We would suggest that given the overall poor quality of studies found in the review there seems to be no rationale for going on to conduct a meta-analysis. One common pitfall of any meta-analysis is that if you put only poor-quality data in, you will get poor-quality data out. Consequently, this meta-analysis would seem to add little to the current evidence base with regard to antipsychotics and diabetes, except, perhaps, the confirmation that the studies on this subject are heterogeneous and generally of poor quality.

If one does want to consider whether a significant relationship exists between antipsychotic use and diabetes, or a metabolic syndrome, then the CATIE study[2] would seem to provide reasonably robust evidence that such a relationship does exist. This large, randomised, prospective study, carried out over a period of 18 months, has data collected at baseline and following the introduction of antipsychotic, and demonstrates clinically and statistically significant adverse changes in blood glucose, weight and cholesterol. This is particularly the case for those patients commenced on olanzapine.

Declaration of interest

R.P. has received speakers' honoraria from Janssen-Cilag, Eli Lilly and Wyeth Pharmaceuticals.

1 Smith M, Hopkins D, Peveler RC, Holt RI, Woodward M, Ismail K. First- *v.* second-generation antipsychotics and risk for diabetes in schizophrenia: systematic review and meta-analysis. *Br J Psychiatry* 2008; **192**: 406–11.

2 Lieberman JA, Stroup TS, McEvoy JP, Swartz MS, Rosenheck RA, Perkins DO, et al. Effectiveness of antipsychotic drugs in patients with chronic schizophrenia. *N Engl J Med* 2005; **353**: 1209–23.

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Authors' reply: We acknowledge Smith & Porter's interest in the reasons for why we did not focus on the relationship between merely starting any antipsychotic and developing diabetes, but instead reviewed the evidence for an association between diabetes and type of antipsychotic medication. There has been increasing concern that second-generation antipsychotics may be more diabetogenic than first-generation antipsychotics in patients with schizophrenia. Despite this concern, there is a lack of good evidence to support this apparent phenomenon and so it was essential to carry out our systematic review prior to developing guidelines for diabetes screening and management.

We agree with Smith & Porter that our paper has found strong heterogeneity between studies which is clearly an important finding from our study. It is only by undertaking systematic reviews that one can determine that heterogeneity exists. Therefore, without our systematic review this would not have been clear. Our meta-analysis uses random effects methodology, which means we have analysed the average effect over the studies. This is a meaningful concept in the presence of heterogeneity. As for looking at absolute risks, the heterogeneity between studies is so great as to make even random effects pooling absurd. This is why pooled analyses virtually always pool relative risks rather than risk differences.

Smith & Porter have highlighted our conclusions that methodological limitations were found in most studies. As current evidence is poor, it should not be used alone in making clinical decisions concerning diabetes screening and management for patients with schizophrenia. Regardless of whether first- or second-generation antipsychotics are prescribed, routine screening for diabetes in all patients with schizophrenia should be undertaken.

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Pharmacology and human morality

Maybe I am missing something but what is new in the proposition Spence has outlined?[1] When a Yanomani tribesman snorts a powerful concoction of hallucinogens he does so as part of a ritual that includes the shamanistic healing of others in the tribe and maintaining tribal cohesion through tradition. When a footballer plays on despite injury, with pain relieved by analgesia, he does this in part for his team and fans. When a Peruvian highlander chews coca leaves so that he can work longer hours he does so to keep his family fed; and the same applies to the kratom user in the Far East. When millions of soldiers took amphetamines to enable them to fight for longer hours, thereby exposing themselves to ever greater dangers, they did so to win what they believed to be just wars. When a mother solicits fertility treatment so as to produce a child that will not only add to the family, but also potentially save the life of another sibling, the use of these potentially dangerous drugs is largely driven by the mother's need to save the other child. When groups of men gather every afternoon in the Yemen and chew qat, this is a social activity enhanced by the use of qat. In the Middle East, coffee shops have always served this purpose, providing socially stimulating conversation, and do so in Europe to this day. Tobacco has had a similar use in many countries and alcohol has done much the same, despite the harm associated with the use of both of these substances. Psychiatrists, on a small scale, have started to use what some term empathogens (i.e. MDMA) so that they can better understand and help their patients (although the less charitable question their motives).

I think we would be splitting hairs to argue that taking a drug to achieve a moral end is fundamentally different from achieving a moral end through use of a drug; they exist on a continuum. Drugs simply allow us to explore and alter our behaviour and thoughts. How we use this allowance is up to us.

1 Spence SA. Can pharmacology help enhance human morality? *Br J Psychiatry* 2008; **193**: 179–80.

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In a recent editorial, Spence stated that the pharmacological interventions currently available in psychiatry also improve moral behaviour.[1] He subsequently argued that there is no fundamental difference with moral enhancement therapy, medication specifically developed to increase moral behaviour. Spence gave the example of a patient who continues to take antipsychotic medication because he knows he can be violent when unwell and he wants to prevent risks to others.

Spence asserted that whether an intervention assists in 'moral enhancement' or not crucially depends upon the goals of the

patient concerned, i.e. the 'ends' he or she is pursuing. However, 'the goals of the patient concerned' can be problematic in the cognitive enhancement debate and this formulation can conceal important ethical issues.

