

Cancer and schizophrenia

The negative finding of the recent paper by Goldacre *et al* (2005) is an important addition to studies attempting to confirm or disprove the 'epidemiologic puzzle' (Jablensky & Lawrence, 2001), but the evidence remains ambiguous regarding the overall risk of cancer in people with schizophrenia. In three of five comparisons with reference populations conducted between 1992 and 2003 (see Grinshpoon *et al*, 2005), males with schizophrenia had a reduced risk of cancer. No reduction was found among females in four comparisons but decreased risk was reported in one of two comparisons of both males and females. Two recent studies (Dalton *et al*, 2005; Grinshpoon *et al*, 2005) mostly found reduced risk. When evaluating these results, it is important to recall that people with schizophrenia face many health and service hazards that may increase their risk for cancer (Grinshpoon *et al*, 2005). We therefore suggest that results in this area should not be stopped prematurely, especially since one study (Lichtermann *et al*, 2001), but not another (Dalton *et al*, 2004), found a reduced risk of cancer among first-degree relatives of patients with schizophrenia, an indication of a genetic factor (Park *et al*, 2004).

The study by Goldacre *et al* (2005) had some limitations, as acknowledged by the authors. We wonder whether a diagnosis of schizophrenia at the time of the first admission may not constitute an additional limitation. Patients admitted with an early diagnosis of schizophrenia but who later received other psychiatric diagnoses might have diluted the risk (Carney *et al*, 2004), whereas others who did not have a diagnosis of schizophrenia on first admission but did on later contact might have been lost to the enquiry. We also wonder whether the decision to exclude some people from the reference population for selected cancers was sound. Admittedly, dietary factors may be imputed for those conditions selected for elimination as well as for cancer risk. We look forward to a repetition of the analysis after their inclusion.

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Authors' reply: We agree that further evidence is needed to gain greater certainty about whether or not cancer risk is altered in people with schizophrenia. By their nature, observational epidemiological studies include more biases and confounding than randomised controlled trials, but the latter are not an option for studying this association.

We included people in the schizophrenia cohort if they had a discharge diagnosis of schizophrenia at any admission and not just at the first admission. We accept that there could be a dilution effect from early misclassification, but it seems unlikely that this would completely reverse any real and substantial inverse association between schizophrenia and cancer.

We excluded people with appendicectomy, haemorrhoids and inguinal hernia from the reference cohort when studying colorectal cancer because we knew, from other work, that they have a significantly increased risk (albeit fairly small). We therefore felt that, in principle, they were inappropriate for the colorectal cancer analyses. However, this was more a decision on principle than one with much practical effect. Comparing the schizophrenia cohort with the reference cohort, including all people in the reference cohort, the rate ratio for cancer of the rectum fell to 0.55 (95% CI 0.31–0.90), compared with

0.57 (0.33–0.93) reported by us. The rate ratio for cancer of the colon, including all the reference cohort, fell to 0.59 (0.39–0.85) compared with 0.72 (0.50–1.01) reported by us. Thus, a result on the borderline of significance became significant; but we consider that it was right to exclude the three reference groups as in the original analysis. None the less, the case does seem to be building, considering results from other studies as well as ours, that there may be a deficit of colorectal cancer in people with schizophrenia. As suggested by Dr Levav and his colleagues, it is unclear whether this is a result of confounding with dietary factors. Finally, we would like to correct a typographical error in the footnote to our table: 'superficial injury and confusion' should have read 'superficial injury and contusion'!

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Schizophrenia, weight gain and atypical antipsychotics

Thakore (2005) highlights the increased prevalence of the metabolic syndrome in schizophrenia. He briefly discusses the relationship between atypical antipsychotic drugs, weight gain and abnormal glucose and lipid metabolism. He rightly concludes that this relationship is poorly understood and that much of the evidence is contradictory or of dubious quality. Unfortunately this narrow focus on the aetiology of the metabolic syndrome risks diverting attention from the urgent need to reduce obesity among people with schizophrenia.

There is good evidence that people with schizophrenia have a high and growing cardiovascular mortality (Ösby *et al*, 2000). Many also have multiple lifestyle-related cardiovascular risk factors such as smoking, lack of exercise and poor diet (Brown *et al*, 1999), none of which are convincingly susceptible to modification. Schizophrenia may also be associated with intrinsic metabolic disadvantage (Thakore, 2005).