosis - All cases (Total cohort)

	IRR Calculation		
		95%CI of RR	
Autoimmune diseases	Adjusted Incidence Rate Ratio	LL	UL
Neuroinflammatory/Ophthalmic autoimmune diseases	2.132	0.566	8.038

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted for other covariates: age group [9-17] and [18-25], healthcare resources utilization in quartile regions (North England, South England, Midlands & Ireland Scotland Wales), live attenuated & adjuvanted & other vaccines in the follow-up period

Table 369 Incidence rate of Other autoimmune diseases in Male Cohorts - Onset Diagnosis - All cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Concurrent Male	56	64897	86.291	65.183	112.056
Historical Male	48	64891	73.970	54.540	98.073

LL, UL = 95% Lower and Upper exact confidence limits

Table 370 Incidence rate ratios of Other autoimmune diseases in Male Cohorts - Onset Diagnosis - All cases (Total cohort)

	IRR Calculation					
		95%CI of RR			95%CI of RR	
Autoimmune diseases	Crude Incidence Rate Ratio	LL	UL	Adjusted Incidence Rate Ratio	LL	UL
Other autoimmune diseases	1.167	0.793	1.715	1.186	0.806	1.746

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted by age group: age group [9-17] and [18-25]

Table 371 Incidence rate difference of Other autoimmune diseases in Male Cohorts - Onset Diagnosis - All cases (Total cohort)

Characteristics	IRD Calculation
IRD(exp-unexp OR conc-hist)	12.321

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 372 Incidence rate ratios of Other autoimmune diseases in Male Cohorts (covariates adjusted) - Onset Diagnosis - All cases (Total cohort)

	IRR Calculation		
		95%CI of RR	
Autoimmune diseases	Adjusted Incidence Rate Ratio	LL	UL
Other autoimmune diseases	1.160	0.788	1.709

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted for other covariates: age group [9-17] and [18-25], healthcare resources utilization in quartile, regions (North England, South England, Midlands & Ireland Scotland Wales), any vaccines during the year prior to the reference date

Table 373 Incidence rate of Acute Disseminated Encephalomyelitis in Female Cohorts - Onset Diagnosis - All cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Exposed Female	1	64852	1.542	0.039	8.591
Non-Exposed Female	0	64893	0.000	0.000	5.685

LL, UL = 95% Lower and Upper exact confidence limits

Table 374 Incidence rate of Ankylosing Spondylitis in Male Cohorts - Onset Diagnosis - Confirmed cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Concurrent Male	0	64897	0.000	0.000	5.684
Historical Male	1	64891	1.541	0.039	8.586

LL, UL = 95% Lower and Upper exact confidence limits

Table 375 Incidence rate of Ankylosing Spondylitis in Female Cohorts - Onset Diagnosis - All cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Exposed Female	1	64852	1.542	0.039	8.591
Non-Exposed Female	0	64893	0.000	0.000	5.685

LL, UL = 95% Lower and Upper exact confidence limits

Table 376 Incidence rate of Ankylosing Spondylitis in Male Cohorts - Onset Diagnosis - All cases (Total cohort)

				95% CI	
Cohort	**Number of cases**	**Person-time (in years)**	**Incidence Rate (per 100,000 PY)**	**LL**	**UL**
Concurrent Male	0	64897	0.000	0.000	5.684
Historical Male	2	64891	3.082	0.373	11.134

LL, UL = 95% Lower and Upper exact confidence limits

Table 377 Incidence rate of Peripheral neuropathies and plexopathies in Female Cohorts - Onset Diagnosis - All cases (Total cohort)

				95% CI	
Cohort	**Number of cases**	**Person-time (in years)**	**Incidence Rate (per 100,000 PY)**	**LL**	**UL**
Exposed Female	0	64852	0.000	0.000	5.688
Non-Exposed Female	1	64893	1.541	0.039	8.586

LL, UL = 95% Lower and Upper exact confidence limits

Table 378 Incidence rate of Autoimmune Thyroiditis in Female Cohorts - Onset Diagnosis - Confirmed cases (Total cohort)

				95% CI	
Cohort	**Number of cases**	**Person-time (in years)**	**Incidence Rate (per 100,000 PY)**	**LL**	**UL**
Exposed Female	23	64852	35.465	22.482	53.215
Non-Exposed Female	15	64893	23.115	12.937	38.125

LL, UL = 95% Lower and Upper exact confidence limits

Table 379 Incidence rate ratios of Autoimmune Thyroiditis in Female Cohorts - Onset Diagnosis - Confirmed cases (Total cohort)

	IRR Calculation					
		95%CI of RR			95%CI of RR	
Autoimmune diseases	**Crude Incidence Rate Ratio**	**LL**	**UL**	**Adjusted Incidence Rate Ratio**	**LL**	**UL**
Autoimmune Thyroiditis	1.534	0.801	2.940	1.533	0.800	2.938

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted by age group: age group [9-17] and [18-25]

Table 380 Incidence rate difference of Autoimmune Thyroiditis diseases in Female Cohorts - Onset Diagnosis - Confirmed cases (Total cohort)

Characteristics	**IRD Calculation**
IRD(exp-unexp OR conc-hist)	12.350

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 381 Incidence rate ratios of Autoimmune Thyroiditis in Female Cohorts (covariates adjusted) - Onset Diagnosis - Confirmed cases (Total cohort)

	IRR Calculation		
		95%CI of RR	
Autoimmune diseases	Adjusted Incidence Rate Ratio	LL	UL
Autoimmune Thyroiditis	1.336	0.695	2.567

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted for other covariates: age group [9-17] and [18-25], healthcare resources utilization in quartile, regions (North England, South England, Midlands & Ireland Scotland Wales), any vaccines during the year prior to the reference date

Table 382 Incidence rate of Autoimmune Thyroiditis in Male Cohorts - Onset Diagnosis - Confirmed cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Concurrent Male	2	64897	3.082	0.373	11.133
Historical Male	0	64891	0.000	0.000	5.685

LL, UL = 95% Lower and Upper exact confidence limits

Table 383 Incidence rate difference of Autoimmune Thyroiditis diseases in Male Cohorts - Onset Diagnosis - Confirmed cases (Total cohort)

Characteristics	IRD Calculation
IRD(exp-unexp OR conc-hist)	3.082

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 384 Incidence rate of Autoimmune Thyroiditis in Female Cohorts - Onset Diagnosis - All cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Exposed Female	48	64852	74.014	54.572	98.132
Non-Exposed Female	46	64893	70.886	51.898	94.552

LL, UL = 95% Lower and Upper exact confidence limits

Table 385 Incidence rate ratios of Autoimmune Thyroiditis in Female Cohorts - Onset Diagnosis - All cases (Total cohort)

	IRR Calculation					
		95%CI of RR			95%CI of RR	
Autoimmune diseases	Crude Incidence Rate Ratio	LL	UL	Adjusted Incidence Rate Ratio	LL	UL
Autoimmune Thyroiditis	1.044	0.697	1.565	1.044	0.697	1.564

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted by age group: age group [9-17] and [18-25]

Table 386 Incidence rate difference of Autoimmune Thyroiditis diseases in Female Cohorts - Onset Diagnosis - All cases (Total cohort)

Characteristics	IRD Calculation
IRD(exp-unexp OR conc-hist)	3.128

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 387 Incidence rate ratios of Autoimmune Thyroiditis in Female Cohorts (covariates adjusted) - Onset Diagnosis - All cases (Total cohort)

	IRR Calculation		
		95%CI of RR	
Autoimmune diseases	Adjusted Incidence Rate Ratio	LL	UL
Autoimmune Thyroiditis	0.926	0.617	1.391

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted for other covariates: age group [9-17] and [18-25], healthcare resources utilization in quartile, regions (North England, South England, Midlands & Ireland Scotland Wales), any vaccines during the year prior to the reference date

Table 388 Incidence rate of Autoimmune Thyroiditis in Male Cohorts - Onset Diagnosis - All cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Concurrent Male	10	64897	15.409	7.389	28.338
Historical Male	8	64891	12.328	5.322	24.292

LL, UL = 95% Lower and Upper exact confidence limits

Table 389 Incidence rate ratios of Autoimmune Thyroiditis in Male Cohorts - Onset Diagnosis - All cases (Total cohort)

	IRR Calculation					
		95%CI of RR			95%CI of RR	
Autoimmune diseases	Crude Incidence Rate Ratio	LL	UL	Adjusted Incidence Rate Ratio	LL	UL
Autoimmune Thyroiditis	1.250	0.493	3.167	1.251	0.493	3.179

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted by age group: age group [9-17] and [18-25]

Table 390 Incidence rate difference of Autoimmune Thyroiditis diseases in Male Cohorts - Onset Diagnosis - All cases (Total cohort)

Characteristics	IRD Calculation
IRD(exp-unexp OR conc-hist)	3.081

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 391 Incidence rate ratios of Autoimmune Thyroiditis in Male Cohorts (covariates adjusted) - Onset Diagnosis - All cases (Total cohort)

	IRR Calculation		
		95%CI of RR	
Autoimmune diseases	Adjusted Incidence Rate Ratio	LL	UL
Autoimmune Thyroiditis	0.246	0.067	0.898

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted for other covariates: age group [9-17] and [18-25], healthcare resources utilization in quartile regions (North England, South England, Midlands & Ireland Scotland Wales), live attenuated & adjuvanted & other vaccines in the follow-up period

Table 392 Incidence rate of Autoimmune Uveitis in Female Cohorts - Onset Diagnosis - All cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Exposed Female	3	64852	4.626	0.954	13.519
Non-Exposed Female	7	64893	10.787	4.337	22.225

LL, UL = 95% Lower and Upper exact confidence limits

Table 393 Incidence rate ratios of Autoimmune Uveitis in Female Cohorts - Onset Diagnosis - All cases (Total cohort)

	IRR Calculation					
		95%CI of RR			95%CI of RR	
Autoimmune diseases	Crude Incidence Rate Ratio	LL	UL	Adjusted Incidence Rate Ratio	LL	UL
Autoimmune Uveitis	0.429	0.111	1.658	0.428	0.111	1.656

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted by age group: age group [9-17] and [18-25]

Table 394 Incidence rate difference of Autoimmune Uveitis in Female Cohorts - Onset Diagnosis - All cases (Total cohort)

Characteristics	IRD Calculation
IRD(exp-unexp OR conc-hist)	-6.161

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 395 Incidence rate ratios of Autoimmune Uveitis in Female Cohorts (covariates adjusted) - Onset Diagnosis - All cases (Total cohort)

	IRR Calculation		
		95%CI of RR	
Autoimmune diseases	Adjusted Incidence Rate Ratio	LL	UL
Autoimmune Uveitis	0.453	0.115	1.775

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted for other covariates: age group [9-17] and [18-25], healthcare resources utilization in quartile, regions (North England, South England, Midlands & Ireland Scotland Wales), any vaccines during the year prior to the reference date

Table 396 Incidence rate of Autoimmune Uveitis in Male Cohorts - Onset Diagnosis - All cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Concurrent Male	6	64897	9.245	3.393	20.123
Historical Male	3	64891	4.623	0.953	13.511

LL, UL = 95% Lower and Upper exact confidence limits

Table 397 Incidence rate ratios of Autoimmune Uveitis in Male Cohorts - Onset Diagnosis - All cases (Total cohort)

	IRR Calculation					
		95%CI of RR			95%CI of RR	
Autoimmune diseases	Crude Incidence Rate Ratio	LL	UL	Adjusted Incidence Rate Ratio	LL	UL
Autoimmune Uveitis	2.000	0.500	7.996	2.121	0.527	8.536

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted by age group: age group [9-17] and [18-25]

Table 398 Incidence rate difference of Autoimmune Uveitis in Male Cohorts - Onset Diagnosis - All cases (Total cohort)

Characteristics	IRD Calculation
IRD(exp-unexp OR conc-hist)	4.622

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 399 Incidence rate ratios of Autoimmune Uveitis in Male Cohorts (covariates adjusted) - Onset Diagnosis - All cases (Total cohort)

	IRR Calculation		
		95%CI of RR	
Autoimmune diseases	Adjusted Incidence Rate Ratio	LL	UL
Autoimmune Uveitis	2.151	0.535	8.650

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted for other covariates: age group [9-17] and [18-25], healthcare resources utilization in quartile, regions (North England, South England, Midlands & Ireland Scotland Wales), any vaccines during the year prior to the reference date

Table 400 Incidence rate of Autoimmune Crohn diseases in Female Cohorts - Onset Diagnosis - Confirmed cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Exposed Female	11	64852	16.962	8.467	30.349
Non-Exposed Female	9	64893	13.869	6.342	26.328

LL, UL = 95% Lower and Upper exact confidence limits

Table 401 Incidence rate ratios of Crohn diseases in Female Cohorts - Onset Diagnosis - Confirmed cases (Total cohort)

	IRR Calculation					
		95%CI of RR			95%CI of RR	
Autoimmune diseases	Crude Incidence Rate Ratio	LL	UL	Adjusted Incidence Rate Ratio	LL	UL
Crohn diseases	1.223	0.507	2.951	1.226	0.508	2.959

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted by age group: age group [9-17] and [18-25]

Table 402 Incidence rate difference of Autoimmune Crohn diseases in Female Cohorts - Onset Diagnosis - Confirmed cases (Total cohort)

Characteristics	IRD Calculation
IRD(exp-unexp OR conc-hist)	3.093

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 403 Incidence rate ratios of Crohn diseases in Female Cohorts (covariates adjusted) - Onset Diagnosis - Confirmed cases (Total cohort)

	IRR Calculation		
		95%CI of RR	
Autoimmune diseases	Adjusted Incidence Rate Ratio	LL	UL
Crohn diseases	1.088	0.448	2.642

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted for other covariates: age group [9-17] and [18-25], healthcare resources utilization in quartile, regions (North England, South England, Midlands & Ireland Scotland Wales), any vaccines during the year prior to the reference date

Table 404 Incidence rate of Crohn diseases in Male Cohorts - Onset Diagnosis - Confirmed cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Concurrent Male	15	64897	23.114	12.936	38.122
Historical Male	8	64891	12.328	5.322	24.292

LL, UL = 95% Lower and Upper exact confidence limits

Table 405 Incidence rate ratios of Crohn diseases in Male Cohorts - Onset Diagnosis - Confirmed cases (Total cohort)

	IRR Calculation					
		95%CI of RR			95%CI of RR	
Autoimmune diseases	Crude Incidence Rate Ratio	LL	UL	Adjusted Incidence Rate Ratio	LL	UL
Crohn diseases	1.875	0.795	4.422	1.941	0.820	4.593

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted by age group: age group [9-17] and [18-25]

Table 406 Incidence rate difference of Crohn diseases in Male Cohorts - Onset Diagnosis - Confirmed cases (Total cohort)

Characteristics	IRD Calculation
IRD(exp-unexp OR conc-hist)	10.785

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 407 Incidence rate of Crohn diseases in Female Cohorts - Onset Diagnosis - All cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Exposed Female	13	64852	20.046	10.673	34.279
Non-Exposed Female	9	64893	13.869	6.342	26.328

LL, UL = 95% Lower and Upper exact confidence limits

Table 408 Incidence rate ratios of Crohn diseases in Female Cohorts - Onset Diagnosis - All cases (Total cohort)

	IRR Calculation					
		95%CI of RR			95%CI of RR	
Autoimmune diseases	Crude Incidence Rate Ratio	LL	UL	Adjusted Incidence Rate Ratio	LL	UL
Crohn diseases	1.445	0.618	3.381	1.448	0.619	3.389

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted by age group: age group [9-17] and [18-25]

Table 409 Incidence rate difference of Crohn diseases in Female Cohorts - Onset Diagnosis - All cases (Total cohort)

Characteristics	IRD Calculation
IRD(exp-unexp OR conc-hist)	6.177

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 410 Incidence rate ratios of Crohn diseases in Female Cohorts (covariates adjusted) - Onset Diagnosis - All cases (Total cohort)

	IRR Calculation		
		95%CI of RR	
Autoimmune diseases	Adjusted Incidence Rate Ratio	LL	UL
Crohn diseases	1.286	0.546	3.024

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted for other covariates: age group [9-17] and [18-25], healthcare resources utilization in quartile, regions (North England, South England, Midlands & Ireland Scotland Wales), any vaccines during the year prior to the reference date

Table 411 Incidence rate of Crohn diseases in Male Cohorts - Onset Diagnosis - All cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Concurrent Male	16	64897	24.654	14.092	40.037
Historical Male	10	64891	15.410	7.390	28.340

LL, UL = 95% Lower and Upper exact confidence limits

Table 412 Incidence rate ratios of Crohn diseases in Male Cohorts - Onset Diagnosis - All cases (Total cohort)

	IRR Calculation					
		95%CI of RR			95%CI of RR	
Autoimmune diseases	Crude Incidence Rate Ratio	LL	UL	Adjusted Incidence Rate Ratio	LL	UL
Crohn diseases	1.600	0.726	3.525	1.638	0.741	3.619

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted by age group: age group [9-17] and [18-25]

Table 413 Incidence rate difference of Crohn diseases in Male Cohorts - Onset Diagnosis - All cases (Total cohort)

Characteristics	IRD Calculation
IRD(exp-unexp OR conc-hist)	9.244

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 414 Incidence rate of Inflammatory bowel diseases in Female Cohorts - Onset Diagnosis - Confirmed cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Exposed Female	1	64852	1.542	0.039	8.591
Non-Exposed Female	0	64893	0.000	0.000	5.685

LL, UL = 95% Lower and Upper exact confidence limits

Table 415 Incidence rate of Inflammatory bowel diseases in Male Cohorts - Onset Diagnosis - Confirmed cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Concurrent Male	0	64897	0.000	0.000	5.684
Historical Male	2	64891	3.082	0.373	11.134

LL, UL = 95% Lower and Upper exact confidence limits

Table 416 Incidence rate of Inflammatory bowel diseases in Female Cohorts - Onset Diagnosis - All cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Exposed Female	2	64852	3.084	0.373	11.140
Non-Exposed Female	1	64893	1.541	0.039	8.586

LL, UL = 95% Lower and Upper exact confidence limits

Table 417 Incidence rate difference of Inflammatory bowel diseases in Female Cohorts - Onset Diagnosis - All cases (Total cohort)

Characteristics	IRD Calculation
IRD(exp-unexp OR conc-hist)	1.543

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 418 Incidence rate of Inflammatory bowel diseases in Male Cohorts - Onset Diagnosis - All cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Concurrent Male	0	64897	0.000	0.000	5.684
Historical Male	3	64891	4.623	0.953	13.511

LL, UL = 95% Lower and Upper exact confidence limits

Table 419 Incidence rate of Juvenile Rheumatoid Arthritis in Female Cohorts - Onset Diagnosis - Confirmed cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Exposed Female	1	64852	1.542	0.039	8.591
Non-Exposed Female	3	64893	4.623	0.953	13.510

LL, UL = 95% Lower and Upper exact confidence limits

Table 420 Incidence rate difference of Juvenile Rheumatoid Arthritis in Female Cohorts - Onset Diagnosis - Confirmed cases (Total cohort)

Characteristics	IRD Calculation
IRD(exp-unexp OR conc-hist)	-3.081

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 421 Incidence rate of Juvenile Rheumatoid Arthritis in Male Cohorts - Onset Diagnosis - Confirmed cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Concurrent Male	1	64897	1.541	0.039	8.585
Historical Male	3	64891	4.623	0.953	13.511

LL, UL = 95% Lower and Upper exact confidence limits

Table 422 Incidence rate difference of Juvenile Rheumatoid Arthritis in Male Cohorts - Onset Diagnosis - Confirmed cases (Total cohort)

Characteristics	IRD Calculation
IRD(exp-unexp OR conc-hist)	-3.082

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 423 Incidence rate of Juvenile Rheumatoid Arthritis in Female Cohorts - Onset Diagnosis - All cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Exposed Female	1	64852	1.542	0.039	8.591
Non-Exposed Female	3	64893	4.623	0.953	13.510

LL, UL = 95% Lower and Upper exact confidence limits

Table 424 Incidence rate difference of Juvenile Rheumatoid Arthritis in Female Cohorts - Onset Diagnosis - All cases (Total cohort)

Characteristics	IRD Calculation
IRD(exp-unexp OR conc-hist)	-3.081

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 425 Incidence rate of Juvenile Rheumatoid Arthritis in Male Cohorts - Onset Diagnosis - All cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Concurrent Male	1	64897	1.541	0.039	8.585
Historical Male	4	64891	6.164	1.680	15.783

LL, UL = 95% Lower and Upper exact confidence limits

Table 426 Incidence rate difference of Juvenile Rheumatoid Arthritis in Male Cohorts - Onset Diagnosis - All cases (Total cohort)

Characteristics	IRD Calculation
IRD(exp-unexp OR conc-hist)	-4.623

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 427 Incidence rate of Multiple Sclerosis in Female Cohorts - Onset Diagnosis - Confirmed cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Exposed Female	1	64852	1.542	0.039	8.591
Non-Exposed Female	1	64893	1.541	0.039	8.586

LL, UL = 95% Lower and Upper exact confidence limits

Table 428 Incidence rate difference of Multiple Sclerosis in Female Cohorts - Onset Diagnosis - Confirmed cases (Total cohort)

Characteristics	IRD Calculation
IRD(exp-unexp OR conc-hist)	0.001

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 429 Incidence rate of Multiple Sclerosis in Female Cohorts - Onset Diagnosis - All cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Exposed Female	1	64852	1.542	0.039	8.591
Non-Exposed Female	1	64893	1.541	0.039	8.586

LL, UL = 95% Lower and Upper exact confidence limits

Table 430 Incidence rate difference of Multiple Sclerosis in Female Cohorts - Onset Diagnosis - All cases (Total cohort)

Characteristics	IRD Calculation
IRD(exp-unexp OR conc-hist)	0.001

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 431 Incidence rate of Optic Neuritis in Male Cohorts - Onset Diagnosis - Confirmed cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Concurrent Male	1	64897	1.541	0.039	8.585
Historical Male	0	64891	0.000	0.000	5.685

LL, UL = 95% Lower and Upper exact confidence limits

Table 432 Incidence rate of Optic Neuritis in Female Cohorts - Onset Diagnosis - All cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Exposed Female	1	64852	1.542	0.039	8.591
Non-Exposed Female	1	64893	1.541	0.039	8.586

LL, UL = 95% Lower and Upper exact confidence limits

Table 433 Incidence rate difference of Optic Neuritis in Female Cohorts - Onset Diagnosis - All cases (Total cohort)

Characteristics	IRD Calculation
IRD(exp-unexp OR conc-hist)	0.001

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 434 Incidence rate of Optic Neuritis in Male Cohorts - Onset Diagnosis - All cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Concurrent Male	2	64897	3.082	0.373	11.133
Historical Male	0	64891	0.000	0.000	5.685

LL, UL = 95% Lower and Upper exact confidence limits

Table 435 Incidence rate of Psoriatic Arthritis in Female Cohorts - Onset Diagnosis - Confirmed cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Exposed Female	1	64852	1.542	0.039	8.591
Non-Exposed Female	1	64893	1.541	0.039	8.586

LL, UL = 95% Lower and Upper exact confidence limits

Table 436 Incidence rate difference of Psoriatic Arthritis in Female Cohorts - Onset Diagnosis - Confirmed cases (Total cohort)

