17 September 2025
EMA/761521/2021

Data analysis report

Drug utilisation and patient characterisation of statin usage

Administrative details of the data analysis	
Substance(s)	Statins: Atorvastatin, Fluvastatin, Lovastatin, Pravastatin, Rosuvastatin, Simvastatin, any statin
Condition/ADR(s)	N/A
Short title of topic	Statin prescribing in primary care
Regulatory procedure	N/A
Rapporteur's country	N/A
Requester name and contact details	N/A
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1. Milestones

Milestone	Planned date
Study protocol drafted	11/6/2024
Study report drafted	28/2/2025
Study report finalised	17/9/2025

2. Brief description of the study

A simple descriptive study to measure exposure to statin therapy in primary care. These data will be used to inform decision making by the EMA TDA-RWE team and the around the feasibility of a larger Darwin EU network study.

3. Rationale and background

Statins are the standard type of medicine used to reduce cholesterol. Statins are used to treat certain forms of high blood cholesterol levels and to reduce the risk of heart disease and the rate of death in patients with atherosclerotic cardiovascular disease or diabetes. The arteries become narrower due to fatty materials building up on their inside walls. [1]

The Periodic Safety Update Reports (PSURs) and PSUR single assessment procedures (PSUSAs) for simvastatin, fenofibrate / simvastatin, amlodipine / atorvastatin, pitavastatin, and rosuvastatin/ Omega-3-acid ethyl esters are due in 2025. Further, the PSUR for atorvastatin / perindopril, valsartan / rosuvastatin, fenofibrate / pravastatin, and lovastatin are due in 2026. Knowledge on usage of these drugs, as well as a patient characterisation of patients using these drugs may support these regulatory procedures.

The use of statins increased in United Kingdom, Denmark, Spain and Italy between 2010 and 2018, as described by García Rodríguez et al. [2] In a rapid review of studies in 2015 to 2020, the most common lipid management therapy was statins, and commonly reported comorbidities were hypertension, diabetes and obesity. [3] Less is known about the usage of statins in Europe in more recent years.

To support these regulatory PSUSA procedures, we investigated the usage of statins in IMRD UK and IQVIA DA Germany in 2010 to 2023. We estimated the incidence of new prescriptions of statins, and counts of subsequent prescriptions of statins. We characterized patients who were prescribed statins, in terms of demographics, cardiovascular diagnoses, previous statin prescriptions and switching to another statin.

4. Research question (RQ) and objectives

4.1. Objective 1: Incidence of prescriptions

1. What was the annual incidence of the prescription of individual statins and any statin, stratified by age group and sex?
2. What were the lines of therapy for incident statin users? I.e. what were the proportions of first, second and third line of treatment?

4.2. Objective 2: Characterisation of statin users

3. What was the duration (mean, SD) of continuous individual statin and any statin prescriptions (non-incident), stratified by age, sex, or cardiovascular diagnosis?
4. What were the most common cardiovascular diagnoses, close to the initiation date, for each of the individual statins, and any statin (non-incident)?
5. In patients who were prescribed statins in the study period, which earlier statin(s) were they prescribed, up to 1 or 5 years before? And how many?

5. Research methods

5.1. Study design

This was a longitudinal observational cohort study.

For the incidence rates (objective 1, RQ 1-2) a new user design was used. For the lines of therapy, the first line of treatment was required to be incident. For these analyses, the index date was the date of the first (incident) of any statin prescription.

For the characterisation of patients who were prescribed statins (objective 2, RQ 3-5), no limitations were applied with respect to new usage. For these analyses, the index date was the date that the respective statin was first prescribed in the study period.

5.2. Setting and study population

The study population was the general population (IMRD UK) and patients visiting general practices (IQVIA DA DE).

The study period was 2010 to 2023 (the last full year of the databases).

5.3. Variables

Individual statins: Atorvastatin, Fluvastatin, Lovastatin (IQVIA DA DE only), Pitavastatin (IQVIA DA DE only), Pravastatin, Rosuvastatin, Simvastatin.

Any statin: any of the above statins.

Cardiovascular: any disorder of cardiovascular system, including descendants.

The data sources have been mapped to the Observational Medical Outcomes Partnership (OMOP) Common Data Model (CDM). For code lists, see Annex 1.

5.4. Data sources

The following databases were used: IQVIA™ Medical Research Data (IMRD) May 2024 UK (IMRD UK), IQVIA™ Disease Analyser Germany June 2024 (IQVIA DA DE). For brief descriptions of these databases, see Annex 2.

5.5. Statistical analysis

5.5.1. Main statistical methods

Patients who were observable for less than 365 days before the index date were excluded.

5.5.1.1. Objective 1: Incidence of prescriptions

For this objective, the cohorts were the entire sample in the database (overall, stratified by age group and by sex). When incident (first line) statin prescriptions were recorded, a person stopped contributing to the person-time.

For RQ 1, descriptive statistics of statin prescriptions, stratified by age group, sex and overall were provided as tabulated incidence rates and as figures. Confidence intervals were calculated according to the method by Ulm. [4]

For RQ 2, time was divided into 180 day intervals. Prescriptions of statins were tabulated as counts and percentages for each interval. Prescriptions of different statins within the same interval were recorded as concurrent prescriptions, where these prescriptions was also recorded in an adjacent interval, were assumed to be switches.

These were provided overall and stratified by age group and sex, for patients with and without a history of a SNOMED code for any circulatory system disorder.

5.5.1.2. Objective 2: Characterisation of statin users

For this objective, patients entered a statin cohort on the day that they were first prescribed the respective statin. They could contribute to multiple cohorts.

For RQ 3, for statin prescriptions where the number of days supplied was not available, 30 days of supply was assumed. Patients were assumed to be continuously treated if any gap between treated/supplied days was less than 180 days. Subsequently, the number of treated days was counted, and mean and standard deviation (SD) were provided overall, stratified by sex, and stratified by presence of a SNOMED code for a circulatory system disorder before entering the respective statin cohort.

For RQ 4, for each statin cohort, the SNOMED code for a circulatory system disorder closest to statin initiation date (not incident), 365 days before or 30 days after the initiation date was selected. In case of ties the first was selected. The count and percentage for each code was tabulated.

For RQ 5, for each statin cohort (except any statin), for each patient upon cohort entry, any previous statin prescriptions were recorded. Counts and percentages were tabulated. Also, the number of previous statins was calculated and reported as mean, SD, median, interquartile range (IQR) and percentiles.

5.5.2. Sensitivity analysis

No sensitivity analysis was performed.

5.6. Quality control

The study was conducted according to the ENCePP code of conduct (European Medicines Agency 2018).

Standard operating procedures or internal process guidance were adhered to for the conduct of the study. These procedures include rules for secure and confidential data storage, quality-control procedures for all aspects of the study from protocol development to the reporting of the results.

All documents underwent at least one round a review by an experienced reviewer, while the results from the statistical analysis will be either reviewed or checked via double coding.

The quality control of the data is the responsibility of the data holder.

5.7. Software

Analyses were performed by EMA researchers using IHD and R, version 4.1.2. Specifically, the data were retrieved and the analytic datasets were created in IHD. For the drug utilisation studies, the initial analyses were performed in IHD, and summarised and visualised in R. For the incidence rates, analyses and visualisation were performed in R with the epiR and ggplot2 packages, respectively.

6. Results

In accordance with database rules on the management of low cell counts, cells with low numbers (<6 in the IMRD database) were removed prior to publication of this report. Additional cells may have been redacted (events/patients typically being rounded up to the nearest 10) if needed in order to ensure that the aforementioned low cell counts cannot be re-identified. This may include both events/patients and follow-up times.

In IQVIA DA DE, the numbers of pitavastatin prescriptions were (nearly) zero. Results specific for pitavastatin have been omitted, but pitavastatin prescriptions have been included in the 'any statin' cohort.

6.1. Research question 1: incidence

The number of results for the incidence of statin initiation were very large. Hence, these results were displayed as figures (below) and provided as csv files in Annex 3.

IQVIA DA DE

The incidence of statin prescribing increased over the period 2010 to 2023. In IQVIA DA DE, an increase in statin prescribing occurred in 2016. This was followed by a decrease until 2019, when it subsequently began to increase again (Figure 1).

The incidence of simvastatin prescribing decreased over the period 2010 to 2023, and peaked in 2016. In contrast, the incidence of atorvastatin prescribing over the period 2010 to 2023 gradually increased and was highest in 2023. The incidence of rosuvastatin prescribing increased from 2018. By 2023, atorvastatin had the highest incidence of prescribing, followed by rosuvastatin and then simvastatin (which previously the highest incidence between 2010 and 2016). The incidence of other statin prescribing was low or absent.

Statin prescribing in IQVIA DA DE by age category and sex

The incidence of statin initiation under the age of 40 years was very low. In older age categories, the incidence of statin initiation increased and peaked in the age group 65-74 before falling in those aged 75 years and above. The trends in the incidence of statin prescribing per age group were similar to those seen in the overall population. The incidence of statin prescribing was higher in men than in women and was consistent across age categories. However, the trends in the incidence of statin prescribing in men and women were similar (Figure 2 and 3).

IMRD UK

The incidence of statin prescribing increased over the period 2010 to 2023 in IMRD UK. However, the incidence of statin prescribing remained fairly stable until 2019 when it decreased before increasing again in 2021, being highest in 2023 (Figure 4).

The incidence of simvastatin prescribing gradually decreased over the period 2010 to 2023. In contrast, the incidence of atorvastatin prescribing over the period 2010 to 2023 gradually increased and was highest in 2023. The incidence of rosuvastatin prescribing increased from 2021 but incidence was relatively low in comparison to incidence of atorvastatin and simvastatin. From 2015, atorvastatin had the highest incidence of prescribing among all statins, whilst simvastatin had the highest incidence of prescribing before 2015. The incidence of other statin prescribing was low or absent.

Statin prescribing in IMRD UK by age category and sex

The incidence of statin initiation under the age of 40 years was also very low. In older age categories, the incidence of statin initiation increased and peaked in the age group 65-74 before falling in those aged 75 years and above. The trends in the incidence of statin prescribing per age group were similar to those seen in the overall population. The incidence of statin prescribing was higher in men than in women and was consistent across age categories. However, the trends in the incidence of statin prescribing in men and women were similar (Figure 5 and 6).

