The destabilization of mental health, which may manifest through the presence of common mental disorders (eg, anxiety, depression), can have substantial deleterious consequences on myriad aspects of biological, social, and emotional health in both adults and children. Throughout the formative stages of childhood development, adverse experiences, occurring as a result of actions or conditions uncontrollable by children, can bear strongly on critical aspects of healthy psychological development, including resilience against undue social stress, the formation of strong social bonds (eg, school friendships), and the avoidance of longer-term anxiety and depression. Adverse events experienced during childhood have been reported to have negative impacts that may persist well into adulthood.1

The work of Pierce et al2 characterizes the associations between adverse events experienced in childhood and disrupted social-psychological development and diminished opportunities for educational flourishing. In this large-scale, longitudinal, retrospective observational cohort study, Pierce et al2 use data available from Swedish registries to evaluate evidence for the (causally interpretable) adjusted association of adverse events experienced in childhood with the development of anxiety and depression (ie, common mental disorders) and average performance in school in a cohort of more than 160 000 Swedish children followed up from birth until their twenty-first birthday. By using the g-computation framework,3 a suite of statistical methods for the analysis of observational study data, to estimate associations while adjusting for possibly complex time-varying confounding, the authors uncover significant evidence of a protective association between preventing adverse events and the prevalence of common mental disorders (a reduction of 2.6%, from an observed 10.2% to an expected 7.6%) as well as a positive association with educational attainment (an expected increase of 0.149 SDs for grades). Their thoughtful analysis ought to be informative of the potential preventive efforts targeted at curbing adverse events experienced in childhood, including the types of adversities to target, subgroups most harmed by adverse events, and which developmental points in childhood may be most responsive to candidate interventions. Furthermore, this work shows how the application of (bio)statistical techniques developed in recent decades and extensively studied in the statistical and epidemiologic methodology literature, may facilitate the extraction of insights for future study by subject matter and clinical experts and may inform the design of targeted interventions intended to alleviate the impacts of such adversities.

Two key issues that arise in the work of Pierce et al2 merit further discussion: the use of analytic methods to evaluate the possible effects of hypothetical interventions that are not themselves well defined, and the promises and pitfalls of research findings derived from observational studies relative to those extracted from randomized clinical trials. In their analysis of the Swedish registry data, these authors consider how the associations—or, under well-studied assumptions, the causal effects—of “preventing childhood adversity could provide notable improvements in the rates of common mental disorders.”2 While informative, an important next step in any impactful analysis would be to formulate a set of well-specified interventions that could be carried out in practice and frame an analysis in terms of such well-defined counterfactual contrasts. For example, the authors found that preventing parental separation provided for the greatest improvement, yet such a vague intervention constitutes not only a violation of the consistency rule in causal inference4 but also fails to suggest a plausible intervention (eg, marriage counseling to prevent parental separation), which may yet fail in practice; thus, one is left to interpret the substantive results of this hypothetical
analysis in terms of implausible interventions (eg, marriage counseling that can never fail). Outside of such a pragmatic framing, candidate interventions may incur severe and unintended consequences—that is, What does it mean to deliver marriage counseling that never fails? Would one really expect for unhappy marriages carried forward by fiat to positively impact children’s social-psychological health? A focus on carefully defined and specific interventions—those in line with the consistency rule—are necessary to inform future substantive research. Without such specificity and clarity, any such analysis is limited to the realm of the hypothetical.

Turning now to the reliability of insights extracted from observational studies, Pierce et al² note that “randomized trials for childhood adversities are rarely ethical and often unfeasible,” yet stop short of invoking a causal interpretation of their findings. While the vagueness of the interventions considered surely limit such an interpretation (per prior remarks on the consistency rule), the fact that the consideration of such a problem is limited to observational study research ought not be disqualifying. The vast array of causal-analytic and statistical methods available in the modern quantitative researcher’s arsenal provide tools sufficient to safely extract causal insights from observational studies—when subject matter knowledge can be used as a guide and when a surfeit of relevant data is available for analytic studies (as is the case here). In large-scale observational studies such as this one, modern analytic methods allow adjustment for the numerous confounding variables routinely collected in modern databases (eg, as with national registries), and sensitivity analyses can—indeed, must—be used to provide a measure of the reliability of scientific conclusions drawn from observational data.⁵ While randomization provides substantial inferential safeguards, an overly cautious adherence to randomized clinical trials, although they may well justifiably be the highest standard for causal inference, limits the scope of scientific inquiry to the readily and easily manipulable and, by extension, damages the mission of public health by casting doubt on findings that suggest benefits from the potential amelioration of important issues, such as childhood adversities. One wonders what good deference to a highest standard is when said standard simply cannot be applied—in fact, it was despite dogma about the virtues of randomization,⁶ not because of randomized clinical trials, that an irrefutable causal link between smoking and cancer was established many decades ago.⁷ How many impactful health findings are today still hindered by such dogma and a relative lack of awareness of today's causal-analytic toolbox?