Characteristics	IRD Calculation
IRD(exp-unexp OR conc-hist)	0.001

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 437 Incidence rate of Psoriatic Arthritis in Female Cohorts - Onset Diagnosis - All cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Exposed Female	2	64852	3.084	0.373	11.140
Non-Exposed Female	1	64893	1.541	0.039	8.586

LL, UL = 95% Lower and Upper exact confidence limits

Table 438 Incidence rate difference of Psoriatic Arthritis in Female Cohorts - Onset Diagnosis - All cases (Total cohort)

Characteristics	IRD Calculation
IRD(exp-unexp OR conc-hist)	1.543

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 439 Incidence rate of Rheumatoid Arthritis in Female Cohorts - Onset Diagnosis - Confirmed cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Exposed Female	2	64852	3.084	0.373	11.140
Non-Exposed Female	0	64893	0.000	0.000	5.685

LL, UL = 95% Lower and Upper exact confidence limits

Table 440 Incidence rate difference of Autoimmune Type 1 Diabetes Mellitus in Female Cohorts - Onset Diagnosis - Confirmed cases (Total cohort)

Characteristics	IRD Calculation
IRD(exposed-unexposed)	-13.819

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = IRexposed - IRnon-exposed

Table 441 Incidence rate of Rheumatoid Arthritis in Female Cohorts - Onset Diagnosis - All cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Exposed Female	2	64852	3.084	0.373	11.140
Non-Exposed Female	1	64893	1.541	0.039	8.586

LL, UL = 95% Lower and Upper exact confidence limits

Table 442 Incidence rate difference of Rheumatoid Arthritis in Female Cohorts - Onset Diagnosis - All cases (Total cohort)

Characteristics	IRD Calculation
IRD(exp-unexp OR conc-hist)	1.543

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 443 Incidence rate of Rheumatoid Arthritis in Male Cohorts - Onset Diagnosis - Confirmed cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Concurrent Male	1	64897	1.541	0.039	8.585
Historical Male	0	64891	0.000	0.000	5.685

LL, UL = 95% Lower and Upper exact confidence limits

Table 444 Incidence rate difference of Rheumatoid Arthritis in Male Cohorts - Onset Diagnosis - Confirmed cases (Total cohort)

Characteristics	IRD Calculation
IRD(exp-unexp OR conc-hist)	1.541

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 445 Incidence rate of Autoimmune Type 1 Diabetes Mellitus in Female Cohorts - Onset Diagnosis - Confirmed cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Exposed Female	11	64852	16.962	8.467	30.349
Non-Exposed Female	20	64893	30.820	18.826	47.599

LL, UL = 95% Lower and Upper exact confidence limits

Table 446 Incidence rate ratios of Type 1 Diabetes Mellitus in Female Cohorts - Onset Diagnosis - Confirmed cases (Total cohort)

	IRR Calculation					
		95%CI of RR			95%CI of RR	
Autoimmune diseases	Crude Incidence Rate Ratio	LL	UL	Adjusted Incidence Rate Ratio	LL	UL
Type 1 Diabetes Mellitus	0.550	0.264	1.149	0.551	0.264	1.149

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted by age group: age group [9-17] and [18-25]

Table 447 Incidence rate difference of Autoimmune Type 1 Diabetes Mellitus in Female Cohorts - Onset Diagnosis - Confirmed cases (Total cohort)

Characteristics	IRD Calculation
IRD(exp-unexp OR conc-hist)	-13.858

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 448 Incidence rate ratios of Type 1 Diabetes Mellitus in Female Cohorts (covariates adjusted) - Onset Diagnosis - Confirmed cases (Total cohort)

	IRR Calculation		
		95%CI of RR	
Autoimmune diseases	Adjusted Incidence Rate Ratio	LL	UL
Type 1 Diabetes Mellitus	0.566	0.270	1.188

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted for other covariates: age group [9-17] and [18-25], healthcare resources utilization in quartile, regions (North England, South England, Midlands & Ireland Scotland Wales), any vaccines during the year prior to the reference date

Table 449 Incidence rate of Type 1 Diabetes Mellitus in Male Cohorts - Onset Diagnosis - Confirmed cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Concurrent Male	23	64897	35.441	22.466	53.179
Historical Male	12	64891	18.492	9.555	32.303

LL, UL = 95% Lower and Upper exact confidence limits

Table 450 Incidence rate ratios of Type 1 Diabetes Mellitus in Male Cohorts - Onset Diagnosis - Confirmed cases (Total cohort)

	IRR Calculation					
		95%CI of RR			95%CI of RR	
Autoimmune diseases	Crude Incidence Rate Ratio	LL	UL	Adjusted Incidence Rate Ratio	LL	UL
Type 1 Diabetes Mellitus	1.916	0.954	3.851	1.899	0.944	3.822

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted by age group: age group [9-17] and [18-25]

Table 451 Incidence rate difference of Autoimmune Type 1 Diabetes Mellitus in Male Cohorts - Onset Diagnosis - Confirmed cases (Total cohort)

Characteristics	IRD Calculation
IRD(exp-unexp OR conc-hist)	16.948

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 452 Incidence rate ratios of Type 1 Diabetes Mellitus in Male Cohorts (covariates adjusted) - Onset Diagnosis - Confirmed cases (Total cohort)

	IRR Calculation		
		95%CI of RR	
Autoimmune diseases	Adjusted Incidence Rate Ratio	LL	UL
Type 1 Diabetes Mellitus	1.887	0.937	3.802

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted for other covariates: age group [9-17] and [18-25], healthcare resources utilization in quartile, regions (North England, South England, Midlands & Ireland Scotland Wales), any vaccines during the year prior to the reference date

Table 453 Incidence rate of Type 1 Diabetes Mellitus in Female Cohorts - Onset Diagnosis - All cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Exposed Female	11	64852	16.962	8.467	30.349
Non-Exposed Female	20	64893	30.820	18.826	47.599

LL, UL = 95% Lower and Upper exact confidence limits

Table 454 Incidence rate ratios of Type 1 Diabetes Mellitus in Female Cohorts - Onset Diagnosis - All cases (Total cohort)

	IRR Calculation					
		95%CI of RR			95%CI of RR	
Autoimmune diseases	Crude Incidence Rate Ratio	LL	UL	Adjusted Incidence Rate Ratio	LL	UL
Type 1 Diabetes Mellitus	0.550	0.264	1.149	0.551	0.264	1.149

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted by age group: age group [9-17] and [18-25]

Table 455 Incidence rate difference of Autoimmune Type 1 Diabetes Mellitus in Female Cohorts - Onset Diagnosis - All cases (Total cohort)

Characteristics	IRD Calculation
IRD(exp-unexp OR conc-hist)	-13.858

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 456 Incidence rate ratios of Type 1 Diabetes Mellitus in Female Cohorts (covariates adjusted) - Onset Diagnosis - All cases (Total cohort)

	IRR Calculation		
		95%CI of RR	
Autoimmune diseases	Adjusted Incidence Rate Ratio	LL	UL
Type 1 Diabetes Mellitus	0.566	0.270	1.188

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted for other covariates: age group [9-17] and [18-25], healthcare resources utilization in quartile, regions (North England, South England, Midlands & Ireland Scotland Wales), any vaccines during the year prior to the reference date

Table 457 Incidence rate of Type 1 Diabetes Mellitus in Male Cohorts - Onset Diagnosis - All cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Concurrent Male	23	64897	35.441	22.466	53.179
Historical Male	14	64891	21.575	11.795	36.198

LL, UL = 95% Lower and Upper exact confidence limits

Table 458 Incidence rate ratios of Type 1 Diabetes Mellitus in Male Cohorts - Onset Diagnosis - All cases (Total cohort)

	IRR Calculation					
		95%CI of RR			95%CI of RR	
Autoimmune diseases	Crude Incidence Rate Ratio	LL	UL	Adjusted Incidence Rate Ratio	LL	UL
Type 1 Diabetes Mellitus	1.643	0.845	3.192	1.645	0.845	3.202

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted by age group: age group [9-17] and [18-25]

Table 459 Incidence rate difference of Autoimmune Type 1 Diabetes Mellitus in Male Cohorts - Onset Diagnosis - All cases (Total cohort)

Characteristics	IRD Calculation
IRD(exp-unexp OR conc-hist)	13.866

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 460 Incidence rate ratios of Type 1 Diabetes Mellitus in Male Cohorts (covariates adjusted) - Onset Diagnosis - All cases (Total cohort)

	IRR Calculation		
		95%CI of RR	
Autoimmune diseases	Adjusted Incidence Rate Ratio	LL	UL
Type 1 Diabetes Mellitus	1.640	0.842	3.195

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted for other covariates: age group [9-17] and [18-25], healthcare resources utilization in quartile, regions (North England, South England, Midlands & Ireland Scotland Wales), any vaccines during the year prior to the reference date

Table 461 Incidence rate of Autoimmune Ulcerative Colitis in Female Cohorts - Onset Diagnosis - Confirmed cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Exposed Female	6	64852	9.252	3.395	20.137
Non-Exposed Female	0	64893	0.000	0.000	5.685

LL, UL = 95% Lower and Upper exact confidence limits

Table 462 Incidence rate of Ulcerative Colitis in Male Cohorts - Onset Diagnosis - Confirmed cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Concurrent Male	4	64897	6.164	1.679	15.781
Historical Male	4	64891	6.164	1.680	15.783

LL, UL = 95% Lower and Upper exact confidence limits

Table 463 Incidence rate difference of Ulcerative Colitis in Male Cohorts - Onset Diagnosis - Confirmed cases (Total cohort)

Characteristics	IRD Calculation
IRD(exp-unexp OR conc-hist)	-0.001

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 464 Incidence rate of Ulcerative Colitis in Female Cohorts - Onset Diagnosis - All cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Exposed Female	6	64852	9.252	3.395	20.137
Non-Exposed Female	1	64893	1.541	0.039	8.586

LL, UL = 95% Lower and Upper exact confidence limits

Table 465 Incidence rate difference of Ulcerative Colitis in Female Cohorts - Onset Diagnosis - All cases (Total cohort)

Characteristics	IRD Calculation
IRD(exp-unexp OR conc-hist)	7.711

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 466 Incidence rate of Ulcerative Colitis in Male Cohorts - Onset Diagnosis - All cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Concurrent Male	4	64897	6.164	1.679	15.781
Historical Male	4	64891	6.164	1.680	15.783

LL, UL = 95% Lower and Upper exact confidence limits

Table 467 Incidence rate difference of Ulcerative Colitis in Male Cohorts - Onset Diagnosis - All cases (Total cohort)

Characteristics	IRD Calculation
IRD(exp-unexp OR conc-hist)	-0.001

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 468 Incidence rate of Idiopathic Thrombocytopenia Purpura in Female Cohorts - Onset Diagnosis - Confirmed cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Exposed Female	1	64852	1.542	0.039	8.591
Non-Exposed Female	1	64893	1.541	0.039	8.586

LL, UL = 95% Lower and Upper exact confidence limits

Table 469 Incidence rate difference of Idiopathic Thrombocytopenia Purpura in Female Cohorts - Onset Diagnosis - Confirmed cases (Total cohort)

Characteristics	IRD Calculation
IRD(exp-unexp OR conc-hist)	0.001

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 470 Incidence rate of Idiopathic Thrombocytopenia Purpura in Male Cohorts - Onset Diagnosis - Confirmed cases (Total cohort)

				95% CI	
Cohort	**Number of cases**	**Person-time (in years)**	**Incidence Rate (per 100,000 PY)**	**LL**	**UL**
Concurrent Male	0	64897	0.000	0.000	5.684
Historical Male	1	64891	1.541	0.039	8.586

LL, UL = 95% Lower and Upper exact confidence limits

Table 471 Incidence rate of Idiopathic Thrombocytopenia Purpura in Female Cohorts - Onset Diagnosis - All cases (Total cohort)

				95% CI	
Cohort	**Number of cases**	**Person-time (in years)**	**Incidence Rate (per 100,000 PY)**	**LL**	**UL**
Exposed Female	1	64852	1.542	0.039	8.591
Non-Exposed Female	1	64893	1.541	0.039	8.586

LL, UL = 95% Lower and Upper exact confidence limits

Table 472 Incidence rate difference of Idiopathic Thrombocytopenia Purpura in Female Cohorts - Onset Diagnosis - All cases (Total cohort)

Characteristics	**IRD Calculation**
IRD(exp-unexp OR conc-hist)	0.001

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 473 Incidence rate of Idiopathic Thrombocytopenia Purpura in Male Cohorts - Onset Diagnosis - All cases (Total cohort)

				95% CI	
Cohort	**Number of cases**	**Person-time (in years)**	**Incidence Rate (per 100,000 PY)**	**LL**	**UL**
Concurrent Male	0	64897	0.000	0.000	5.684
Historical Male	1	64891	1.541	0.039	8.586

LL, UL = 95% Lower and Upper exact confidence limits

Table 474 Frequency of autoimmune diseases during the one year follow-up period by exposed/non-exposed status - in 9-17 years old - Main Analysis - Confirmed and Non-Confirmed cases (Total cohort)

		EXP N = 58736		NNEXP N = 58655		MALE N = 59242		HIST N = 56232		Total N = 232865	
Characteristics	**Categories**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**
Co-primary endpoints within 1 year follow-up period	Neuroinflammatory/Ophthalmic autoimmune diseases	4	6.81	6	10.23	2	3.38	1	1.78	13	5.58
	Other autoimmune diseases	45	76.61	38	64.79	25	42.20	14	24.90	122	52.39
Individual autoimmune diseases within 1 year follow-up period	Acute disseminated encephalomyelitis	1	1.70	0	0.00	0	0.00	0	0.00	1	0.43
	Autoimmune Thyroiditis	24	40.86	17	28.98	2	3.38	1	1.78	44	18.90
	Autoimmune Uveitis	2	3.41	5	8.52	1	1.69	0	0.00	8	3.44
	Crohn diseases	6	10.22	4	6.82	3	5.06	2	3.56	15	6.44
	Guillain-Barre Syndrome	0	0.00	0	0.00	1	1.69	1	1.78	2	0.86
	Idiopathic Thrombocytopenia Purpura	1	1.70	1	1.70	0	0.00	0	0.00	2	0.86
	Juvenile Rheumatoid Arthritis	1	1.70	0	0.00	0	0.00	1	1.78	2	0.86
	Optic Neuritis	1	1.70	1	1.70	0	0.00	0	0.00	2	0.86
	Psoriatic Arthritis	1	1.70	1	1.70	0	0.00	0	0.00	2	0.86
	Rheumatoid Arthritis	1	1.70	0	0.00	0	0.00	0	0.00	1	0.43
	Type 1 Diabetes Mellitus	7	11.92	14	23.87	18	30.38	8	14.23	47	20.18
	Ulcerative Colitis	4	6.81	1	1.70	2	3.38	2	3.56	9	3.86

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n = number of subjects in a given category
Per 100000 = n/Number of subjects with available results*100000
Neuroinflammatory/Ophthalmic autoimmune diseases included: Multiple Sclerosis, Transverse Myelitis, Optic Neuritis, Guillain Barré Syndrome, Acute dissiminated encephalomyelitis, Autoimmune Peripheral neuropathies & plexopathies and Autoimmune Uveitis. Note: that 1 AD was classified as Other AD
Follow-up period 1 year for all the cohorts

Table 475 Frequency of autoimmune diseases during the one year follow-up period by exposed/non-exposed status - in 18-25 years old - Main Analysis - Confirmed and Non-Confirmed cases (Total cohort)

		EXP N = 6228		NNEXP N = 6318		MALE N = 5732		HIST N = 8733		Total N = 27011	
Characteristics	**Categories**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**
Co-primary endpoints within 1 year follow-up period	Neuroinflammatory/Ophthalmic autoimmune diseases	0	0.00	1	15.83	1	17.45	1	11.45	3	11.11
	Other autoimmune diseases	6	96.34	3	47.48	3	52.34	5	57.25	17	62.94
Individual autoimmune diseases within 1 year follow-up period	Autoimmune Thyroiditis	2	32.11	0	0.00	0	0.00	2	22.90	4	14.81
	Autoimmune Uveitis	0	0.00	0	0.00	1	17.45	1	11.45	2	7.40
	Crohn diseases	2	32.11	1	15.83	1	17.45	0	0.00	4	14.81
	Idiopathic Thrombocytopenia Purpura	0	0.00	0	0.00	0	0.00	2	22.90	2	7.40
	Inflammatory Bowel Diseases	0	0.00	0	0.00	0	0.00	1	11.45	1	3.70
	Multiple Sclerosis	0	0.00	1	15.83	0	0.00	0	0.00	1	3.70
	Other AD	1	16.06	0	0.00	0	0.00	0	0.00	1	3.70
	Type 1 Diabetes Mellitus	1	16.06	2	31.66	2	34.89	0	0.00	5	18.51

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n = number of subjects in a given category
Per 100000 = n/Number of subjects with available results*100000
Neuroinflammatory/Ophthalmic autoimmune diseases included: Multiple Sclerosis, Transverse Myelitis, Optic Neuritis, Guillain Barré Syndrome, Acute dissiminated encephalomyelitis, Autoimmune Peripheral neuropathies & plexopathies and Autoimmune Uveitis. Note: that 1 AD was classified as Other AD
Follow-up period 1 year for all the cohorts

Table 476 Frequency of autoimmune diseases during the one year follow-up period by exposed/non-exposed status - in 9-17 years old - Main Analysis - Confirmed cases (Total cohort)

		EXP N = 58736		NNEXP N = 58655		MALE N = 59242		HIST N = 56232		Total N = 232865	
Characteristics	**Categories**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**
Co-primary endpoints within 1 year follow-up period	Neuroinflammatory/Ophthalmic autoimmune diseases	0	0.00	0	0.00	1	1.69	1	1.78	2	0.86
	Other autoimmune diseases	33	56.18	24	40.92	23	38.82	12	21.34	92	39.51
Individual autoimmune diseases within 1 year follow-up period	Autoimmune Thyroiditis	14	23.84	4	6.82	0	0.00	0	0.00	18	7.73
	Crohn diseases	4	6.81	4	6.82	3	5.06	1	1.78	12	5.15
	Guillain-Barre Syndrome	0	0.00	0	0.00	1	1.69	1	1.78	2	0.86
	Idiopathic Thrombocytopenia Purpura	1	1.70	1	1.70	0	0.00	0	0.00	2	0.86
	Juvenile Rheumatoid Arthritis	1	1.70	0	0.00	0	0.00	1	1.78	2	0.86
	Psoriatic Arthritis	1	1.70	1	1.70	0	0.00	0	0.00	2	0.86
	Rheumatoid Arthritis	1	1.70	0	0.00	0	0.00	0	0.00	1	0.43
	Type 1 Diabetes Mellitus	7	11.92	14	23.87	18	30.38	8	14.23	47	20.18
	Ulcerative Colitis	4	6.81	0	0.00	2	3.38	2	3.56	8	3.44

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n = number of subjects in a given category
Per 100000 = n/Number of subjects with available results*100000
Neuroinflammatory/Ophthalmic autoimmune diseases included: Multiple Sclerosis, Transverse Myelitis, Optic Neuritis, Guillain Barré Syndrome, Acute disseminated encephalomyelitis, Autoimmune Peripheral neuropathies & plexopathies and Autoimmune Uveitis. Note: that 1 AD was classified as Other AD
Follow-up period 1 year for all the cohorts

Table 477 Frequency of autoimmune diseases during the one year follow-up period by exposed/non-exposed status - in 18-25 years old - Main Analysis - Confirmed cases (Total cohort)

		EXP N = 6228		NNEXP N = 6318		MALE N = 5732		HIST N = 8733		Total N = 27011	
Characteristics	**Categories**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**
Co-primary endpoints within 1 year follow-up period	Neuroinflammatory/Ophthalmic autoimmune diseases	0	0.00	1	15.83	0	0.00	0	0.00	1	3.70
	Other autoimmune diseases	5	80.28	3	47.48	3	52.34	3	34.35	14	51.83
Individual autoimmune diseases within 1 year follow-up period	Autoimmune Thyroiditis	1	16.06	0	0.00	0	0.00	0	0.00	1	3.70
	Crohn diseases	2	32.11	1	15.83	1	17.45	0	0.00	4	14.81
	Idiopathic Thrombocytopenia Purpura	0	0.00	0	0.00	0	0.00	2	22.90	2	7.40
	Inflammatory Bowel Diseases	0	0.00	0	0.00	0	0.00	1	11.45	1	3.70
	Multiple Sclerosis	0	0.00	1	15.83	0	0.00	0	0.00	1	3.70
	Other AD	1	16.06	0	0.00	0	0.00	0	0.00	1	3.70
	Type 1 Diabetes Mellitus	1	16.06	2	31.66	2	34.89	0	0.00	5	18.51

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n = number of subjects in a given category
Per 100000 = n/Number of subjects with available results*100000
Neuroinflammatory/Ophthalmic autoimmune diseases included: Multiple Sclerosis, Transverse Myelitis, Optic Neuritis, Guillain Barré Syndrome, Acute dissiminated encephalomyelitis, Autoimmune Peripheral neuropathies & plexopathies and Autoimmune Uveitis. Note: that 1 AD was classified as Other AD
Follow-up period 1 year for all the cohorts

Table 478 Incidence rate of Neuroinflammatory/Ophthalmic autoimmune diseases in Female Cohorts in [9-17] years old - Confirmed cases (Total cohort)

				95% CI	
Cohort	**Number of cases**	**Person-time (in years)**	**Incidence Rate (per 100,000 PY)**	**LL**	**UL**
Exposed Female	0	58513	0.00	0.00	6.30
Non-Exposed Female	0	58537	0.00	0.00	6.30

LL, UL = 95% Lower and Upper exact confidence limits

Table 479 Incidence rate of Neuroinflammatory/Ophthalmic autoimmune diseases in Male Cohorts in [9-17] years old - Confirmed cases (Total cohort)

				95% CI	
Cohort	**Number of cases**	**Person-time (in years)**	**Incidence Rate (per 100,000 PY)**	**LL**	**UL**
Exposed Male	1	59136	1.69	0.04	9.42
Non-Exposed Male	1	56152	1.78	0.05	9.92

LL, UL = 95% Lower and Upper exact confidence limits

Table 480 Incidence rate ratios of Neuroinflammatory/Ophthalmic diseases in Male Cohorts in [9-17] years old - Confirmed cases (Total cohort)

	IRR Calculation		
		95%CI of RR	
Autoimmune diseases	**Incidence Rate Ratio**	**LL**	**UL**
Neuroinflammatory/Ophthalmic autoimmune diseases	0.949	0.059	15.177

Table 481 Incidence rate of Other autoimmune diseases in Female Cohorts in [9-17] years old - Confirmed cases (Total cohort)

				95% CI	
Cohort	**Number of cases**	**Person-time (in years)**	**Incidence Rate (per 100,000 PY)**	**LL**	**UL**
Exposed Female	33	58513	56.40	38.82	79.20
Non-Exposed Female	24	58537	41.00	26.27	61.00

LL, UL = 95% Lower and Upper exact confidence limits

Table 482 Incidence rate ratios of Other autoimmune diseases in Female Cohorts in [9-17] years old - Confirmed cases (Total cohort)

	IRR Calculation		
		95%CI of RR	
Autoimmune diseases	Incidence Rate Ratio	LL	UL
Other autoimmune diseases	1.375	0.813	2.326