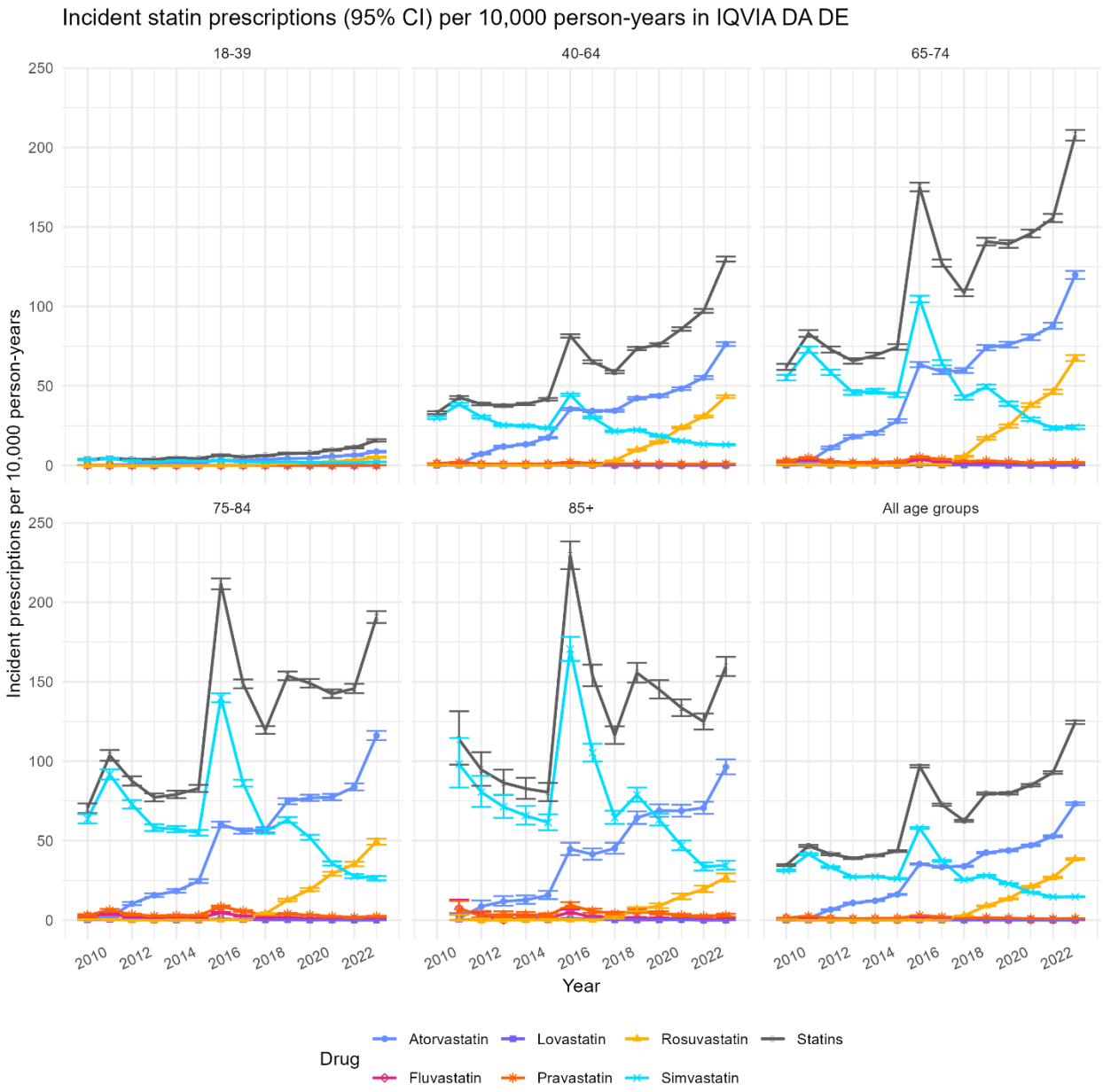

Figure 1. Incident statin prescriptions (95% CI) per 10,000 person-years in IQVIA DA DE

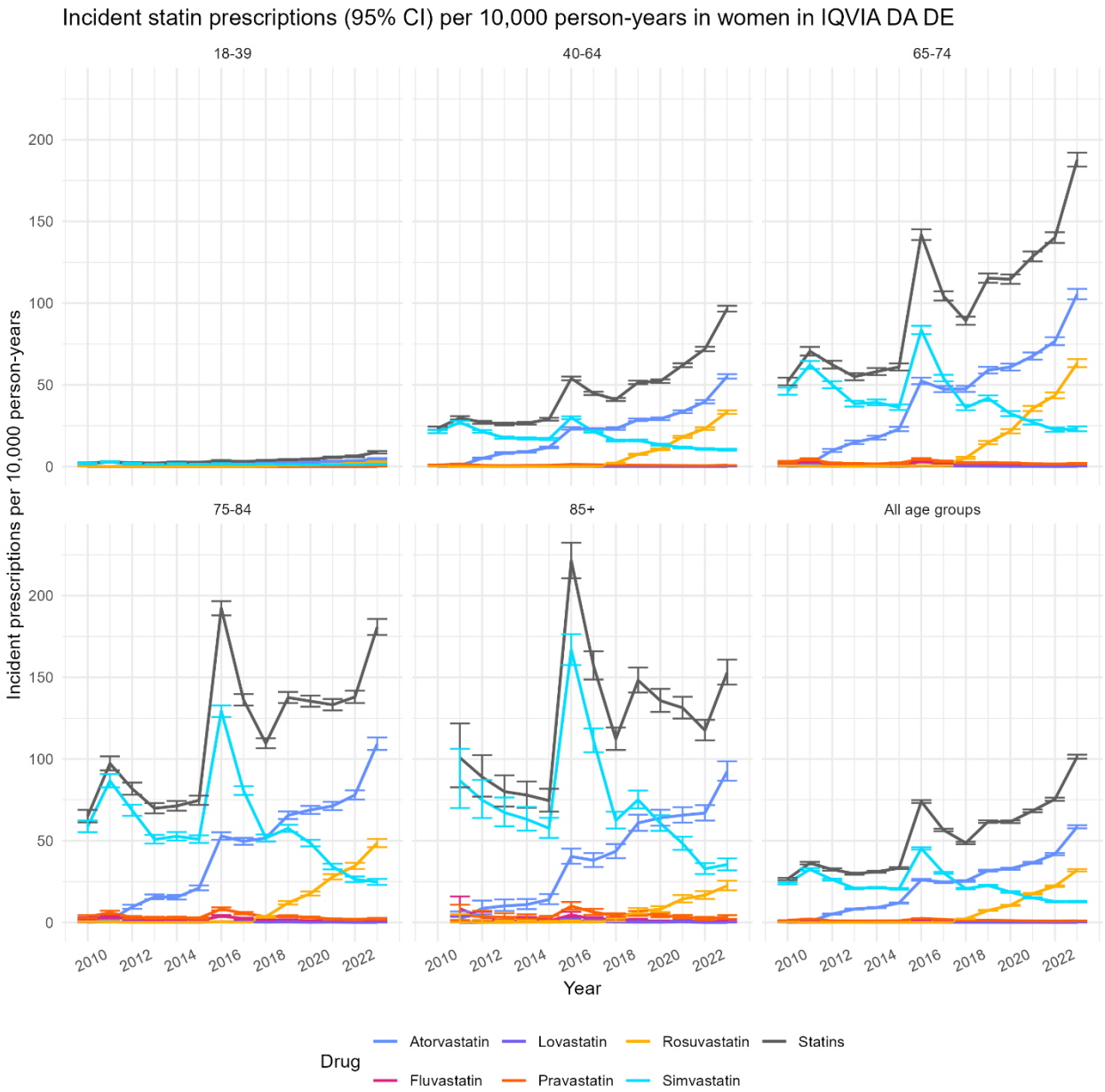

Figure 2. Incident statin prescriptions (95% CI) per 10,000 person-years in women in IQVIA DA DE

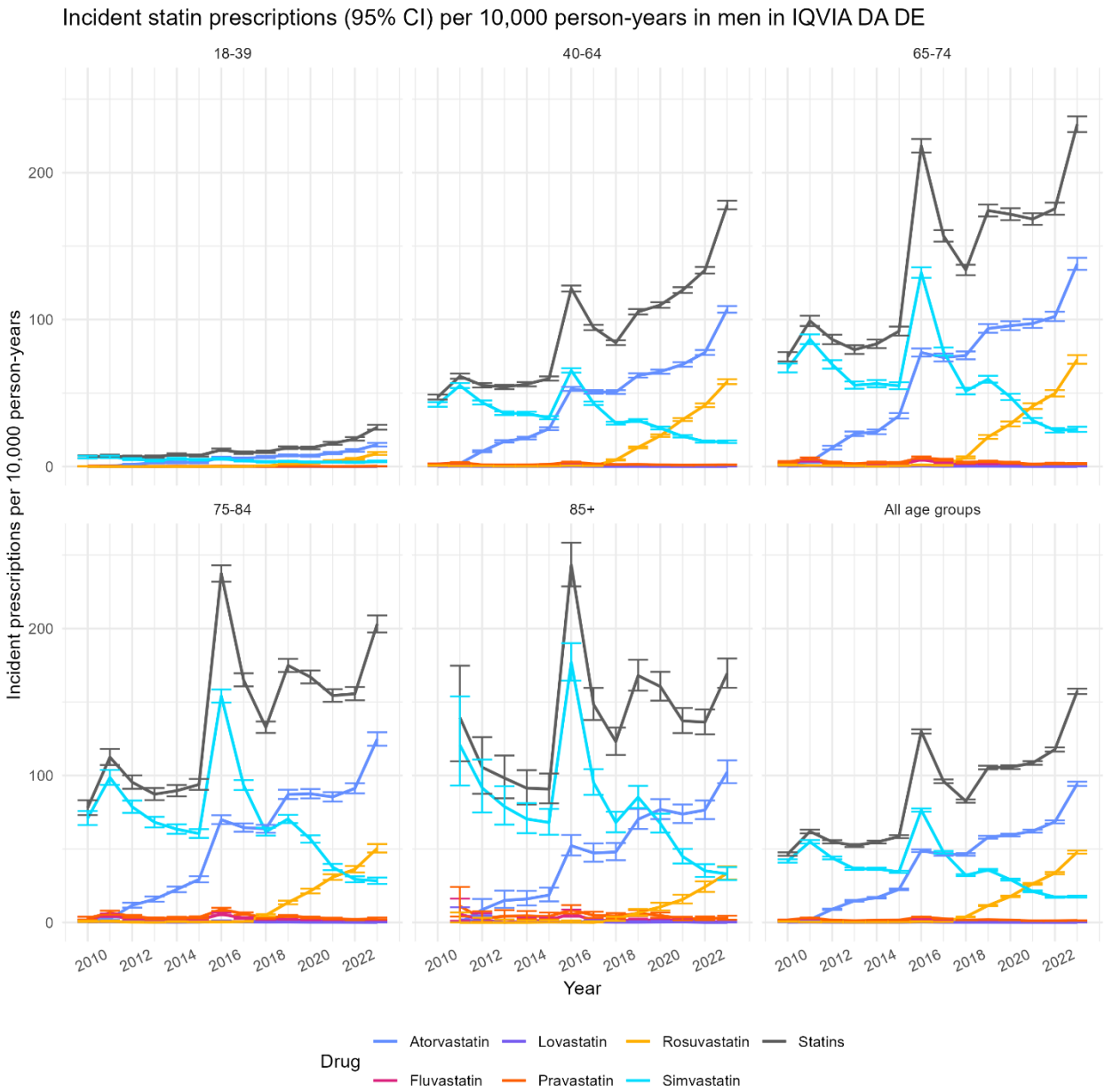

Figure 3. Incident statin prescriptions (95% CI) per 10,000 person-years in men in IQVIA DA DE

