of covariates for propensity score matching in our study. Specifically, the authors recommended matching all variables (including American Society of Anesthesiologists class, weight loss, steroid use, diabetes, hypertension, serum bilirubin, serum albumin, surgical approach, operative time, Pringle maneuver, concurrent ablation, race, and serum transaminase levels) that differ between the 2 groups, as "These factors could impact postoperative complications theoretically. . .." Although we agree that choosing an appropriate set of covariates for propensity score matching analysis is critically important, for several reasons outlined here, we respectfully disagree that the addition of other variables in the matching processing would have been statistically appropriate or "would greatly solidify the conclusions of the study."

First, it is important to remember that the purpose of propensity score matching is to balance 2 groups based on their likelihood of receiving an intervention. In other words, the groups should be matched based on factors that have been shown to determine receipt of neoadjuvant therapy, not of developing postoperative complications. In our study, the selected variables included in the matching process were based on clinical factors that are known to influence decision making about the administration of neoadjuvant chemotherapy.[2] Second, although minor differences in select baseline characteristics are observed post-matching, we purposely avoided adding extraneous variables (eg steroid use, diabetes, and race), which might reduce the final sample size of the study population and reduce statistical power to detect differences in the primary and secondary outcomes. Third, as the propensity score model is constructed from variables believed to influence receipt of neoadjuvant chemotherapy, certain variables, such as operative time and use of Pringle maneuver, would not be appropriate for matching, given that they occur after the receipt of neoadjuvant therapy. Fourth, although propensity score matching was used to minimize bias in the selection of patients for neoadjuvant therapy, multivariate logistic regression techniques were also used after matching to minimize the risk of confounding of other variables on the outcomes of interest (ie morbidity and mortality). Finally, although transaminase levels could represent an important measure of preoperative liver function, we chose not to use them in the matching because of the high rate of missing data and because the reported values in the NSQIP data set are those immediately before operation, they could have potentially been influenced by neoadjuvant therapy in the intervention group.

Once again, we sincerely appreciate the comments and questions from Zhang and colleagues on our recent study. Although we are confident in the statistical approach used in our study, we hope that future studies using novel methodological approaches will further clarify the role of neoadjuvant therapy for colorectal liver metastases.

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Use of Donation after Cardiac Death Donors at the University of Southern California

J Emamaullee, MD, PhD, Navpreet Kaur, MD, Linda Sher, MD, FACS, Yuri Genyk, MD, FACS
Los Angeles, CA

We read with interest the recent publication by Luckett and colleagues, "Use of Hepatitis C Virus Antibody-Positive Donor Livers in Hepatitis C Nonviremic Liver Transplant Recipients,"[1] which outlined their important work on this topic. As a high-volume liver transplant program in United Network for Organ Sharing region 5, which has the highest mean Model for End-Stage Liver Disease score at transplantation of any region of the US, we are acutely aware of the shortage of donor organs and how critical it is to use every possible organ, including hepatitis C virus-positive livers.[2] When reviewing the print version of the April 2019 issue of the *Journal*, we were able to review the transcribed discussion that occurred when this article was presented at the Southern Surgical Association Meeting in December 2018. Comments were provided by several leaders in our field, including John Cameron, MD, John Goss, MD, and Ron Busuttil, MD, among others. Although most of the discussion centered around the use of hepatitis C virus-positive donors, one specific comment stated "At the University of Southern California, they do not use donation after cardiac death (DCD) donors, which I was pretty shocked to hear, especially in a high-acuity area." This specific comment was troubling to our program, as it is false. We consider every organ offer very carefully and have developed our own criteria for using

donation after cardiac death donors. This is based on a comprehensive national survey and United Network for Organ Sharing analysis of donation after cardiac death outcomes, which were completed at the direction of one of our own surgeons, Dr Linda Sher, as part of the American Society of Transplant Surgeons Scientific Studies Committee, with funding from our local organ procurement organization, One Legacy.[3]

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Causation in Interventional Observational Studies

Thomas R McLean, MD, JD, FACS
Shawnee, KS

In a recent issue of the *Journal*, Turner and colleagues[1] described how, after their hospital was identified as an American College of Surgeons NSQIP outlier for *Clostridium difficile* (*C difficile*) infection, a series of interventions was associated with a substantial reduction in *C difficile* infection over the next year. The article is well written and there is no question that Dr Turner's hospital put a lot of time and effort into quality improvement. But because this article does not contemplate ergodicity (ie the dynamics of complex systems), whether the interventions caused the reduction in the rate of *C difficile* infection remains open.

Ergodicity concerns how much a system will fluctuate over time due to randomness alone.[2] If healthcare delivery occurred in a perfect ergodic system, then given an infinite amount of time, a provider's healthcare metrics (eg NSQIP) would spend time at every level of the quality of care spectrum. At the other end of the healthcare delivery's ergodic continuum is the absorption barrier, where once you are at a certain level of quality (good or bad), then absent intervention, your quality of care will remain at that level indefinitely. An implied assumption of Turner and colleagues'[1] article (and for that matter almost all observational quality improvement articles) is that a provider's quality of care is fixed by an absorption barrier. This implied assumption allows the reader license to believe that the Dr Turner and colleagues' interventions caused the observed improvement in quality of care.

Although perfect ergodicity is not a hallmark of our healthcare system (as discussed later), it is very unlikely that the quality of care delivered by a provider is "fixed in stone" by an absorption barrier. Here it is not important to determine the exact level of ergodicity in our healthcare system, only that some degree of randomness is present. Once we allow that randomness plays a part in healthcare delivery, it becomes clear that the outcomes of interventional observational studies have a large component of regression to the mean. In the 2011 book, *Thinking, Fast and Slow*, Nobel Laureate Daniel Kahneman[3] pointed out the fallacy that positive feedback improved a pilot's skills. A pilot's performance on a particular flight reflects the pilot's overall skill plus a certain degree of random fluctuation in that skill. Accordingly, improvement in a pilot's performance after receiving feedback (a form of intervention) was due to regression to the mean, not the feedback. Similarly, randomness in healthcare delivery means that observational studies demonstrating improved healthcare delivery post intervention have more to do with regression to the mean than evidence that the intervention cause improved quality of care.

I do not believe that healthcare delivery is perfectly ergodic. Providers who deliver suboptimal healthcare because of a lack of intelligence, laziness, substance abuse, or alcoholism will never deliver outstanding healthcare because of random fluctuations in that provider's abilities. But because our healthcare system exists somewhere on the continuum between perfect ergodicity and an absorption barrier, regression to the mean haunts every observational study to improve healthcare delivery.

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