Table 483 Incidence rate of Other autoimmune diseases in Male Cohorts in [9-17] years old - Confirmed cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Exposed Male	23	59136	38.89	24.66	58.36
Non-Exposed Male	12	56152	21.37	11.04	37.33

LL, UL = 95% Lower and Upper exact confidence limits

Table 484 Incidence rate ratios of Other autoimmune diseases in Male Cohorts in [9-17] years old - Confirmed cases (Total cohort)

	IRR Calculation		
		95%CI of RR	
Autoimmune diseases	Incidence Rate Ratio	LL	UL
Other autoimmune diseases	1.820	0.905	3.657

Table 485 Incidence rate of Neuroinflammatory/Ophthalmic autoimmune diseases in Female Cohorts in [18-25] years old - Confirmed cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Exposed Female	0	6192	0.00	0.00	59.58
Non-Exposed Female	1	6304	15.86	0.40	88.38

LL, UL = 95% Lower and Upper exact confidence limits

Table 486 Incidence rate of Neuroinflammatory/Ophthalmic autoimmune diseases in Male Cohorts in [18-25] years old - Confirmed cases (Total cohort)

				95% CI	
Cohort	**Number of cases**	**Person-time (in years)**	**Incidence Rate (per 100,000 PY)**	**LL**	**UL**
Exposed Male	0	5722	0.00	0.00	64.46
Non-Exposed Male	0	8717	0.00	0.00	42.32

LL, UL = 95% Lower and Upper exact confidence limits

Table 487 Incidence rate of Other autoimmune diseases in Female Cohorts in [18-25] years old - Confirmed cases (Total cohort)

				95% CI	
Cohort	**Number of cases**	**Person-time (in years)**	**Incidence Rate (per 100,000 PY)**	**LL**	**UL**
Exposed Female	5	6192	80.76	26.22	188.46
Non-Exposed Female	3	6304	47.59	9.81	139.07

LL, UL = 95% Lower and Upper exact confidence limits

Table 488 Incidence rate ratios of Other autoimmune diseases in Female Cohorts in [18-25] years old - Confirmed cases (Total cohort)

	IRR Calculation		
		95%CI of RR	
Autoimmune diseases	**Incidence Rate Ratio**	**LL**	**UL**
Other autoimmune diseases	1.694	0.405	7.087

Table 489 Incidence rate of Other autoimmune diseases in Male Cohorts in [18-25] years old - Confirmed cases (Total cohort)

				95% CI	
Cohort	**Number of cases**	**Person-time (in years)**	**Incidence Rate (per 100,000 PY)**	**LL**	**UL**
Exposed Male	3	5722	52.43	10.81	153.21
Non-Exposed Male	3	8717	34.42	7.10	100.58

LL, UL = 95% Lower and Upper exact confidence limits

Table 490 Incidence rate ratios of Other autoimmune diseases in Male Cohorts in [18-25] years old - Confirmed cases (Total cohort)

	IRR Calculation		
		95%CI of RR	
Autoimmune diseases	Incidence Rate Ratio	LL	UL
Other autoimmune diseases	1.523	0.307	7.547

Table 491 Incidence rate of Neuroinflammatory/Ophthalmic autoimmune diseases in Female Cohorts in [9-17] years old - All cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Exposed Female	4	58513	6.84	1.86	17.50
Non-Exposed Female	6	58537	10.25	3.76	22.31

LL, UL = 95% Lower and Upper exact confidence limits

Table 492 Incidence rate ratios of Neuroinflammatory/Ophthalmic diseases in Female Cohorts in [9-17] years old - All cases (Total cohort)

	IRR Calculation		
		95%CI of RR	
Autoimmune diseases	Incidence Rate Ratio	LL	UL
Neuroinflammatory/Ophthalmic autoimmune diseases	0.667	0.188	2.362

Table 493 Incidence rate of Neuroinflammatory/Ophthalmic autoimmune diseases in Male Cohorts in [18-25] years old - All cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Exposed Male	2	59136	3.38	0.41	12.22
Non-Exposed Male	1	56152	1.78	0.05	9.92

LL, UL = 95% Lower and Upper exact confidence limits

Table 494 Incidence rate ratios of Neuroinflammatory/Ophthalmic autoimmune diseases in Male Cohorts in [18-25] years old - All cases (Total cohort)

	IRR Calculation		
		95%CI of RR	
Autoimmune diseases	Incidence Rate Ratio	LL	UL
Neuroinflammatory/Ophthalmic autoimmune diseases	1.899	0.172	20.939

Table 495 Incidence rate of Other autoimmune diseases in Female Cohorts in [9-17] years old - All cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 10,000 PY)	LL	UL
Exposed Female	45	58513	7.69	5.61	10.29
Non-Exposed Female	38	58537	6.49	4.59	8.91

LL, UL = 95% Lower and Upper exact confidence limits

Table 496 Incidence rate ratios of Other autoimmune diseases in Female Cohorts in [9-17] years old - All cases (Total cohort)

	IRR Calculation		
		95%CI of RR	
Autoimmune diseases	Incidence Rate Ratio	LL	UL
Other autoimmune diseases	1.184	0.769	1.824

Table 497 Incidence rate of Other autoimmune diseases in Male Cohorts in [18-25] years old - All cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Exposed Male	25	59136	42.28	27.36	62.41
Non-Exposed Male	14	56152	24.93	13.63	41.83

LL, UL = 95% Lower and Upper exact confidence limits

Table 498 Incidence rate ratios of Other autoimmune diseases in Male Cohorts in [18-25] years old - All cases (Total cohort)

	IRR Calculation		
		95%CI of RR	
Autoimmune diseases	Incidence Rate Ratio	LL	UL
Other autoimmune diseases	1.695	0.881	3.261

Table 499 Incidence rate of Neuroinflammatory/Ophthalmic autoimmune diseases in Female Cohorts in [18-25] years old - Confirmed cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Exposed Female	0	6192	0.00	0.00	59.58
Non-Exposed Female	1	6304	15.86	0.40	88.38

LL, UL = 95% Lower and Upper exact confidence limits

Table 500 Incidence rate of Neuroinflammatory/Ophthalmic autoimmune diseases in Male Cohorts in [18-25] years old - All cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Exposed Male	1	5722	17.48	0.44	97.37
Non-Exposed Male	1	8717	11.47	0.29	63.92

LL, UL = 95% Lower and Upper exact confidence limits

Table 501 Incidence rate ratios of Neuroinflammatory/Ophthalmic diseases in Male Cohorts in [18-25] years old - All cases (Total cohort)

	IRR Calculation		
		95%CI of RR	
Autoimmune diseases	Incidence Rate Ratio	LL	UL
Neuroinflammatory/Ophthalmic autoimmune diseases	1.523	0.095	24.353

Table 502 Incidence rate of Other autoimmune diseases in Female Cohorts in [18-25] years old - Confirmed cases (Total cohort)

				95% CI	
Cohort	**Number of cases**	**Person-time (in years)**	**Incidence Rate (per 10,000 PY)**	**LL**	**UL**
Exposed Female	6	6192	9.69	3.56	21.09
Non-Exposed Female	3	6304	4.76	0.98	13.91

LL, UL = 95% Lower and Upper exact confidence limits

Table 503 Incidence rate ratios of Other autoimmune diseases in Female Cohorts in [18-25] years old - Confirmed cases (Total cohort)

	IRR Calculation		
		95%CI of RR	
Autoimmune diseases	**Incidence Rate Ratio**	**LL**	**UL**
Other autoimmune diseases	2.032	0.508	8.127

Table 504 Incidence rate of Other autoimmune diseases in Male Cohorts in [18-25] years old - All cases (Total cohort)

				95% CI	
Cohort	**Number of cases**	**Person-time (in years)**	**Incidence Rate (per 100,000 PY)**	**LL**	**UL**
Exposed Male	3	5722	52.43	10.81	153.21
Non-Exposed Male	5	8717	57.36	18.62	133.86

LL, UL = 95% Lower and Upper exact confidence limits

Table 505 Incidence rate ratios of Other autoimmune diseases in Male Cohorts in [18-25] years old - All cases (Total cohort)

	IRR Calculation		
		95%CI of RR	
Autoimmune diseases	**Incidence Rate Ratio**	**LL**	**UL**
Other autoimmune diseases	0.914	0.218	3.824

Table 506 Incidence rate of Autoimmune Thyroiditis in Female Cohorts in [9-17] years old - Confirmed cases (Total cohort)

				95% CI	
Cohort	**Number of cases**	**Person-time (in years)**	**Incidence Rate (per 100,000 PY)**	**LL**	**UL**
Exposed Female	14	58513	23.93	13.08	40.14
Non-Exposed Female	4	58537	6.83	1.86	17.50

LL, UL = 95% Lower and Upper exact confidence limits

Table 507 Incidence rate ratios of Autoimmune Thyroiditis in Female Cohorts in [9-17] years old - Confirmed cases (Total cohort)

	IRR Calculation		
		95%CI of RR	
Autoimmune diseases	**Incidence Rate Ratio**	**LL**	**UL**
Autoimmune Thyroiditis	3.500	1.152	10.632

Table 508 Incidence rate of Crohn diseases in Female Cohorts in [9-17] years old - Confirmed cases (Total cohort)

				95% CI	
Cohort	**Number of cases**	**Person-time (in years)**	**Incidence Rate (per 100,000 PY)**	**LL**	**UL**
Exposed Female	4	58513	6.84	1.86	17.50
Non-Exposed Female	4	58537	6.83	1.86	17.50

LL, UL = 95% Lower and Upper exact confidence limits

Table 509 Incidence rate ratios of Crohn diseases in Female Cohorts in [9-17] years old - Confirmed cases (Total cohort)

	IRR Calculation		
		95%CI of RR	
Autoimmune diseases	**Incidence Rate Ratio**	**LL**	**UL**
Crohn diseases	1.000	0.250	3.998

Table 510 Incidence rate of Type 1 Diabetes Mellitus in Female Cohorts in [9-17] years old - Confirmed cases (Total cohort)

				95% CI	
Cohort	**Number of cases**	**Person-time (in years)**	**Incidence Rate (per 100,000 PY)**	**LL**	**UL**
Exposed Female	7	58513	11.96	4.81	24.65
Non-Exposed Female	14	58537	23.92	13.08	40.13

LL, UL = 95% Lower and Upper exact confidence limits

Table 511 Incidence rate ratios of Type 1 Diabetes Mellitus in Female Cohorts in [9-17] years old - Confirmed cases (Total cohort)

	IRR Calculation		
		95%CI of RR	
Autoimmune diseases	**Incidence Rate Ratio**	**LL**	**UL**
Type 1 Diabetes Mellitus	0.500	0.202	1.239

Table 512 Incidence rate of Type 1 Diabetes Mellitus in Male Cohorts in [9-17] years old - Confirmed cases (Total cohort)

				95% CI	
Cohort	**Number of cases**	**Person-time (in years)**	**Incidence Rate (per 100,000 PY)**	**LL**	**UL**
Exposed Male	18	59136	30.44	18.04	48.11
Non-Exposed Male	8	56152	14.25	6.15	28.07

LL, UL = 95% Lower and Upper exact confidence limits

Table 513 Incidence rate ratios of Type 1 Diabetes Mellitus in Male Cohorts in [9-17] years old - Confirmed cases (Total cohort)

	IRR Calculation		
		95%CI of RR	
Autoimmune diseases	**Incidence Rate Ratio**	**LL**	**UL**
Type 1 Diabetes Mellitus	2.136	0.929	4.912

Table 514 Incidence rate of Autoimmune Thyroiditis in Female Cohorts in [9-17] years old - All cases (Total cohort)

				95% CI	
Cohort	**Number of cases**	**Person-time (in years)**	**Incidence Rate (per 100,000 PY)**	**LL**	**UL**
Exposed Female	24	58513	41.02	26.28	61.03
Non-Exposed Female	17	58537	29.04	16.92	46.50

LL, UL = 95% Lower and Upper exact confidence limits

Table 515 Incidence rate ratios of Autoimmune Thyroiditis in Female Cohorts in [9-17] years old - All cases (Total cohort)

	IRR Calculation		
		95%CI of RR	
Autoimmune diseases	**Incidence Rate Ratio**	**LL**	**UL**
Autoimmune Thyroiditis	1.412	0.758	2.628

Table 516 Incidence rate of Crohn diseases in Female Cohorts in [9-17] years old - All cases (Total cohort)

				95% CI	
Cohort	**Number of cases**	**Person-time (in years)**	**Incidence Rate (per 100,000 PY)**	**LL**	**UL**
Exposed Female	6	58513	10.25	3.76	22.32
Non-Exposed Female	4	58537	6.83	1.86	17.50

LL, UL = 95% Lower and Upper exact confidence limits

Table 517 Incidence rate ratios of Crohn diseases in Female Cohorts in [9-17] years old - All cases (Total cohort)

	IRR Calculation		
		95%CI of RR	
Autoimmune diseases	**Incidence Rate Ratio**	**LL**	**UL**
Crohn diseases	1.500	0.423	5.315

Table 518 Incidence rate of Type 1 Diabetes Mellitus in Female Cohorts in [9-17] years old - All cases (Total cohort)

				95% CI	
Cohort	**Number of cases**	**Person-time (in years)**	**Incidence Rate (per 100,000 PY)**	**LL**	**UL**
Exposed Female	7	58513	11.96	4.81	24.65
Non-Exposed Female	14	58537	23.92	13.08	40.13

LL, UL = 95% Lower and Upper exact confidence limits

Table 519 Incidence rate ratios of Type 1 Diabetes Mellitus in Female Cohorts in [9-17] years old - All cases (Total cohort)

	IRR Calculation		
		95%CI of RR	
Autoimmune diseases	**Incidence Rate Ratio**	**LL**	**UL**
Type 1 Diabetes Mellitus	0.500	0.202	1.239

Table 520 Incidence rate of Type 1 Diabetes Mellitus in Male Cohorts in [9-17] years old - All cases (Total cohort)

				95% CI	
Cohort	**Number of cases**	**Person-time (in years)**	**Incidence Rate (per 100,000 PY)**	**LL**	**UL**
Exposed Male	18	59136	30.44	18.04	48.11
Non-Exposed Male	8	56152	14.25	6.15	28.07

LL, UL = 95% Lower and Upper exact confidence limits

Table 521 Incidence rate ratios of Type 1 Diabetes Mellitus in Male Cohorts in [9-17] years old - All cases (Total cohort)

	IRR Calculation		
		95%CI of RR	
Autoimmune diseases	**Incidence Rate Ratio**	**LL**	**UL**
Type 1 Diabetes Mellitus	2.136	0.929	4.912

Table 522 Incidence rate of Autoimmune Thyroiditis in Female Cohorts in [18-25] years old - Confirmed cases (Total cohort)

				95% CI	
Cohort	**Number of cases**	**Person-time (in years)**	**Incidence Rate (per 100,000 PY)**	**LL**	**UL**
Exposed Female	1	6192	16.15	0.41	89.99
Non-Exposed Female	0	6304	0.00	0.00	58.52

LL, UL = 95% Lower and Upper exact confidence limits

Table 523 Incidence rate of Autoimmune Thyroiditis in Male Cohorts in [18-25] years old - Confirmed cases (Total cohort)

				95% CI	
Cohort	**Number of cases**	**Person-time (in years)**	**Incidence Rate (per 100,000 PY)**	**LL**	**UL**
Exposed Male	0	5722	0.00	0.00	64.46
Non-Exposed Male	0	8717	0.00	0.00	42.32

LL, UL = 95% Lower and Upper exact confidence limits

Table 524 Incidence rate of Crohn diseases in Female Cohorts in [18-25] years old - Confirmed cases (Total cohort)

				95% CI	
Cohort	**Number of cases**	**Person-time (in years)**	**Incidence Rate (per 100,000 PY)**	**LL**	**UL**
Exposed Female	2	6192	32.30	3.91	116.69
Non-Exposed Female	1	6304	15.86	0.40	88.38

LL, UL = 95% Lower and Upper exact confidence limits

Table 525 Incidence rate of Type 1 Diabetes Mellitus in Male Cohorts in [18-25] years old - Confirmed cases (Total cohort)

				95% CI	
Cohort	**Number of cases**	**Person-time (in years)**	**Incidence Rate (per 100,000 PY)**	**LL**	**UL**
Exposed Male	2	5722	34.95	4.23	126.25
Non-Exposed Male	0	8717	0.00	0.00	42.32

LL, UL = 95% Lower and Upper exact confidence limits

Table 526 Incidence rate of Autoimmune Thyroiditis in Female Cohorts in [18-25] years old - All cases (Total cohort)

				95% CI	
Cohort	**Number of cases**	**Person-time (in years)**	**Incidence Rate (per 100,000 PY)**	**LL**	**UL**
Exposed Female	2	6192	32.30	3.91	116.69
Non-Exposed Female	1	6305	15.86	0.40	88.37

LL, UL = 95% Lower and Upper exact confidence limits

Table 527 Incidence rate of Autoimmune Thyroiditis in Male Cohorts in [18-25] years old - All cases (Total cohort)

				95% CI	
Cohort	**Number of cases**	**Person-time (in years)**	**Incidence Rate (per 100,000 PY)**	**LL**	**UL**
Exposed Male	0	5722	0.00	0.00	64.46
Non-Exposed Male	2	8717	22.94	2.78	82.88

LL, UL = 95% Lower and Upper exact confidence limits

Table 528 Incidence rate of Crohn diseases in Female Cohorts in [18-25] years old - All cases (Total cohort)

				95% CI	
Cohort	**Number of cases**	**Person-time (in years)**	**Incidence Rate (per 100,000 PY)**	**LL**	**UL**
Exposed Female	2	6192	32.30	3.91	116.69
Non-Exposed Female	1	6304	15.86	0.40	88.38

LL, UL = 95% Lower and Upper exact confidence limits

Table 529 Incidence rate of Crohn diseases in Male Cohorts in [18-25] years old - All cases (Total cohort)

				95% CI	
Cohort	**Number of cases**	**Person-time (in years)**	**Incidence Rate (per 100,000 PY)**	**LL**	**UL**
Exposed Male	1	5722	17.48	0.44	97.37
Non-Exposed Male	0	8717	0.00	0.00	42.32

LL, UL = 95% Lower and Upper exact confidence limits

Table 530 Incidence rate of Type 1 Diabetes Mellitus in Female Cohorts in [18-25] years old - All cases (Total cohort)

				95% CI	
Cohort	**Number of cases**	**Person-time (in years)**	**Incidence Rate (per 100,000 PY)**	**LL**	**UL**
Exposed Female	1	6192	16.15	0.41	89.99
Non-Exposed Female	2	6305	31.72	3.84	114.59

LL, UL = 95% Lower and Upper exact confidence limits

Table 531 Incidence rate of Type 1 Diabetes Mellitus in Male Cohorts in [18-25] years old - All cases (Total cohort)

				95% CI	
Cohort	**Number of cases**	**Person-time (in years)**	**Incidence Rate (per 100,000 PY)**	**LL**	**UL**
Exposed Male	2	5722	34.95	4.23	126.25
Non-Exposed Male	0	8717	0.00	0.00	42.32

LL, UL = 95% Lower and Upper exact confidence limits

Table 532 Incidence rate of Other autoimmune diseases after Cervarix dose 1 in Exposed cohort- Confirmed and Non-Confirmed cases (Total cohort)

			95% CI	
Number of cases	**Person-time (in years)**	**Incidence Rate (per 10,000 PY)**	**LL**	**UL**
18	11037	16.31	9.67	25.78

LL, UL = 95% Lower and Upper exact confidence limits

Table 533 Incidence rate of Other autoimmune diseases after Cervarix dose 1 in Exposed cohort- Confirmed cases (Total cohort)

			95% CI	
Number of cases	**Person-time (in years)**	**Incidence Rate (per 10,000 PY)**	**LL**	**UL**
15	11037	13.59	7.61	22.42

LL, UL = 95% Lower and Upper exact confidence limits

Table 534 Incidence rate of Other autoimmune diseases after Cervarix dose 2 in Exposed cohort- Confirmed and Non-Confirmed cases (Total cohort)

			95% CI	
Number of cases	Person-time (in years)	Incidence Rate (per 10,000 PY)	LL	UL
22	25298	8.70	5.45	13.17

LL, UL = 95% Lower and Upper exact confidence limits

Table 535 Incidence rate of Other autoimmune diseases after Cervarix dose 2 in Exposed cohort- Confirmed cases (Total cohort)

			95% CI	
Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
15	25298	59.29	33.19	97.80

LL, UL = 95% Lower and Upper exact confidence limits

Table 536 Incidence rate of Other autoimmune diseases after Cervarix dose 3 in Exposed cohort- Confirmed and Non-Confirmed cases (Total cohort)

			95% CI	
Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
7	25048	27.95	11.24	57.58

LL, UL = 95% Lower and Upper exact confidence limits

Table 537 Incidence rate of Other autoimmune diseases after Cervarix dose 3 in Exposed cohort- Confirmed cases (Total cohort)

			95% CI	
Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
5	25048	19.96	6.48	46.58

LL, UL = 95% Lower and Upper exact confidence limits

Table 538 Incidence rate of Other autoimmune diseases after Cervarix dose 4 in Exposed cohort- Confirmed and Non-Confirmed cases (Total cohort)

			95% CI	
Number of cases	Person-time (in years)	Incidence Rate (per 10,000 PY)	LL	UL
0	54	0.00	0.00	680.49

LL, UL = 95% Lower and Upper exact confidence limits

Table 539 Incidence rate of Other autoimmune diseases after Cervarix dose 4 in Exposed cohort- Confirmed cases (Total cohort)

			95% CI	
Number of cases	Person-time (in years)	Incidence Rate (per 10,000 PY)	LL	UL
0	54	0.00	0.00	680.49

LL, UL = 95% Lower and Upper exact confidence limits

Table 540 Incidence rate of Neuroinflammatory/Ophthalmic autoimmune diseases after Cervarix dose 1 in Exposed cohort - Confirmed and Non-Confirmed cases (Total cohort)

			95% CI	
Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
1	11039	9.06	0.23	50.47

LL, UL = 95% Lower and Upper exact confidence limits

Table 541 Incidence rate of Neuroinflammatory/Ophthalmic autoimmune diseases after Cervarix dose 1 in Exposed cohort- Confirmed cases (Total cohort)

			95% CI	
Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
0	11039	0.00	0.00	33.42

LL, UL = 95% Lower and Upper exact confidence limits

Table 542 Incidence rate of Neuroinflammatory/Ophthalmic autoimmune diseases after Cervarix dose 2 in Exposed cohort-Confirmed and Non-Confirmed cases (Total cohort)

			95% CI	
Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
2	25303	7.90	0.96	28.55

LL, UL = 95% Lower and Upper exact confidence limits

Table 543 Incidence rate of Neuroinflammatory/Ophthalmic autoimmune diseases after Cervarix dose 2 in Exposed cohort-Confirmed cases (Total cohort)

			95% CI	
Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
0	25303	0.00	0.00	14.58

LL, UL = 95% Lower and Upper exact confidence limits

Table 544 Incidence rate of Neuroinflammatory/Ophthalmic autoimmune diseases after Cervarix dose 3 in Exposed cohort-Confirmed and Non-Confirmed cases (Total cohort)

			95% CI	
Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
1	25051	3.99	0.10	22.24

LL, UL = 95% Lower and Upper exact confidence limits

Table 545 Incidence rate of Neuroinflammatory/Ophthalmic autoimmune diseases after Cervarix dose 3 in Exposed cohort-Confirmed cases (Total cohort)