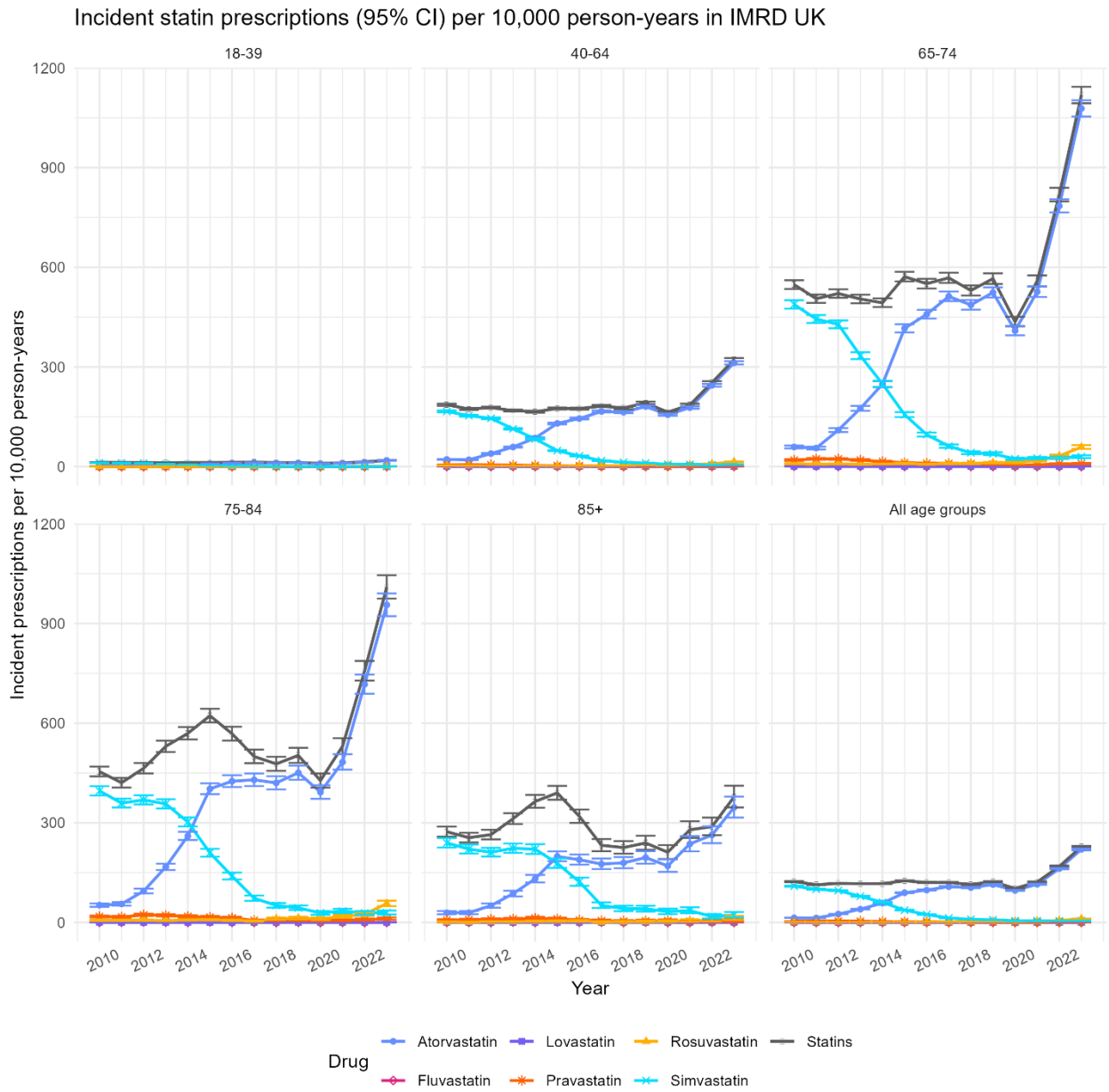

Figure 4. Incident statin prescriptions (95% CI) per 10,000 person-years in IMRD UK

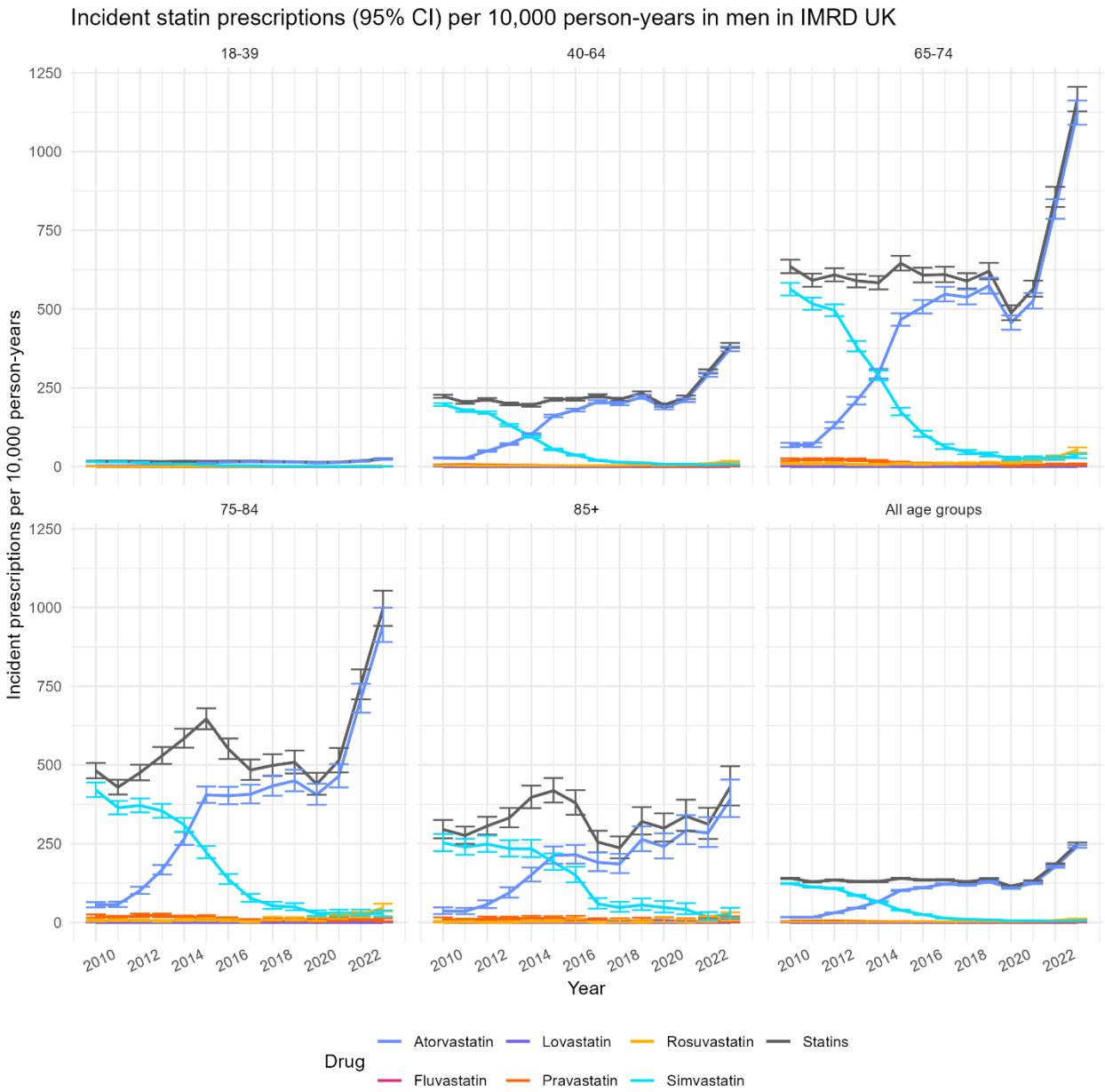

Figure 5. Incident statin prescriptions (95% CI) per 10,000 person-years in men in IMRD UK

