Response to: 'Statins in systemic lupus erythematosus' by Abud-Mendoza

It was with great interest that we read the correspondence of Abud-Mendoza[1] on our recent paper in which we described a decreased risk of developing systemic lupus erythematosus (SLE) in statin users who continued their therapy for >1 year.[2]

We agree that prevention of cardiovascular disease in rheumatic diseases is of great importance.[3] Whether statins decrease disease activity in SLE is, however, controversial since a recent meta-analysis of five controlled trials did not suggest any significant effect of statin therapy on Systemic Lupus Erythematosus Disease Activity Index.[4]

Unfortunately, in the UK's Clinical Practice Research Datalink (CPRD)—an ongoing primary care database of anonymised medical records from general practitioners that was used in our study—no measurements for SLE activity before or after initiating statin therapy are available.[2] We, however, do not think that statin therapy is superior to hydroxychloroquine (HCQ) as therapy to reduce relapses and thrombotic events in SLE. HCQ does not only prevent relapses in SLE but also has anti-atherogenic effects and is, in contrast to statins, associated with a reduced risk of development of diabetes mellitus.[5–7]

Abud-Mendoza wondered whether inclusion of patients <40 years changed our findings.[1] When we included these patients and excluded patients with SLE before the index date, we identified 539 431 statin users and 539 431 non-users after using a matched random sampling approach (1:1). The index date ('baseline') was defined as the date of the first prescription of a statin; that is, 'statin user'. Each statin user was matched to one control ('non-user') based on age, sex and general practice at index date, with the index date of the control being the same as that of the statin user. The characteristics at baseline are presented in table 1 and are in line with the characteristics that have been shown in Table 1 in our paper.[2] Statin users and non-users had similar distributions of age (statin users: mean age, 62.7 years; and non-users: 61.9 years) and sex (statin users and non-users: 47.7% women). In our study population aged ≥16 years, the incidence rate was the same as the incidence rate in our recent study,[2] 0.7 cases per 10 000 person-years.

Compared with our previous findings, we found similar associations between statin use and the risk of SLE, only slightly attenuated. Among patients aged ≥16 years, current statin users had a risk of developing SLE which was comparable to that of non-users ($HR_{adjusted}$, 0.81; 95% CI 0.57 to 1.15). Moreover, current statin users who continued therapy for >1 year had a 34% decreased risk of developing SLE ($HR_{adjusted}$, 0.66; 95% CI 0.44 to 0.98) (table 2).

Finally, Abud-Mendoza wondered whether we had information regarding adverse events related to statins.[1] Since our study objective was to assess the association between the statin use and the risk of SLE, we had no access to other study outcomes than SLE. However, several population-based studies using CPRD data have found adverse events of statins such as rhabdomyolysis and cataract.[8 9]

We conclude that statins are probably safe in SLE but that more research is needed to assess the benefit/risk profile of statins in other autoimmune rheumatic diseases such as polymyalgia rheumatica.[10]

Table 1 Baseline characteristics of statin users and non-statin users aged ≥16 years

Baseline characteristics	Statin users (n=539 431)	Non-users (n=539 431)
Duration of follow-up (years)		
Mean (SD)	4.5 (3.4)	4.1 (2.6)
Sex, n (%)		
Female	257 202 (47.7)	257 202 (47.7)
Age (years)		
Mean (SD)	62.7 (12.7)	61.9 (13.5)
Age by category, years (%)		
≤59	238 092 (44.1)	252 672 (46.8)
60–79	242 331 (44.9)	221 013 (41.0)
80+	59 008 (11.0)	65 746 (12.2)
BMI (kg/m^2)		
Mean (SD)	27.3 (7.8)	21.0 (11.6)
Unknown BMI	29 566 (5.5)	111 025 (20.6)
Smoking status, n (%)		
Non-smoker	224 945 (41.7)	242 946 (45.0)
Ex-smoker	168 229 (31.2)	113 898 (21.1)
Smoker	122 289 (22.7)	106 473 (19.8)
Unknown smoking status	23 968 (4.4)	76 114 (14.1)
Drinking status, n (%)		
Non-drinker	68 056 (12.6)	56 286 (10.4)
Ex-drinker	33 857 (6.3)	21 352 (4.0)
Drinker	370 711 (68.7)	333 313 (61.8)
Unknown drinking status	66 807 (12.4)	128 480 (23.8)
Drug use within previous six months, n (%)		
Antihypertensive agents	329 228 (61.0)	124 612 (23.1)
Fibrates	8960 (1.7)	903 (0.2)
Ezetimibe	2077 (0.4)	133 (0.02)
Antidiabetic agents	129 816 (24.1)	18 793 (3.5)
Aspirin	146 641 (27.2)	36 973 (6.9)
Anti-arrhythmic agents	20 961 (3.9)	11 436 (2.1)
NSAIDs	205 971 (38.2)	89 882 (16.7)
Proton pump inhibitors	87 041 (16.1)	48 796 (9.1)
Hormone replacement therapy or oral contraceptives	21 958 (4.1)	21 150 (3.9)
Oral corticosteroids	18 098 (3.4)	15 701 (2.9)
Antibiotics	49 306 (9.1)	37 394 (6.9)
Anticonvulsants	11 401 (2.1)	8282 (1.5)
Antipsychotics	5896 (1.1)	6291 (1.2)
Antidepressants	120 425 (22.3)	98 630 (18.3)
History of disease ever before, n (%)		
Hypertension*	329 257 (61.0)	124 621 (23.1)
Hyperlipidaemia	160 221 (29.7)	12 839 (2.4)
Diabetes†	130 198 (24.1)	18 962 (3.5)
Cardiovascular diseases	176 908 (32.8)	47 839 (8.9)
Cerebrovascular disease	60 552 (11.2)	17 110 (3.2)
Cancer	35 380 (6.6)	40 220 (7.5)
Psoriasis	20 821 (3.9)	17 095 (3.2)
Inflammatory bowel disease	5298 (1.0)	5297 (1.0)
COPD	21 165 (3.9)	20 866 (3.9)
Asthma	64 470 (12.0)	55 677 (10.3)
Dementia	5079 (0.9)	8611 (1.6)
Depression	75 507 (14.0)	50 671 (9.4)

*Diagnosis of hypertension or use of antihypertensive agents.
†Diagnosis of diabetes mellitus or use of antidiabetic therapy.
BMI, body mass index; COPD, chronic obstructive pulmonary disease; NSAIDs, non-steroidal anti-inflammatory drugs.

Table 2 Risk of systemic lupus erythematosus (SLE) in statin users compared with non-statin users aged ≥16 years

	SLE (n)	IR*	Age and sex-adjusted HR (95% CI)	Fully adjusted HR (95% CI)†
No statin use	98	0.6	1.00	1.00
Past statin use	24	1.0	1.70 (1.08 to 2.66)	1.39 (0.86 to 2.23)
Recent statin use	21	1.1	1.66 (0.99 to 2.78)	1.32 (0.76 to 2.28)
Current statin use	124	0.6	1.04 (0.78 to 1.38)	0.81 (0.57 to 1.15)
≤1 year	70	2.0	1.43 (0.97 to 2.10)	1.12 (0.73 to 1.72)
>1 year	54	0.3	0.86 (0.62 to 1.21)	0.66 (0.44 to 0.98)

*Incidence rate is calculated for each recency of statin use by dividing the number of events by the person time within each given recency of use.
†Adjusted for age, sex, practice, smoking, cardiovascular diseases, hyperlipidaemia, hypertension, diabetes and use of non-steroid anti-inflammatory drugs.
IR, incidence rate (per 10 000 person-years).

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