DEPRESCRIBING STATINS-IS IT ETHICAL?

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midlife glucose levels and reducing incipient risk of dementia. Although Cintosun and colleagues note that a large number of participants and the ability to follow them for up to 4 decades strengthened our observational study, they present some methodological concerns, which we would like to address. We do not claim to make any causal inferences about random measured blood glucose levels and dementia-related death but point to a clear risk association. Cintosun and colleagues do not mention that we adjusted for education (related to socioeconomic status) and cardiovascular disorders but were unable to include data on hospitalizations. Adjusting for relevant confounders is important, but we do not view it likely that factors such as vitamin deficiencies or thyroid disorders would alter the association between glucose level and dementia-related death, as Cintosun and colleagues suggest. We performed a wide assessment with variables such as depressive symptoms, anxiety, and alcohol, including a sensitivity analysis restricting the follow-up to the age of 65 (early-onset dementia), and the results did not differ to a significant degree. Although the above-mentioned factors are deemed independent risk factors of dementia, their importance when evaluating high glucose levels and dementia-related death is uncertain. In response to Cintosun’s concern regarding the use of dementia-related death, we included all registered deaths with dementia on the death certificate as the underlying or accompanying cause, and in understanding the mechanism of cause-specific dementia mortality, the use of dementia-related death as an outcome in observational studies is considered valid. Furthermore, a validation study of Norwegian death certificates in dementia in nursing home residents showed high specificity. Using data from a large case-control study of dementia-related death (n = 561), we found that the risk of dementia-related death in individuals with various apolipoprotein E genotypes were comparable with risk ratios from studies using clinical diagnoses as the end point, suggesting that dementia-related death could prove useful as a proxy for clinical dementia diagnoses in epidemiological studies.

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To the Editor: I believe that Gnjidic and colleagues may not have given a fair account of the benefits of statin treatment in older adults. In a population-based study, they did not find significantly less dementia in statin users (although point estimate was clearly below unity) but nevertheless noted significantly lower mortality in statin users than nonusers. The totality of the evidence in older adults, and even in frail individuals and those with multimorbidity, supports this finding. Gnjidic and colleagues may also have misinterpreted the review of Desai and colleagues by stating that there is growing evidence of adverse effects of statins.

Why “growing”? The possibility of adverse effects on muscle has been known since statins were introduced, and to the best of my knowledge, nothing new has emerged, except that statins do not cause all muscle aches during statin treatment. The possibility of diabetes mellitus is a more recently recognized adverse effect, but the clinical significance of statin-associated diabetes mellitus is unknown because, paradoxically, statin treatment improves the prognosis of individuals with diabetes mellitus. There is a list of conditions linked to statin use, such as cataract and erectile dysfunction, but results are inconsistent, and confounding by indication cannot usually be excluded. Alternatively, other potential benefits such as fewer complications from venous thromboembolism, less pancreatitis, less chronic obstructive pulmonary disease-related mortality, and lower prostate cancer-specific mortality have emerged, but these possibilities have received much less attention.

Given the lower mortality of older statin users in many studies, including the study of Gnjidic and colleagues, is it ethical to suggest trials—for individuals who...
are not in a terminal stage—in which statins are depre-
scribed?

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RESPONSE TO TIMO E. STRANDBERG
To the Editor: We thank Professor Strandberg1 for his valuable comments and interest in our recently published letter to the editor.2 The aim of our study was to deter-
mine associations between statin use and incident dementia according to disease severity and multimorbidty, but since the publication of our letter, a new Cochrane review has shed additional light on the topic.3 This Cochrane review concludes that current evidence does not support the role of statins for prevention of dementia, which is in agree-
ment with our study findings.

Ensuring rational statin use in older adults is challeng-
ing because clinical trial data in older adults with multimor-
bidity and polypharmacy are limited. In addition, as people age, treatment goals may change from extending duration of life to maintaining function and quality of life.4 Therefore, more research is warranted to generate information about benefits and side effects of statins in real-world data from older adults. Research into deprescribing medications is an emerging area and requires robust evidence to inform clin-
ical decisions.5 The need for evidence-based deprescribing guidelines for a range of medication classes including statins was highlighted in a recent Delphi process.6

We appreciate Professor Strindberg’s comments, and we support more research efforts to inform rational drug prescribing for older adults worldwide.

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