those who withdrew, redo the intention-to-treat analysis and calculate dichotomous weight change outcomes. This, however, would still not resolve the basic problem with regard to quality in individual studies. Well-designed, large-scale pragmatic trials with longer periods of follow-up are needed before undertaking further review in this area, an implication which has been acknowledged by the authors.

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Dimple George, Academic CT3, Wolfson Research Institute, Durham University Queen's Campus, Stockton-on-Tees, UK. Email: georgedimple@hotmail.com; **J. G. Reilly**, **Mona-Lisa Kwentoh** Tees, Esk and Wear Valleys NHS Foundation Trust and School for Medicine and Health, Durham Univeristy Queen's Campus, Stockton-on-Tees, UK

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Authors' reply: We would like to thank George *et al* for their comments. However, we believe that some clarification is needed regarding the outcomes and procedures of our meta-analysis.

First, we agree that percentage of weight gain is a more appropriate measure to assess weight gain compared with body weight change. In fact, somewhere else we have pointed to 'the importance of reporting percentage of weight gain, as absolute body weight changes may be deceptive, concealing the real extent of this side effect on those who experience weight gain'.[1] To put it more simply, research shows that up to 80% of individuals being treated with antipsychotics suffer significant gain in body weight. As a result, patients taking antipsychotics are more likely to gain 20 kg than they are to lose 20 kg. Indeed, weight-management interventions do not usually produce weight loss but they attenuate antipsychotic-induced weight gain.[2] For these reasons, data on weight change is unlikely to overestimate the effectiveness of weight management interventions as George *et al* contend. To illustrate this further, in a previous randomised controlled trial (RCT) of weight-management interventions we assessed the proportion of patients that gained more than 7% of their baseline body weight. Patients in the control group gained 6.9 kg compared with 3.9 kg in the intervention group. These absolute gains were translated into 78.8% in the control group increasing their baseline weight by more than 7% *v.* 39.9% in the intervention group.[3]

George *et al* also commented on the quality of the included trials as a potential threat to the reliability of the results. First, it should be pointed out that only RCTs were included – in three of them we were able to pool relevant data with the help of the authors. Second, we performed several sensitivity analyses to determine the robustness of our findings to the exclusion of low-quality trials and exclusion of small trials.[4] The exclusion of these studies affected the overall effect size and confidence intervals only marginally. Importantly, there was notable consistency across all study estimates, which was reflected in the robustness of the findings across analytic methods. Thus, our findings are unlikely to be biased by these issues.

After examining all the available evidence, it is now possible to conclude that large-scale pragmatic trials with longer follow-up are needed to make further progress in this area as George *et al* state.

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2 Álvarez-Jiménez M, Hetrick SE, González-Blanch C, Gleeson JF, McGorry PD. Non-pharmacological management of antipsychotic-induced weight gain: systematic review and meta-analysis of randomised controlled trials. *Br J Psychiatry* 2008; **193**: 101–7.

3 Álvarez-Jiménez M, González-Blanch C, Vázquez-Barquero JL, Pérez-Iglesias R, Martínez-García O, Pérez-Pardal T, et al. Attenuation of antipsychotic-induced weight gain with early behavioral intervention in drug-naive first-episode psychosis patients. A randomized controlled trial. *J Clin Psychiatry* 2006; **67**: 1253–60.

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Mario Álvarez-Jiménez, ORYGEN Research Centre, University of Melbourne, Australia, and University Hospital 'Marqués de Valdecilla', Department of Psychiatry, University of Cantabria School of Medicine, Santander, Spain. Email: malvarez@unimelb.edu.au; **Sarah E. Hetrick**, ORYGEN Research Centre, University of Melbourne, Australia; **César González-Blanch**, University Hospital 'Marqués de Valdecilla', Department of Psychiatry, University of Cantabria School of Medicine, Santander, Spain; **John F. Gleeson**, ORYGEN Research Centre, and Department of Psychiatry, University of Melbourne, and NorthWestern Mental Health Programme, Melbourne, Australia; **Patrick D. McGorry**, ORYGEN Research Centre, University of Melbourne, Australia

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Aetiological significance of middle-ear disease in schizophrenia

We read the study by Mason *et al*[1] with great interest. The authors conclude that there is an association between middle-ear disease and schizophrenia which may have aetiological significance. However, the authors have based their conclusions on a case–control study, which is susceptible to biases and effects of confounding factors; we would like to raise concerns about these conclusions.

First, we would like to highlight the strong possibility of selection bias as this study design is particularly prone to it. In this case, at the sample selection stage, no precautions were taken to ensure that the person selecting the patients was masked to the study hypothesis. This could lead to bias towards selecting patients with middle-ear disease and schizophrenia.

Case–control studies are more susceptible to bias and confounding factors than are cohort studies. In order to establish the association, it is recommended that we should have an odds ratio >4,[2] because the higher the odds ratio, the stronger the association. However, Mason *et al* have concluded about the association when the odds ratio is <4, which could be as a result of bias alone. This raises strong doubts about the validity of the authors' conclusions.

We would request that the authors clarify these issues.

1 Mason P, Rimmer M, Richman A, Garg G, Johnson J, et al. Middle-ear disease and schizophrenia: case–control study. *Br J Psychiatry* 2008; **193**: 192–6.