			95% CI	
Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
0	25051	0.00	0.00	14.73

LL, UL = 95% Lower and Upper exact confidence limits

Table 546 Incidence rate of Neuroinflammatory/Ophthalmic autoimmune diseases after Cervarix dose 4 in Exposed cohort- Confirmed and Non-Confirmed cases (Total cohort)

			95% CI	
Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
0	54	0.00	0.00	6804.9

LL, UL = 95% Lower and Upper exact confidence limits

Table 547 Incidence rate of Neuroinflammatory/Ophthalmic autoimmune diseases after Cervarix dose 4 in Exposed cohort- Confirmed cases (Total cohort)

			95% CI	
Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
0	54	0.00	0.00	6804.9

LL, UL = 95% Lower and Upper exact confidence limits

Table 548 Incidence rate of Autoimmune thyroiditis after Cervarix dose 1 in Exposed cohort- Confirmed and Non-Confirmed cases (Total cohort)

			95% CI	
Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
9	11038	81.53	37.28	154.78

LL, UL = 95% Lower and Upper exact confidence limits

Table 549 Incidence rate of Autoimmune thyroiditis after Cervarix dose 1 in Exposed cohort- Confirmed cases (Total cohort)

			95% CI	
Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
6	11038	54.36	19.95	118.31

LL, UL = 95% Lower and Upper exact confidence limits

Table 550 Incidence rate of Autoimmune thyroiditis after Cervarix dose 2 in Exposed cohort- Confirmed and Non-Confirmed cases (Total cohort)

			95% CI	
Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
10	25301	39.52	18.95	72.69

LL, UL = 95% Lower and Upper exact confidence limits

Table 551 Incidence rate of Autoimmune thyroiditis after Cervarix dose 2 in Exposed cohort- Confirmed cases (Total cohort)

			95% CI	
Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
5	25301	19.76	6.42	46.12

LL, UL = 95% Lower and Upper exact confidence limits

Table 552 Incidence rate of Autoimmune thyroiditis after Cervarix dose 3 in Exposed cohort- Confirmed and Non-Confirmed cases (Total cohort)

			95% CI	
Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
6	25049	23.95	8.79	52.14

LL, UL = 95% Lower and Upper exact confidence limits

Table 553 Incidence rate of Autoimmune thyroiditis after Cervarix dose 3 in Exposed cohort- Confirmed cases (Total cohort)

			95% CI	
Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
4	25049	15.97	4.35	40.89

LL, UL = 95% Lower and Upper exact confidence limits

Table 554 Incidence rate of Autoimmune thyroiditis after Cervarix dose 4 in Exposed cohort- Confirmed and Non-Confirmed cases (Total cohort)

			95% CI	
Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
0	54	0.00	0.00	6804.9

LL, UL = 95% Lower and Upper exact confidence limits

Table 555 Incidence rate of Autoimmune thyroiditis after Cervarix dose 4 in Exposed cohort- Confirmed cases (Total cohort)

			95% CI	
Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
0	54	0.00	0.00	6804.9

LL, UL = 95% Lower and Upper exact confidence limits

Table 556 Incidence rate of Crohn diseases after Cervarix dose 1 in Exposed cohort- Confirmed and Non-Confirmed cases (Total cohort)

			95% CI	
Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
2	11039	18.12	2.19	65.45

LL, UL = 95% Lower and Upper exact confidence limits

Table 557 Incidence rate of Crohn diseases after Cervarix dose 1 in Exposed cohort- Confirmed cases (Total cohort)

			95% CI	
Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
2	11039	18.12	2.19	65.45

LL, UL = 95% Lower and Upper exact confidence limits

Table 558 Incidence rate of Crohn diseases after Cervarix dose 2 in Exposed cohort- Confirmed and Non-Confirmed cases (Total cohort)

			95% CI	
Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
5	25302	19.76	6.42	46.12

LL, UL = 95% Lower and Upper exact confidence limits

Table 559 Incidence rate of Crohn diseases after Cervarix dose 2 in Exposed cohort- Confirmed cases (Total cohort)

			95% CI	
Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
3	25302	11.86	2.45	34.65

LL, UL = 95% Lower and Upper exact confidence limits

Table 560 Incidence rate of Crohn diseases after Cervarix dose 3 in Exposed cohort- Confirmed and Non-Confirmed cases (Total cohort)

			95% CI	
Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
0	25051	0.00	0.00	14.73

LL, UL = 95% Lower and Upper exact confidence limits

Table 561 Incidence rate of Crohn diseases after Cervarix dose 3 in Exposed cohort- Confirmed cases (Total cohort)

			95% CI	
Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
0	25051	0.00	0.00	14.73

LL, UL = 95% Lower and Upper exact confidence limits

Table 562 Incidence rate of Crohn diseases after Cervarix dose 4 in Exposed cohort- Confirmed and Non-Confirmed cases (Total cohort)

			95% CI	
Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
0	54	0.00	0.00	6804.9

LL, UL = 95% Lower and Upper exact confidence limits

Table 563 Incidence rate of Crohn diseases after Cervarix dose 4 in Exposed cohort- Confirmed cases (Total cohort)

			95% CI	
Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
0	54	0.00	0.00	6804.9

LL, UL = 95% Lower and Upper exact confidence limits

Table 564 Incidence rate of Type 1 Diabetes Mellitus after Cervarix dose 1 in Exposed cohort- Confirmed and Non-Confirmed cases (Total cohort)

			95% CI	
Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
2	11039	18.12	2.19	65.45

LL, UL = 95% Lower and Upper exact confidence limits

Table 565 Incidence rate of Type 1 Diabetes Mellitus after Cervarix dose 1 in Exposed cohort- Confirmed cases (Total cohort)

			95% CI	
Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
2	11039	18.12	2.19	65.45

LL, UL = 95% Lower and Upper exact confidence limits

Table 566 Incidence rate of Type 1 Diabetes Mellitus after Cervarix dose 2 in Exposed cohort- Confirmed and Non-Confirmed cases (Total cohort)

			95% CI	
Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
4	25303	15.81	4.31	40.48

LL, UL = 95% Lower and Upper exact confidence limits

Table 567 Incidence rate of Type 1 Diabetes Mellitus after Cervarix dose 2 in Exposed cohort- Confirmed cases (Total cohort)

			95% CI	
Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
4	25303	15.81	4.31	40.48

LL, UL = 95% Lower and Upper exact confidence limits

Table 568 Incidence rate of Type 1 Diabetes Mellitus after Cervarix dose 3 in Exposed cohort- Confirmed and Non-Confirmed cases (Total cohort)

			95% CI	
Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
0	25051	0.00	0.00	14.73

LL, UL = 95% Lower and Upper exact confidence limits

Table 569 Incidence rate of Type 1 Diabetes Mellitus after Cervarix dose 3 in Exposed cohort- Confirmed cases (Total cohort)

			95% CI	
Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
0	25051	0.00	0.00	14.73

LL, UL = 95% Lower and Upper exact confidence limits

Table 570 Incidence rate of Type 1 Diabetes Mellitus after Cervarix dose 4 in Exposed cohort- Confirmed and Non-Confirmed cases (Total cohort)

			95% CI	
Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
0	54	0.00	0.00	6804.9

LL, UL = 95% Lower and Upper exact confidence limits

Table 571 Incidence rate of Type 1 Diabetes Mellitus after Cervarix dose 4 in Exposed cohort- Confirmed cases (Total cohort)

			95% CI	
Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
0	54	0.00	0.00	6804.9

LL, UL = 95% Lower and Upper exact confidence limits

Table 572 Number of Other Autoimmune diseases by CTRL/RISK period - Main Analysis - Main SCCS- All cases (Total cohort)

		Gr 1 N = 95	
Follow Up Period	Categories	n	%
ctrl	AD Event	44	100
risk	AD Event	51	100
Overall total	AD Event	95	100

N = number of subjects
n = number of subjects in a given category
% = n / Number of subjects with available results x 100
Main analysis of coprimary endpoints: risk period lasts 12months after the first Cervarix dose

Table 573 Number of Other Autoimmune diseases by CTRL/RISK period - Main Analysis - Main SCCS - All cases

		95%CI		
	Relative Incidence	LL	UL	P-value
Risk period VS Control period	1.1591	0.7744	1.7348	0.4730

Table 574 Number of Diabetes diseases by CTRL/RISK period - Main Analysis - All cases (Total cohort)

		Gr 1 N = 15	
Follow Up Period	**Categories**	**n**	**%**
ctrl	AD Event	7	100
risk	AD Event	8	100
Overall total	AD Event	15	100

N = number of subjects
n = number of subjects in a given category
% = n / Number of subjects with available results x 100
Main analysis of coprimary endpoints: risk period lasts 12months after the first Cervarix dose

Table 575 Number of Diabetes diseases by CTRL/RISK period - Main Analysis - All cases

		95%CI		
	Relative Incidence	**LL**	**UL**	**P-value**
Risk period VS Control period	1.1429	0.4144	3.1516	0.7964

Table 576 Number of Thyroiditis diseases by CTRL/RISK period - Main Analysis - All cases (Total cohort)

		Gr 1 N = 52	
Follow Up Period	**Categories**	**n**	**%**
ctrl	AD Event	26	100
risk	AD Event	26	100
Overall total	AD Event	52	100

N = number of subjects
n = number of subjects in a given category
% = n / Number of subjects with available results x 100
Main analysis of coprimary endpoints: risk period lasts 12months after the first Cervarix dose

Table 577 Number of Thyroiditis diseases by CTRL/RISK period - Main Analysis - All cases

		95%CI		
	Relative Incidence	LL	UL	P-value
Risk period VS Control period	1.0000	0.5807	1.7222	1.0000

Table 578 Number of Crohn diseases by CTRL/RISK period - Main Analysis - All cases (Total cohort)

		Gr 1 N = 11	
Follow Up Period	Categories	n	%
ctrl	AD Event	3	100
risk	AD Event	8	100
Overall total	AD Event	11	100

N = number of subjects
n = number of subjects in a given category
% = n / Number of subjects with available results x 100
Main analysis of coprimary endpoints: risk period lasts 12months after the first Cervarix dose

Table 579 Number of Crohn diseases by CTRL/RISK period - Main Analysis - - Main SCCS - All cases

		95%CI		
	Relative Incidence	LL	UL	P-value
Risk period VS Control period	2.6667	0.7075	10.0512	0.1474

Table 580 Number of Neuroinflammatory/Ophthalmic diseases by CTRL/RISK period - Main Analysis - Main SCCS - All cases (Total cohort)

		Gr 1 N = 12	
Follow Up Period	**Categories**	**n**	**%**
ctrl	AD Event	8	100
risk	AD Event	4	100
Overall total	AD Event	12	100

N = number of subjects
n = number of subjects in a given category
% = n / Number of subjects with available results x 100
Main analysis of coprimary endpoints: risk period lasts 12months after the first Cervarix dose

Table 581 Number of Neuroinflammatory/Ophthalmic diseases by CTRL/RISK period - Main Analysis - Main SCCS - All cases

		95%CI		
	Relative Incidence	**LL**	**UL**	**P-value**
Risk period VS Control period	0.5000	0.1506	1.6604	0.2577

Table 582 Number of Other Autoimmune diseases by CTRL/RISK period - Main Analysis - Sensitivity SCCS - All cases (Total cohort)

		Gr 1 N = 89	
Follow Up Period	**Categories**	**n**	**%**
ctrl	AD Event	39	100
risk	AD Event	50	100
Overall total	AD Event	89	100

N = number of subjects
n = number of subjects in a given category
% = n / Number of subjects with available results x 100
Sensitivity analysis of coprimary endpoints: risk period lasts until 6 months after the last Cervarix dose

Table 583 Number of Other Autoimmune diseases by CTRL/RISK period - Main Analysis - Sensitivity SCCS - All cases

		95%CI		
	Relative Incidence	LL	UL	P-value
Risk period VS Control period	1.2351	0.8038	1.8980	0.3353

Table 584 Number of Neuroinflammatory/Ophthalmic diseases by CTRL/RISK period - Main Analysis - Sensitivity SCCS - All cases (Total cohort)

		Gr 1 N = 13	
Follow Up Period	Categories	n	%
ctrl	AD Event	9	100
risk	AD Event	4	100
Overall total	AD Event	13	100

N = number of subjects
n = number of subjects in a given category
% = n / Number of subjects with available results x 100
Sensitivity analysis of coprimary endpoints: risk period lasts until 6 months after the last Cervarix dose

Table 585 Number of Neuroinflammatory/Ophthalmic diseases by CTRL/RISK period - Main Analysis - Sensitivity Analysis - All cases

		95%CI		
	Relative Incidence	LL	UL	P-value
Risk period VS Control period	0.5872	0.1763	1.9552	0.3857

Table 586 Number of Other Autoimmune diseases by CTRL/RISK period - Main Analysis - Main SCCS- Confirmed cases (Total cohort)

		Gr 1 N = 66	
Follow Up Period	**Categories**	**n**	**%**
ctrl	AD Event	28	100
risk	AD Event	38	100
Overall total	AD Event	66	100

N = number of subjects
n = number of subjects in a given category
% = n / Number of subjects with available results x 100
Main analysis of coprimary endpoints: risk period lasts 12months after the first Cervarix dose

Table 587 Number of Other Autoimmune diseases by CTRL/RISK period - Main Analysis - Main SCCS - Confirmed cases

		95%CI		
	Relative Incidence	**LL**	**UL**	**P-value**
Risk period VS Control period	1.3571	0.8330	2.2112	0.2201

Table 588 Number of Diabetes diseases by CTRL/RISK period - Main Analysis - Confirmed cases (Total cohort)

		Gr 1 N = 15	
Follow Up Period	**Categories**	**n**	**%**
ctrl	AD Event	7	100
risk	AD Event	8	100
Overall total	AD Event	15	100

N = number of subjects
n = number of subjects in a given category
% = n / Number of subjects with available results x 100
Main analysis of coprimary endpoints: risk period lasts 12months after the first Cervarix dose

Table 589 Number of Diabetes diseases by CTRL/RISK period - Main Analysis - Confirmed cases

		95%CI		
	Relative Incidence	LL	UL	P-value
Risk period VS Control period	1.1429	0.4144	3.1516	0.7964

Table 590 Number of Thyroiditis diseases by CTRL/RISK period - Main Analysis - Confirmed cases (Total cohort)

		Gr 1 N = 26	
Follow Up Period	Categories	n	%
ctrl	AD Event	11	100
risk	AD Event	15	100
Overall total	AD Event	26	100

N = number of subjects
n = number of subjects in a given category
% = n / Number of subjects with available results x 100
Main analysis of coprimary endpoints: risk period lasts 12months after the first Cervarix dose

Table 591 Number of Thyroiditis diseases by CTRL/RISK period - Main Analysis - Confirmed cases

		95%CI		
	Relative Incidence	LL	UL	P-value
Risk period VS Control period	1.3636	0.6263	2.9689	0.4346

Table 592 Number of Neuroinflammatory/Ophthalmic diseases by CTRL/RISK period - Main Analysis - Main SCCS - Confirmed cases (Total cohort)

		Gr 1 N = 2	
Follow Up Period	Categories	n	%
ctrl	AD Event	2	100
Overall total	AD Event	2	100

N = number of subjects
n = number of subjects in a given category
% = n / Number of subjects with available results x 100
Main analysis of coprimary endpoints: risk period lasts 12months after the first Cervarix dose

Table 593 Number of Neuroinflammatory/Ophthalmic diseases by CTRL/RISK period - Main Analysis - Main SCCS - Confirmed cases

		95%CI		
	Relative Incidence	LL	UL	P-value
Risk period VS Control period	0.0000	0.0000	.	0.9984

Table 594 Number of Other Autoimmune diseases by CTRL/RISK period - Main Analysis - Sensitivity SCCS - Confirmed cases (Total cohort)

		Gr 1 N = 64	
Follow Up Period	Categories	n	%
ctrl	AD Event	26	100
risk	AD Event	38	100
Overall total	AD Event	64	100

N = number of subjects
n = number of subjects in a given category
% = n / Number of subjects with available results x 100
Sensitivity analysis of coprimary endpoints: risk period lasts until 6 months after the last Cervarix dose

Table 595 Number of Other Autoimmune diseases by CTRL/RISK period - Main Analysis - Sensitivity SCCS - Confirmed cases

		95%CI		
	Relative Incidence	LL	UL	P-value
Risk period VS Control period	1.4097	0.8439	2.3547	0.1896

Table 596 Number of Neuroinflammatory/Ophthalmic diseases by CTRL/RISK period - Main Analysis - Sensitivity SCCS - Confirmed cases (Total cohort)

		Gr 1 N = 2	
Follow Up Period	**Categories**	**n**	**%**
ctrl	AD Event	2	100
Overall total	AD Event	2	100

N = number of subjects
n = number of subjects in a given category
% = n / Number of subjects with available results x 100
Sensitivity analysis of coprimary endpoints: risk period lasts until 6 months after the last Cervarix dose

Table 597 Number of Neuroinflammatory/Ophthalmic diseases by CTRL/RISK period - Main Analysis - Sensitivity Analysis - Confirmed cases

		95%CI		
	Relative Incidence	**LL**	**UL**	**P-value**
Risk period VS Control period	0.0000	0.0000	.	0.9984

Table 598 Incidence Rate Ratio for diabetes adjusted for male effect (Total cohort)

	IRR Calculation					
		95%CI of RR			95%CI of RR	
Autoimmune diseases	**Crude Incidence Rate Ratio**	**LL**	**UL**	**Adjusted Incidence Rate Ratio**	**LL**	**UL**
Diabetes vaccine adjusted effect	0.200	0.062	0.652	0.300	0.109	0.825

Table 599 Sat Scan Results-Main analysis: Exposed Female cohort – Temporal windows = 60 days

Endpoints	Confirmed or All cases	Start – End Date (period of analysis)	Time frame of the most likely cluster	Time (in days) between reference date end cluster's start	Number of Observed/Expected cases in cluster	Observed/Expected Ratio	Relative Risk	P-value
Neuroinflammatory/ Ophthalmic diseases	All	2008/11/02 - 2009/8/24	2008/11/2 - 2008/11/28	62	2 / 0.64	3.13	3.99	0.9957
Other AI	All	2008/9/1 - 2009/9/1	2008/9/19 - 2008/9/21	18	4 / 0.72	5.55	5.76	0.9214
	Confirmed	2008/9/10 - 2009/9/1	2008/10/5 - 2008/10/6	34	3 / 0.34	8.78	9.18	0.8759
Crohn's disease	All	2008/9/21 - 2009/7/11	2008/10/5 - 2008/10/9	34	3 / 0.24	12.60	15.76	0.4099
	Confirmed	2008/9/21 - 2009/7/11	2008/10/5 - 2008/10/9	34	3 / 0.20	14.70	19.27	0.2978
Diabetes Type I	All	2008/10/14 - 2009/7/13	2008/10/14 - 2008/10/20	43	4 / 0.41	9.75	12.67	0.1224
Thyroiditis disease	All	2008/9/1 - 2009/9/1	2008/12/22 - 2009/1/2	112	7 / 1.57	1.57	4.45	0.3509
	Confirmed	2008/9/17 - 2009/9/1	2008/12/22 - 2009/1/1	112	4 / 0.79	5.09	5.87	0.8439

Table 600 Sat Scan Results-Main analysis Non-Exposed Female cohort – Temporal windows = 60 days

Endpoints	Confirmed or All cases	Start – End Date	Time frame of the most likely cluster	Time (in days) between reference date end cluster's start	Number of Observed/Expected cases in cluster	Observed/Expected Ratio	Relative Risk	P-value
Neuroinflammatory/ Ophthalmic diseases	All	2008/10/15 - 2009/7/20	2009/2/24 - 2009/3/15	176	2 / 0.50	3.99	5.18	0.9770
Other AI	All	2008/9/1 - 2009/7/26	2008/12/28 - 2008/12/31	118	5 / 0.51	9.79	10.98	0.0871
	Confirmed	2008/9/1 - 2009/7/13	2008/12/29 - 2008/12/31	119	3 / 0.26	11.70	13.04	0.4772
Thyroiditis disease	All	2008/9/1 - 2009/7/21	2008/12/28 - 2008/12/29	118	2 / 0.11	18.00	20.13	0.8248

Table 601 Sat Scan Results-Main analysis Concurrent Male cohort – Temporal windows = 60 days

Endpoints	Confirmed or All cases	Start – End Date	Time frame of the most likely cluster	Time (in days) between reference date end cluster's start	Number of Observed/Expected cases in cluster	Observed/Expected Ratio	Relative Risk	P-value
Neuroinflammatory/ Ophthalmic diseases	All	2009/3/7 - 2009/5/29	2009/3/7 - 2009/3/12	187	2 / 0.21	9.33	23.00	0.4105
Other AI	All	2008/9/6 - 2009/8/16	2008/9/6 - 2008/9/7	5	4 / 0.16	24.64	28.58	0.0154
	Confirmed	2008/9/6 - 2009/8/16	2008/9/6 - 2008/9/7	5	4 / 0.15	26.54	31.18	0.0109
Diabetes Type I	All	2008/9/6 - 2009/8/16	2008/9/6 - 2008/9/7	5	4 / 0.13	30.00	36.11	0.0055
	Confirmed	2008/9/6 - 2009/8/16	2008/9/6 - 2008/9/7	5	4 / 0.13	30.00	36.11	0.0055

Table 602 Sat Scan Results-Main analysis Historical Male cohort – Time Aggregation = 60 days

Endpoints	Confirmed or All cases	Start – End Date	Time frame of the most likely cluster	Time (in days) between reference date end cluster's start	Number of Observed/Expected cases in cluster	Observed/Expected Ratio	Relative Risk	P-value
Neuroinflammatory/ Ophthalmic diseases	All	2008/10/31 - 2009/6/10	No clusters were found. All areas scanned had either only one case or an equal or fewer number of cases than expected.					
Other AI	All	2008/10/11 - 2009/8/31	2009/2/8 - 2009/2/9	160	2 / 0.12	17.11	19.00	0.8580
	Confirmed	2008/10/11 - 2009/8/31	2008/10/11 - 2008/10/12	39	2 / 0.092	21.67	24.85	0.6928
Diabetes Type I	All	2008/11/8 - 2009/8/31	2009/2/26 - 2009/3/1	175	2 / 0.19	10.61	12.21	0.9263
	Confirmed	2008/11/25 - 2009/8/31	2009/2/26 - 2009/3/1	174	2 / 0.17	11.67	13.80	0.8649

Table 603 Sat Scan Results-Main analysis Exposed Female cohort – Temporal windows = 120 days

Endpoints	Confirmed or All cases	Start – End Date	Time frame of the most likely cluster	Time (in days) between reference date end cluster's start	Number of Observed/Expected cases in cluster	Observed/Expected Ratio	Relative Risk	P-value
Neuroinflammatory/ Ophthalmic diseases	All	2008/11/2 - 2009/8/24	2008/11/2 - 2008/11/28	62	2 / 0.64	3.13	3.99	0.9958
Other AI	All	2008/9/1 - 2009/9/1	2008/9/19 - 2008/9/21	18	4 / 0.72	5.55	5.76	0.9238
	Confirmed	2008/9/10 - 2009/9/1	2008/10/5 - 2008/10/6	34	3 / 0.34	8.78	9.18	0.8798
Crohn's disease	All	2008/9/21 - 2009/7/11	2008/10/5 - 2008/10/9	34	3 / 0.24	12.60	15.76	0.4161
	Confirmed	2008/9/21 - 2009/7/11	2008/10/5 - 2008/10/9	34	3 / 0.20	14.70	19.27	0.3055
Diabetes Type I	All	2008/10/14 - 2009/7/13	2008/10/14 - 2008/10/20	43	4 / 0.41	9.75	12.67	0.1307
Thyroiditis disease	All	2008/9/1 - 2009/9/1	2008/12/22 - 2009/1/2	112	7 / 1.57	4.45	5.04	0.3611
	Confirmed	2008/9/17 - 2009/9/1	2008/12/22 - 2009/1/1	112	4 / 0.79	5.09	5.87	0.8500

