

Cancer Risk in Parents of Patients With Schizophrenia

TO THE EDITOR: Reassuring as it is to see that a recent record linkage study from Denmark by Susanne Oksbjerg Dalton, M.D., Ph.D., et al. (1) accurately replicated our previous finding of a reduced incidence of cancer in the parents of patients with schizophrenia in Finland compared with the general population (2), I was surprised to recognize that this difference vanished when parents whose children were free of schizophrenia were chosen as the comparison group instead. Thus, the authors made a point that our common finding with the general population as the reference group should be invalid, and they claimed a “healthy parenthood effect” as the critical source of bias. However, when testing our genetic hypothesis, they should have considered parents exposed to cancer risk throughout their lifetime. I am not sure whether their method of having follow-up for cancer in parents starts only at the birth of the first child or, alternatively, at the birth (or age at disease onset) of the first child with schizophrenia might have biased their finding of equal cancer risk (e.g., given that some studies find schizophrenia risk to depend on birth order, e.g., Kemppainen et al. [3]). Also, the “healthy parenthood effect” they introduced from a Danish study that found parents of children with cancer at no higher incidence than the general population (4) did not receive general support from several other population studies in parents of individuals with cancer at a younger age (5–7), and it seems counterintuitive at least since a significant proportion of cancer at a younger age is known to occur on a genetic basis. In fact, the only other retrievable large population study that compared cancer risk between the relatives of patients with cancer and the relatives of otherwise deceased persons from Utah (instead of the general population) still found familial cancer risk increased (8). Therefore, I doubt the general validity of the “healthy parenthood effect.” It would have been useful to see whether cancer risk in the Danish comparison group of parous individuals with no child affected by schizophrenia was indeed lower than in the general population, including parous and nonparous individuals. Unfortunately, the lack of resources does not currently permit me to replicate, in turn, selection of a parous comparison group from the Finnish population register and analyses similar to those of the Danish study. Meanwhile, I commend the colleagues from Denmark for drawing benefit from the excellent epidemiological material available in Nordic countries, and I hope that other appropriate registers (e.g., Hemminki et al. [9]) will contribute.

References

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Dr. Dalton and Colleagues Reply

TO THE EDITOR: We introduced the healthy parenthood effect as a proposed explanation for the observed change in results according to which comparison group was used in our study of cancer risk in the parents of schizophrenic offspring. We compared the cancer rates in the parents of schizophrenic offspring (exposed group) to those of other parents, which we consider to be the most correct, and found no difference in cancer risk. When we included persons who had not had any children and used the general population rates of cancer as the comparison, a method similar to that of Dr. Lichtermann and colleagues, we also observed a reduced risk of several forms of cancer, in line with the findings of our Finnish colleagues. It is unlikely that our results were biased by the choice of start of follow-up because we followed up from the time of birth of the schizophrenic offspring in the exposed group in both analyses. We do not think that the results published by our Finnish colleagues are specific to the parents of schizophrenic patients but more generally to being parents. The healthy parenthood effect denotes selective processes that lead to the forming or initiation of a family and, second, to the maintenance of a relatively regular and healthy lifestyle when living a family life. This would probably mean that parents, compared to all adults, smoke less, drink less, exercise more, and so forth. The results that we highlight from the literature in our article as supporting the notion of a healthy parenthood effect include mainly cancer forms with a large environmental component. To the best of our knowledge, there have been no studies of the risk of cancer in parents in general and, as Dr. Lichtermann points out, most studies of cancer risk in cancer families will reflect the high-risk nature and report the higher risk of some forms of cancer with a large familial component. However, the study by Westergaard et al. (1996)—apart from reporting a high risk of testicular cancer in the fathers and brothers of testicular cancer patients—did indeed also find a reduced risk of overall cancer, a reduction mainly carried by reduced lung cancer and gastrointestinal cancer risk. The differences in cancer risk based on whether the exposed group is compared to only other parents or the total population in Denmark must somehow be connected to