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Commentary: Putting natural experiments in context

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An experiment is a question which science poses to Nature and a measurement is the recording of Nature's answer.

— Max Planck (1858-1947)

A natural experiment refers to a situation that is not experimental but is treated as if it was. Mokashi and colleagues¹ use this principle to analyze the results of aortic root replacement with valve reimplantation. The investigators capitalized on nature's allocation of patients to have bicuspid or tricuspid valves. Propensity scores were derived using the native valve type as the dependent variable in a logistic regression and 1:1 matching was accomplished. Although not statistically significant, at 5 years severe aortic insufficiency and a higher gradient were more common in the bicuspid valve group.

Propensity score methods are a widely used for removing the effects of confounding in observational trials when estimating the effects of treatment on outcomes. The original publication by Rosenbaum and Rubin² identified that treatment assignment could be strongly ignorable as long as 2 conditions are upheld: first, that every subject has a nonzero probability to receive either treatment; and second, that the treatment assignment should be independent of the outcomes conditional on the observed baseline covariates. The first condition is not supported in the current experiment because a patient with a tricuspid valve has zero probability of having a bicuspid valve. However, as the authors have stated, this is no longer dogma.³ This type of analysis will become increasingly popular, providing new avenues of questioning we can engage in. As for the second condition, an analysis is viable as long as there are no clinically relevant unmeasured confounders. This is a challenge in the current study because we know there are

Max Planck (1858-1947)—Nobel laureate and the originator of modern quantum theory.

CENTRAL MESSAGE

Natural experiments provide a window into the surgical world with a new perspective on what questions remain.

likely genotypic and phenotypic differences in these 2 groups of patients that could be related to the outcome, yet these differences cannot be identified with current demographic characteristics. For example, histologic dissimilarities in the aortic annulus in patients with a bicuspid valve could significantly influence subsequent root remodeling after repair.⁴

Natural experiments provide intriguing data about the world we live in and the surgery we use to make that world a better place. Even if I am not entirely convinced of the validity of the analysis, taken at face value this natural experiment tells us that probably outcomes after bicuspid valve reimplantation at the time of root replacement are not as good as those seen after tricuspid valve reimplantation. The not-natural experimental comparison that would inform our practice is aortic valve replacement versus reimplantation at the time of root replacement in patients with bicuspid valves, but it is unlikely that these data will be forthcoming. Today's question is a ball that has been kicked down the road because nature's answer is to pose a new riddle.

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