

## CORRESPONDENCE

e-mail submissions to [correspondence@lancet.com](mailto:correspondence@lancet.com)

## Dementia and statins

Sir—The case-control observational study by Hershel Jick and colleagues (Nov 11, 1627)<sup>1</sup> raises some important questions over and above researchers' own caveats.

First, the diagnosis of dementia was based on a clinical assessment by family physicians, which is only a first step towards a diagnosis. Quantitative screening is needed to ascertain loss of cognition, such as the mini-mental state examination.<sup>2</sup> A score of less than 24 should lead to a more specific diagnostic assessment.<sup>3</sup> Moreover, causes of cognitive failure other than dementia proper, should be excluded, such as pharmacologically or toxicologically induced disturbances of brain function.

Second, Jick and colleagues mention the possibility that the reduced risk for statins could be caused by characteristics of the statin recipients that are associated with a lower risk of dementia. They should have expanded this point, since they were close to touching on the fundamental weakness of the study: bias by indication. Sociological experience shows a group of intelligent, well informed, alert, mostly urban patients. If they develop hypercholesterolaemia, they frequently demand and obtain the most modern lipid-lowering agents. By contrast, other patients, generally of lower socioeconomic status, are less aware of cardiovascular risk factors and treatment trends. In the Systolic Hypertension in Europe trial,<sup>4</sup> age on leaving school was a major determinant of cognitive function, measured by the mini-mental state questionnaire.

This type of preordained selection might partly explain the negative association between dementia and the use of statins, rather than a pharmacological action of this drug class.

Willem H Birkenhäger, Ji-Guang Wang,

\*Jan A Staessen

Erasmus University, Rotterdam, Netherlands; and \*Study Coordinating Centre, Hypertension Unit, Campus Gasthuisberg, University of Leuven, B-3000 Leuven, Belgium (e-mail: [jan.staessen@med.kuleuven.ac.be](mailto:jan.staessen@med.kuleuven.ac.be))

1 Jick H, Zornberg GL, Jick SS, Seshadri S, Drachman DA. Statins and the risk of dementia. *Lancet* 2000; **356**: 1627–31.

2 Folstein MF, Folstein SE, McHugh PR. "Mini-Mental State": a practical method for grading the cognitive state of patients for the

clinician. *J Psychiatr Res* 1975; **12**: 189–98.

3 Diagnostic and Statistical Manual of Mental Disorders, 4th edn. Washington DC, USA: American Psychiatric Association, 1994.

4 Forette F, Seux ML, Staessen JA, et al. Prevention of dementia in randomised double-blind placebo-controlled Systolic Hypertension in Europe (Syst-Eur) trial. *Lancet* 1998; **352**: 1347–51.

Sir—Hershel Jick and colleagues<sup>1</sup> found a striking inverse association between the use of statins and dementia.<sup>1</sup> They admit that case-control studies merely identify associations, not causal links, which could be the case in their study.

Since 87% of participants were older than 70 years, the use of statins in this population was probably affected by many factors, including state of health, quality of life, and prognosis. Healthy people in their 70s will not be denied statins. Indeed treatment in such individuals at high risk of cardiovascular events has a low number needed to treat, which suggests cost effectiveness.<sup>2</sup> Nearly all guidelines advise caution in prescribing statins to people with non-cardiovascular diseases that impair prognosis for a healthy life.<sup>3</sup> A person who has dementia is much less likely than someone without to be prescribed statins. In Jick and colleagues' study, only 12 (4.2%) of 284 cases were receiving statins, compared with 100 (9.3%) of 1080 controls. The proportion of people receiving statins is strikingly low among cases and fairly low even in the controls.

Many randomised prospective trials of statins shed light on the effect of these drugs on the development of dementia. Jick and colleagues should nevertheless be congratulated on highlighting an important imbalance in the prescription of statins. If it is confirmed, what should be debated is whether statins should or should not be withheld from people with dementia.

BMYC and CRK are council members of the Institute of Cardiovascular Science and Medicine, University of Hong Kong.

\*Bernard M Y Cheung, Cyrus R Kumana

Department of Medicine, University of Hong Kong, Queen Mary Hospital, Pokfulam, Hong Kong, China (e-mail: [mycheung@hkucc.hku.hk](mailto:mycheung@hkucc.hku.hk))

1 Jick H, Zornberg GL, Jick SS, Seshadri S, Drachman DA. Statins and the risk of dementia. *Lancet* 2000; **356**: 1627–31.

2 Kumana CR, Cheung BMY, Lauder IJ. Impact of statins in different circumstances. *JAMA* 1999; **282**: 1899–901.

3 Second report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel II). *Circulation* 1994; **89**: 1329–445.

## Authors' reply

Sir—In reply to W H Birkenhäger and colleagues, we point out that in another study of the effects of oestrogen-replacement therapy on the development of Alzheimer's disease we carefully assessed 80 case records of patients recorded as having dementia or Alzheimer's disease, through the General Practice Research Database. 90% met stringent criteria for the diagnosis.<sup>1</sup>

We controlled for patients' general practice in our analysis. Although general practice provides only an indirect indicator of socioeconomic status and education, we suspect that it substantially controls for these factors, as well as for the acumen of and criteria for diagnosing dementia of the individual physicians. We suggest that specific choice of drugs, as well as the decision to treat hyperlipidaemia is not involved in any selection bias, since treatment with non-statin lipid-lowering agents had no effect on the risk of dementia.

Birkenhäger and colleagues allude to the pharmacological action of statins. However, statins have beneficial effects on vascular endothelium through the increase in activity of endothelial nitric-oxide synthase and the reduction of endothelin-1,<sup>2,3</sup> and their effects in reducing heart disease and stroke<sup>4,5</sup> exceed their lipid-lowering actions.

B M Y Cheung and C R Kumana seem to assume that we studied prevalent cases of dementia. We included only incident cases of dementia. Therefore the data on statin use relate only to the time before the diagnosis. The indication for use was hyperlipidaemia in all statins users. The negative association between statins and dementia was present for all durations of treatment, including 4 or more years before the date of first diagnosis. Our results provide information on the use of statins before