Comments on Thavendiranathan et al. Do Blood Tests Cause Anemia in Hospitalized Patients?

To the Editor:—I am concerned about important methodological problems in the recent article by Thavendiranathan et al.¹ The exclusion criteria seem overly restrictive. For example, though blood loss is difficult to quantify clinically, the amount of hemoglobin (Hgb) transfused is not, and could have been included in the analyses as a continuous variable. In addition, several other exclusions could have been eliminated by using indicator variables. The authors report their continuous variables in Table 1 as if they were normally distributed. I suspect that they are not, especially for an important variable like mean volume of phlebotomy for which they report a very large calculated standard deviation. Interquartile ranges would have been more informative. I'm not sure why the authors prescreened their candidate variables in the model using univariate analyses. This approach overfits models and leads to confidence intervals that are not appropriate.² The authors also do not report if they adjusted for the clustering of patients in their analyses.

The authors report that Hgb concentration (C) on admission is strongly associated with drop in Hgb C during hospitalization but this is at least partially an artifact of how they set up their regression equation. Because the change in Hgb C (the dependent portion of the regression equation) is calculated as admission Hgb C minus discharge Hgb C, then Hgb C on admission when introduced on the independent side of the equation must perforce be associated with change in Hgb C.

A method like ordinary least squares regression can indicate the importance of an independent variable such as phlebotomy volume compared with all other variables in the model by producing partial R^2 's for each independent variable in the model. In addition, by reporting adjusted R^2 the analyst can give the reader some idea of how well the model performs. These statistics are especially important for studies of changes in Hgb C that are susceptible to confounding by indication—the sicker the patient the greater the indication for blood drawing and the greater the effect on Hgb C.³ Unfortunately, the authors do not report these statistics.

Finally, the authors suggest that the Hgb C drop they observed is clinically significant but their references to this statement are a textbook of hematology and a 1994 article that references an earlier edition of the same textbook.^{4,5}—**Norman A. Desbiens, MD**, University of Tennessee College of Medicine, Department of Medicine, Chattanooga, TN, USA.

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In Reply:—Dr. Desbiens makes several helpful suggestions and comments regarding alternate approaches to our analysis. We would like to specifically respond to a number of his comments.

First, we imposed stringent exclusion criteria to ensure that the changes in hemoglobin/hematocrit values seen were solely because of phlebotomy. Rather than controlling for these potential confounders as Dr. Desbiens suggests, we chose to restrict our sample to a more homogenous population. Practically, we would expect that the effect of phlebotomy in patients with gastrointestinal hemorrhage would be no different for patients with cellulitis.

Second, we disagree that pre-screening candidate variables with univariate analysis leads to over-fitting. This is particularly true because we had more than 400 observations and only 7 potential predictors. Repeating our analysis including all potential predictors provides identical results to those we obtained.

Third, whether or not to include a baseline measurement in analyses of change scores is controversial. We disagree that baseline hemoglobin is perforce correlated with hemoglobin change, although Dr. Desbiens is correct that it may be. We performed an unconditional analysis as suggested and found equivalent results.

Overall, we are confident that analytic methods described in our paper produced results that are robust in terms of the final conclusion: blood drawing for diagnostic studies in internal medicine inpatients causes anemia.—**Dinesh Thavendiranathan, MD, MSc, Akshay Bagai, MD**, Department of Medicine, University of Toronto, Toronto, Ontario, Canada; **Allan S. Detsky, MD, PhD**, Department of Medicine, University of Toronto, Toronto, Ontario; Health Policy, Management and Evaluation, University of Toronto, Ontario, Canada; and Department of Medicine, University of Health Network and Mount Sinai Hospital, Toronto, Ontario, Canada; **Nitesh K. Choudhry, MD, PhD**, Division of Pharmacoepidemiology and Pharmacoeconomics, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, USA.

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