Table 604 Sat Scan Results-Main analysis Non-Exposed Female cohort – Temporal windows = 120 days

Endpoints	Confirmed or All cases	Start – End Date	Time frame of the most likely cluster	Time (in days) between reference date end cluster's start	Number of Observed/Expected cases in cluster	Observed/Expected Ratio	Relative Risk	P-value
Neuroinflammatory/ Ophthalmic diseases	All	2008/10/15 - 2009/7/20	2009/2/24 - 2009/3/15	176	2 / 0.50	3.99	5.18	0.9784
Other AI	All	2008/9/1 - 2009/7/26	2008/12/28 - 2008/12/31	118	5 / 0.51	9.79	10.98	0.0911
	Confirmed	2008/9/1 - 2009/7/13	2008/12/29 - 2008/12/31	119	3 / 0.26	11.70	13.04	0.4862
Thyroiditis disease	All	2008/9/1 - 2009/7/21	2008/12/28 - 2008/12/29	483	2 / 0.11	18.00	20.13	0.8285

Table 605 Sat Scan Results-Main analysis Concurrent Male cohort – Temporal windows = 120 days

Endpoints	Confirmed or All cases	Start – End Date	Time frame of the most likely cluster	Time (in days) between reference date end cluster's start	Number of Observed/Expected cases in cluster	Observed/Expected Ratio	Relative Risk	P-value
Other AI	All	2008/9/6 - 2009/8/16	2008/9/6 - 2008/9/7	5	4 / 0.16	24.64	28.58	0.0161
	Confirmed	2008/9/6 - 2009/8/16	2008/9/6 - 2008/9/7	5	4 / 0.15	26.54	31.18	0.0114
Diabetes Type I	All	2008/9/6 - 2009/8/16	2008/9/6 - 2008/9/7	5	4 / 0.13	30.00	36.11	0.0059
	Confirmed	2008/9/6 - 2009/8/16	2008/9/6 - 2008/9/7	5	4 / 0.13	30.00	36.11	0.0059

Table 606 Sat Scan Results-Main analysis Historical Male cohort – Temporal windows = 120 days

Endpoints	Confirmed or All cases	Start – End Date	Time frame of the most likely cluster	Time (in days) between reference date end cluster's start	Number of Observed/Expected cases in cluster	Observed/Expected Ratio	Relative Risk	P-value
Neuroinflammatory/ Ophthalmic diseases	All	2008/10/31 - 2009/6/10	No clusters were found. All areas scanned had either only one case or an equal or fewer number of cases than expected.					
Other AI	All	2008/10/11 - 2009/8/31	2009/2/8 - 2009/2/9	160	2 / 0.12	17.11	19.00	0.8621
	Confirmed	2008/10/11 - 2009/8/31	2008/10/11 - 2008/10/12	40	2 / 0.092	21.67	24.85	0.6980
Diabetes Type I	All	2008/11/8 - 2009/8/31	2009/2/26 - 2009/3/1	178	2 / 0.19	10.61	12.21	0.9282
	Confirmed	2008/11/25 - 2009/8/31	2009/2/26 - 2009/3/1	178	2 / 0.17	11.67	13.80	0.8701

Table 607 Sat Scan Results Imputed date Exposed Female cohort – Temporal windows = 60 days

Endpoints	Confirmed or All cases	Start – End Date	Time frame of the most likely cluster	Time after reference date when the cluster starts (in days)	Number of Observed/Expected cases in cluster	Observed/Expected Ratio	Relative Risk	P-value
Neuroinflammatory/ Ophthalmic diseases	All	2008/11/2 - 2009/8/24	2009/4/9 - 2009/4/22	368	2 / 0.38	5.29	6.71	0.9596
Other AI	All	2008/9/1 - 2009/9/1	2008/11/13 - 2008/11/13	73	3 / 0.28	10.87	11.17	0.8360
	Confirmed	2008/9/8 - 2009/9/1	2008/10/5 - 2008/10/6	34	3 / 0.36	8.28	8.64	0.9181
Crohn's disease	Confirmed	2008/9/8 - 2009/7/11	2008/10/5 - 2008/10/9	34	3 / 0.21	14.17	18.12	0.3417
Diabetes Type I	All	2008/10/14 - 2009/7/13	2008/10/14 - 2008/10/20	43	4 / 0.46	8.67	10.86	0.2369
	Confirmed	2008/9/19 - 2009/8/8	2009/3/27 - 2009/3/27	207	2 / 0.034	58.91	71.78	0.2048
Thyroiditis disease	All	2008/9/1 - 2009/9/1	2008/12/22 - 2008/12/27	112	5 / 0.93	5.35	5.77	0.5980
	Confirmed	2008/9/17 - 2009/9/1	2009/1/25 - 2009/1/26	146	2 / 0.15	13.46	14.50	0.9661

Table 608 Sat Scan Results Imputed date Non-Exposed Female cohort – Temporal windows = 60 days

Endpoints	Confirmed or All cases	Start – End Date	Time frame of the most likely cluster	Time after reference date when the cluster starts (in days)	Number of Observed/Expected cases in cluster	Observed/Expected Ratio	Relative Risk	P-value
Neuroinflammatory/ Ophthalmic diseases	All	2008/9/10 - 2009/7/20	2008/10/15 - 2008/10/15	44	2 / 0.029	69.78	89.43	0.1499
Other AI	All	2008/9/1 - 2009/7/26	2008/12/28 - 2008/12/31	118	7 / 0.64	10.86	12.36	0.0028
	Confirmed	2008/9/1 - 2009/7/13	2008/12/28 - 2008/12/31	118	5 / 0.42	11.97	13.93	0.0337
Thyroiditis disease	All	2008/9/1 - 2009/7/21	2008/12/28 - 2008/12/31	118	3 / 0.33	9.00	10.00	0.8307

Table 609 Sat Scan Results Imputed date Concurrent Male cohort – Temporal windows = 60 days

Endpoints	Confirmed or All cases	Start – End Date	Time frame of the most likely cluster	Time after reference date when the cluster starts (in days)	Number of Observed/Expected cases in cluster	Observed/Expected Ratio	Relative Risk	P-value
Neuroinflammatory/ Ophthalmic diseases	All	2009/1/23 - 2009/6/29	2009/5/4 - 2009/5/4	245	2 / 0.044	45.14	62.80	0.1688
	Confirmed	2009/3/07 - 2009/6/29	No clusters were found. All areas scanned had either only one case or an equal or fewer number of cases than expected		2/ -			
Other AI	All	2008/9/6 - 2009/8/16	2008/9/6 - 2008/9/7	5	4 / 0.22	18.16	20.18	0.0415
	Confirmed	2008/9/6 - 2009/8/16	2008/9/6 - 2008/9/7	5	4 / 0.19	20.91	23.66	0.0213

Table 610 Sat Scan Results Imputed date Historical Male cohort – Temporal windows = 60 days

Endpoints	Confirmed or All cases	Start – End Date	Time frame of the most likely cluster	Time after reference date when the cluster starts (in days)	Number of Observed/Expected cases in cluster	Observed/Expected Ratio	Relative Risk	P-value
Neuroinflammatory/ Ophthalmic diseases	All	2008/10/31 - 2009/6/10	2009/5/13 - 2009/6/10	254	2 / 0.52	3.84	6.69	0.8536
Other AI	All	2008/9/6 - 2009/8/31	2009/4/19 - 2009/4/25	230	4 / 0.56	7.09	8.07	0.5143
	Confirmed	2008/10/11 - 2009/8/31	2008/10/11 - 2008/10/12	40	2 / 0.12	17.11	19.00	0.8580

Table 611 Sat Scan Results Imputed date Exposed Female cohort – Temporal windows = 120 days

Endpoints	Confirmed or All cases	Start – End Date	Time frame of the most likely cluster	Time after reference date when the cluster starts (in days)	Number of Observed/Expected cases in cluster	Observed/Expected Ratio	Relative Risk	P-value
Neuroinflammatory/Ophthalmic diseases	All	2008/11/2 - 2009/8/24	2009/4/9 - 2009/4/22	220	2 / 0.38	5.29	6.71	0.9623
Other AI	All	2008/9/1 - 2009/9/1	2008/11/13 - 2008/11/13	73	3 / 0.28	10.87	11.17	0.8402
	Confirmed	2008/9/8 - 2009/9/1	2008/10/5 - 2008/10/6	34	3 / 0.36	8.28	8.64	0.9202
Crohn's disease	All							
	Confirmed	2008/9/8 - 2009/7/11	2008/10/5 - 2008/10/9	34	3 / 0.21	14.17	18.12	0.3477
Diabetes Type I	All	2008/10/14 - 2009/7/13	2008/10/14 - 2008/10/20	43	4 / 0.46	8.67	10.86	0.2462
	Confirmed	2008/9/19 - 2009/8/8	2009/3/27 - 2009/3/27	207	2 / 0.034	58.91	71.78	0.2099
Thyroiditis disease	All							
	Confirmed	2008/9/17 - 2009/9/1	2009/1/25 - 2009/1/26	146	2 / 0.15	13.46	14.50	0.9672

Table 612 Sat Scan Results Imputed date Non-Exposed Female cohort – Temporal windows = 120 days

Endpoints	Confirmed or All cases	Start – End Date	Time frame of the most likely cluster	Time after reference date when the cluster starts (in days)	Number of Observed/Expected cases in cluster	Observed/Expected Ratio	Relative Risk	P-value
Neuroinflammatory/ Ophthalmic diseases	All	2008/9/10 - 2009/7/20	2008/10/15 - 2008/10/15	44	2 / 0.029	69.78	89.43	0.1540
Other AI	All	2008/9/1 - 2009/7/26	2008/12/28 - 2008/12/31	118	7 / 0.64	10.86	12.36	0.0031
	Confirmed	2008/9/1 - 2009/7/13	2008/12/28 - 2008/12/31	118	5 / 0.42	11.97	13.93	0.0360
Thyroiditis disease	All	2008/9/1 - 2009/7/21	2008/12/28 - 2008/12/31	118	3 / 0.33	9.00	10.00	0.8350

Table 613 Sat Scan Results Imputed date Concurrent Male cohort – Temporal windows = 120 days

Endpoints	Confirmed or All cases	Start – End Date	Time frame of the most likely cluster	Time after reference date when the cluster starts (in days)	Number of Observed/Expected cases in cluster	Observed/Expected Ratio	Relative Risk	P-value
Neuroinflammatory/ Ophthalmic diseases	All	2009/1/23 - 2009/6/29	2009/5/4 - 2009/5/4	245	2 / 0.044	45.14	62.80	0.1757
Other AI	All	2008/9/6 - 2009/8/16	2008/9/6 - 2008/9/7	5	4 / 0.22	18.16	20.18	0.0436
	Confirmed	2008/9/6 - 2009/8/16	2008/9/6 - 2008/9/7	5	4 / 0.19	20.91	23.66	0.0226

Table 614 Sat Scan Results Imputed date Historical Male cohort – Temporal windows = 120 days

Endpoints	Confirmed or All cases	Start – End Date	Time frame of the most likely cluster	Time after reference date when the cluster starts (in days)	Number of Observed/Expected cases in cluster	Observed/Expected Ratio	Relative Risk	P-value
Neuroinflammatory/ Ophthalmic diseases	All	2008/10/31 - 2009/6/10	2009/5/13 - 2009/6/10	254	2 / 0.52	3.84	6.69	0.8688
Other AI	All	2008/9/6 - 2009/8/31	2009/4/19 - 2009/4/25	230	4 / 0.56	7.09	8.07	0.5251
	Confirmed	2008/10/11 - 2009/8/31	2008/10/11 - 2008/10/12	40	2 / 0.12	17.11	19.00	0.8621

Table 615 Sat Scan Results Diagnosis date Exposed Female cohort – Temporal windows = 60 days

Endpoints	Confirmed or All cases	Start – End Date	Time frame of the most likely cluster	Time after reference date when the cluster starts (in days)	Number of Observed/Expected cases in cluster	Observed/Expected Ratio	Relative Risk	P-value
Neuroinflammatory/ Ophthalmic diseases	All	2008/12/18 - 2009/8/25	2009/8/24 - 2009/8/25	357	2 / 0.048	41.83	62.25	0.2000
Other AI	All	2008/9/2 - 2009/8/31	2008/12/15 - 2008/12/22	105	8 / 1.93	4.14	4.45	0.2895
	Confirmed	2008/9/21 - 2009/8/31	2008/12/15 - 2008/12/24	105	8 / 1.68	4.76	5.36	0.1177
Crohn's disease	All	2008/9/27 - 2009/8/10	2008/11/16 - 2008/11/17	76	2 / 0.082	24.46	28.73	0.6020
	Confirmed	2008/9/27 - 2009/8/10	2008/11/16 - 2008/11/17	76	2 / 0.069	28.91	35.11	0.4722
Diabetes Type I	All	2008/9/21 - 2009/5/21	2009/1/17 - 2009/1/19	138	2 / 0.14	14.73	17.78	0.7554
	Confirmed	2008/9/21 - 2009/5/21	2009/1/17 - 2009/1/19	138	2 / 0.14	14.73	17.78	0.7554
Thyroiditis disease	All	2008/9/2 - 2009/8/27	2009/4/15 - 2009/6/8	226	18 / 7.33	2.45	3.33	0.0943
	Confirmed	2008/9/22 - 2009/8/13	2008/12/16 - 2008/12/22	106	4 / 0.49	8.10	9.59	0.3449

Table 616 Sat Scan Results Diagnosis date Non-Exposed Female cohort – Temporal windows = 60 days

Endpoints	Confirmed or All cases	Start – End Date	Time frame of the most likely cluster	Time after reference date when the cluster starts (in days)	Number of Observed/Expected cases in cluster	Observed/Expected Ratio	Relative Risk	P-value
Neuroinflammatory/ Ophthalmic diseases	All	2008/9/18 - 2009/8/20	2008/10/18 - 2008/11/14	47	4 / 0.83	4.81	7.36	0.6813
Other AI	All	2008/9/6 - 2009/8/31	2008/12/28 - 2009/2/6	118	18 / 9.79	1.84	2.06	0.9524
	Confirmed	2008/9/13 - 2009/8/30	2009/3/18 - 2009/3/22	198	4 / 0.74	5.42	5.78	0.8708
Diabetes Type I	All	2008/9/13 - 2009/7/26	2009/1/6 - 2009/1/11	127	3 / 0.38	7.93	9.15	0.7421
	Confirmed	2008/9/13 - 2009/7/26	2009/1/6 - 2009/1/11	127	3 / 0.38	7.93	9.15	0.7421
Thyroiditis disease	All	2008/9/6 - 2009/8/21	2009/8/8 - 2009/8/9	339	2 / 0.26	7.61	7.91	1.0000
	Confirmed	2008/10/18 - 2009/7/29	2009/4/12 - 2009/4/13	223	2 / 0.11	19.00	21.77	0.7386

Table 617 Sat Scan Results Diagnosis date Concurrent Male cohort – Temporal windows = 60 days

Endpoints	Confirmed or All cases	Start – End Date	Time frame of the most likely cluster	Time after reference date when the cluster starts (in days)	Number of Observed/Expected cases in cluster	Observed/Expected Ratio	Relative Risk	P-value
Neuroinflammatory/ Ophthalmic diseases	All	2008/11/4 - 2009/7/18	2009/5/12 - 2009/5/12	253	2 / 0.035	57.11	73.14	0.1719
Other AI	All	2008/9/7 - 2009/8/21	2008/12/21 - 2009/2/11	111	21 / 8.50	2.47	3.35	0.0323
	Confirmed	2008/9/7 - 2009/8/21	2008/12/21 - 2009/2/16	111	19 / 7.48	2.54	3.67	0.0314
Diabetes Type I	All	2008/9/7 - 2009/8/21	2009/1/16 - 2009/2/16	137	8 / 2.11	3.79	5.28	0.1995
	Confirmed	2008/9/7 - 2009/8/21	2009/1/16 - 2009/2/16	137	8 / 2.11	3.79	5.28	0.1995
Crohn's disease	All	2008/10/20 - 2009/7/13	2009/1/5 - 2009/1/14	126	4 / 0.60	6.67	8.57	0.5125
	Confirmed	2008/10/20 - 2009/7/13	2009/1/5 - 2009/1/14	126	4 / 0.56	7.12	9.35	0.4581
Thyroiditis disease	All	2008/9/7 - 2009/6/17	2009/5/19 - 2009/5/24	260	3 / 0.21	14.20	19.86	0.2481

Table 618 Sat Scan Results Diagnosis date Historical Male cohort – Temporal windows = 60 days

Endpoints	Confirmed or All cases	Start – End Date	Time frame of the most likely cluster	Time after reference date when the cluster starts (in days)	Number of Observed/Expected cases in cluster	Observed/Expected Ratio	Relative Risk	P-value
Neuroinflammatory/ Ophthalmic diseases	All	2008/10/30 - 2009/6/16	2009/5/21 - 2009/6/16	262	2 / 0.47	4.26	7.52	0.8223
Other AI	All	2008/9/13 - 2009/8/31	2009/1/10 - 2009/1/11	131	3 / 0.27	11.03	11.70	0.6904
	Confirmed	2008/9/13 - 2009/8/31	2009/7/16 - 2009/7/18	318	3 / 0.28	10.70	11.67	0.6080
Diabetes Type I	All	2008/11/22 - 2009/8/31	2009/1/11 - 2009/1/11	132	2 / 0.053	37.73	43.38	0.3800
	Confirmed	2008/12/2 - 2009/8/31	2009/1/11 - 2009/1/11	132	2 / 0.048	42.00	49.45	0.3304
Crohn's disease	All	2008/9/23 - 2009/7/18	2009/7/17 - 2009/7/18	319	2 / 0.067	29.90	37.13	0.4253

Table 619 Sat Scan Results Diagnosis date Exposed Female cohort – Temporal windows = 120 days

Endpoints	Confirmed or All cases	Start – End Date	Time frame of the most likely cluster	Time after reference date when the cluster starts (in days)	Number of Observed/Expected cases in cluster	Observed/Expected Ratio	Relative Risk	P-value
Neuroinflammatory/ Ophthalmic diseases	All	2008/12/18 - 2009/8/25	2009/8/24 - 2009/8/25	357	2 / 0.048	41.83	62.25	0.2109
Other AI	All	2008/9/2 - 2009/8/31	2008/12/15 - 2008/12/22	105	8 / 1.93	4.14	4.45	0.2997
	Confirmed	2008/9/21 - 2009/8/31	2008/12/15 - 2008/12/24	105	8 / 1.68	4.76	5.36	0.1255
Crohn's disease	All	2008/9/27 - 2009/8/10	2008/11/16 - 2008/11/17	76	2 / 0.082	24.46	28.73	0.6074
	Confirmed	2008/9/27 - 2009/8/10	2008/11/16 - 2008/11/17	76	2 / 0.069	28.91	35.11	0.4806
Diabetes Type I	All	2008/9/21 - 2009/5/21	2009/1/17 - 2009/1/19	138	2 / 0.14	14.73	17.78	0.7622
	Confirmed	2008/9/21 - 2009/5/21	2009/1/17 - 2009/1/19	138	2 / 0.14	14.73	17.78	0.7622
Thyroiditis disease	All	2008/9/2 - 2009/8/27	2009/4/15 - 2009/6/8	226	18 / 7.33	2.45	3.33	0.0991
	Confirmed	2008/9/22 - 2009/8/13	2008/12/16 - 2008/12/22	106	4 / 0.49	8.10	9.59	0.3565

Table 620 Sat Scan Results Diagnosis date Non-Exposed Female cohort – Temporal windows = 120 days

Endpoints	Confirmed or All cases	Start – End Date	Time frame of the most likely cluster	Time after reference date when the cluster starts (in days)	Number of Observed/Expected cases in cluster	Observed/Expected Ratio	Relative Risk	P-value
Neuroinflammatory/ Ophthalmic diseases	All	2008/9/18 - 2009/8/20	2008/10/18 - 2008/11/14	47	4 / 0.83	4.81	7.36	0.6922
Other AI	All	2008/9/6 - 2009/8/31	2008/12/28 - 2009/2/6	118	18 / 9.79	1.84	2.06	0.9544
	Confirmed	2008/9/13 - 2009/8/30	2009/1/28 - 2009/5/19	149	26 / 16.55	1.57	2.14	0.8288
Diabetes Type I	All	2008/9/13 - 2009/7/26	2009/1/6 - 2009/1/11	127	3 / 0.38	7.93	9.15	0.7502
	Confirmed	2008/9/13 - 2009/7/26	2009/1/6 - 2009/1/11	127	3 / 0.38	7.93	9.15	0.7502
Thyroiditis disease	All	2008/9/6 - 2009/8/21	2009/8/8 - 2009/8/9	341	2 / 0.26	7.61	7.91	1.0000
	Confirmed	2008/10/18 - 2009/7/29	2009/3/8 - 2009/6/2	188	10 / 4.58	2.18	4.55	0.5576

Table 621 Sat Scan Results Diagnosis date Concurrent Male cohort – Temporal windows = 120 days

Endpoints	Confirmed or All cases	Start – End Date	Time frame of the most likely cluster	Time after reference date when the cluster starts (in days)	Number of Observed/Expected cases in cluster	Observed/Expected Ratio	Relative Risk	P-value
Neuroinflammatory/ Ophthalmic diseases	All	2008/11/4 - 2009/7/18	2009/5/12 - 2009/5/12	253	2 / 0.035	57.11	73.14	0.1797
Other AI	All	2008/9/7 - 2009/8/21	2008/12/21 - 2009/2/11	111	21 / 8.50	2.47	3.35	0.0344
	Confirmed	2008/9/7 - 2009/8/30	2008/10/20 - 2009/2/16	49	29 / 15.08	1.92	3.59	0.0132
Crohn's disease	All	2008/10/20 - 2009/7/13	2009/1/5 - 2009/1/14	126	4 / 0.60	6.67	8.57	0.5202
	Confirmed	2008/10/20 - 2009/7/13	2009/1/5 - 2009/1/14	126	4 / 0.56	7.12	9.35	0.4649
Thyroiditis disease	All	2008/9/7 - 2009/6/17	2009/5/19 - 2009/5/24	260	3 / 0.21	14.20	19.86	0.2577
Diabetes Type I	All	2008/9/7 - 2009/8/21	2009/1/16 - 2009/2/16	137	8 / 2.11	3.79	5.28	0.2087
	Confirmed	2008/9/7 - 2009/8/21	2009/1/16 - 2009/2/16	137	8 / 2.11	3.79	5.28	0.2087

Table 622 Sat Scan Results Diagnosis date Historical Male cohort – Temporal windows = 120 days