Spence mentioned the concept of meta-responsibility, the fact that somebody can be responsible for becoming irresponsible, in the case of the example that somebody can be responsible for deciding not to take medication.[2] In a somewhat similar way as Mitchell, Frankfurt[3] discussed the difference between first- and second-order desires. One can have a desire for smoking, which is a first-order desire. One can also have a second-order desire, namely the desire not to have the desire for smoking.

One could argue that in the future pharmacological interventions might be able to interfere with second-order desires. Second-order desires according to Frankfurt are the core aspect of personhood. Even if one does not want to go as far as Frankfurt in stating that the second-order desires determine personhood, moral enhancement treatment can be problematic if it could change second-order desires. In that case, people's goals would alter. Contrary to Spence's view, moral enhancement pharmacotherapy can be quite controversial if it interferes with second-order desires.

1 Spence SA. Can pharmacology help enhance human morality? *Br J Psychiatry* 2008; **193**: 179–80.

2 Mitchell EW. Madness and meta-responsibility: the culpable causation of mental disorder and the insanity defence. *J Forensic Psychiatr* 1999; **10**: 597–622.

3 Frankfurt H. Freedom of the will and the concept of a person. *J Philos* 1971; **58**: 5–20.

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Author's reply: The varied correspondence precipitated by my editorial has invoked a great many issues. However, the sole aim of my original piece was to examine whether a current concern with the putative cognitive-enhancing effects of certain medications might be redirected towards the possible enhancement of other human attributes such as moral behaviour.[1] Should this be of interest to psychiatrists? Well, I believe that there is something worth scrutinising within the medical consultation when a patient (a moral agent) considers the likely impact of their future conduct upon others, and the various means via which such conduct might be modulated. Drugs are not the only means by which such modulation might occur but they do provide an interesting example. Nevertheless, as I acknowledged in the editorial, such a juxtaposition of pharmacology with morality risks provoking reflexive responses: strong opinions unencumbered by reflection.

Clearly, the situation in the consulting room with an antisocial or aggressive man is rather different from that outlined by Al-Adwani. We are not talking about the social consumption of stimulants and intoxicants or the enforced ingestion of medicines by combatants in order for them to fight for longer. We are talking about what individual patients might choose to do about their own future behaviours, sometimes under very difficult circumstances; indeed, an antisocial male may not even enjoy a community of peers with whom to consume coca, kratom or qat. I apologise if this was not sufficiently obvious.

With respect to Frankfurt's conjecture that we might all harbour first- and second-order desires, Hubbeling's point is well taken: that if we posit such a hierarchy of desiring processes, then an individual's second-order (pro-social) desire to control an aberrant first-order desire (to react aggressively, to assault someone) might utilise a pharmaceutical agent only, to discover (later on) that the latter had modulated not only the first-order construct but the second-order one as well. The questions arising, here, are: (a) whether such first-order and second-order desires enjoy any empirical demonstration of their existence; and (b) whether, if second-order desires really exist, we are currently managing to avoid affecting them when we prescribe psychotropic medications or engage in any form of dynamic psychotherapy. To my mind, this makes the central question of even greater interest and one deserving of further empirical exploration.

1 Spence SA. Can pharmacology help enhance human morality? *Br J Psychiatry* 2008; **193**: 179–80.

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Duration of untreated psychosis in LAMI countries

I have some reservations regarding the conclusions drawn by Large *et al*[1] in their study on duration of untreated psychosis in low- and middle-income (LAMI) countries. This is because the samples are not really representative of the occurrence of psychosis. It seems, people with untreated psychosis who have recovered or remitted without antipsychotic or medical treatment are excluded from this study. There is enough evidence that in LAMI countries, a substantial proportion of patients with psychosis seek treatment from traditional healers,[2] use indigenous methods based on their non-biomedical beliefs[3] or pathways to care.[4,5] Perhaps, many of those who fail to respond to these methods seek psychiatric help. Thus, the sample which reaches psychiatric services is a biased one. In clinical practice, we do encounter patients who have had previous episodes of psychosis which remitted spontaneously or by indigenous methods. Studies on duration of untreated psychosis should be community or general population based to overcome the confounding effects of non-psychiatric treatments and biased sampling. This is true more so for LAMI countries where such non-medical services are popular, in contrast to high-income countries[6] with well-organised health services, where any patient with psychosis is likely to reach psychiatric services without the pathway to care through non-psychiatric methods. This limitation needs a mention by the authors.[1]

1 Large M, Farooq S, Nielssen O, Slade T. Relationship between gross domestic product and duration of untreated psychosis in low- and middle-income countries. *Br J Psychiatry* 2008; **193**: 272–8.

2 Razali SM, Mohd Yasin MA. Complementary treatment of psychotic and epileptic patients in Malaysia. *Transcult Psychiatry* 2008; **45**: 455–69.

3 Sarvanan B, Jakob KS, Deepak MG, Prince M, David AS, Bhugra D. Perceptions about psychosis and psychiatric services: a qualitative study from Vellore, India. *Soc Psychiatry Psychiatr Epidemol* 2008; **43**: 231–8.

4 Kulhara P. Transcultural variations in schizophrenia: some research issues. *Indian J Psychiatry* 2001; **43**: 1–4.

5 Chong SA, Mythili, Lum A, Chan YH, McGorry P. Determinants of duration of untreated psychosis and the pathway to care in Singapore. *Int J Soc Psychiatry* 2005; **51**: 55–62.

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