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Letter to the Editors

Statin use is associated with reduced depressive symptoms in Europeans, but increased symptoms in ethnic minorities in the UK: an observational study

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Proposed as potential mood-enhancing therapy [1], evidence linking statin use with depression remains conflicting [2]. Marked ethnic differences exist in rates of cardiovascular disease (CVD), depression and responses to some drugs [3, 4], and yet ethnic minority groups (EMGs) have been under-represented in statin trials and no studies have examined ethnic differences in the statin–depression relationship.

Cross-sectional data from a population-based tri-ethnic study [5] were available on 638 White Europeans, 487 South Asians and 208 African-Caribbeans. Depression (score of ≥4/10 on the ethnically-validated Geriatric Depression Scale [6]), and other psychosocial, behavioural, anthropometric and medication history data were collected. Statin use was identified by prescription from participant/GP records (as were CVD and hypertension). Diabetes was identified from medical records, diagnosis recall or oral glucose tolerance test [5].

Statin use was modelled as a predictor for depression in logistic regression analyses, with ethnicity by statin use interaction terms included. Models were also stratified by ethnicity. In a 77% male sample (mean age 70 years), 56% of participants were receiving statins (48% White European, 68% South Asian, 52% African-Caribbean). Of those on statins, South Asian and African-Caribbean participants were significantly more likely to report depression compared with Europeans (OR 2.00, 95% CI 1.25, 3.21 and 2.96, 95% 1.67, 5.24), respectively). The similar relationship between statin use and depression in South Asians and African-Caribbeans (Table 1) meant their data were pooled. In ethnically-stratified model 1, statin use was not related to depression in Europeans, whereas among EMGs, depression was significantly higher in people on statins (full sample: ethnicity–statin interaction, $P = 0.11$). After full adjustment, analyses showed a non-significant trend towards a protective effect of statin use on depression in Europeans and a deleterious effect in EMGs (full sample: ethnicity–statin interaction, $P = 0.041$).

A few explanations could exist for this differential relationship between statin use and depression. '*Presentation bias*' (different presentation of depression by a particular ethnic group to health care professionals could increase the likelihood of detection/treatment of other conditions) was explored with depression somatization, by correlating depressive symptoms with self-reported health. No group demonstrated elevated depression somatization, with the same strength and direction of relationship observed across all groups. Depression was measured using a screening tool rather than clinical diagnosis; often a study limitation, here it reduced 'presentation bias' likelihood, since depression may not have been discussed with GPs.

Another possibility is that the statin–depression association was confounded by CVD due to the established bi-directional relationship between depression and CVD. To examine whether, among EMGs, depression is a stronger predictor of CVD or *vice versa*, we adjusted for CVD in the main models (4–5) and stratified the fully-adjusted model by CVD status in sensitivity analyses. The same results were observed across groups irrespective of CVD prevalence (results not shown), indicating that the statin–depression link did not result from statin use acting as a proxy for CVD.

Therefore, our results may reflect a true ethnic difference in the impact of statins on depression. Ethnic differences in response to statins could elicit direct and indirect effects on depression, i.e. across ethnicities, there could be a differential influence of statins on lipid sub-fractions or of statins' protective effects on cerebrovascular processes, both of which could impact mood. Alternatively, EMGs could be more vulnerable to statin-induced side effects, influencing depression.

EMGs receiving statins in this sample were over twice as likely to report depression as Europeans. To our knowledge, this is the first study to examine ethnic differentials in the statin–depression relationship. We acknowledge our dataset's limitations, in particular its cross-sectional nature precluding causal interpretations and limited study power. However our aim was to highlight these findings and we urge others to interrogate existing clinical trial/health care databases, as well as including sufficient EMG numbers in future studies. Given the

Table 1

Risk of major depression according to statin use across ethnic groups

	White European (n = 638)	South Asian and African Caribbean† (n = 695)	
Not on statins % depressed	9.6	11.9	
On statins % depressed	9.8	19.5*	
	Risk of depression according to statin use OR (95% CI)		**Ethnic–statin interaction P value**
Model 1: age and gender	1.03 (0.60, 1.76)	1.91 (1.22, 3.01)‡	0.11
Model 2: model 1 + manual labour and stressful life events	0.96 (0.56, 1.65)	1.89 (1.20, 2.99)	0.087
Model 3: model 1 + smoking, alcohol intake and physical activity	0.84 (0.47, 1.49)	1.81 (1.14, 2.87)	0.085
Model 4: model 1 + BMI, diabetes, hypertension and CVD	0.58 (0.29, 1.15)	1.66 (0.98, 2.83)	0.036
Model 5: Full adjustment	0.54 (0.26, 1.13)	1.67 (0.97, 2.88)	0.041
In sample with total cholesterol > 3mmol l^{-1}§:			
Full adjustment	0.52 (0.24, 1.13)	1.60 (0.91, 2.79)	0.049

Significant ethnic group difference of $P < 0.05$. BMI body mass index. CVD cardiovascular disease. †South Asians only: % depressed - not on statins = 10.2%, on statins = 17.9%. For African-Caribbeans only: % depressed - not on statins = 14.6%, on statins = 24.8%*. ‡South Asians only: OR 1.94, 95% CI 1.07, 3.52, P = 0.13 for ethnic–statin interaction. African-Caribbeans only: OR 2.19, 95% CI 1.05, 4.57, P = 0.16 for ethnic–statin interaction. §To assess the potential confounding role of very low cholesterol, the sample was restricted to those participants with total cholesterol of >3mmol l^{-1}.

pervasiveness of statins and predisposition towards CVD and depression among certain groups [3, 4], this finding has potentially serious implications for the mental health of thousands of EMGs being treated with statins.

Competing Interests

All authors have completed the Unified Competing Interest form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare no support from any organization for the submitted work, no financial relationships with any organizations that might have an interest in the submitted work in the previous 3 years and no other relationships or activities that could appear to have influenced the submitted work.

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