an overall increased risk for birth defects with first-trimester exposure to any selective serotonin reuptake inhibitors but later studies with more efficient designs such as the case–control approach started showing low-to-moderate increased risks for the more commonly occurring birth defects such as heart defects, neural tube defects and oral clefts. Therefore, using a cohort approach would have resulted again in a null finding, contrary to Rajkumar & Jacob's comments.

We excluded pregnancies ending with abortion or miscarriage per design since malformation outcomes of these foetuses were not available in the Quebec Pregnancy Registry. We agree that this resulted in prevalent cases of malformations in our study but this is highly comparable to studies performed in similar populations. We do not, however, agree that this methodological choice resulted in biasing our study estimates towards the null. Indeed, although Hemels et al[3] reported an association between antidepressant use during pregnancy and risk of spontaneous abortion, this was based on women's self-report and likely resulted in an overestimation of the rate of miscarriage and an underestimation of the rate of abortion, hence a significant association.

Major congenital malformations are structural abnormalities that affect the way a person looks and require medical and/or surgical treatment. Minor defects are abnormalities that do not cause serious health or social problems. Major defects were the focus of interest in our study and, although the risk of minor malformations is interesting, it is a different research question. Several other authors have previously made this distinction.[4,5]

We agree that results from observational studies always need to be interpreted with caution. However, given that from an ethical point of view it is almost impossible to randomise pregnant women to receive medications not known to be safe for the foetus, the collection and follow-up of observational data is the only ethical way to close the knowledge gap between the limited value of animal studies and human pregnancy exposures.

Finally, our study was not designed to look at the effect of the duration of specific antidepressants on the risk of specific major congenital malformations. Therefore, we only looked at duration of antidepressant use during the first trimester of gestation and its risk for major congenital malformations, all types and all malformations combined. Results should be interpreted in this context.

1 Ramos E, St-André M, Rey E, Oraichi D, Bérard A. Duration of antidepressant use during pregnancy and risk of major congenital malformations. Br J Psychitary 2008; **192**: 344–50.

2 Hernández-Díaz S, Hernán MA, Meyer K, Werler MM, Mitchell AA. Case-crossover and case-time-control designs in birth defects epidemiology. Am J Epidemiol 2003; **158**: 385–91.

3 Hemels MEH, Einarson A, Koren G, Lanctôt KL, Einarson TR. Antidepressant use during pregnancy and the rates of spontaneous abortions: a meta-analysis. Ann Pharmacother 2005; **39**: 803–9.

4 Simon GE, Cunningham ML, Davis RL. Outcomes of prenatal antidepressant exposure. Am J Psychiatry 2002; **159**: 2055–61.

5 Chambers CD, Johnson KA, Dick LM, Felix RJ, Jones KL. Birth outcomes in pregnant women taking fluoxetine. N Engl J Med 1996; **335**: 1010–5.

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Structural equation modelling in developmental psychiatry

The paper Green & Dunn[1] may prove to be of merit in the interpretation of causal relationships between interventions and outcomes. In particular, the recommendation that randomised controlled trial (RCT) methodology should be embedded within statistical methods from observation studies is long overdue. Such an approach would greatly assist in the interpretation of results which seem completely counterintuitive to those in everyday clinical practice. One such result is the finding of Byford et al[2] that cognitive–behavioural therapy provides no added or separate advantage to selective serotonin reuptake inhibitors in the treatment of adolescent depression.

I have a quibble with the length of time it has taken for basic concepts on causality introduced by Green & Dunn to appear in psychiatric research. These concepts have been commonplace in social science research for more than 20 years and their section on causal inference in analysis is little more than a primer. For a more complete coverage of principles of causality, I can recommend Judea Pearl's book, *Causality: Models, Reasoning and Inference.*[3]

Is there any particular reason why Green & Dunn, having put their toes in the water by introducing basic concepts on causality, have not taken their paper further or are we to await a follow-up? In particular, why is there no mention of structural equation modelling, otherwise known as covariance structure analysis? Structural equation modelling has been extensively used in social science research for the past 20 years and adaptations of the method such as multiple-indicator, multiple-cause (MIMIC) seem to address the issues on confounding variables adequately without the need to revert to RCT methodology. It would be interesting to hear from Green & Dunn their thoughts as to how necessary would RCT methods be in developmental psychiatry research whenever a structural equation model is being employed.

1 Green J, Dunn G. Using intervention trials in developmental psychiatry to illuminate basic science. Br J Psychiatry 2008; **192**: 323–5.

2 Byford S, Barrett B, Roberts C, Wilkinson P, Dubicka B, Kelvin RG, White L, Ford C, Breen S, Goodyer I. Cost-effectiveness of selective serotonin reuptake inhibitors and routine specialist care with and without cognitive–behavioural therapy in adolescents with major depression. Br J Psychiatry 2007; **191**: 521–7.

3 Pearl J. *Causality: Models, Reasoning and Inference*. Cambridge University Press, 2000.

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Authors' reply: We thank Dr MacFarlane for his favourable comments on our views. The development of research designs that can rigorously test the complexities of mental health intervention and also have face validity to clinicians is at the centre of our concern. In a brief editorial we could do no more than whet the readers' appetites. There was no mention of structural equation modelling because of lack of space, and not because we do not have sympathies with the technique. In fact, one of us (G.D.) has taught structural equation modelling for nearly 20 years.[1] When used wisely and with correctly specified models, structural equation modelling approaches can be very powerful – but they do not obviate the need for good design (including the randomisation in an RCT). In particular, MacFarlane is mistaken when he suggests that the use of structural equation modelling (MIMIC)