Endpoints	Confirmed or All cases	Start – End Date	Time frame of the most likely cluster	Time after reference date when the cluster starts (in days)	Number of Observed/Expected cases in cluster	Observed/Expected Ratio	Relative Risk	P-value
Neuroinflammatory/ Ophthalmic diseases	All	2008/10/31 - 2009/6/16	2009/5/21 - 2009/6/16	262	2 / 0.47	4.24	7.48	0.8385
Other AI	All	2008/9/13 - 2009/8/31	2009/1/10 - 2009/1/11	131	3 / 0.27	11.03	11.70	0.6966
	Confirmed	2008/9/13 - 2009/8/31	2009/7/16 - 2009/7/18	318	3 / 0.28	10.70	11.67	0.6172
Diabetes Type I	All	2008/11/22 - 2009/8/31	2009/1/11 - 2009/1/11	132	2 / 0.053	37.73	43.38	0.3863
	Confirmed	2008/12/2 - 2009/8/31	2009/1/11 - 2009/1/11	132	2 / 0.048	42.00	49.45	0.3385
Crohn's disease	All	2008/9/23 - 2009/7/18	2009/7/17 - 2009/7/18	319	2 / 0.067	29.90	37.13	0.4365

Table 623 Geographical distribution of the two co-primary endpoints - Confirmed cases (Total cohort)

			EXP N = 64964		NNEXP N = 64973		MALE N = 64974		HIST N = 64965		Total N = 259876	
Region in category	**Practice Region**	**Categories**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Ireland Scotland Wales	Northern Ireland	Neuroinflammatory Ophthalmic autoimmune diseases	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
		Other autoimmune diseases	1	100	5	100	0	0.0	1	100	7	100
	Scotland	Neuroinflammatory Ophthalmic autoimmune diseases	0	0.0	0	0.0	1	20.0	0	0.0	1	7.7
		Other autoimmune diseases	5	100	2	100	4	80.0	1	100	12	92.3
	Wales	Neuroinflammatory Ophthalmic autoimmune diseases	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
		Other autoimmune diseases	3	100	1	100	3	100	0	0.0	7	100
Midlands	East Midlands	Neuroinflammatory Ophthalmic autoimmune diseases	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
		Other autoimmune diseases	4	100	1	100	2	100	2	100	9	100
	West Midlands	Neuroinflammatory Ophthalmic autoimmune diseases	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
		Other autoimmune diseases	4	100	0	0.0	1	100	3	100	8	100
North England	North East	Neuroinflammatory Ophthalmic autoimmune diseases	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
		Other autoimmune diseases	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	North West	Neuroinflammatory Ophthalmic autoimmune diseases	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
		Other autoimmune diseases	3	100	4	100	7	100	1	100	15	100
	Yorkshire & The Humber	Neuroinflammatory Ophthalmic autoimmune diseases	0	0.0	0	0.0	0	0.0	1	100	1	16.7
		Other autoimmune diseases	1	100	1	100	3	100	0	0.0	5	83.3
South England	East of England	Neuroinflammatory Ophthalmic autoimmune diseases	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
		Other autoimmune diseases	2	100	4	100	2	100	5	100	13	100
	London	Neuroinflammatory Ophthalmic autoimmune diseases	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
		Other autoimmune diseases	1	100	2	100	0	0.0	1	100	4	100
	South Central	Neuroinflammatory Ophthalmic autoimmune diseases	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
		Other autoimmune diseases	7	100	2	100	2	100	0	0.0	11	100
	South East Coast	Neuroinflammatory Ophthalmic autoimmune diseases	0	0.0	1	50.0	0	0.0	0	0.0	1	16.7
		Other autoimmune diseases	4	100	1	50.0	0	0.0	0	0.0	5	83.3
	South West	Neuroinflammatory Ophthalmic autoimmune diseases	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
		Other autoimmune diseases	3	100	4	100	2	100	1	100	10	100
Overall total	Overall total	Neuroinflammatory Ophthalmic autoimmune diseases	0	0.0	1	3.6	1	3.7	1	6.3	3	2.8
		Other autoimmune diseases	38	100	27	96.4	26	96.3	15	93.8	106	97.2

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort

HIST = Non Exposed Historical Male Cohort
N = number of subjects
n/% = number / percentage of subjects in a given category

Table 624 Geographical distribution of the two co-primary endpoints - All cases (Total cohort)

			EXP N = 64964		NNEXP N = 64973		MALE N = 64974		HIST N = 64965		Total N = 259876	
Region in category	**Practice Region**	**Categories**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Ireland Scotland Wales	Northern Ireland	Neuroinflammatory Ophthalmic autoimmune diseases	0	0.0	0	0.0	0	0.0	1	50.0	1	9.1
		Other autoimmune diseases	2	100	7	100	0	0.0	1	50.0	10	90.9
	Scotland	Neuroinflammatory Ophthalmic autoimmune diseases	1	14.3	0	0.0	1	20.0	0	0.0	2	10.5
		Other autoimmune diseases	6	85.7	4	100	4	80.0	3	100	17	89.5
	Wales	Neuroinflammatory Ophthalmic autoimmune diseases	0	0.0	1	16.7	0	0.0	0	0.0	1	7.7
		Other autoimmune diseases	4	100	5	83.3	3	100	0	0.0	12	92.3
Midlands	East Midlands	Neuroinflammatory Ophthalmic autoimmune diseases	1	20.0	0	0.0	0	0.0	0	0.0	1	10.0
		Other autoimmune diseases	4	80.0	1	100	2	100	2	100	9	90.0
	West Midlands	Neuroinflammatory Ophthalmic autoimmune diseases	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
		Other autoimmune diseases	6	100	0	0.0	1	100	3	100	10	100
North England	North East	Neuroinflammatory Ophthalmic autoimmune diseases	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
		Other autoimmune diseases	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	North West	Neuroinflammatory Ophthalmic autoimmune diseases	0	0.0	1	16.7	0	0.0	0	0.0	1	5.3
		Other autoimmune diseases	4	100	5	83.3	8	100	1	100	18	94.7
	Yorkshire & The Humber	Neuroinflammatory Ophthalmic autoimmune diseases	0	0.0	1	50.0	0	0.0	1	100	2	28.6
		Other autoimmune diseases	1	100	1	50.0	3	100	0	0.0	5	71.4
South England	East of England	Neuroinflammatory Ophthalmic autoimmune diseases	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
		Other autoimmune diseases	2	100	5	100	2	100	5	100	14	100
	London	Neuroinflammatory Ophthalmic autoimmune diseases	0	0.0	1	33.3	0	0.0	0	0.0	1	20.0
		Other autoimmune diseases	1	100	2	66.7	0	0.0	1	100	4	80.0
	South Central	Neuroinflammatory Ophthalmic autoimmune diseases	1	10.0	1	20.0	1	33.3	0	0.0	3	16.7
		Other autoimmune diseases	9	90.0	4	80.0	2	66.7	0	0.0	15	83.3
	South East Coast	Neuroinflammatory Ophthalmic autoimmune diseases	0	0.0	1	33.3	1	50.0	0	0.0	2	16.7
		Other autoimmune diseases	5	100	2	66.7	1	50.0	2	100	10	83.3
	South West	Neuroinflammatory Ophthalmic autoimmune diseases	1	12.5	1	16.7	0	0.0	0	0.0	2	11.8
		Other autoimmune diseases	7	87.5	5	83.3	2	100	1	100	15	88.2
Overall total	Overall total	Neuroinflammatory Ophthalmic autoimmune diseases	4	7.3	7	14.6	3	9.7	2	9.5	16	10.3
		Other autoimmune diseases	51	92.7	41	85.4	28	90.3	19	90.5	139	89.7

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort

HIST = Non Exposed Historical Male Cohort
N = number of subjects
n/% = number / percentage of subjects in a given category

Table 625 Geographical distribution of thyroiditis cases - Confirmed cases (Total cohort)

			EXP N = 15		NNEXP N = 4		Total N = 19	
Region in category	**Practice Region**	**Categories**	**n**	**%**	**n**	**%**	**n**	**%**
Ireland Scotland Wales	Northern Ireland	Autoimmune Thyroiditis	1	100	-	-	1	100
	Scotland	Autoimmune Thyroiditis	2	100	-	-	2	100
	Wales	Autoimmune Thyroiditis	2	100	-	-	2	100
Midlands	West Midlands	Autoimmune Thyroiditis	2	100	-	-	2	100
North England	North West	Autoimmune Thyroiditis	-	-	2	100	2	100
South England	East of England	Autoimmune Thyroiditis	1	100	-	-	1	100
	London	Autoimmune Thyroiditis	-	-	1	100	1	100
	South Central	Autoimmune Thyroiditis	3	100	-	-	3	100
	South East Coast	Autoimmune Thyroiditis	2	100	1	100	3	100
	South West	Autoimmune Thyroiditis	2	100	-	-	2	100
Overall total	Overall total	Autoimmune Thyroiditis	15	100	4	100	19	100

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n/% = number / percentage of subjects in a given category

Table 626 Geographical distribution of thyroiditis cases - All cases (Total cohort)

			EXP N = 26		NNEXP N = 18		MALE N = 2		HIST N = 3		Total N = 49	
Region in category	**Practice Region**	**Categories**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Ireland Scotland Wales	Northern Ireland	Autoimmune Thyroiditis	1	100	3	100	-	-	-	-	4	100
	Scotland	Autoimmune Thyroiditis	3	100	1	100	-	-	1	100	5	100
	Wales	Autoimmune Thyroiditis	3	100	4	100	-	-	-	-	7	100
Midlands	West Midlands	Autoimmune Thyroiditis	4	100	-	-	-	-	-	-	4	100
North England	North West	Autoimmune Thyroiditis	1	100	3	100	1	100	-	-	5	100
South England	East of England	Autoimmune Thyroiditis	1	100	1	100	-	-	-	-	2	100
	London	Autoimmune Thyroiditis	-	-	1	100	-	-	-	-	1	100
	South Central	Autoimmune Thyroiditis	4	100	2	100	-	-	-	-	6	100
	South East Coast	Autoimmune Thyroiditis	3	100	2	100	1	100	2	100	8	100
	South West	Autoimmune Thyroiditis	6	100	1	100	-	-	-	-	7	100
Overall total	Overall total	Autoimmune Thyroiditis	26	100	18	100	2	100	3	100	49	100

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n/% = number / percentage of subjects in a given category

Table 627 Geographical distribution of Diabetes Type 1 cases - Confirmed cases (Total cohort)

			EXP N = 8		NNEXP N = 16		MALE N = 20		HIST N = 8		Total N = 52	
Region in category	**Practice Region**	**Categories**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Ireland Scotland Wales	Northern Ireland	Type 1 Diabetes Mellitus	-	-	5	100	-	-	-	-	5	100
	Scotland	Type 1 Diabetes Mellitus	2	100	1	100	1	100	1	100	5	100
	Wales	Type 1 Diabetes Mellitus	-	-	-	-	3	100	-	-	3	100
Midlands	East Midlands	Type 1 Diabetes Mellitus	1	100	-	-	2	100	2	100	5	100
	West Midlands	Type 1 Diabetes Mellitus	1	100	-	-	1	100	2	100	4	100
North England	North West	Type 1 Diabetes Mellitus	1	100	-	-	6	100	-	-	7	100
	Yorkshire & The Humber	Type 1 Diabetes Mellitus	-	-	1	100	3	100	-	-	4	100
South England	East of England	Type 1 Diabetes Mellitus	1	100	3	100	1	100	2	100	7	100
	London	Type 1 Diabetes Mellitus	-	-	-	-	-	-	1	100	1	100
	South Central	Type 1 Diabetes Mellitus	-	-	2	100	2	100	-	-	4	100
	South East Coast	Type 1 Diabetes Mellitus	1	100	-	-	-	-	-	-	1	100
	South West	Type 1 Diabetes Mellitus	1	100	4	100	1	100	-	-	6	100
Overall total	Overall total	Type 1 Diabetes Mellitus	8	100	16	100	20	100	8	100	52	100

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n/% = number / percentage of subjects in a given category

Table 628 Geographical distribution of Diabetes Type 1 cases - All cases (Total cohort)

			EXP N = 8		NNEXP N = 16		MALE N = 20		HIST N = 8		Total N = 52	
Region in category	**Practice Region**	**Categories**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Ireland Scotland Wales	Northern Ireland	Type 1 Diabetes Mellitus	-	-	5	100	-	-	-	-	5	100
	Scotland	Type 1 Diabetes Mellitus	2	100	1	100	1	100	1	100	5	100
	Wales	Type 1 Diabetes Mellitus	-	-	-	-	3	100	-	-	3	100
Midlands	East Midlands	Type 1 Diabetes Mellitus	1	100	-	-	2	100	2	100	5	100
	West Midlands	Type 1 Diabetes Mellitus	1	100	-	-	1	100	2	100	4	100
North England	North West	Type 1 Diabetes Mellitus	1	100	-	-	6	100	-	-	7	100
	Yorkshire & The Humber	Type 1 Diabetes Mellitus	-	-	1	100	3	100	-	-	4	100
South England	East of England	Type 1 Diabetes Mellitus	1	100	3	100	1	100	2	100	7	100
	London	Type 1 Diabetes Mellitus	-	-	-	-	-	-	1	100	1	100
	South Central	Type 1 Diabetes Mellitus	-	-	2	100	2	100	-	-	4	100
	South East Coast	Type 1 Diabetes Mellitus	1	100	-	-	-	-	-	-	1	100
	South West	Type 1 Diabetes Mellitus	1	100	4	100	1	100	-	-	6	100
Overall total	Overall total	Type 1 Diabetes Mellitus	8	100	16	100	20	100	8	100	52	100

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n/% = number / percentage of subjects in a given category

Table 629 Geographical distribution of Crohn's disease - Confirmed cases (Total cohort)

			EXP N = 6		NNEXP N = 5		MALE N = 4		HIST N = 1		Total N = 16	
Region in category	**Practice Region**	**Categories**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Ireland Scotland Wales	Scotland	Crohn diseases	1	100	1	100	2	100	-	-	4	100
	Wales	Crohn diseases	1	100	-	-	-	-	-	-	1	100
Midlands	East Midlands	Crohn diseases	2	100	1	100	-	-	-	-	3	100
	West Midlands	Crohn diseases	-	-	-	-	-	-	1	100	1	100
North England	North West	Crohn diseases	-	-	2	100	1	100	-	-	3	100
South England	London	Crohn diseases	-	-	1	100	-	-	-	-	1	100
	South Central	Crohn diseases	2	100	-	-	-	-	-	-	2	100
	South West	Crohn diseases	-	-	-	-	1	100	-	-	1	100
Overall total	Overall total	Crohn diseases	6	100	5	100	4	100	1	100	16	100

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n/% = number / percentage of subjects in a given category

Table 630 Geographical distribution of Crohn's disease - All cases (Total cohort)

			EXP N = 8		NNEXP N = 5		MALE N = 4		HIST N = 2		Total N = 19	
Region in category	**Practice Region**	**Categories**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Ireland Scotland Wales	Northern Ireland	Crohn diseases	1	100	-	-	-	-	-	-	1	100
	Scotland	Crohn diseases	1	100	1	100	2	100	1	100	5	100
	Wales	Crohn diseases	1	100	-	-	-	-	-	-	1	100
Midlands	East Midlands	Crohn diseases	2	100	1	100	-	-	-	-	3	100
	West Midlands	Crohn diseases	-	-	-	-	-	-	1	100	1	100
North England	North West	Crohn diseases	-	-	2	100	1	100	-	-	3	100
South England	London	Crohn diseases	-	-	1	100	-	-	-	-	1	100
	South Central	Crohn diseases	3	100	-	-	-	-	-	-	3	100
	South West	Crohn diseases	-	-	-	-	1	100	-	-	1	100
Overall total	Overall total	Crohn diseases	8	100	5	100	4	100	2	100	19	100

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n/% = number / percentage of subjects in a given category

Table 631 Frequency of autoimmune diseases during the one year follow-up period by exposed/non-exposed status - Main Analysis - Confirmed and Non-Confirmed cases (N=AD) (Total cohort)

		EXP N = 64964		NNEXP N = 64973		MALE N = 64974		HIST N = 64965		Total N = 259876	
Characteristics	**Categories**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**
Individual autoimmune diseases within 1 year follow-up period	ACUTE DISSEMINATED ENCEPHALOMYELITIS	1	1.54	0	0.00	0	0.00	0	0.00	1	0.38
	AI HYPOTHYROIDITIS	22	33.86	15	23.09	2	3.08	1	1.54	40	15.39
	AUTOIMMUNE UVEITIS	2	3.08	5	7.70	2	3.08	1	1.54	10	3.85
	CROHN'S DISEASE	8	12.31	5	7.70	4	6.16	2	3.08	19	7.31
	DOWN SYNDROME	1	1.54	0	0.00	0	0.00	1	1.54	2	0.77
	GUILLAIN-BARRÉ SYNDROME	0	0.00	0	0.00	1	1.54	1	1.54	2	0.77
	IDIOPATHIC THROMBOCYTOPENIC PURPURA (ITP)	1	1.54	1	1.54	0	0.00	2	3.08	4	1.54
	INFLAMMATORY BOWEL	0	0.00	0	0.00	0	0.00	1	1.54	1	0.38
	JUVENILE RHEUMATOID ARTHRITIS (JRA)	1	1.54	0	0.00	0	0.00	1	1.54	2	0.77
	MULTIPLE SCLEROSIS	0	0.00	1	1.54	0	0.00	0	0.00	1	0.38
	OPTIC NEURITIS	1	1.54	1	1.54	0	0.00	0	0.00	2	0.77
	OTHER AUTOIMMUNE DISEASES	1	1.54	0	0.00	0	0.00	0	0.00	1	0.38
	PSORIATIC ARTHRITIS	1	1.54	1	1.54	0	0.00	0	0.00	2	0.77
	RHEUMATOID ARTHRITIS (RA)	1	1.54	0	0.00	0	0.00	0	0.00	1	0.38
	THYROTOXICOSIS	3	4.62	3	4.62	0	0.00	1	1.54	7	2.69
	TYPE 1 DIABETES MELLITUS	8	12.31	16	24.63	20	30.78	8	12.31	52	20.01
	ULCERATIVE COLITIS	4	6.16	1	1.54	2	3.08	2	3.08	9	3.46

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n = number of subjects in a given category
Per 100000 = n/Number of subjects with available results*100000
Neuroinflammatory/Ophthalmic autoimmune diseases included: Multiple Sclerosis, Transverse Myelitis, Optic Neuritis, Guillain Barré Syndrome, Acute disseminated encephalomyelitis, Autoimmune Peripheral neuropathies & plexopathies
and Autoimmune Uveitis. Note: that 1 AD was classified as Other AD
Follow-up period 1 year for all the cohorts
One subject has simultaneously diabetes and thyroid diseases

Table 632 Classification of thyroiditis cases - All cases (Total cohort)

	EXP N = 26		NNEXP N = 18		MALE N = 2		HIST N = 3		Total N = 49	
Categories	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
DOWN SYNDROME	1	3.8	0	-	0	-	1	33.3	2	4.1
AI HYPOTHYROIDITIS	22	84.6	15	83.3	2	100	1	33.3	40	81.6
THYROTOXICOSIS	3	11.5	3	16.7	0	-	1	33.3	7	14.3

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n/% = number / percentage of subjects in a given category

Table 633 HES linkage - All cases (Total cohort)

		EXP N = 26		NNEXP N = 18		MALE N = 2		HIST N = 3		Total N = 49	
DIS_	**Categories**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
AI HYPOTHYROIDITIS	No	10	45.5	8	53.3	1	50.0	1	100	20	50.0
	Yes	12	54.5	7	46.7	1	50.0	0	0.0	20	50.0
DOWN SYNDROME	No	0	0.0	-	-	-	-	1	100	1	50.0
	Yes	1	100	-	-	-	-	0	0.0	1	50.0
THYROTOXICOSIS	No	0	0.0	2	66.7	-	-	0	0.0	2	28.6
	Yes	3	100	1	33.3	-	-	1	100	5	71.4
Overall total	No	10	38.5	10	55.6	1	50.0	2	66.7	23	46.9
	Yes	16	61.5	8	44.4	1	50.0	1	33.3	26	53.1

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n/% = number / percentage of subjects in a given category

Table 634 Incidence rate of Hypotyroiditis in Female Cohorts - Main Analysis - All cases (Total cohort)

				95% CI	
Cohort	**Number of cases**	**Person-time (in years)**	**Incidence Rate (per 100,000 PY)**	**LL**	**UL**
Exposed Female	22	64705	34.001	21.308	51.477
Non-Exposed Female	15	64841	23.133	12.948	38.155

LL, UL = 95% Lower and Upper exact confidence limits

Table 635 Incidence rate ratios of Hypothyroiditis in Female Cohorts - Main Analysis - All cases (Total cohort)

	IRR Calculation					
		95%CI of RR			95%CI of RR	
Autoimmune diseases	**Crude Incidence Rate Ratio**	**LL**	**UL**	**Adjusted Incidence Rate Ratio**	**LL**	**UL**
Hypothyroiditis	1.469	0.762	2.831	1.468	0.761	2.829

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted by age group: age group [9-17] and [18-25]

Table 636 Incidence rate difference of Hypothyroiditis diseases in Female Cohorts - Main Analysis - All cases (Total cohort)

Characteristics	IRD Calculation
IRD(exp-unexp OR conc-hist)	10.867

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 637 Incidence rate ratios of Hypothyroiditis in Female Cohorts (covariates adjusted) - Main Analysis - All cases (Total cohort)

	IRR Calculation		
		95%CI of RR	
Autoimmune diseases	Adjusted Incidence Rate Ratio	LL	UL
Hypothyroiditis	1.368	0.707	2.647

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted for other covariates: age group [9-17] and [18-25], healthcare resources utilization in quartile, regions (North England, South England, Midlands & Ireland Scotland Wales), any vaccines during the year prior to the reference date

Table 638 Incidence rate of Hypotyroiditis in Male Cohorts - Main Analysis - All cases (Total cohort)

				95% CI	
Cohort	Number of cases	Person-time (in years)	Incidence Rate (per 100,000 PY)	LL	UL
Concurrent Male	2	64859	3.084	0.373	11.139
Historical Male	1	64868	1.542	0.039	8.589

LL, UL = 95% Lower and Upper exact confidence limits

Table 639 Incidence rate ratios of Hypothyroiditis in Male Cohorts - Main Analysis - All cases (Total cohort)

	IRR Calculation					
		95%CI of RR			95%CI of RR	
Autoimmune diseases	Crude Incidence Rate Ratio	LL	UL	Adjusted Incidence Rate Ratio	LL	UL
Hypothyroiditis	2.000	0.181	22.055	1.899	0.172	20.939

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted by age group: age group [9-17] and [18-25]

Table 640 Incidence rate difference of Hypothyroiditis diseases in Male Cohorts - Main Analysis - All cases (Total cohort)

Characteristics	IRD Calculation
IRD(exp-unexp OR conc-hist)	1.542

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 641 Incidence rate ratios of Hypothyroiditis in Male Cohorts (covariates adjusted) - Main Analysis - All cases (Total cohort)

	IRR Calculation		
		95%CI of RR	
Autoimmune diseases	Adjusted Incidence Rate Ratio	LL	UL
Hypothyroiditis	1.708	0.154	18.948

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted for other covariates: age group [9-17] and [18-25], healthcare resources utilization in quartile, regions (North England, South England, Midlands & Ireland Scotland Wales), any vaccines during the year prior to the reference date

Table 642 Frequency of autoimmune diseases during the one year follow-up period by exposed/non-exposed status - Main Analysis - Confirmed cases (N=AD) (Total cohort)