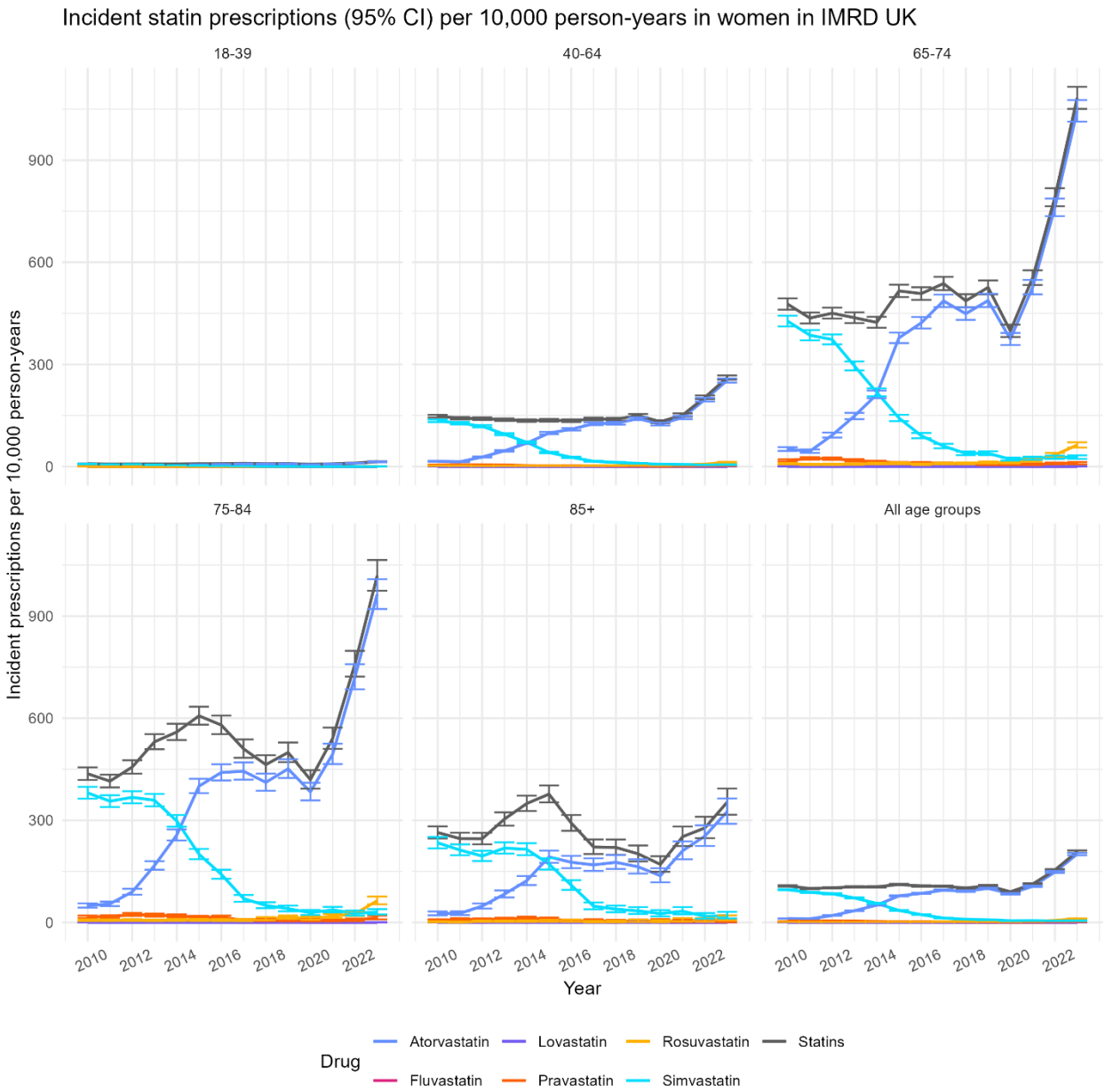

Figure 6. Incident statin prescriptions (95% CI) per 10,000 person-years in women in IMRD UK

6.2. Research question 2: Lines of statin therapy

A line of therapy for this analysis is defined as what was prescribed within 180 days following statin initiation. The most common line of statin therapy in the entire study period in IQVIA DA DE (44.2%; Table 1 and Figure 7) and IMRD UK (81.5%; Table 2 and Figure 8) was atorvastatin only. The next most common lines of statin therapy were simvastatin only (27.5% in In IQVIA DA DE, and 6.2% in IMRD UK). The third most common lines of therapy were Rosuvastatin only in IQVIA DA DE (11.7%) and first simvastatin followed by atorvastatin in IMRD UK (3.3%). The fourth most common lines of statin therapy were simvastatin followed by atorvastatin in IQVIA DA DE (4.8%) and atorvastatin followed by rosuvastatin in IMRD UK (2.3%). Lines of therapy including 3 or more statins were observed with frequencies below 0.5% and are not reported.

For the two most commonly prescribed statin lines of therapy in IMRD 37.2% of patients initiating simvastatin were prescribed another statin subsequently compared to 6.2% of patients prescribed atorvastatin. Corresponding numbers for IQVIA DA DE were 21.4% and 9.9% respectively, whilst the figure for rosuvastatin in IQVIA DA DE was 6.5%.

Lines of therapy stratified by circulatory system disorder status, age and sex are provided in Annex 4.

Table 1. Counts and percentages of the most common lines of statin therapy in IQVIA DA DE.

Line 1	Line 2	Count	Percentage
Atorvastatin		186,972	44.2
Simvastatin		116,054	27.5
Rosuvastatin		49,450	11.7
Simvastatin	Atorvastatin	20,380	4.8
Atorvastatin	Rosuvastatin	13,524	3.2
Simvastatin	Rosuvastatin	5,909	1.4
Pravastatin		5,901	1.4
Atorvastatin	Simvastatin	2,717	0.6
Rosuvastatin	Atorvastatin	2,400	0.6
Fluvastatin		2,149	0.5
Other		17,284	4.1
Total		422,740	100

Notes: Only lines of therapy occurring in at least 0.5% of patients are shown. Empty cells for Line 2 indicate this line of therapy includes only one statin. Lines of therapy including more than 2 statins all had frequencies below 0.5%.

Table 2. Counts and percentages of the most common lines of statin therapy in IMRD UK.

Line 1	Line 2	Count	Percentage
Atorvastatin		143,779	81.5
Simvastatin		10,987	6.2
Simvastatin	Atorvastatin	5,763	3.3
Atorvastatin	Rosuvastatin	4,025	2.3
Atorvastatin	Simvastatin	2,162	1.2
Rosuvastatin		2,146	1.2
Atorvastatin	Pravastatin	1,407	0.8
Pravastatin		826	0.5
Other		5,323	3.0
Total		176,418	100

Notes: Only lines of therapy occurring in at least 0.5% of patients are shown. Empty cells for Line 2 indicate this line of therapy includes only one statin. Lines of therapy including more than 2 statins all had frequencies below 0.5%.

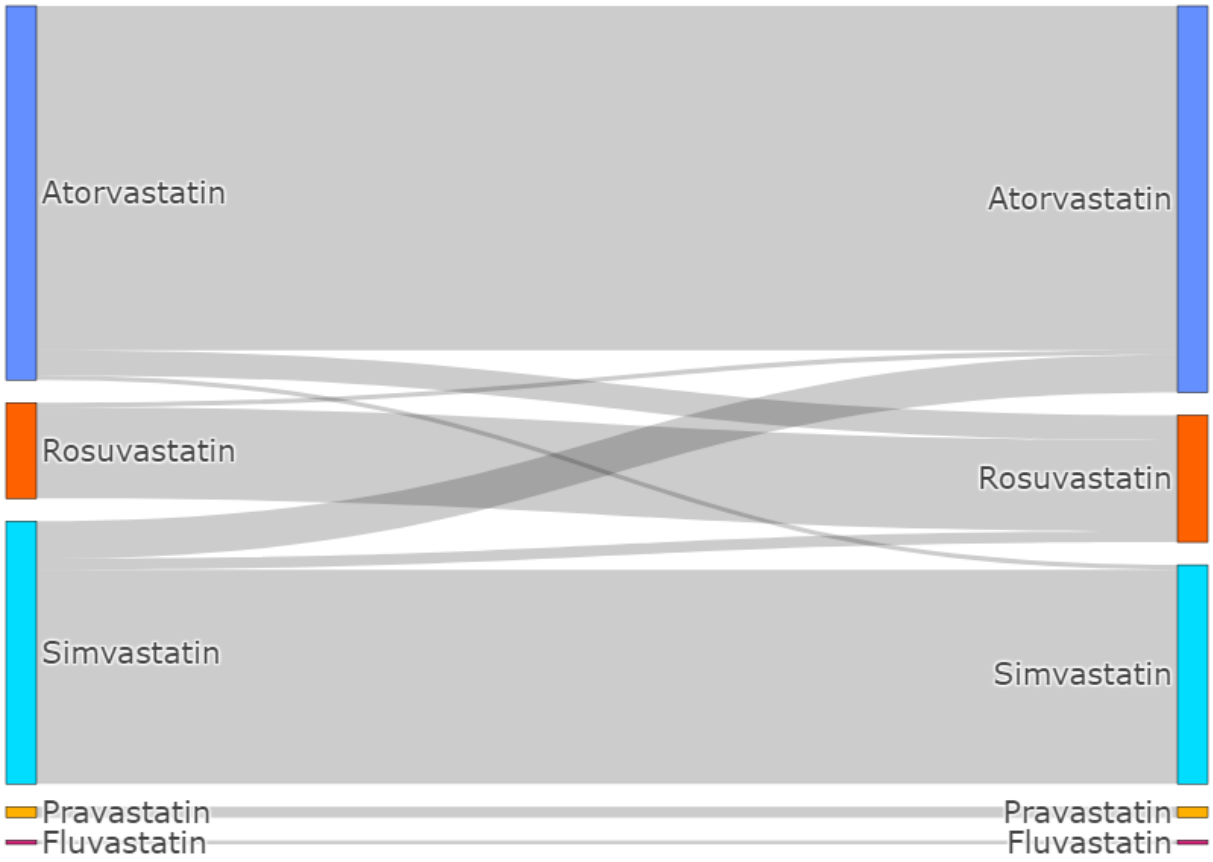

Figure 7. Lines of statin therapy occurring for at least 0.5% of the patients in IQVIA DA DE.

