Commentary: Strengths and limitations of the discordant twin-pair design in social epidemiology. Where do we go from here?

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It has become increasingly recognized that many of the associations between various exposures and health outcomes measured in adulthood are confounded by social and behavioural factors acting early in life,¹ and recent research has questioned whether socio-economic position (SEP) in adulthood in fact has an additional impact on adult health beyond the influence of one’s childhood environment and genetic make-up.²

The traditional way to examine the independent influence of adult SEP on differences in health outcomes is to use multivariable models, which mutually adjust for early and late social factors. However, such analyses may not provide sufficient adjustment for all the factors that constitute childhood social environment, and close correlation between early and late social factors may present serious statistical challenges. Alternative approaches for dealing with confounding are designs that approximate the conditions of a true experiment. One such approach is the discordant twin-pair design employed by Fujiwara and Kawachi³ in their well-designed and innovative study. Here, the authors compare health status in twin pairs who are discordant on educational status in adulthood, but are matched fully or partly on genetic make-up and rearing environment. Such a study on twin-pair discordant on exposure provides a useful analogue to the idealized counterfactual design, and failure to observe an association within discordant twin pairs would imply that a previously observed association between an exposure and an outcome is attributable to common genetic or shared environmental factors. In addition, differences in the magnitude of association between monozygotic and dizygotic twins may serve to further disentangle the respective effects of genetic and familial environmental effects.

However, as enchanting as this approach may seem, as with everything else, it has a price: in this case, the flip side of the coin is the fact that the statistical power in the fixed-effects analyses is dramatically limited, resulting in highly imprecise estimates. The implication of this is that these ‘unconfounded’ estimates may in fact be further away from the ‘true value’, which we are trying to estimate, due to the large imprecision of estimates.⁴ A consequence of this is that authors are left with considerable room for interpretation of results and, in some cases, interpretation tends to border on arbitrariness. To illustrate this point, we would like to call attention to a discussion paper by Lundborg,⁵ which essentially is based on the same data (MIDUS survey, first data collection wave) as the paper by Fujiwara and Kawachi, although dizygotic same-sex twin pairs were not included. Despite the fact that the results in the two papers appear to be fairly similar, the authors

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of the two papers seem to reach diverging conclusions, i.e. different degrees of support for confounding of the association between education and various health outcomes and behaviours from genetic and early environmental factors. The purpose of pointing out this discrepancy is solely to highlight the pitfalls of this otherwise alluring method to handle confounding in social epidemiology and to encourage cautious interpretation of the results of the fixed-effect analyses.

Obviously, a way to overcome the sample size limitation of the discordant twin-pair design is to embark on analysis of larger twin datasets that will allow sufficient statistical power even in the fixed-effects analyses. Furthermore, larger twin datasets may also enable us to address harder end points of great public health interest such as mortality and incidence of disease.

However, there is another inherent problem in the discordant twin-pair design, which cannot be solved by increasing sample size. That is the selection issue owing to the fact that twins who are discordant on educational status in adulthood may be a selected group, who are special in the sense that in spite of identical genes and rearing environment, they differ in their educational accomplishments. The reasons for such differences in education pose an interesting research question, although reflections on this issue will perhaps be most relevant in cases where studies fail to demonstrate health differences in the fixed-effect analyses within twin-pair discordant on educational status.

So far, the few available twin studies on social inequality in health are not consistent and many of them suffer from imprecise estimation of effects. In addition, the comparison of studies is hampered by the fact that different SEP indicators are used in different studies, and evidence suggests that different indicators have different impact on health.6

For instance, a study among 308 American female twin pairs7 showed no differences in the fixed-effects analyses for self-rated health, medication use, physical activity and blood pressure and lipids if discordance was defined on the basis of educational status. In contrast to this, the fixed-effect analyses of discordance defined on the basis of occupational social class generally showed a significantly worse health situation of the twin with a low-social class compared with the twin with a higher social class.

As such, it would also be interesting to further explore the effect of different social indicators using the discordant twin design.

In conclusion, the discordant twin-pair design is truly a promising and innovative approach that provides a clever method for dealing with genetic and early environmental confounding. But in order to improve our work we have to acknowledge its limitations. The next step will be to await studies using larger twin datasets that allow more precise estimation of effects and enable us to address a wider range of health outcomes and various social indicators.

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References