2 Sackett DL, Straus SE, Richardson WS, Rosenberg W, Haynes RB. *Evidence-Based Medicine. How to Practice and Teach EBM*. Churchill Livingstone, 2000.

Ashok K. Jainer, Coventry & Warwickshire Partnership Trust, Caludon Centre, Coventry CV2 2TE, UK. Email: ashokjainer@hotmail.com; **Supriya M. Shivanandaswamy**, Coventry & Warwickshire Partnership Trust, Caludon Centre, Coventry, UK

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Author's reply: Jainer & Shivanandaswamy's comments about the problems of bias in case–control studies are well made. However, our study[1] was designed to avoid such problems by recruiting all patients with a likely diagnosis of schizophrenia in contact with general practitioners in a defined catchment area. There was no possibility of influencing the selection of individuals

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since they were all patients with a diagnosis of schizophrenia on a community mental health team's case-load.

The community mental health team concerned looked after an area of high socio-economic deprivation and the study included patients who had drifted down the social scale from more affluent rural areas where one would expect a lower prevalence of middle-ear disease. If there is any bias in this study it is likely to favour the null hypothesis rather than that suggested by Jainer & Shivanandaswamy.

In addition, perhaps the most striking finding in this study was the excess of left-sided middle-ear disease. In this case, the odds ratio of 4.15 meets the recommendation of Sackett *et al*[2] that an odds ratio of greater than 4 should be used to establish an association in case–control studies.

1 Mason P, Rimmer M, Richman A, Garg G, Johnson J, et al. Middle-ear disease and schizophrenia: case–control study. *Br J Psychiatry* 2008; **193**: 192–6.

2 Sackett DL, Straus SE, Richardson WS, Rosenberg W, Haynes RB. *Evidence-Based Medicine. How to Practice and Teach EBM*. Churchill Livingstone, 2000.

Peter R. Mason, Cheshire and Wirral Partnership NHS Foundation Trust, The Stein Centre, St Catherine's Hospital, Derby Road, Birkenhead CH42 0LQ, UK. Email: peter.mason@cwp.nhs.uk

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DSM–V: should PTSD be in a class of its own?

Principles of diagnostic taxonomy suggest that disorders of a specific class, or spectrum, should aggregate more with each other than with disorders from another class. Results of recent comorbidity studies raise questions about whether this is true for post-traumatic stress disorder (PTSD) – which has been classified as an anxiety disorder since DSM–III – and the implications for where the diagnosis should be located in DSM–V.

Several factor analyses of diagnostic data from epidemiological and clinical samples suggest that PTSD covaries more strongly with disorders defined by anhedonia, worry and rumination (i.e. the unipolar mood disorders and generalised anxiety disorder) than with ones characterised by pathological fear and avoidance (e.g. the phobias, panic/agoraphobia and obsessive–compulsive disorder).[1] However, classifying PTSD among these 'anxious-misery' disorders provides a poor fit to the data because PTSD is conditional on trauma exposure and, in new-onset cases, typically develops before its comorbid conditions. For example, when PTSD and major depression co-occur following trauma exposure, PTSD usually precedes or develops concurrently with the depression. New-onset major depression that develops in the wake of trauma rarely precedes or develops in the absence of PTSD.[2] This implies a causal influence of PTSD on comorbid psychopathology and suggests a distinct phenomenology which should be reflected in its diagnostic class membership within DSM.

Developmental studies have shown that adult psychopathology is often foreshadowed by childhood and/or adolescent problems in the same domain. Along these lines, many adults with anxiety disorders report histories of juvenile anxiety disorders but they do not typically report juvenile externalising disorders. The exception to this is found among samples of individuals with PTSD where adult patients frequently have histories of childhood externalising disorders.[3] Twin studies align with this finding and have shown that PTSD shares genetic influences with both internalising- and externalising-spectrum diagnoses.[4] Other work suggests that many adults with PTSD exhibit a predominantly externalising pattern of comorbidity characterised by problems in the domain of impulse-control, antisociality and substance misuse.[5] These findings raise concern about conceptualising PTSD simply as the manifestation of a vulnerability to anxiety-related psychopathology.

Since its third edition, the DSM has taken a largely descriptive, as opposed to aetiological, approach to defining and classifying disorders. The most notable exception to this is the PTSD diagnosis, which specifies a causal relationship between trauma exposure and symptom development. We believe that the most appropriate location for PTSD in DSM–V would be among a class of disorders precipitated by serious adverse life events, i.e. a spectrum of traumatic stress disorders. Candidates for inclusion would include PTSD, acute stress disorder, adjustment disorder, a traumatic grief or bereavement-related diagnosis, and possibly complex PTSD. These disorders are the product of an environmental pathogen (i.e. a traumatic stressor) operating on individual diatheses that span the spectrum of human variation in vulnerability to psychopathology. This diathesis–stress interaction can result in extensive heterogeneity in the phenotypic expression of psychopathology – pathological anxiety being just one manifestation of the process.

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Mark W. Miller, VA Boston Healthcare System, National Center for PTSD, USA. Email: mark.miller5@va.gov; **Patricia A. Resick**, **Terence M. Keane**, VA Boston Healthcare System, National Center for PTSD, USA

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Correction

Interventions for people bereaved through suicide: systematic review. *BJP*; **193**: 438–43. Reference 5 should read: Hawton K, Simkin S. Helping people bereaved by suicide. Their needs require special attention. *BMJ* 2003; **327**: 177–8.

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