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## Seeking causal inference with ecological and hybrid designs

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We thank Carol Hogue for her insightful commentary (1) on our article (2) and the broader issue of pregnancy loss. Hogue argues persuasively that pregnancy loss remains an important public health problem. Hogue also describes the poor data quality of pregnancy loss registration in the U.S. We fully agree with this assessment and add that such a limitation precludes rigorous inquiry in the U.S. regarding individual and population-level causes of pregnancy loss. Epidemiologists, therefore, often turn to registries in Europe, such as the Danish registry we used for our analysis.

Whereas we agree with much of Hogue's commentary, we clarify and extend two areas. The first involves the choice of study design when attempting to infer causal relationships. The second pertains to our examination of economic downturns and a new recommendation of wider use of hybrid strategies that borrow strengths from both individual and ecological analyses.

Much criticism of social epidemiology centers on its being "casual about causality" in its study design (3, p.796). This criticism relates to the inability to rule out confounding by a common cause. Let us assume that researchers interested in stressful life events and pregnancy outcomes carefully measure both processes in a prospective cohort study. Next, assume that the researchers find a positive relation between these variables. Approximating a counterfactual of "stressed" women by using unexposed women proves challenging since women are not randomly assigned stressful life events. In particular, unmeasured factors that precede both stressful events during pregnancy and the adverse pregnancy outcome (e.g., social or health selection into environments that increase risk of stressful events) remain viable threats to validity. Given the potential of strong unmeasured confounding by a common cause, at least one discipline—economics—eschews traditional covariate modeling when attempting to infer causality (4). Within this context, in our study we contend that use of a plausibly exogenous exposure—that is, an external exposure whose timing is independent of common causes of exposure and outcome at the level of the individual—minimizes confounding. Examination of

economic downturns in Denmark follows in the spirit of the quasi-experimental design in that acute economic downturns "assign" stressful life events randomly in time to some gravid cohorts.

Hogue notes the limitation that, absent individual-level data on unemployment, our ecological analysis cannot inform interventions on high-risk subgroups. Whereas we agree with Hogue, we remind epidemiologists of two points. First, confounding by a common cause remains a plausible rival in most studies of individual unemployment. Second, much public policy turns on "net effects" considerations (5). A recent review on the Great Recession (6), moreover, challenges Hogue's assertion that "unexpected economic downturn[s] . . . affect at most a small minority of families" (1, p. XXX). Lost hours from underemployment, lost assets, marital instability, and fear of unemployment itself represent but a few adversities among the overwhelming fraction of persons who remain employed during downturns.

To assess the putative mechanisms we describe above, and to identify high-risk subgroups, we agree with Hogue that detailed surveys of new mothers (e.g., Pregnancy Risk Assessment Monitoring System) and other sources of individual income and employment information would complement our time-series study. We suggest that a hybrid strategy can leverage the strengths of both approaches. Combination of detailed individual-level surveys with ecological data on exogenous exposures may provide a minimally biased estimate (due to quasi-randomization of exposure assignment) while also illuminating mechanistic pathways. Such a hybrid approach could, for instance, examine whether state-level economic downturns precede pregnancy loss or unhealthy maternal behaviors (7). These hybrid designs, if applied more routinely than at present, may render social epidemiology less vulnerable to the critique that it favors descriptive over causal estimation.

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