		EXP N = 64964		NNEXP N = 64973		MALE N = 64974		HIST N = 64965		Total N = 259876	
Characteristics	**Categories**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**	**n**	**Per 100000**
Individual autoimmune diseases within 1 year follow-up period	AI HYPOTHYROIDITIS	12	18.47	4	6.16	0	0.00	0	0.00	16	6.16
	CROHN DISEASES	6	9.24	5	7.70	4	6.16	1	1.54	16	6.16
	DOWN SYNDROME	1	1.54	0	0.00	0	0.00	0	0.00	1	0.38
	GUILLAIN-BARRÉ SYNDROME	0	0.00	0	0.00	1	1.54	1	1.54	2	0.77
	IDIOPATHIC THROMBOCYTOPENIC PURPURA (ITP)	1	1.54	1	1.54	0	0.00	2	3.08	4	1.54
	INFLAMMATORY BOWEL	0	0.00	0	0.00	0	0.00	1	1.54	1	0.38
	JUVENILE RHEUMATOID ARTHRITIS (JRA)	1	1.54	0	0.00	0	0.00	1	1.54	2	0.77
	MULTIPLE SCLEROSIS	0	0.00	1	1.54	0	0.00	0	0.00	1	0.38
	OTHER AUTOIMMUNE DISEASES	1	1.54	0	0.00	0	0.00	0	0.00	1	0.38
	PSORIATIC ARTHRITIS	1	1.54	1	1.54	0	0.00	0	0.00	2	0.77
	RHEUMATOID ARTHRITIS (RA)	1	1.54	0	0.00	0	0.00	0	0.00	1	0.38
	THYROTOXICOSIS	2	3.08	0	0.00	0	0.00	0	0.00	2	0.77
	TYPE 1 DIABETES MELLITUS	8	12.31	16	24.63	20	30.78	8	12.31	52	20.01
	ULCERATIVE COLITIS	4	6.16	0	0.00	2	3.08	2	3.08	8	3.08

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n = number of subjects in a given category
Per 100000 = n/Number of subjects with available results*100000
Neuroinflammatory/Ophthalmic autoimmune diseases included: Multiple Sclerosis, Transverse Myelitis, Optic Neuritis, Guillain Barré Syndrome, Acute disseminated encephalomyelitis, Autoimmune Peripheral neuropathies & plexopathies
and Autoimmune Uveitis. Note: that 1 AD was classified as Other AD
Follow-up period 1 year for all the cohorts
One subject has simultaneously diabetes and thyroid diseases

Table 643 Classification of thyroiditis cases - Confirmed cases (Total cohort)

	EXP N = 15		NNEXP N = 4		Total N = 19	
Categories	**n**	**%**	**n**	**%**	**n**	**%**
Down syndrome	1	6.7	0	-	1	5.3
hypothyroiditis	12	80.0	4	100	16	84.2
thyrotoxicosis	2	13.3	0	-	2	10.5

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n = number of subjects in a given category
% = n / Number of subjects with available results x 100

Table 644 HES linkage - All cases (Total cohort)

		EXP N = 15		NNEXP N = 4		Total N = 19	
DIS_	**Categories**	**n**	**%**	**n**	**%**	**n**	**%**
AI HYPOTHYROIDITIS	No	7	58.3	1	25.0	8	50.0
	Yes	5	41.7	3	75.0	8	50.0
DOWN SYNDROME	No	0	0.0	-	-	0	0.0
	Yes	1	100	-	-	1	100
THYROTOXICOSIS	No	0	0.0	-	-	0	0.0
	Yes	2	100	-	-	2	100
Overall total	No	7	46.7	1	25.0	8	42.1
	Yes	8	53.3	3	75.0	11	57.9

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
N = number of subjects
n = number of subjects in a given category
% = n / Number of subjects with available results x 100

Table 645 Incidence rate of Hypothyroiditis in Female Cohorts - Main Analysis - Confirmed cases (Total cohort)

				95% CI	
Cohort	**Number of cases**	**Person-time (in years)**	**Incidence Rate (per 100,000 PY)**	**LL**	**UL**
Exposed Female	12	64705	18.546	9.583	32.396
Non-Exposed Female	4	64841	6.169	1.681	15.795

LL, UL = 95% Lower and Upper exact confidence limits

Table 646 Incidence rate ratios of Hypothyroiditis in Female Cohorts - Main Analysis - Confirmed cases (Total cohort)

	IRR Calculation					
		95%CI of RR			95%CI of RR	
Autoimmune diseases	**Crude Incidence Rate Ratio**	**LL**	**UL**	**Adjusted Incidence Rate Ratio**	**LL**	**UL**
Hypothyroiditis	3.004	0.969	9.315	3.003	0.968	9.310

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted by age group: age group [9-17] and [18-25]

Table 647 Incidence rate difference of Hypothyroiditis diseases in Female Cohorts - Main Analysis - Confirmed cases (Total cohort)

Characteristics	**IRD Calculation**
IRD(exp-unexp OR conc-hist)	12.377

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
Incidence Rate Difference = (IRexposed - IRnon-exposed) for female cohorts OR (IRconcurrent - IRhistorical) for male cohorts

Table 648 Incidence rate ratios of Hypothyroiditis in Female Cohorts (covariates adjusted) - Main Analysis - Confirmed cases (Total cohort)

	IRR Calculation		
		95%CI of RR	
Autoimmune diseases	**Adjusted Incidence Rate Ratio**	**LL**	**UL**
Hypothyroiditis	2.835	0.909	8.840

EXP = Exposed Cohort
NNEXP = Non Exposed Historical Female Cohort
MALE = Non Exposed Concurrent Male Cohort
HIST = Non Exposed Historical Male Cohort
IRR adjusted for other covariates: age group [9-17] and [18-25], healthcare resources utilization in quartile, regions (North England, South England, Midlands & Ireland Scotland Wales), any vaccines during the year prior to the reference date

Annex 1 List of stand-alone documents

Number	Document reference number	Date	Title
1.	116239	17-MAR-2015	Annex 1: List of stand-alone documents
2.	116239	17-MAR-2015	Annex 2: Glossary of Terms
3.	116239	17-MAR-2015	Annex 3: Trademarks
4.	116239	17-MAR-2015	Annex 4: Changes in the conduct of the study
5.	116239	17-MAR-2015	Annex 5: Pallas Methodology Report
6.	116239	17-MAR-2015	Annex 6: Additional information
7.	116239	17-MAR-2015	Annex 7: Report sign-off

Annex 2 Glossary of Terms

Coded:	Information is associated with a subject number i.e. a code number. Coded information can only be linked back to the individual via a key code i.e. a listing of the research participant and their code. Within the pharmaceutical industry coding data is the usual mechanism used for protecting an individual's research data. The key code is kept secure, usually by the investigator, and GSK researchers cannot identify the research individual other than in exceptional and controlled circumstances.
Cohort study:	A form of epidemiology study where subjects in a study population are classified according to their exposure status and followed over time (prospective / retrospective) to ascertain the outcome(s) (disease).
Eligible:	Qualified for enrolment into the study based upon strict adherence to inclusion/exclusion criteria.
eTrack:	GSK's tracking tool for clinical/epidemiological trials.
Medcode	The Medcodes are the abbreviated terms which mean CPRD GOLD medical codes. Medcodes consisting of READ codes are used to enter medical diagnosis in the CPRD GOLD database.
Non-interventional (observational) Human Subject Research:	Studies where medicinal products, should they be administered, are prescribed in normal (routine) medical practice. No medical care or medical/scientific procedures as required in a research protocol are administered to participants except as part of routine medical care.

Post-Authorization Safety Study (PASS)	A pharmacoepidemiological study or a clinical trial carried out in accordance with the terms of the marketing authorisation, conducted with the aim of identifying or quantifying a safety hazard relating to an authorised medicinal product. This includes all GSK sponsored non-interventional studies and clinical trials conducted anywhere in the world that are in accordance with the terms of the European marketing authorisation and where the investigation of safety is the specific stated objective.
Self-control case-series (SCCS):	Statistical method for assessing the association between a transient exposure and an adverse event. The method was developed to study adverse reactions to vaccines. The method uses only cases; no controls are required as the cases act as their own controls. Each case's given observation time is divided into control and risk periods. Risk periods are defined during or after the exposure. The method estimates a relative incidence rate, that is, the incidence in risk periods relative to the incidence in control periods. Time-varying confounding factors such as age can be allowed for by dividing up the observation period further into age categories. An advantage of the method is that confounding factors that do not vary with time, such as genetics, location, socio-economic status are controlled for implicitly.
Study population:	Sample of population of interest.
Subject:	Term used throughout the protocol to denote an individual who has been contacted in order to participate or participates in the clinical/epidemiological study, or a person about whom some medical information have been recorded in a database.
Subject number:	A unique number identifying a subject, assigned to each subject consenting to participate in the study.

Annex 3 Trademarks

The following trademarks are used in the present report.

Note: In the body of the report (including the synopsis), the names of the vaccines/products and/or medications will be written without the superscript symbol ™ or ® and in italics.

Trademarks of the GlaxoSmithKline group of companies	**Generic description**
Cervarix	Bivalent human papillomavirus (types 16, 18) recombinant vaccine

Trademarks not owned by the GlaxoSmithKline group of companies	**Generic description**
Gardasil® (Merck & CO., Inc.)	Quadrivalent human papillomavirus (types 6, 11, 16, 18) recombinant vaccine

Annex 4 Changes in the conduct of the study

Not applicable.

Annex 5 Pallas Methodology Report

[redacted]

An observational cohort study to assess the risk of autoimmune diseases in adolescent and young adult women aged 9 to 25 years exposed to Cervarix® in the United Kingdom

EPI-HPV-040 VS UK (e-track 116239)

Methodology for subject profile and free text review from CPRD, and data entry in RDE

Version 2

Rotterdam, 15 September, 2014

[redacted], PhD
[redacted], MSc
[redacted], MSc

[redacted]

A study commissioned by GlaxoSmithKline Vaccines

2 Summary of CPRD profiles review and RDE entry. *Pallas 13 August 2014, version 2.*

Project team

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Internal medicine expert	
Neurology expert	
Ophthalmology expert	
Rheumatology expert	

Contents

1 Introduction

Cervarix is GlaxoSmithKline (GSK) Vaccines' bivalent recombinant vaccine against human papillomavirus (HPV, types 16 and 18). A pooled safety analysis of data from 57,580 adolescent and adult females aged 9 years and above, of whom 33,339 received at least one dose of HPV vaccine, showed the vaccine to be generally well tolerated in women of all ages.

To address a regulatory commitment made in 2009 to the United States Food and Drug Administration, GSK initiated an observational cohort study in the USA (e-track: 113522, EPI-HPV-015) to assess the risk of autoimmune diseases (AIDs) within 12 months following the administration of at least one dose of Cervarix (exposed) versus a non-Cervarix vaccinated cohort (unexposed). Because of the current low Cervarix uptake in the USA which is anticipated to stay at a low level over the next few years, GSK proposed an alternative epidemiological study using the Clinical Practice Research Datalink General Practitioner OnLine database (CPRD GOLD) in the UK to fulfil the post-marketing commitment. The UK has had sufficient Cervarix vaccination coverage to, in theory, enable data acquisition. A public immunisation programme targeting girls between 12 and 13 years of age including a catch-up programme for young women up to 18 years was undertaken during the academic year 2008/09. CPRD is the world's largest computerised database of linked anonymised longitudinal medical records from primary care.

Background incidence rates of AIDs in the UK and USA for male and female subjects that were derived from published literature are similar in magnitude between the two countries.

Pallas has been asked to review all subject profiles extracted from the CPRD. The subject profiles contain a medical chronological overview of each subject, including diagnoses, symptoms, laboratory tests, vaccinations, prescribed medication, etc. For some of these events so called 'free text' is available (e.g. hospital discharge report, letter from a specialist, administration, etc.). Pallas has been asked to collect relevant information from these subject profiles, to request relevant free text associated with certain events and to import the data into Remote Data Entry (RDE). This report complements the protocol and gives a summary of the methods used to review the subject profiles, to review the requested free texts and to import all relevant data in RDE.

In section 2.1-2.2 the subject profiles are described; in section 2.3 the decisions regarding the free text requests are presented and in section 3 the decisions that were made regarding the type of data that was extracted from the profiles and free text, and the rules used to enter the data in RDE are explained. In sections 4 and 5 the roles of the GSK safety physician and RTI physician and the roles of the external experts in determining the diagnosis of a new onset autoimmune disease (NOAD) are described. In section 6 some limitations of the study are listed.

2 Subject profile review

2.1 Number of subject profiles

Pallas received 1,053 subject profiles from GSK. These subject profiles were divided into 19 autoimmune disease groups based on algorithm requests performed by GSK:

- Ankylosing spondylitis (AS), n= 12
- Crohn's disease, n= 69
- Diabetes mellitus type I, n= 265
- Guillain-Barré syndrome (GBS), n= 8
- Autoimmune haemolytic anaemia, n= 1
- Autoimmune hepatitis, n= 3
- Inflammatory bowel disease (IBD), n= 237
- Idiopathic thrombocytopenic purpura (ITP), n= 30
- Juvenile rheumatoid arthritis (JRA), n= 30
- Multiple sclerosis (MS), n= 3
- Optic neuritis, n= 8
- Psoriatic arthritis, n= 2
- Rheumatoid arthritis (RA), n= 14
- Systemic lupus erythematosus (SLE), n= 14
- Autoimmune thyroiditis , n= 244
- Transverse myelitis (TM), n= 8
- Ulcerative colitis, n= 40
- Autoimmune uveitis, n= 62
- Other demyelinating diseases, n= 3

For each subject, these algorithms flagged a so called 'event' possibly belonging to one of the autoimmune disease groups. The date corresponding to this event is referred to as the 'event date'. Pallas reviewed these subject profiles and the corresponding free text to investigate wether the events flagged by the algorithms were indeed NOADs of interest to this study.

2.2 Review of subject profiles

Pallas reviewed all subject profiles. The following information was considered relevant:

- HPV vaccinations
- Pandemic flu vaccinations
- Other vaccinations
- Diagnosis of NOADs
- Date of first symptom of NOADs
- Date of diagnosis of NOADs
- Date of first abnormal (laboratory) test result related to NOADs (with the normal ranges of the test, if applicable)
- Medication prescribed for NOADs, including the start and end dates

During the subject profile review by Pallas, telephone conferences with GSK and RTI were scheduled to discuss complex subject profiles and to make decisions regarding the type of information that should be considered relevant. Minutes of these TCs are available through Pallas and GSK.

After review of the subject profiles by Pallas, requests for free text were sent to GSK. GSK requested these free texts from the CPRD.

2.3 Decisions for the request of free text from subject profiles

The following sections discuss the decisions that were made with regard to the request of free text from the subject profiles. In Section 2.3.1, the methods for data request from CPRD are explained, Section 2.3.2 gives an overview of the general decisions that were made regarding all profiles, and Sections 2.3.3-2.3.13 list the disease-specific rules for the request of free text (mostly regarding the request of lab results).

2.3.1 Methods regarding the request of free text

There were two sources of data in the subject profiles, data from CPRD and data from 'Hospital Episodes Statistics' (HES). Free text could be requested for CPRD data with a non-0 code in the 'textid' column. No free text could be requested for HES data. After review of the first batch of free text, another batch of free text requests was sent to CPRD. This second batch included subjects for whom some questions remained and potentially relevant additional free text was available.

No free text was requested for a subject profile if:

- The autoimmune disease found by the algorithm was already diagnosed before the start of the study period, i.e. there was no *new onset* autoimmune disease.
- The diagnosis found by the algorithm was clearly not autoimmune, i.e. there was no new onset *autoimmune* disease.

These subjects are considered as non-cases (see section 2.4).

The relevant symptoms and laboratory tests for NOAD diagnosis were based on textbooks (and consultation of the GSK safety physician and RTI physician) and not on standardized lists of operational criteria provided by GSK. See the reference list for a list of frequently used textbooks.

2.3.2 General

- Free text of the diagnosis flagged by the algorithm (i.e. the event) in the subject profile was always requested. Note: this 'event date' is not necessarily the date of diagnosis.
- If multiple diagnostic codes for NOADs were reported in the profile, associated free texts for all diseases were requested.
- In general, free text for symptoms up to one year prior to the diagnosis was requested. The reason for this is that onset of most autoimmune diseases are (sub)acute. The one year threshold was crossed if very disease-specific symptoms were found, such as arthritis or skin manifestations for SLE. Free text for letters from specialists, 'seen in xxx clinic' etc. was requested when the subject profile was not deemed sufficiently clear (e.g. uncertainty about laboratory results, medicine use, symptoms or (date of) diagnosis).
- In case of any doubt, the free text was requested.

Laboratory tests

- Free texts for relevant laboratory tests were requested when the data in the 'lab_results' column was not sufficient, i.e. when the data were incomplete (e.g. no units of measurement) or when 'Data not entered' was written in this column. In some cases, the free text was also requested when no normal range of the laboratory test was available.
- The free texts of several (repeated or different) laboratory tests were requested when it was not clear which one (if any) had abnormal results.
- The date of the first laboratory test with abnormal results might be before, on or soon after the date of diagnosis. Laboratory tests conducted later after the diagnosis were not considered relevant, as medications given soon after the diagnosis might influence the lab result.
- Free text was not requested for laboratory tests related to a differential diagnosis other than the NOAD of interest.

Medication:

- In general, free text for medication was not requested.

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2.3.3 Ankylosing spondylitis (AS)

- The following laboratory tests were considered to be relevant for AS:
  - Human leukocyte antigen (HLA) B27 screening test
  - X-rays
  - If the tests listed above are not present, C-reactive protein can be used

2.3.4 Diabetes mellitus type I

- The following laboratory tests were considered to be relevant for diabetes mellitus type 1:
  - Glucose tests
  - HbA1c tests
- Pallas did not request free text for diabetes-related laboratory tests if there was already a result in the lab_results column (e.g. abnormal).
- For subjects with an abnormal blood glucose test, free text was not requested for other diabetes-tests done on the same day and for which the results are not known ("Data not entered").
- In several profiles of subjects with a clear diagnosis of type 1 diabetes and with insulin prescriptions throughout the profile, a type 2 diabetes diagnosis was also reported once or twice. There were no prescriptions of medicines related to diabetes mellitus type 2. These subjects were considered to have diabetes mellitus type 1 and not diabetes mellitus type 2.

2.3.5 Autoimmune hepatitis

- The following laboratory tests were considered to be relevant:
  - Liver biopsy
  - Antinuclear antibody (ANA)
  - Anti-smooth muscle antibody (SMA)
  - Liver/kidney microsomal antibody (LKM-1, LKM-2, LKM-3, anti-LC1)
  - Anti-soluble liver antigen (SLA/LP)
  - Anti-mitochondrial antibody (AMA)
  - Increased IgG level or gammaglobulin
  - Atypical pANCA should be requested when all other antibodies are negative (ANCA = antineutrophil cytoplasmic antibodies)
- "Bilirubin and urobilin in urine" were considered relevant as first abnormal lab test if none of the above mentioned tests were found.

2.3.6 Inflammatory bowel disease, Crohn's disease and ulcerative colitis

- The only test considered a relevant test for IBD was a colonoscopy or endoscopy. Free text for colonoscopies/endoscopies with unknown results were requested. Other laboratory tests were not considered to be relevant.
- If in subjects with "non-infectious gastroenteritis and colitis" or "irritable bowel syndrome" an endoscopy/colonoscopy had been performed or the subject was seen in a specialized clinic for that process, the free text was requested.

2.3.7 Idiopathic thrombocytopenic purpura (ITP)

- The only lab test that was considered to be relevant for ITP was the platelet count.

2.3.8 Juvenile rheumatoid arthritis (JRA)

- There are no JRA-specific laboratory tests. The following general tests were considered to be relevant:
  - Rheumatoid factor
  - ESR (high)
  - C-reactive protein (high)
  - Neutrophilia
  - Thrombocytosis
  - ANA-positive
- Psoriatic arthritis and juvenile arthritis are considered NOADs in subjects already diagnosed with psoriasis.

2.3.9 Optic neuritis

- The following laboratory tests were considered relevant for optic neuritis:
  - Magnetic resonance imaging (MRI)
  - Visual evoked response

2.3.10 Rheumatoid arthritis (RA)

- The following laboratory tests were considered relevant for rheumatoid arthritis:
  - Rheumatoid factor
  - Rheumatoid arthritis particle agglutination test
  - Anti-cyclic citrullinated peptide antibody level
  - If the tests listed above are not present, erythrocyte sedimentation rate (ESR) or C-reactive protein were used.

2.3.11 Systemic lupus erythematosus (SLE)

- The following laboratory tests were considered to be the most relevant for SLE:
  - tests for ANA,
  - anti-phospholipid antibodies,
  - dsDNA,
  - anti-Smith antibodies
  - Complement 3 and 4 (low)
  - Computed tomography (CT) or MRI scans
- Full blood count is unspecific but the results could support the diagnosis of SLE and therefore this lab test was included when the disease-specific lab tests were unavailable.

2.3.12 Autoimmune thyroiditis

- The following laboratory tests were considered to be relevant for hypothyroidism (Hashimoto's thyroiditis, atrophic thyroiditis, postpartum thyroiditis) and hyperthyroidism (Graves' disease):
  - Thyroid-peroxidase antibody,
  - Antibodies to thyroid stimulating hormone (TSH) receptor (Thyroid stimulating immunoglobulins, Thyroid growth immunoglobulins, Thyrotrophin Binding-Inhibiting Immunoglobulins),
  - Thyroglobulin,
  - Other thyroid auto-antibodies
  - TSH = high (hypothyroidism) or low (hyperthyroidism)
  - T4 level = typically low (hypothyroidism) or high (hyperthyroidism) (it was noted that hypothyroidism can start with high T4 levels before proceeding to low T4 levels and that this is suggestive of autoimmune disease)
  - T3 level = high (hyperthyroidism)
  - Radioiodine uptake test

2.3.13 Autoimmune uveitis

- There are no uveitis-specific laboratory tests. The following general tests were considered to be relevant:
  - Eye-related tests
  - Antibody tests or tests indicating an underlying AID (e.g. rheumatoid factor). There are no specific tests other than the ones for the associated autoimmune diseases.
  - The diagnosis is made by split lamp examination but that is not specific of the cause.
- For cases with hyphaema as event, without any further indication of uveitis, but also no other event implicating that it was not uveitis (e.g. injury: traumatic injury is the most common cause and neovascularization and tumours can also cause hyphaema), free text was requested, since hyphaema can be caused by uveitis.

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2.4 No NOAD

During subject profile review 420 subjects were not considered to have a NOAD. For these subjects no free text was requested. After free text review another 167 subjects were not considered to have a NOAD. For all these subjects 'no' was ticked in the Pallas column in RDE for the question "did the subject report any NOADs during the follow-up period?". A complete overview of the number of excluded subjects per group of autoimmune diseases according to the algorithm can be found in the table below.