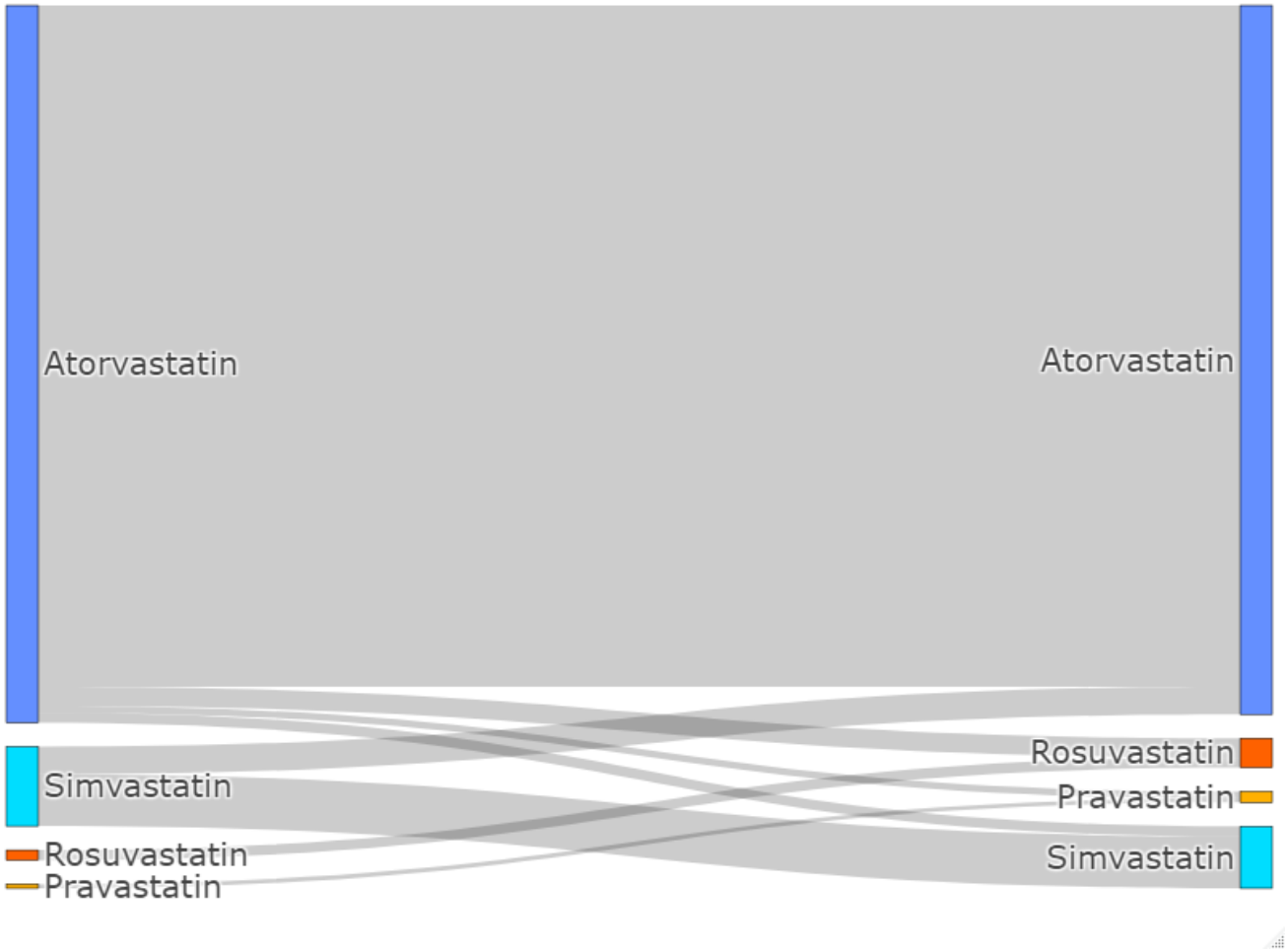

Figure 8. Lines of statin therapy occurring for at least 0.5% of the patients in IMRD UK.

6.3. Research question 3: Duration of continuous treatment

In IQVIA DA DE (Table 3), the overall mean number of days of continuous treatment across the study period was 745 days. A large variation of this was observed: the standard deviatiation equaled 921 days, larger than the mean.

In IMRD UK (Table 4), the overall mean number of days of continuous treatment across the study period was 1,455 days. A large variation of this was observed: the standard deviatiation equaled 1,223 days.

In both databases, for the any statin cohort and for each individual statin cohort, the mean number of days of continuous treatment was greater for men than for women, though these differences were relatively small.

Patients who had a circulatory system disorder code before their first statin prescription, had a higher mean number of days of continuous treatment than those who did not, for the any statin cohort and individual statin cohorts, in both databases (Tables 5 and 6).

In both databases, the mean duration of continuous treatment of any statin was greatest for the age group 65-74, though this varied for individual statins (Table 7 and 8).

Table 3. Duration of continuous treatment, overall and stratified by sex, in IQVIA DA DE.

Cohort	Statistic	Women	Men	Overall
Any statin	N patients	287,322	339,846	627,545
	Mean days (SD)	716.83 (898.93)	768.75 (938.67)	744.72 (920.90)
Atorvastatin	N patients	151,263	192,789	344,232
	Mean days (SD)	547.90 (718.18)	607.70 (765.32)	581.27 (745.45)
Fluvastatin	N patients	4,820	5,509	10,334
	Mean days (SD)	656.36 (861.40)	718.22 (879.80)	689.31 (871.61)
Lovastatin	N patients	832	687	1,520
	Mean days (SD)	714.87 (862.88)	791.09 (903.54)	748.87 (881.93)
Pravastatin	N patients	9,998	9,883	19,897
	Mean days (SD)	679.13 (872.54)	691.95 (865.83)	685.27 (868.96)
Rosuvastatin	N patients	55,852	67,085	122,984
	Mean days (SD)	369.78 (432.52)	401.98 (459.36)	387.30 (447.61)
Simvastatin	N patients	132,702	150,795	283,696
	Mean days (SD)	804.06 (943.91)	832.49 (955.23)	818.83 (949.90)

Table 4. Duration of treatment, overall and stratified by sex, in IMRD UK

Cohort	Statistic	Women	Men	Overall
Any statin	N patients	197,268	235,549	432,829
	Mean days (SD)	1,424.36 (1,211.77)	1,480.22 (1,231.79)	1,454.74 (1,223.02)
Atorvastatin	N patients	147,749	180,359	328,117
	Mean days (SD)	1,132.93 (1,097.15)	1,198.96 (1,122.87)	1,169.22 (1,111.85)
Fluvastatin	N patients	393	367	760
	Mean days (SD)	988.23 (1,094.87)	1,197.54 (1,107.43)	1,089.31 (1,105.19)
Pravastatin	N patients	9,307	9,355	18,662
	Mean days (SD)	1,117.03 (1,140.40)	1,199.66 (1,154.39)	1,158.45 (1,148.15)
Rosuvastatin	N patients	12,158	12,263	24,421
	Mean days (SD)	847.99 (1,020.46)	886.40 (1,042.71)	867.28 (1,031.85)
Simvastatin	N patients	68,463	79,641	148,110
	Mean days (SD)	1,426.41 (1,173.92)	1,457.75 (1,186)	1,443.24 (1,180.52)

Table 5. Duration of continuous treatment, stratified by historical presence of a SNOMED circulatory system disorder code, in IQVIA DA DE

Cohort	Statistic	No circulatory system disorder code before initiation	Circulatory system disorder code before initiation
Any statin	N	86,611	540,934
	Mean (SD)	488.27 (735.86)	785.78 (940.70)
Atorvastatin	N	46,435	297,797
	Mean (SD)	422.19 (628.75)	606.08 (759.03)
Fluvastatin	N	871	9,463
	Mean (SD)	453.37 (712.65)	711.02 (881.68)
Lovastatin	N	132	1,388
	Mean (SD)	404.11 (626.60)	781.66 (895.74)
Pravastatin	N	2,069	17,828
	Mean (SD)	453.10 (713.93)	712.22 (881.26)
Rosuvastatin	N	15,523	107,461
	Mean (SD)	305.87 (387.95)	399.06 (454.38)
Simvastatin	N	31,976	251,720
	Mean (SD)	535.47 (800.05)	854.82 (961.32)

Table 6. Duration of continuous treatment, stratified by historical presence of a SNOMED circulatory system disorder code, in IMRD UK

Cohort	Statistic	No circulatory system disorder code before initiation	Circulatory system disorder code before initiation
Any statin	N patients	109,208	323,621
	Mean (SD)	1,204.34 (1,190.99)	1,539.24 (1,222.12)
Atorvastatin	N patients	84,331	243,786
	Mean (SD)	943.86 (1,036.88)	1,247.17 (1,126.19)
Fluvastatin	N patients	96	664
	Mean (SD)	926.49 (1,074.70)	1,112.85 (1,108.34)
Pravastatin	N patients	3,221	15,441
	Mean (SD)	1,055.32 (1,128.57)	1,179.96 (1,151.06)
Rosuvastatin	N patients	5,034	19,387
	Mean (SD)	796.77 (991.75)	885.58 (1,041.25)
Simvastatin	N patients	31,753	116,357
	Mean (SD)	1,363 (1,210.96)	1,465.14 (1,171.13)

Table 7. Duration of continuous treatment, stratified by age group, in IQVIA DA DE

Cohort	Statistic	18-39	40-64	65-74	75-84	85+
Any statin	N patients	11,458	249,061	176,344	156,384	34,027
	Mean (SD)	401.71 (633.99)	727.19 (922.94)	808.53 (974.80)	766.52 (906.15)	560.81 (685.41)
Atorvastatin	N patients	6,634	144,393	96,719	79,521	16,876
	Mean (SD)	378.45 (578.77)	591.21 (764.54)	614.74 (777.97)	572.53 (714.29)	427.05 (529.24)
Fluvastatin	N patients	82	3,170	3,330	3,188	557
	Mean (SD)	402.41 (611.49)	624.48 (840.85)	719.49 (913.66)	744.86 (883.67)	606.95 (700.44)
Lovastatin	N patients	5	357	479	567	110
	Mean (SD)	528.20 (1,063.52)	596.92 (836.27)	741.44 (917.61)	871.95 (890.56)	662.28 (728.02)
Pravastatin	N patients	198	5,800	5,847	6,390	1,577
	Mean (SD)	381.03 (628.46)	648.50 (865.89)	740.91 (917.72)	716.83 (869.51)	539.17 (681.95)
Rosuvastatin	N patients	2,230	53,530	37,541	25,456	4,178
	Mean (SD)	262.19 (332.75)	389.32 (447.05)	394.15 (457.46)	395.37 (452.95)	318.38 (362.61)
Simvastatin	N patients	3,700	97,390	80,205	82,968	19,357
	Mean (SD)	408.28 (651.40)	798.73 (964.39)	894.93 (1,001.81)	833.91 (926.91)	620.76 (722.88)

Table 8. Duration of continuous treatment, stratified by age group, in IMRD UK

Cohort	Statistic	18-39	40-64	65-74	75-84	85+
Any statin	N patients	12,606	189,524	124,223	80,773	25,532
	Mean (SD)	886.54 (1,041.05)	1,403.92 (1,242.18)	1,651 (1,260.49)	1,501.27 (1,162.19)	1,013.83 (889.53)
Atorvastatin	N patients	10,410	153,476	93,284	55,642	15,188
	Mean (SD)	764.15 (937.73)	1,146.84 (1,120.56)	1,294.73 (1,157.27)	1,184.92 (1,069.64)	847.05 (820.88)
Fluvastatin	N patients	14	253	237	198	58
	Mean (SD)	1,272.29 (1,140.27)	978.86 (1,068.74)	1,129.58 (1,193.35)	1,229.08 (1,112.98)	885.24 (749.38)
Pravastatin	N patients	227	6,043	6,419	4,740	1,199
	Mean (SD)	643.35 (843.73)	1,054.55 (1,136.37)	1,245.90 (1,203.95)	1,242.10 (1,139.30)	985.61 (874.61)
Rosuvastatin	N patients	591	10,002	8,158	4,884	767
	Mean (SD)	661.96 (855.88)	889.08 (1,044.49)	915.49 (1,069.54)	802.21 (984.20)	645.53 (792.37)
Simvastatin	N patients	2,631	52,982	44,417	34,858	13,194
	Mean (SD)	925.14 (1,056.60)	1,405.42 (1,213.50)	1,635.09 (1,225.76)	1,465.09 (1,123.15)	996.52 (855.23)

6.4. Research question 4: Disorders of the circulatory system

Most patients who were prescribed a statin had a SNOMED code for a circulatory system disorder before the first prescription, for the any statin cohort and for individual statin cohorts, in both databases (Table 5 and 6).

