

# Correspondence

## First, do no harm

I welcomed the special article by Bailey *et al.*<sup>1</sup> I share the authors' concern over the 'scandal of premature mortality' and note their recommendation to urgently review antipsychotic medication when certain adverse effects are experienced (rapid early weight gain or cardiometabolic blood disturbance). The authors do not implicate any particular antipsychotics, but guidelines suggest that clozapine and olanzapine are the most likely antipsychotics to be associated with these side-effects.<sup>2</sup> Neither do the authors suggest what the outcome of such a review might be, although I deduce it is implicit in the recommendation that reducing the dose or switching antipsychotic would be likely possible outcomes. I do, however, have one concern with this suggestion which relates to the risk–benefit balance of antipsychotics.

Tiihonen *et al.*<sup>3</sup> present data from a large study which examined the effects of antipsychotics on all-cause mortality, suicide and deaths from ischaemic heart disease; one strength of this study is the examination of all-cause mortality. The researchers found that in people with schizophrenia antipsychotic use is associated with a reduced risk of death (by about a third) when compared with no antipsychotic treatment (hazard ratio 0.68, 95% confidence interval 0.65–0.71); clozapine was associated with a substantially lower risk of all-cause mortality as well as suicide. No pronounced differences between antipsychotics (including clozapine and olanzapine) were noted for mortality from ischaemic heart disease.

Thus, if a patient is switched from clozapine to an alternative antipsychotic, their risk of death may in fact be increased rather than reduced. Further, switching antipsychotics (even olanzapine) does not appear to be associated with a reduction in risk of all-cause mortality or even death from ischaemic heart disease. Given that switching antipsychotic medication is associated with harm, for example by increasing risk of relapse,<sup>4</sup> this leads me to question the wisdom of Bailey *et al.*'s recommendation to urgently review the antipsychotic prescription in the circumstances they describe.

There may be other reasons for switching antipsychotics but Tiihonen *et al.*'s findings suggest that reducing the 'scandal of premature mortality' is not one of them. This raises a dilemma for practising clinicians as to how to proceed in these circumstances.

- 1 Bailey S, Gerada C, Lester H, Shiers D. The cardiovascular health of young people with severe mental illness: addressing an epidemic within an epidemic. *Psychiatrist* 2012; **36**: 375–8.
- 2 Taylor D, Paton C. *Maudsley Prescribing Guidelines in Psychiatry* (11th edn). Wiley–Blackwell, 2012.
- 3 Tiihonen J, Lönnqvist J, Wahlbeck K, Klaukka T, Niskanen L, Tanskanen A, et al. 11-year follow-up of mortality in patients with schizophrenia: a population-based cohort study (FIN11 study). *Lancet* 2009; **374**: 620–7.
- 4 Weiden P. Switching antipsychotic medications: not enough, too often, or just right. *Am J Psychiatry* 2011; **168**: 882–4.

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## Cardiovascular disease and schizophrenia: do we know enough?

We find the aims of Bailey *et al.*<sup>1</sup> laudable. However, we would like to add a note of caution. Our main concern is that many of the recommendations are not based on evidence. Bailey *et al.* assume that people with schizophrenia are the same as the general population, the so-called 'ecological fallacy'. The authors describe potential differences such as the increased risk of metabolic abnormalities including diabetes which pre-date the prescription of antipsychotics. Therefore, it cannot be assumed that what is effective in the general population will be equally effective in people with schizophrenia. For example, controversy surrounds the diabetogenic effect of statins in the general population and Nielsen *et al.*<sup>2</sup> demonstrated that lipid-lowering medication was a greater risk factor for the development of diabetes in a cohort of people with schizophrenia than was 'high-risk' antipsychotic medication. Furthermore, a Finnish cohort study<sup>3</sup> replicated the finding of poor outcomes for cardiovascular disorders in patients with schizophrenia and reiterated that the excess morbidity could not be explained by prescription rates of lipid-lowering drugs.

Bailey *et al.* present a comprehensive overview of cardiovascular risk management and although we may be guilty of the same assumption as the authors, we would like to emphasise the importance of cardiorespiratory fitness as a modifiable risk factor. Its significance is often neglected or understated, with guidelines emphasising medical management. However, Kilbourne *et al.*<sup>4</sup> reported that physical inactivity (hazard ratio 1.66, 95 CI 1.59–1.74) was a greater risk factor than smoking (hazard ratio 1.32, 95% CI 1.26–1.39) for cardiovascular mortality in a cohort of people with schizophrenia. The complexity of mortality risk factors in early schizophrenia is further illustrated when one examines the relationship between body mass index (BMI) and suicide in the general population. Suicide, and not cardiovascular disease, is the major mortality risk in younger people with schizophrenia. An emerging paradox is linking an inverse association between BMI and suicide risk in the general population; hence a lower BMI may reduce cardiovascular risk but increase suicide risk.<sup>5</sup> Whereas there is emerging evidence that patients with schizophrenia are receiving medical treatment for cardiovascular risk factors,<sup>3</sup> there is little evidence so far that this has reduced mortality.<sup>1</sup>

If the people with schizophrenia are seen as a high cardiovascular risk population with attendant early and aggressive medical intervention, the impact on core symptom outcomes needs to be studied as some of the antipsychotics with the greatest liability for metabolic side-effects are also the more effective. Clearly, more research is required to understand the relative importance of mortality risk factors in schizophrenia and their management.<sup>5</sup>

### Declaration of interest

R.E.H. and M.B. have received research funding and hospitality from pharmaceutical companies. H.W. is an ex-Lilly employee.