[Three of the authors respond:]

We thank Micheal Guirguis for his valuable comments on our paper.[1] One of the limitations of our work, which we discussed in the article, was that we did not assay the active metabolite of clopidogrel directly but, rather, performed a platelet aggregation test with adenosine diphosphate as an indirect marker of the active clopidogrel metabolite, as done by previous investigators. Therefore, we were not able to rule out the involvement of factors other than the interaction of the active metabolite and the platelet adenosine diphosphate receptor.

We agree with Guirguis that pharmacokinetic–pharmacodynamic data are needed to confirm individual variations in clopidogrel metabolism. However, such data have not yet been collected because of the difficulty in assaying the active metabolite of clopidogrel. Some researchers are investigating clopidogrel metabolism using various methods,[2–4] and we are looking forward to applying their findings to clinical studies in the near future.

We appreciate the suggestion by Craig McLachlan and associates of the possibility of rebound atherothrombotic events after cessation of clopidogrel administration in susceptible people, such as those with the non-expressor genotype for the 3A5 isoenzyme of the cytochrome P450 3A system. In our study, patients in the non-expressor group experienced more atherothrombotic events than those in the expressor group, and events after 1 month occurred only in the non-expressor group. However, all patients who experienced atherothrombotic events after 1 month were taking both clopidogrel and ASA at the time. Therefore, our data cannot be used to address the issue of whether people with the non-expressor genotype for the 3A5 isoenzyme of the cytochrome P450 3A system may be more vulnerable to atherothrombotic events after cessation of clopidogrel administration. However, it is possible that these patients are more sensitive to rebound effects on platelet aggregation in the setting of inhibition of the CYP3A4 isoenzyme. The issue raised by McLachlan and associates is an important one and warrants further study.

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Driving and dementia

As a result of the work of Nathan Herrmann and colleagues[1] we now have an improved understanding of the factors involved in driving cessation among people with dementia. Of particular interest was the finding that living in a jurisdiction with mandatory reporting did not significantly increase the risk of driving cessation. This leads one to question the utility of mandatory reporting, which may deter patients with dementia from relaying concerns about deterioration in their level of functioning to their physician.

Perhaps we are missing a more important issue associated with driving cessation if we focus unduly on safety rather than on mobility. Driving cessation is associated with significant difficulty in accessing services[2] and is an independent risk factor for entry to a nursing home.[3] Easy access to transportation is a key factor in maintaining the health and independence of older people and promotes social inclusion.[4,5]

Concern has been expressed that older people are discriminated against in public discussions about driving and health because of the emphasis on safety at the expense of a balanced perspective of the importance of both mobility and safety to health and social inclusion.[6] As physicians, we need to be mindful of the enabling aspects of driving assessment (e.g., by an appropriate focus on arthritis, vision and medication review[7]), as well as the need to actively support other forms of facilitated transport (people who stop driving are usually not able to manage the rigours of public transportation).[8] It is also important that any public health discourse support outdoor mobility and transportation for our patients.

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