The most common circulatory system disorder SNOMED code closest to index date was Essential hypertension, for the any statin cohort and each individual statin cohort, in both databases (Table 9 and 10). In IQVIA DA DE, the next most common circulatory system disorder SNOMED code closest to index date was Chronic ischemic heart disease, for the any statin cohort and each individual statin cohort except rosuvastatin, where Coronary arteriosclerosis was the second most common. This was followed by Chronic ischemic heart disease for the rosuvastatin cohort, and by Coronary arteriosclerosis for the other individual statin cohorts and the any statin cohort.

In IMRD UK, the next most common circulatory system disorder SNOMED code closest to index date was Hypertensive disorder, for the any statin cohort and each individual statin cohort except rosuvastatin, for which this was Ischemic heart disease. This was followed by Hypertensive disorder for the Rosuvastatin cohort, and by Ischemic heart disease for the other individual statin cohorts and the any statin cohort.

Table 9. Circulatory system disorder SNOMED codes closest to statin initiation date (not incidence), 365 days before or 30 days after the initiation date in IQVIA DA DE

OMOP ID and SNOMED code	Any statin	Atorvastatin	Fluvastatin	Lovastatin	Pravastatin	Rosuvastatin	Simvastatin
320128 - Essential hypertension [SNOMED 59621000]	154,261 (39.59%)	77,758 (35.18%)	2,677 (41.94%)	498 (51.45%)	5,212 (42.43%)	25,750 (34.43%)	79,246 (44.57%)
315286 - Chronic ischemic heart disease [SNOMED 413838009]	32,028 (8.22%)	19,038 (8.61%)	572 (8.96%)	76 (7.85%)	1,000 (8.14%)	6,484 (8.67%)	14,964 (8.42%)
317576 - Coronary arteriosclerosis [SNOMED 53741008]	26,794 (6.88%)	18,559 (8.40%)	426 (6.67%)	42 (4.34%)	679 (5.53%)	6,981 (9.33%)	9,577 (5.39%)
321052 - Peripheral vascular disease [SNOMED 400047006]	9,391 (2.41%)	5,345 (2.42%)	136 (2.13%)	22 (2.27%)	275 (2.24%)	1,597 (2.14%)	4,607 (2.59%)
4068155 - Atrial arrhythmia [SNOMED 17366009]	8,500 (2.18%)	4,748 (2.15%)	138 (2.16%)	27 (2.79%)	296 (2.41%)	1,306 (1.75%)	4,197 (2.36%)
4153380 - Disorder of carotid artery [SNOMED 371160000]	8,237 (2.11%)	5,208 (2.36%)	108 (1.69%)	13 (1.34%)	209 (1.70%)	2,071 (2.77%)	2,790 (1.57%)
381316 - Cerebrovascular accident [SNOMED 230690007]	7,845 (2.01%)	4,768 (2.16%)	61 (0.96%)	7 (0.72%)	284 (2.31%)	735 (0.98%)	3,624 (2.04%)
316437 - Cerebral atherosclerosis [SNOMED 55382008]	7,640 (1.96%)	4,696 (2.12%)	107 (1.68%)	7 (0.72%)	179 (1.46%)	2,501 (3.34%)	1,837 (1.03%)
316139 - Heart failure [SNOMED 84114007]	7,563 (1.94%)	4,267 (1.93%)	145 (2.27%)	19 (1.96%)	248 (2.02%)	1,128 (1.51%)	3,943 (2.22%)
373503 - Transient cerebral ischemia [SNOMED 266257000]	6,926 (1.78%)	4,229 (1.91%)	60 (0.94%)	5 (0.52%)	210 (1.71%)	767 (1.03%)	2,968 (1.67%)
314666 - Old myocardial infarction [SNOMED 1755008]	6,015 (1.54%)	3,755 (1.70%)	133 (2.08%)	9 (0.93%)	173 (1.41%)	1,215 (1.62%)	2,776 (1.56%)
318443 - Arteriosclerotic vascular disease [SNOMED 72092001]	5,489 (1.41%)	3,232 (1.46%)	70 (1.10%)	12 (1.24%)	139 (1.13%)	1,489 (1.99%)	1,721 (0.97%)

4181705 - Varicose veins of lower extremity without ulcer AND without inflammation [SNOMED 297713002]	5,304 (1.36%)	2,746 (1.24%)	84 (1.32%)	23 (2.38%)	194 (1.58%)	1,014 (1.36%)	2,584 (1.45%)
319034 - Hypertensive heart disease without congestive heart failure [SNOMED 60899001]	4,817 (1.24%)	2,512 (1.14%)	81 (1.27%)	21 (2.17%)	170 (1.38%)	926 (1.24%)	2,342 (1.32%)
4154290 - Paroxysmal atrial fibrillation [SNOMED 282825002]	4,556 (1.17%)	2,797 (1.27%)	95 (1.49%)	7 (0.72%)	162 (1.32%)	961 (1.28%)	1,928 (1.08%)
44784217 - Cardiac arrhythmia [SNOMED 698247007]	4,272 (1.10%)	2,270 (1.03%)	65 (1.02%)	14 (1.45%)	158 (1.29%)	803 (1.07%)	1,955 (1.10%)
439846 - Left heart failure [SNOMED 85232009]	4,177 (1.07%)	2,713 (1.23%)	64 (1%)	6 (0.62%)	126 (1.03%)	994 (1.33%)	1,719 (0.97%)
312327 - Acute myocardial infarction [SNOMED 57054005]	4,027 (1.03%)	2,908 (1.32%)	26 (0.41%)	2 (0.21%)	85 (0.69%)	655 (0.88%)	1,416 (0.80%)
315558 - Atherosclerosis of arteries of the extremities [SNOMED 51274000]	3,891 (1%)	2,496 (1.13%)	63 (0.99%)	3 (0.31%)	85 (0.69%)	782 (1.05%)	1,665 (0.94%)
321318 - Angina pectoris [SNOMED 194828000]	3,879 (1%)	2,540 (1.15%)	83 (1.30%)	12 (1.24%)	99 (0.81%)	788 (1.05%)	1,590 (0.89%)

Totals for individual statins do not sum op to the value for any statins, as patients may have different statin prescriptions, and therefore appear in multiple cohorts.

The 20 most common circulatory system disorder codes closest to initiation date are shown, as measured in the any statin cohort, and sorted according to the any statin cohort.

Table 10. Circulatory system disorder SNOMED codes closest to statin initiation date (not incidence), 365 days before or 30 days after the initiation date in IMRD UK

OMOP ID and SNOMED code	Any statin	Atorvastatin	Fluvastatin	Pravastatin	Rosuvastatin	Simvastatin
320128 - Essential hypertension [SNOMED 59621000]	69,706 (41.28%)	56,543 (40.48%)	120 (38.22%)	3,010 (40.09%)	4,066 (38.44%)	21,340 (42.32%)
316866 - Hypertensive disorder [SNOMED 38341003]	16,954 (10.04%)	12,011 (8.60%)	31 (9.87%)	895 (11.92%)	710 (6.71%)	6,630 (13.15%)
4185932 - Ischemic heart disease [SNOMED 414545008]	9,869 (5.84%)	7,596 (5.44%)	26 (8.28%)	552 (7.35%)	881 (8.33%)	3,181 (6.31%)
313217 - Atrial fibrillation [SNOMED 49436004]	7,060 (4.18%)	5,406 (3.87%)	22 (7.01%)	389 (5.18%)	434 (4.10%)	2,517 (4.99%)
381316 - Cerebrovascular accident [SNOMED 230690007]	6,306 (3.73%)	6,030 (4.32%)	10 (3.18%)	171 (2.28%)	273 (2.58%)	1,442 (2.86%)
373503 - Transient cerebral ischemia [SNOMED 266257000]	5,478 (3.24%)	4,937 (3.53%)	<6	216 (2.88%)	279 (2.64%)	1,435 (2.85%)
4270024 - Acute non-ST segment elevation myocardial infarction [SNOMED 401314000]	3,983 (2.36%)	4,662 (3.34%)	<6	78 (1.04%)	305 (2.88%)	316 (0.63%)
321318 - Angina pectoris [SNOMED 194828000]	3,515 (2.08%)	2,760 (1.98%)	18 (5.73%)	201 (2.68%)	315 (2.98%)	1,166 (2.31%)
195562 - Hemorrhoids [SNOMED 70153002]	3,448 (2.04%)	2,552 (1.83%)	<6	202 (2.69%)	247 (2.34%)	1,218 (2.42%)
312327 - Acute myocardial infarction [SNOMED 57054005]	3,076 (1.82%)	2,844 (2.04%)	7 (2.23%)	102 (1.36%)	164 (1.55%)	602 (1.19%)
4296653 - Acute ST segment elevation myocardial infarction [SNOMED 401303003]	2,513 (1.49%)	2,764 (1.98%)	<6	25 (0.33%)	160 (1.51%)	105 (0.21%)
321052 - Peripheral vascular disease [SNOMED 400047006]	1,984 (1.17%)	1,622 (1.16%)	<6	80 (1.07%)	147 (1.39%)	631 (1.25%)
318736 - Migraine [SNOMED 37796009]	1,797 (1.06%)	1,493 (1.07%)	<6	62 (0.83%)	132 (1.25%)	508 (1.01%)
316139 - Heart failure [SNOMED 84114007]	1,778 (1.05%)	1,581 (1.13%)	<6	62 (0.83%)	133 (1.26%)	474 (0.94%)
317576 - Coronary arteriosclerosis [SNOMED 53741008]	1,550 (0.92%)	1,551 (1.11%)	<6	81 (1.08%)	220 (2.08%)	263 (0.52%)
4154290 - Paroxysmal atrial fibrillation [SNOMED 282825002]	1,443 (0.85%)	1,141 (0.82%)	7 (2.23%)	89 (1.19%)	110 (1.04%)	490 (0.97%)

318169 - Varicose veins of lower extremity [SNOMED 72866009]	1,263 (0.75%)	927 (0.66%)		62 (0.83%)	65 (0.61%)	476 (0.94%)
4215140 - Acute coronary syndrome [SNOMED 394659003]	1,108 (0.66%)	1,243 (0.89%)		32 (0.43%)	94 (0.89%)	137 (0.27%)
381591 - Cerebrovascular disease [SNOMED 62914000]	1,047 (0.62%)	794 (0.57%)	<6	47 (0.63%)	62 (0.59%)	385 (0.76%)
4133004 - Deep venous thrombosis [SNOMED 128053003]	938 (0.56%)	695 (0.50%)	<6	39 (0.52%)	42 (0.40%)	342 (0.68%)

Totals for individual statins do not sum op to the value for any statins, as patients may have different statin prescriptions, and therefore appear in multiple cohorts.