NOAD according to algorithm	Number of subjects with no NOAD
Ankylosing spondylitis	9
Diabetes mellitus type I	176
Guillain-Barré syndrome	5
Autoimmune haemolytic anaemia	0
Autoimmune hepatitis	0
IBD, Crohn's disease, ulcerative colitis	Crohn: 18 IBD: 213 Ulcerative colitis: 16
Idiopathic thrombocytopenic purpura	22
Juvenile rheumatoid arthritis	16
Multiple sclerosis	0
Optic neuritis	0
Psoriatic arthritis	0
Rheumatoid arthritis	3
Systemic lupus erythematosus	8
Autoimmune thyroiditis	57
Transverse myelitis	7
Autoimmune uveitis	34
Other	3

In some subjects, two events were flagged, but only one was a NOAD according to Pallas. These are not included in the above table. For these subjects, data entry was done for the "true" NOAD, and "no 2nd NOAD" was reported in the comment box of the other NOAD page in RDE.

2.4.1 General remarks

- Autoimmune diseases that were not listed in the protocol were not considered in the profile review (e.g. Wegener's granulomatosis and juvenile dermatomyositis).
- If the autoimmune disease found by the algorithm was already diagnosed before the start of the study period this subject was not considered to have a NOAD, i.e. there was no *new onset* autoimmune disease.
- In some profiles, the flagged 'event' was not an autoimmune disease. If in addition there was no mention of an autoimmune disease (listed in the protocol) and abnormal lab test or medication suggesting treatment for an autoimmune disease in the subject profile, the subject was considered not to have a new onset *autoimmune* disease. In case of doubt, the free text was always requested.
- In some profiles, a (possible) autoimmune disease was mentioned, yet it was concluded that the subject did not have a NOAD. These cases are explained below.

2.4.2 Diabetes mellitus type I

- Some subjects were noted in the CPRD database to be admitted to the hospital because of a serious event (e.g. motor cycle accident or cancer with several HES diagnoses related to that). Besides these HES diagnoses, a diagnosis of diabetes mellitus (not specified which type) was stated once in the profile. After that, no further diabetes diagnosis was made, nor was insulin prescribed. We concluded that these subjects did not have type 1 diabetes mellitus.

2.4.3 SLE

- Some subjects in the SLE profiles file were found to have antiphospholipid syndrome (APS), without mention of SLE in the subject profile. Pallas requested free text for these cases. If SLE was not mentioned in the free text, these subjects were considered to have no NOAD.

2.4.4 Autoimmune thyroiditis

- Subjects with hypopituitarism prior to hypothyroidism were not considered to have a NOAD.

2.4.5 Uveitis

- A subject with a diagnosis of uveitis within the study period, but with a diagnosis of juvenile rheumatoid arthritis or psoriatic arthritis before the reference date, was considered no NOAD, as uveitis can be a manifestation of these diseases. Note: this was not decided when psoriasis or diabetes mellitus type 1 was already present before the reference date. In these instances the uveitis diagnosis was considered as a NOAD.

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3 Data entry in RDE

In this section, all decisions that were made during data entry are presented. These decisions regard both the type of data that was extracted from the profiles and free text, and data entry in RDE. For each subject there are eight pages in RDE (one on general information, two on vaccination, and five on the presence of NOADs and drug prescription for the NOAD), see the workbook in Appendix II. The general information page was filled in with data extracted directly from CPRD. The other pages contained a column (hereafter called the 'Pallas column') in which Pallas could enter information to complete or correct the information recorded in the so-called 'CPRD column'. First, the general rules that were applied to fill in the Pallas column on multiple RDE pages are stated (section 3.1.1). All following paragraphs are divided according to the different autoimmune diseases. For each disease, the specific rules for data extraction and data entry are described.

3.1 General rules for filling in the Pallas column

The following general rules were used to fill in the Pallas column in RDE:

1. If information was reported in the CPRD column and the same information was found in the subject profile/free text, the Pallas column was left blank.
2. If information was reported in the CPRD column but conflicting information was found in the subject profile/free text, the Pallas column was completed with the new information.
3. If the CPRD column was blank but information was found in the subject profile/free text, the Pallas column was completed with the new information.

Any exceptions and additions to these rules are described below by page in RDE.

3.1.1 General information page

- A subject was considered lost to follow-up if the last date mentioned in the profile was before the end date of the study period. The last date mentioned in the subject profile was used as the "date of lost to follow-up".

3.1.2 HPV Cervarix vaccination page

- Sometimes the second or third HPV dose was selected as the reference date by the CPRD algorithm (while this should be the first dose). This happened when the first HPV dose was not reported in the profile. The algorithm automatically takes the earliest reported HPV dose in the profile (which thus is not necessarily always the first dose). It was decided that there is no need to adjust the reference dates or to exclude these subjects as the algorithm used in CPRD systematically identified the first reported dose of HPV-vaccine.

3.1.3 Other vaccination page

- Vaccines were entered in RDE from one year before the reference date until 30 months after the reference date. Pallas used the comments section of the vaccination page when more than three vaccines other than HPV were administered to one subject. Note that this deviates from the sentence on the vaccination page in RDE, which states that these data should be reported until the end of follow-up.

3.1.4 NOAD page

- If a subject did not have a NOAD, the question "did the subject report any NOAD/s during the follow-up period?" was answered with "no". The rest of the pages were left empty.

3.1.5 NOAD 1, NOAD 2 pages

- "Origin of data": this field concerns the origin of the *diagnosis*. If the diagnosis in the subject profile was listed both in CPRD and HES (even if not on the same date), "CPRD and HES" was selected.
- "Name of NOAD": this field was never completed by Pallas.
- "Category of NOAD": the Pallas column for this field was always completed by Pallas, also when this was in complete agreement with the information reported in the CPRD column. Note: this is an exception to general rule 1 (see section 3.1).
- "Date of 1st symptom of NOAD"/ "Date of first abnormal lab result related to NOAD":
    - If there was no 1st symptom or no abnormal lab test, this field was left blank.
    - If there was a 1st symptom or abnormal lab test, this field was completed. The following rules were applied:
        - If there was no free text belonging to the first symptom, the event date of the first symptom was used as date of first symptom.
        - The table below shows the rules that were applied for different time indications for the symptoms found in the free text.

Time indication in free text	Decision completion in RDE
Last 3-4 weeks	Event date - 3.5 weeks
Last 1-2 months	Event date - 1.5 months
x days/weeks/months/years earlier	Event date - x days/weeks/ months/years
About a month	Event date - 1 month
Since August	August 15th
Since summer	August 6th
Last week	Event date - 1 week
Last month	Event date - 1 month
Last year	1st of July previous year
Over the past year	Event date - 1 year
This month	1st of the month of the free text
Missed period for 2 months	Event date - 2 months
Few/several/couple of days	Event date - 3 days
Few/several/couple of weeks	Event date - 2 weeks
…since age 11	The birth year is known from CPRD (e.g. 1992), however the birth month is not, therefore it is assumed the birth date is 30JUN of that year (e.g. 30JUN1992). Subject is aged X years for one full year (e.g. aged12 from 30JUN2004 up to and including 29JUN2005). We assumed the symptom started in the middle of that year (i.e. 31DEC2004).
Few/several/couple of months	Event date
Few/several/couple of years	Event date
Last year or 2	Event date
For some time	Event date
For a long time	Event date
Occasionally	Event date
"ongoing problem"	Event date
Longstanding	Event date
Recent(ly)	Event date
No (useful) time indication (e.g. irregular menstrual cycle/weight loss/tired all the time, without further mention of how long this symptom has been present)	Event date

    - For some subjects the symptoms started before the reference date. This will be taken into account during data analyses by GSK.

- Rules for the confirmation of "Date of 1st symptom":
  - If the date was entered in RDE -> confirmed.
  - If there was no date of first symptom -> not confirmed.
  - For one subject an exception was made (subject number 3839384) for which Pallas and the experts are not completely sure whether the symptom is indeed related to the NOAD.
- "Date of diagnosis":
  - A date prior to the diagnosis in the subject profile on which comments such as "Looks like diabetes type 1", "likely rheumatoid arthritis", "?SLE" were reported in the free text was not considered as the date of diagnosis (as this is a differential diagnosis).
  - Every event that occurred within the study period up to and including the "date of end of study period" listed on the general information page was included in RDE.
- Rules for the confirmation of "Date of diagnosis":
  - If the date was entered in RDE -> confirmed.
  - If there was doubt about the accuracy of the date of diagnosis -> not confirmed.
- Rules for the confirmation of "Final classification of NOAD":
  - If the diagnosis was mentioned in the profile/free text and there is evidence that it is autoimmune -> confirmed.
  - If there existed some doubt about the diagnosis or there was no indication that it is autoimmune (the latter is only applicable to uveitis and thyroiditis) -> not confirmed.
- "Need of expert review" was ticked:
  - When the GSK and RTI physicians had doubts about the subject and deemed expert review necessary.
  - When the "final classification" was not confirmed (except for autoimmune thyroiditis and uveitis, see section 3.2.6 and 3.2.7).
  - For 10% randomly chosen subjects per NOAD (out of those that were not already sent to the experts). For these subjects, data were only entered in RDE when the expert's opinion differed from that in the Pallas column.
- If there were 2 NOADs according to CPRD but only one according to Pallas, Pallas filled in "No 2nd NOAD" in the comment box of the page for the NOAD that was completed by CPRD but which was deemed not correct after profile/free text review.
- Ideally, normal ranges of lab tests provided in the CPRD-data were used (as calibrations might differ). When these were not provided, textbooks on autoimmune disease or laboratory tests were consulted.

3.1.6 Medication NOAD 1, NOAD 2 pages

- Relevant disease-specific medication was reported up to one year after the diagnosis.
- All medications related to the NOAD of interest were reported on the medication page.
- "Chronic use" of medication was ticked when there was an indication that the medicine was used for more than one month or was prescribed at least twice within 6 consecutive months. This also included two prescriptions within a short period (e.g. one week). No operational definition of chronic use of medication was found in the literature.
- For chronically used medicines, no end date was reported, only a start date. "Not available" was never ticked for the end date.
- In case of no chronic use, generally no information on the end date was available, therefore "not available" was ticked for almost all non-chronically used medicines. Only if the free text mentioned prescription duration or that a certain prescription had been stopped, this could be entered in RDE accordingly.
- GSK provided a list of subjects for which the number of prescription days of some prescribed medications (but not all) was available. Pallas searched in this list for an end date of the medicines reported in RDE that were not already defined as chronic. Unfortunately, these disease-specific medications relevant for this project were never reported in this list.

- If medication for the NOAD of interest was prescribed before the date of diagnosis, the prescription date was considered to be the date of first therapy (i.e. disease-specific medication prior to the diagnosis was reported in RDE).

3.2 Disease-specific decisions

3.2.1 Diabetes mellitus type 1

- "Insulin" was reported in the medication section of RDE, the different types of insulin were not reported separately.
- For several subjects, insulin needles were prescribed soon after the diagnosis, while insulin prescription was some weeks/months after that. Free text was requested for these subjects, but gave no further insight. If it was clear from the profile that it concerned insulin needles, this date was used as start date of insulin use. However, if only needles were reported, this was not used as these could also refer to needles used to check blood glucose.
- A blood glucose test of ≥7mmol/L was considered as abnormal lab test. A blood glucose value between 6 mmol/L and 7 mmol/L, which is indicative of hyperglycemia, was not considered as an abnormal lab test for the purpose of diabetes mellitus type 1.
- HbA1c was used as first abnormal lab test if ≥6.5%.

3.2.2 Autoimmune Hepatitis

- If other causes of hepatitis disease were ruled out and a subject presented with a compatible clinical picture, a diagnosis of autoimmune hepatitis may be made. A liver biopsy was required, however, for a case of autoimmune hepatitis to be classified as confirmed.

3.2.3 IBD/Crohn's disease/ulcerative colitis

- If a colonoscopy/endoscopy was performed on the day of the diagnosis, but no results were reported, it was assumed that the results were abnormal. We also assumed this when the colonoscopy/endoscopy was performed within 3 weeks before the diagnosis. In these cases, it might have taken a while before the results of the biopsy were available for diagnosis.
- Erythema nodosum was considered a symptom of Crohn's disease. It is not specific of Crohn's disease, but if there is no other disease in the profile/free text that could be related to it, then this was used as the first symptom.
- The following medication was considered relevant and were reported in RDE:
    - Azathioprine, 6-mercaptopurine, methotrexate
    - Budesonide
    - Mesalazine, sulfasalazine, olsalazine and balsalazide
    - Prednisolone
    - Methotrexate (+folic acid)
    - Topical 5-aminosalicylic acid (5-ASA)
    - Topical beclomethasone dipropionate
    - Cyclosporine
    - Infliximab, adalimumab, certolizumab pegol, natalizumab
    - Antibiotics such as ciprofloxacin, metronidazole (used for both diseases but evidence of clear benefit exists only for Crohns's disease)
- Antibiotics prescribed before the date of diagnosis were not reported in RDE.
- Antibiotics prescribed after the date of diagnosis on the same day that the subject had e.g. a sore throat, an upper respiratory tract infection, etc. were not reported in RDE.
- The more general antibiotics (e.g. amoxicillin, chloramphenicol, trimethoprim) prescribed after the diagnosis, without any clue that it was prescribed for an infection/sore throat/etc., were reported in RDE.

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3.2.4 JRA

- Subjects with a diagnosis of Still's disease in the profile were classified as JRA if there was no clinical information suggesting acute disease.

3.2.5 Optic neuritis

- The final classification by Pallas of optic neuritis as 'confirmed' did *not* depend on the presence or absence of any autoantibodies. All these cases needed expert review.
- Antibiotics given after a diagnosis of optic neuritis were not reported in RDE.

3.2.6 Autoimmune thyroiditis

- Many subjects were diagnosed with "hypothyroidism" or "hyperthyroidism" without indication of autoimmune disease (i.e. "Hashimoto's disease" or "Graves' disease", etc).
    - If antibodies were found (or there was another indication that the disease is autoimmune), this was entered as a NOAD.
    - If antibodies were within the normal range, the disease was marked as a "not confirmed" NOAD. This is because several tests can be performed, another type of test might have been positive.
    - If there were no test results for antibodies, the "final classification of NOAD" was marked as "not confirmed". In some subjects an abnormal lab test was followed by a normal lab test and then another abnormal lab test. In these subjects the first abnormal lab test was used.
- When a subclinical hypothyroidism diagnosis was made (sometimes but not always followed by a hypothyroidism diagnosis), the subclinical diagnosis was used as date of diagnosis.
- "Underactive thyroid" or "thyroid not at level" reported before the diagnosis was used as date of diagnosis, as these terms can be seen as a synonym of thyroiditis.

3.2.7 Autoimmune uveitis

- Many subjects were diagnosed with uveitis without indication of autoimmune disease (e.g. psoriatic arthritis or rheumatic arthritis):
    - If antibodies were found (or there was another indication that the disease is autoimmune), this was entered as a NOAD.
    - If antibodies were within the normal range, the disease was marked as a "not confirmed" NOAD. This is because several tests can be performed, another type of test might have been positive.
    - If there were no test results for antibodies, the "final classification of NOAD" was marked as "not confirmed". This is because GPs can differ in the degree of information they write down, and therefore it can never be concluded from this that it was not an autoimmune disease.
- Conjunctivitis or episcleritis before the diagnosis of uveitis was not used as the first symptom in the Pallas column. Medication associated with these conditions was also not reported in the medication page in RDE.

4 RTI and GSK physician review

The RTI and GSK physicians reviewed all subjects for which Pallas had some doubts.

- Review of subjects was assigned by disease, so one disease was reviewed by either the RTI or GSK physician. In case one of them had doubts, these subjects were discussed in a telephone conference with Pallas, GSK and both physicians.
- When Pallas finished data entry for one NOAD, all subjects for which Pallas had doubts were sent to one of the physicians for review.
- If the RTI and GSK physicians had doubts about a subject, this subject was reviewed by the experts.

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5 External experts review

A total of five experts in the fields of rheumatology, ophthalmology, internal medicine and neurology reviewed 104 profiles and free texts. The subjects for which Pallas, the GSK safety physician and the RTI physician still had doubts were referred for expert review, as well as a 10% random sample of the remaining profiles per NOAD. The random sample was drawn using a random number generator in SPSS.

The subjects were divided amongst the experts:

- Rheumatologist: juvenile rheumatoid arthritis, psoriatic arthritis, rheumatoid arthritis, ankylosing spondylitis, n=18.
- Ophthalmologist: optic neuritis, uveitis, n=17.
- Internal medicine experts: diabetes mellitus type I, autoimmune hepatitis, inflammatory bowel syndrome, Crohn's disease, ulcerative colitis, idiopathic thrombocytopenic purpura, systemic lupus erythematosus, autoimmune thyroiditis, n=63.
- Neurologist: Guillain-Barré syndrome, multiple sclerosis, transverse myelitis, acute disseminated encephalomyelitis, other demyelinating diseases, n=6.

An Excel file containing a list of subject numbers, gender, year of birth and the outcomes according to Pallas or Pallas and the GSK Safety Physician/ RTI physician as entered in the Pallas column on the NOAD 1 and/or 2 page(s) was sent to each expert, together with the corresponding profiles and free texts for each of these subjects. Any information on HPV vaccination was removed from the files, therefore the experts were blinded with regard to HPV vaccine exposure. The experts recorded the results of their review in the Excel file and sent it back to Pallas.

Any discrepancies were resolved in a telephone conference with each expert, Pallas and the GSK safety physician and/or the RTI physician. Four of these telephone conferences were held, one for each of the four specialties.

The results from the experts were recorded in the 'Expert 1' column in RDE. The final classification as agreed upon during the telephone conference was recorded in the 'Final classification' column in RDE. The expert and final classification columns in RDE were completed for all subjects for which expert review was deemed necessary and the subjects from the 10% random check for which the final classification was different than that recorded in the Pallas column. The expert and final classification columns were not completed for the subjects from the 10% random check for which there were no discrepenacies between the final classification agreed upon during the telephone conference and the Pallas column.

5.1 Random 10% check

For the random check, four subjects were checked by the rheumatologist, three subjects were checked by the ophthalmologist, four subjects were checked by the neurologist and 39 subjects were checked by the internal medicine experts.

5.1.1 Rheumatology

There was one discrepancy between the findings in the Pallas column and the final ascertainment decided upon with the rheumatologist. For one subject with ankylosing spondylitis, no abnormal laboratory results were entered in the Pallas column, whereas the expert pointed out that there was a positive test for HLA-B27 five years after the diagnosis. Generally laboratory tests a long time after the diagnosis were not considered to be relevant, as medications given soon after the diagnosis might

influence the test results. This reason is not applicable to the test for HLA-B27, a gene that is linked to ankylosing spondylitis. Therefore an exception was made.

5.1.2 Opthalmology

The expert decided that for subjects with a uveitis diagnosis, conjunctivitis/episcleritis can be used as the first symptom, as misdiagnoses are very frequent. This was in contrast with what was previously decided by Pallas, GSK and RTI (see section 3.2.7). All subjects not reviewed by the experts were reviewed again by Pallas for the presence of conjunctivitis/episcleritis before the uveitis diagnosis and changes were made in the Pallas column accordingly. Note that this could also change the use of medications, as it was previously decided that medications used for conjunctivitis/episcleritis before the uveitis diagnosis should not be entered in RDE.

There were no other discrepancies.

5.1.3 Neurology

There were no discrepancies between the findings in the Pallas column and the final ascertainment decided upon with the expert for the subjects from the random 10% check.

5.1.4 Internal medicine

Diabetes

There was one discrepancy regarding type 1 diabetes between the findings in the Pallas column and the final ascertainment decided upon with the internal medicine expert. For this subject Pallas mistakenly reported a normal lab test. In the final ascertainment, no lab test was reported as no abnormal lab test was found for this patient.

IBD

The expert decided that for IBD subjects for whom the date of diagnosis precedes the date of the first abnormal lab test, the diagnosis date should be changed to the date of the first abnormal lab test, because the diagnosis is incomplete without an abnormal lab test. All subjects were reviewed again by Pallas on this point and for eight subjects Pallas changed the date of diagnosis accordingly (NB: one of these eight subjects was reviewed by Dr Ramos as part of the random sample, who agreed with the earlier diagnosis date, but Pallas changed this date too).

Additionally, for three IBD subjects without an abnormal lab test the final classification differed between Pallas and the final ascertainment decided upon with the expert. For these subjects Pallas confirmed the final classification of the NOAD, while the expert pointed out that the final classication should be changed to unconfirmed, because an abnormal lab test is necessary for confirmation of the diagnosis. Afterwards the following was decided between GSK, RTI and Pallas:

- Confirmation of IBD: an abnormal colonoscopy (or colonoscopy with unreported results followed by diagnosis) is necessary
- Confirmation of CD and UC: an abnormal colonoscopy (or colonoscopy with unreported results followed by diagnosis) is not necessary, but there should be at least one of the following: 1) a prescription of IBD-specific medication (see 3.2.3, a prescription of only antibiotics was not sufficient), 2) an HES-diagnosis of CD or UC, or 3) a specialist letter indicating diagnosis of CD or UC

Pallas reviewed all IBD, CD and UC subjects without an abnormal lab test (n=27) and applied the above rules accordingly (NB: confirmation of the diagnosis was changed to unconfirmed for one subject).

ITP

There was one discrepancy between data reported by Pallas and the final ascertainment regarding the abnormal lab test of one ITP subject. A slightly abnormal platelet count was entered in the Pallas column (137,000 /µL, normal range 140,000/µL-400,000/µL), whereas the expert chose a later platelet count that was much more abnormal (57,000/µL). The expert pointed out that he did not consider the lab test chosen by Pallas to be diagnostic for ITP; the slightly low values could be attributed to calibration errors

and should therefore not be chosen. Pallas reviewed all other subjects and found no other subject with a nearly normal platelet count as first abnormal lab test.

AI thyroiditis

For four thyroid disease subjects discrepancies existed between data reported in the Pallas column and the final ascertainment decided upon with the expert. For one subject an additional lab test was added by the expert on the same date as an already noted lab test by Pallas. For another subject the expert reported a much earlier lab test and this earlier lab test was reported in the final ascertainment. Finally, for two subjects Pallas mistakenly reported the wrong date of abnormal lab test, whereas the expert reported the correct date.

SLE

At first, one random SLE subject and two non-random SLE subjects were reviewed by the expert. Discrepancies between Pallas and the final ascertainment agreed upon existed for all three subjects in the category of NOAD and corresponding confirmation of the final classification. Pallas confirmed the SLE diagnosis in all three subjects, while the expert pointed out that these subjects did not fulfill enough criteria to confirm the SLE diagnosis. As discrepancies existed for all three subjects, the expert reviewed all other remaining SLE subjects as well (n=5). The following was decided by the expert:

1. If we can confirm that the subject fulfills at least four criteria, it will be a "**confirmed SLE**" (final ascertainment for two subjects).
2. Subjects with three or less criteria, subjects in whom the available data clearly suggest the existence of a systemic autoimmune disease other than SLE, and those with clinical features suggestive of systemic autoimmune disease and positive immunological markers but without the fulfillment of the current classification criteria for a specific systemic autoimmune disease, will be reported as "**confirmed other autoimmune disease**" (final ascertainment for five subjects).
3. In the absence of positive immunological markers, even in the presence of indirect sentences supporting the diagnosis ("hospital say meets the criteria for this diagnosis"), it will be "**no SLE, no auto-immune disease**" (final ascertainment for one subject).

6 Study limitations

- When the first symptom of a NOAD for a subject is known but the date of onset of the symptom is not known (there was no time indication when the first symptom started), the date of first report of this symptom was used as date of first symptom. This is a limitation of the study because we know that in a subset of these subjects the symptom has started (much) earlier.

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APPENDIX I Workbook

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