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Letters to the Editor

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'The association between intelligence and lifespan is mostly genetic'

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We were sadly disappointed to read the recently published article by Arden *et al.*[1] (in press) in the *International Journal of Epidemiology*. This article is one that we believe to be unsound in its conceptualization and execution and which should not have been considered for publication in an epidemiology journal even if it did not suffer from these methodological flaws.

The scientific hypothesis pursued by these authors is that individuals with higher intelligence quotient (IQ) have longer lifespans, that this relationship is due primarily to common causes of both variables and finally that the common causation is primarily genetic rather than environmental. They investigated these relationships in three cohorts of aged same-sex monozygotic and dizygotic twin pairs. There are a number of statistical analyses reported in the paper, and these violate many widely accepted principles of epidemiological analysis and reporting, such as the avoidance of standardized effect estimates[2] and the reliance on null hypothesis significance testing rather than reporting of effect estimates and their imprecision.[3] The paper makes inferences about genetics and environments, but has no direct measures of either set of variables. Rather, the key assumption on which the inference rests is the 'equal environment assumption' (EEA), which is that twins are not exposed to different environments based on their zygosity. This assumption is stated by the authors as a fact, but is not evaluated in these data. When evaluated in previous reports it is sometimes reported to hold approximately,[4] and at other times found to be severely violated.[5]

Unfortunately for Arden *et al.*, however, even if the EEA is approximately valid in the populations studied in this paper, it will not be so in the samples actually analysed. This is because of selection mechanisms that differentially exclude twin pairs based on the similarity of their survival outcomes. For example, to be included in the analyses, at least one twin must have died by the time of the assessment. Therefore, pairs in which both twins live to an advanced age due to shared genetic and environmental advantages are excluded, implying that pairs in which one twin died from a unique genetic or environmental factor have a greater probability of being included. Epidemiologists will recognize survival as a 'collider' in this setting, since it is determined by common genetic and environmental factors as well as by unique genetic and environmental factors.[6] The implication of the collider stratification bias that results from the exclusions is that even if the proportion of shared environmental factors were equal across zygosity groups in the population, it would not be equal in the sample. Because there are several such selection processes present in the design, and because the authors do not reveal how many pairs were excluded from each selection mechanism, it is impossible to anticipate the overall direction and magnitude of the summary bias. For example, in the Danish sample, twin pairs are also excluded if one or both of the pair died before age 70. Thus, even if the study null were true, the dizygotic twins could appear in the analysis to have a stronger association between IQ differences and survival differences from selection bias alone.

But the situation is even worse than this. If at least one twin died by the time of the study assessment, then the pair was included in the analysis, but the survival difference could not be calculated if the second twin was still alive, which was true in about half of the pairs analysed. In that case the authors imputed the death date for this surviving twin by using the national average for a person of the same birth year and sex. This is inappropriate for several reasons, the most important one being that imputing a single point

for missing values underestimates the variance. The true data have a spread, but the mean is concentrated at a single value. In fact, this is exactly why the technique of 'multiple imputation' exists, to avoid this deficiency of plugging in a mean value with no variation, and thereby underestimating standard errors and biasing *P*-values downward. This procedure would be invalid even if the mean estimate were unbiased, but in this case, the actual survival is almost always longer than the life table estimate, because if it were less than the life table estimate, the person would already be dead. Moreover, in some instances, the authors found that the person had already reached their life table estimated survival, and so they assigned this person to die in the same year, once again forcing the twin survival difference in the dataset to be smaller than it is in reality. This error is especially catastrophic for these authors because they use this estimated standard error in their third analysis to estimate the proportion of the association that is genetic rather than environmental. The underestimation of the variance through restriction of the sample and incorrect imputation methodology can easily exaggerate this estimate for the genetic contribution if dizygotic twins are more severely biased than monozygotic twins.

Even more disturbing than these fatal statistical flaws, however, is fact that this paper was favourably reviewed and published in an epidemiology journal. Like the myth of Sisyphus, the psychology of individual differences has repeatedly tried to infiltrate epidemiology, whether in cancer[7] or social[8]subfields. It is a credit to the field as a whole that these incursions have largely remained unsuccessful, and yet here we go again. Arden *et al*. now advocate for a 'cognitive epidemiology', drawing on twin studies and IQ tests, which purportedly has a 'critical role to play ... in public health'. Such claims convey a misunderstanding of the nature of our discipline. Epidemiology is an applied science dealing with the description and understanding of the determinants of disease in populations.[9] Epidemiology contributes to a technology called 'public health', which is an organized effort by society to prevent disease and promote health in populations.[10] To consider IQ, as a marker of a disease or variation in test scores, as a condition to be prevented or treated is absurd. There is no more a cognitive epidemiology than there is a memory, perception or emotional epidemiology. These are basic psychological processes, not diseases, therefore not targets of prevention or treatment. A loss of functional cognition, such as occurs in dementia, can be studied as a disease outcome, but variation in intelligence test scores in the population is not such a quantity. Nor is IQ a well-defined exposure even if it were relevant to public health.[11] The misconception of using IQ or other markers of cognitive performance as causes of disease or death, to be prevented or treated at the population level, has had devastating effects in the past century.[12] It remains unstated what kind of 'public health interventions' the authors have in mind, but given their assertions of hypotheses that are 'crucial to medicine and public health', this is a very ominous omission.

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