The 20 most common circulatory system disorder SNOMED codes closest to initiation date are shown, as measured in the any statin cohort, and sorted according to the any statin cohort.

6.5. Research question 5: Previous statin prescriptions

6.5.1. Percentage of patients with previous prescriptions

IQVIA DA DE

The most common previous statin in the atorvastatin cohort was simvastatin, with 15% (1-year lookback period) and 23% (5-year lookback period) of those who had a atorvastatin prescription in the study period having previous simvastatin prescriptions (Table 11 and 12). The next most common previous statin prescription in this cohort was atorvastatin (6% and 8%), i.e., before the study period.

The most common previous statin in the fluvastatin cohort was fluvastatin, with 31% and 34% of those who had a fluvastatin prescription in the study period having previous fluvastatin prescriptions (i.e., before the study period). The next most common previous statin prescription in this cohort was atorvastatin (13% and 21%).

The most common previous statin in the lovastatin cohort was lovastatin, with 40% and 44% of those who had a lovastatin prescription in the study period having previous lovastatin prescriptions (i.e., before the study period). The next most common previous statin prescription in this cohort was atorvastatin (9% and 17%).

The most common previous statin in the pravastatin cohort was pravastatin, with 27% and 31% of those who had a pravastatin prescription in the study period having previous pravastatin prescriptions (i.e., before the study period). The next most common previous statin prescription in this cohort was simvastatin (11% and 19%).

The most common previous statin in the rosuvastatin cohort was atorvastatin, with 21% and 20% of those who had a rosuvastatin prescription in the study period having previous atorvastatin prescriptions. The next most common previous statin prescription in this cohort was simvastatin (12% and 20%).

The most common previous statin in the simvastatin cohort was simvastatin, with 34% and 40% of those who had a simvastatin prescription in the study period having previous simvastatin prescriptions (i.e., before the study period). The next most common previous statin prescription in this cohort was atorvastatin (2% and 4%).

IMRD UK

The most common previous statin in the atorvastatin cohort was atorvastatin, with 23% (1-year lookback period) and 25% (5-year lookback period) of those who had a atorvastatin prescription in the study period having previous atorvastatin prescriptions (i.e., before the study period; Table 13 and 14). The next most common previous statin prescription in this cohort was simvastatin (17% and 29%).

The most common previous statin in the fluvastatin cohort was fluvastatin, with 51% and 52% of those who had a fluvastatin prescription in the study period having previous fluvastatin prescriptions (i.e., before the study period). The next most common previous statin prescription in this cohort was atorvastatin (20% and 38%).

The most common previous statin in the pravastatin cohort was pravastatin, with 48% and 50% of those who had a pravastatin prescription in the study period having previous pravastatin prescriptions (i.e., before the study period). The next most common previous statin prescription in this cohort was atorvastatin (29% and 44%).

The most common previous statin in the rosuvastatin cohort was atorvastatin, with 43% and 61% of those who had a rosuvastatin prescription in the study period having previous atorvastatin prescriptions. The next most common previous statin prescription in this cohort was rosuvastatin (23% and 24%).

The most common previous statin in the simvastatin cohort was simvastatin, with 80% and 83% of those who had a simvastatin prescription in the study period having previous simvastatin prescriptions (i.e., before the study period). The next most common previous statin prescription in this cohort was atorvastatin (4% and 8%).

6.5.2. Number of unique previous prescriptions

IQVIA DA DE

Across the individual statin cohorts, the mean number of unique other statin prescriptions up to 1 year before index ranged from 0.25 (atorvastatin cohort) to 0.64 (lovastatin cohort), whereas the median ranged from 0 (atorvastatin, pravastatin, rosuvastatin and simvastatin cohorts) to 1 (fluvastatin and lovastatin cohorts). The 10% - 90% percentiles were 0-1 for all cohorts (Table 15).

Across the individual statin cohorts, the mean number of unique other statin prescriptions up to 5 year before index ranged from 0.36 (atorvastatin cohort) to 0.87 (lovastatin cohort), whereas the median ranged from 0 (rosuvastatin and simvastatin cohorts) to 1 (atorvastatin, pravastatin, fluvastatin and lovastatin cohorts). The 10% - 90% percentiles were 0-1 for the atorvastatin, rosuvastatin and simvastatin cohorts, and 0-2 for the fluvastatin, lovastatin and pravastatin cohorts (Table 16).

IMRD UK

Across the individual statin cohorts, the mean number of unique other statin prescriptions up to 1 year before index ranged from 0.42 (atorvastatin cohort) to 0.97 (fluvastatin cohort), whereas the median ranged from 0 (atorvastatin) to 1 (fluvastatin, pravastatin, rosuvastatin and simvastatin cohorts). The 10% - 90% percentiles were 0-1 for the atorvastatin, pravastatin, rosuvastatin and simvastatin cohorts, and 0-2 for the fluvastatin cohort (Table 17).

Across the individual statin cohorts, the mean number of unique other statin prescriptions up to 5 year before index ranged from 0.57 (atorvastatin cohort) to 0.49 (fluvastatin cohort), whereas the median ranged from 0 (atorvastatin) to 1 (fluvastatin, pravastatin, rosuvastatin and simvastatin cohorts). The 10% percentile varied from 0 to 1, and the 90% percentile varied from 1 to 3 (Table 18).

Table 11. Previous statin prescriptions (percentages) in statin cohorts in IQVIA DA DE in a 1-year lookback period

Previous statin	Atorvastatin cohort	Fluvastatin cohort	Lovastatin cohort	Pravastatin cohort	Rosuvastatin cohort	Simvastatin cohort
Atorvastatin	21,905 (6.36%)	1,348 (13.04%)	142 (9.34%)	1,872 (9.41%)	26,088 (21.21%)	7,013 (2.47%)
Fluvastatin	2,038 (0.59%)	3,173 (30.70%)	42 (2.76%)	243 (1.22%)	1,172 (0.95%)	681 (0.24%)
Lovastatin	419 (0.12%)	44 (0.43%)	606 (39.87%)	72 (0.36%)	264 (0.21%)	200 (0.07%)
Pravastatin	2,965 (0.86%)	187 (1.81%)	33 (2.17%)	5,467 (27.48%)	1,585 (1.29%)	772 (0.27%)
Rosuvastatin	5,226 (1.52%)	437 (4.23%)	53 (3.49%)	571 (2.87%)	437 (0.36%)	965 (0.34%)
Simvastatin	52,858 (15.36%)	952 (9.21%)	99 (6.51%)	2,119 (10.65%)	15,044 (12.23%)	96,722 (34.09%)

Table 12. Previous statin prescriptions (percentages) in statin cohorts in IQVIA DA DE in a 5-year lookback period

Previous statin	Atorvastatin cohort	Fluvastatin cohort	Lovastatin cohort	Pravastatin cohort	Rosuvastatin cohort	Simvastatin cohort
Atorvastatin	28,695 (8.34%)	2,132 (20.63%)	253 (16.64%)	2,899 (14.57%)	37,672 (30.63%)	12,024 (4.24%)
Fluvastatin	3,566 (1.04%)	3,530 (34.16%)	58 (3.82%)	423 (2.13%)	1,947 (1.58%)	1,511 (0.53%)
Lovastatin	621 (0.18%)	68 (0.66%)	669 (44.01%)	94 (0.47%)	369 (0.30%)	325 (0.11%)
Pravastatin	5,071 (1.47%)	334 (3.23%)	59 (3.88%)	6,210 (31.21%)	2,609 (2.12%)	1,987 (0.70%)
Rosuvastatin	6,925 (2.01%)	593 (5.74%)	71 (4.67%)	778 (3.91%)	584 (0.47%)	1,381 (0.49%)
Simvastatin	80,592 (23.41%)	1,923 (18.61%)	218 (14.34%)	3,833 (19.26%)	24,471 (19.90%)	114,640 (40.41%)

Table 13. Previous statin prescriptions (percentages) in statin cohorts in IMRD UK in a 1-year lookback period

Previous statin	Atorvastatin cohort	Fluvastatin cohort	Pravastatin cohort	Rosuvastatin cohort	Simvastatin cohort
Atorvastatin	76,130 (23.20%)	151 (19.87%)	5,470 (29.31%)	10,539 (43.16%)	6,589 (4.45%)
Fluvastatin	140 (0.04%)	385 (50.66%)	20 (0.11%)	49 (0.20%)	29 (0.02%)
Pravastatin	3,220 (0.98%)	69 (9.08%)	9,050 (48.49%)	1,276 (5.23%)	407 (0.27%)
Rosuvastatin	1,760 (0.54%)	76 (10%)	623 (3.34%)	5,525 (22.62%)	337 (0.23%)
Simvastatin	56,167 (17.12%)	56 (7.37%)	1,884 (10.10%)	1,913 (7.83%)	118,789 (80.20%)

Table 14. Previous statin prescriptions (percentages) in statin cohorts in IMRD UK in a 5-year lookback period

Previous statin	Atorvastatin cohort	Fluvastatin cohort	Pravastatin cohort	Rosuvastatin cohort	Simvastatin cohort
Atorvastatin	81,647 (24.88%)	289 (38.03%)	8,302 (44.49%)	14,840 (60.77%)	11,655 (7.87%)
Fluvastatin	273 (0.08%)	393 (51.71%)	58 (0.31%)	102 (0.42%)	86 (0.06%)
Pravastatin	6,997 (2.13%)	145 (19.08%)	9,423 (50.49%)	2,453 (10.04%)	1,231 (0.83%)
Rosuvastatin	4,560 (1.39%)	130 (17.11%)	1,102 (5.91%)	5,831 (23.88%)	1,326 (0.90%)
Simvastatin	95,112 (28.99%)	177 (23.29%)	6,682 (35.81%)	5,444 (22.29%)	122,529 (82.73%)

Table 15. Number of unique other statin prescriptions up to 1 year before index in IQVIA DA DE.

Statistic	Atorvastatin	Fluvastatin	Lovastatin	Pravastatin	Rosuvastatin	Simvastatin
N patients	344,232	10,334	1,520	19,897	122,984	283,696
Mean (SD)	0.25 (0.45)	0.59 (0.60)	0.64 (0.61)	0.52 (0.57)	0.36 (0.51)	0.37 (0.49)
Median (IQR)	0 (0-0)	1 (0-1)	1 (0-1)	0 (0-1)	0 (0-1)	0 (0-1)
10% - 90% percentile	0-1	0-1	0-1	0-1	0-1	0-1

N patients indicates the number of patients that have been prescribed the respective statin. The following are statistics on the number of unique other statins these patients have been prescribed before.

Table 16. Number of unique other statin prescriptions up to 5 years before index in IQVIA DA DE.

