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The need for causal-inference methods to answer causal questions

The recent GlobalSurg and COVIDSurg collaboratives' publication is likely to influence care for millions of surgical patients [1]. The authors sought to estimate the effect of pre-operative isolation on postoperative pulmonary complications. This constitutes an impressive global collaboration, and we congratulate the authors. They conclude that isolation is associated with increased risk of postoperative pulmonary complications but we are concerned that this conclusion is not sufficiently evidenced to safely influence practice.

To answer what is an explicitly causal question (the effect of x on y), the authors used regression modelling; a statistical technique for describing associations. The manuscript acknowledges this limitation but nevertheless goes on to assume a causal relationship and recommends relaxing pre-operative isolation requirements. Inappropriately attributing causality to identified associations while simultaneously stating that causation cannot be assumed (sometimes termed 'Schrodinger's Causality') is common, for example occurring in two-thirds of observational studies in a general medical journal in 2018 [2].

Even the identified association between isolation and pulmonary complications might not be robust. There is a complex web of known and unknown relationships between the variables in the COVIDSurg dataset, and other relevant variables were not considered at all, likely for practical reasons. Particular concerns with the current analysis include unmeasured confounding, injudicious statistical adjustments and collider bias.

An inappropriate but often made assumption is that multivariable regression modelling attenuates confounding such that precise, unbiased results can be interpreted in the context of the reported covariates. This is not correct: additional variables can sometimes reduce precision, induce bias, and interpretation is made in the context of all covariates, including unmeasured ones. The relationship between pre-operative isolation and patient outcomes is confounded by (or in the context of) societal isolation guidance, which was not explicitly modelled (i.e. it is an unmeasured confounder). The study's finding that pre-operative isolation is associated with poor outcomes is confounded by the fact that, in accordance with societal guidance, patients who were older and had more comorbidities were generally expected to isolate more than young and relatively fit patients. Thus, the finding could be explained by age and comorbidity rather than implausibly suggesting that an additional 3–14 days of isolation would materially change outcomes for all patients. The authors also adjusted for ASA physical status, which would in most cases be assigned on the day of surgery. The ASA physical status thereby mediates, rather than confounds, any effect of isolation. Adjustment for mediators can both over- or underestimate the total causal effect.

Collider bias occurs when an analysis includes a variable that multiple other variables influence, i.e. the arrows in the causal graph collide at the included variable [3]. This induces spurious correlations that transmit unpredictably through the causal network. Importantly, collider bias can reverse the apparent direction of an effect [3]. Observational research related to COVID-19 is very likely to succumb to collider bias because of the complex relationships between the variables of interest [4].

Without formal adoption of a causal inference approach, it is impossible to draw robust, causal conclusions from the COVIDSurg analyses. Only with judicious use of computing and statistical methods can we facilitate sensible and safe decision making. We congratulate the authors on this impressive dataset but implore a causal-inference approach to data analysis. We invite the authors to put the data in the public domain, similar to SNAP2-EPICCS [5], to facilitate collaboration for causal analysis on this question of importance.

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