Statistic	Atorvastatin	Fluvastatin	Lovastatin	Pravastatin	Rosuvastatin	Simvastatin
N patients	344,232	10,334	1,520	19,897	122,984	283,696
Mean (SD)	0.36 (0.58)	0.83 (0.75)	0.87 (0.77)	0.72 (0.71)	0.55 (0.65)	0.46 (0.54)
Median (IQR)	0 (0-1)	1 (0-1)	1 (0-1)	1 (0-1)	0 (0-1)	0 (0-1)
10% - 90% percentile	0-1	0-2	0-2	0-2	0-1	0-1

N patients indicates the number of patients that have been prescribed the respective statin. The following are statistics on the number of unique other statins these patients have been prescribed before.

Table 17. Number of unique other statin prescriptions up to 1 year before index in IMRD UK

Statistic	Atorvastatin	Fluvastatin	Pravastatin	Rosuvastatin	Simvastatin
N patients	328,117	760	18,662	24,421	148,110
Mean (SD)	0.42 (0.54)	0.97 (0.67)	0.91 (0.52)	0.79 (0.57)	0.85 (0.38)
Median (IQR)	0 (0-1)	1 (1-1)	1 (1-1)	1 (0-1)	1 (1-1)
10% - 90% percentile	0-1	0-2	0-1	0-1	0-1

N patients indicates the number of patients that have been prescribed the respective statin. The following are statistics on the number of unique other statins these patients have been prescribed before.

Table 18. Number of unique other statin prescriptions up to 5 years before index in IMRD UK

Statistic	Atorvastatin	Fluvastatin	Pravastatin	Rosuvastatin	Simvastatin
N patients	328,117	760	18,662	24,421	148,110
Mean (SD)	0.57 (0.73)	1.49 (1)	1.37 (0.74)	1.17 (0.80)	0.92 (0.43)
Median (IQR)	0 (0-1)	1 (1-2)	1 (1-2)	1 (1-2)	1 (1-1)
10% - 90% percentile	0-2	0-3	1-2	0-2	0-1

N patients indicates the number of patients that have been prescribed the respective statin. The following are statistics on the number of unique other statins these patients have been prescribed before.

7. Discussion

7.1. Key results

7.1.1. Incidence

The incidence of statin prescriptions increased from 2010 to 2023 in IQVIA DA DE, whereas the incidence of statin prescriptions was relatively constant in IMRD UK, until it increased in 2021-2023. Simvastatin used to be the most commonly initiated (newly prescribed) statin in both countries, after which atorvastatin was initiated more often. Specifically, in IQVIA DA DE, simvastatin had the highest incidence of initiations from 2010 to 2016, and from 2018 atorvastatin has been the most commonly initiated statin. Also, initiations of rosuvastatin have risen from 2018 to 2023. In IMRD UK, Simvastatin had the highest incidence of initiations from 2010 to 2014, and since 2015 atorvastatin had the highest incidence of initiations. The incidence of statin initiations was higher in men than in women, in both databases.

Reasons for the spike in incidence in Germany in 2016, and smaller spike in the UK in 2014-2015 may relate to differences in guideline changes in recommendations. For example, a Cochrane review was published in 2013 focused on statins for the primary prevention of cardiovascular disease and the UK adjusted its guideline in 2014.[5,6] In contrast guidelines within the EU changed in 2016.[7,8]

7.1.2. Lines of therapy

The most common line of statin therapy in IQVIA DA DE (44.2%; Table 1 and Figure 7) and IMRD UK (81.5%; Table 2 and Figure 8) was Atorvastatin only. The next most common lines of statin therapy were Simvastatin only (27.5% in In IQVIA DA DE, and 6.2% in IMRD UK).

In both databases, the most common first line of therapy was atorvastatin (IQVIA DA DE: 49.1%, IMRD UK: 86.9%), followed by simvastatin (IQVIA DA DE: 34.9%, IMRD UK: 9.9%), and then rosuvastatin (IQVIA DA DE: 12.5%, IMRD UK 1.4%).

Among patients prescribed atorvastatin as first line, and who were prescribed a second line treatment, rosuvastatin was the most common second line treatment (3.2% of the total in IQVIA DA DE, 2.3% of the total in IMRD UK, Table 1). Among patients prescribed simvastatin as first line, and who were prescribed a second line treatment, atorvastatin was the most common second line treatment (4.8% of the total in IQVIA DA DE, 3.3% of the total in IMRD UK).

7.1.3. Duration of continuous treatment

In IQVIA DA DE, the overall mean number of days of continuous treatment was 745 days, whereas in IMRD UK (Table 8), the overall mean number of days of continuous treatment was 1,455 days.

Overall, in men and in women, duration of continuous treatment was longest for simvastatin, followed by lovastatin in IQVIA DA DE. Overall and in men, duration of continuous treatment was longest for simvastatin in IMRD UK, followed by pravastatin and atorvastatin. In women, this was longest for simvastatin, followed by atorvastatin and then pravastatin, in IMRD UK. Duration of continuous

treatment was longer in patients who had a SNOMED circulatory system disorder code before initiation than those who did not have such a code before initiation, in IQVIA DA DE and IMRD UK.

The greater mean duration of continuous treatment in patients aged 65-74 than in those 85+ is likely be due to a lack of follow-up time for the older patients.

7.1.4. Common disorders of the circulatory system

The most common SNOMED circulatory system disorder code closest to index date were Essential hypertension (IQVIA DA DE), and Hypertensive disorder (IMRD UK). Other common SNOMED circulatory system disorder codes closest to index date were Chronic ischemic heart disease, Coronary arteriosclerosis (IQVIA DA DE) and Ischemic heart disease (IMRD UK).

7.1.5. Previous statin prescriptions

In patients who were prescribed statins in the study period, the most common statin prescriptions they had before the study period, on overall were atorvastatin and simvastatin.

7.2. Interpretation

Simvastatin was the most commonly newly prescribed statin at the start of the study period. By the end, nearly all statin prescriptions were either atorvastatin, rosuvastatin or simvastatin. More people initiated another statin within 180 days when prescribed simvastatin compared to other statins. These data may be useful to support the planning and design of other observational studies examining the side effect profile of statins.

7.3. Limitations

The shorter duration of continuous treatment in IQVIA DA DE than in IMRD UK may be a result of different healthcare systems and privacy protection. Whereas GP practices in IMRD UK contain lifetime records for patients, records transfer when patients move to another practice, and includes (some) health and care information from other care providers, practices in IQVIA DA DE do not include data from other care providers, do not share data when patients visit another practice. This may artificially reduce the observed duration of continuous treatment in IQVIA DA DE.

In IQVIA DA DE, the denominator for incidence rates is calculated using the recording of healthcare encounters. Patients' time at risk runs, at maximum, from their first to their last healthcare encounter. Patients who do not have any healthcare encounter in the last year(s) of the study are not included in the denominator for that/those year(s). This leads to an artificially high observed incidence rate in the last year(s)

7.3.1. Lines of statin therapy

A larger proportion of simvastatin users switched to another statin than for other first line statins. This can at least partially be explained by the difference in initiation dates for different statins or reduced tolerance to simvastatin. At the start of the study period, simvastatin was the most commonly prescribed statin, meaning that these patients had more time to switch to another statin than those who initiated atorvastatin or rosuvastatin closer to the study end date.

8. Conclusion

The incidence of statin initiation has increased from 2010 to 2023 in both IQVIA DA DE and IMRD UK. However, the incidence of statin initiations was relatively constant in IMRD UK, until it increased more recently from 2021-2023. Simvastatin used to be the most commonly newly initiated statin, and since 2018 (IQVIA DA DE) and 2015 (IMRD UK) atorvastatin was initiated more often. A higher proportion of people initiating simvastatin were prescribed another statin in 180 days compared to the atorvastatin and rosuvastatin.

Overall, in men and in women, duration of continuous treatment was longest for simvastatin, followed by lovastatin in IQVIA DA DE. Overall and in men, duration of continuous treatment was longest for simvastatin in IMRD UK, followed by pravastatin and atorvastatin. In women, this was longest for simvastatin, followed by atorvastatin and then pravastatin, in IMRD UK. In both databases, duration of continuous treatment was longer in patients who had a SNOMED code for a disorder of the circulatory system before initiation than those who did.

9. References

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Annexes

Annex 1 - Codelists

Statins

Atorvastatin - RxNorm and Extensi

Fluvastatin - RxNorm and Extensi

Lovastatin - RxNorm and Extension - ATL

Pitavastatin - RxNorm and Extensi

Pravastatin - RxNorm and Extensi

Rosuvastatin - RxNorm and Extensi

Simvastatin - RxNorm and Extensi

Circulatory system disorders as defined by SNOMED

Disorder of cardiovascular syste

Annex 2 - Information on Databases and Healthcare systems included

IQVIA™ Medical Research Data (IMRD) UK

IMRD UK is a primary care database from the UK. GPs play a gatekeeper role in the healthcare system in the UK, as they are responsible for delivering primary health care and specialist referrals. Over 98% of the UK-resident population is registered with a GP, so that GP patient records are broadly representative of the UK population in general. Patients are affiliated to a practice, which centralizes the medical information from GPs, specialist referrals, hospitalizations, and tests.

IQVIA™ Disease Analyzer Germany

IQVIA™ Disease Analyzer Germany collects computerised information from specialised and general primary care practices throughout Germany since 1992. Around 3% of general practitioners (GP) practices are included, which covers all patients consulting a practice. Data from IQVIA™ Disease Analyzer Germany have been shown to be reasonably representative of German healthcare statistics for demographics and certain diseases and is considered one of the largest national medical databases worldwide. IQVIA™ Disease Analyzer Germany includes more than 2,500 practices and 3,100 physicians (13 speciality groups) representing over 15,000,000 patients. This database used to be named IMS® Germany and some use of this terminology may persist.

The quality of IQVIA™ Disease Analyzer data is ensured by a series of continuous QA controls and data refinement. These include checking incoming data for criteria such as completeness and correctness, (e.g. linkage between diagnoses and prescriptions), and standardizing certain data values such as laboratory test results in order to enable reliable analysis.

Ethical approval

EMA has blanket approval to perform simple descriptive analysis of IMRD UK and IQVIA DA DE and no further permissions were required.

Annex 3 – Incidence of statin prescriptions tables

Incidence IMRD UK May 2024.csv

Incidence IQVIA DA DE June 2024.csv

Annex 4 – Lines of therapy stratified by circulatory system disorder status (CVD), age and sex


Lines of therapy - DE - no CVD.xlsx


Lines of therapy - DE - CVD.xlsx


Lines of therapy - UK - no CVD.xlsx


Lines of therapy - UK - CVD.xlsx