diagnostic process, we believe it would be insufficient for practical resolution without making some proposal for the medical teams. In addition, with regard to medical practice with multiple divisions, factors of handoffs could have considerable influence on diagnostic errors. One retrospective study showed that failures in handoffs were one of the leading factors that contributed to diagnostic errors (2). Starmer et al (3) proved that implementing interventions at handoff points was associated with reductions in medical errors. With additional attempts to clarify the divisions involved in each part of a diagnostic process, including handoffs, the work by Bergl et al (1) would be more useful for providing specific suggestion for improving diagnostic errors in ICU settings.

Second, a narrower and specific target cohort would be better to gain further suggestive consequences. Patients admitted from the ward would have considerable differences from those admitted from the emergency department; the various factors include prior probability of diseases and backgrounds. By investigating them separately, more accurate and practical epidemiology and solutions of diagnostic errors will be obtained.

Third, the evaluation should include problems newly occurring after the first 24 hours of ICU admissions as well as initial problems during the first 24 hours of ICU admissions. Attention should be given to various complications, such as device-related complications, ventilator-associated pneumonia, and delirium, during ICU stay. Furthermore, prevention and reduction of long-term complications of critical care, including post-intensive care syndrome, are one of the major topics of modern intensive care (4). It is anticipated that diagnostic errors have a certain level of association with these complications as well as with problems during the first 24 hours of ICU admissions.

Medical errors in ICUs, including diagnostic errors, are potentially highly diverse and complicated. Constant and cumulative effort in the morbidity and mortality conference (5) would be helpful for patient safety improvement. Additionally, further prospective research in the field of adult intensive care is needed.

The authors have disclosed that they do not have any potential conflicts of interest.

ACKNOWLEDGMENTS
We would like to thank Editage (www.editage.com) for English language editing.

Junky Ishii, MD, Kohei Ota, MD, PhD, Nobuaki Shime, MD, PhD, Department of Emergency and Critical Care Medicine, Graduate School of Biomedical and Health Sciences, Hiroshima University, Hiroshima, Japan

REFERENCES
1. Bergl PA, Taneja A, El-Kareh R, et al: Frequency, Risk Factors, Causes, and Consequences of Diagnostic Errors in Critically Ill Medical Patients: A Retrospective Cohort Study. Crit Care Med 2019; 47:e902–e910
2. Gandhi TK, Kachalia A, Thomas EJ, et al: Missed and delayed diagnoses in the ambulatory setting: A study of closed malpractice claims. Ann Intern Med 2006; 146:488–496
3. Starmer AJ, Spector ND, Srivastava R, et al; I-PASS Study Group: Changes in medical errors after implementation of a handoff program. N Engl J Med 2014; 371:1803–1812
4. Desai SV, Law TJ, Needham DM: Long-term complications of critical care. Crit Care Med 2011; 39:371–379
5. Frey B, Doell C, Klawuer D, et al: The morbidity and mortality conference in pediatric intensive care as a means for improving patient safety. Pediatr Crit Care Med 2016; 17:67–72

DOI: 10.1097/CCM.0000000000004250

The authors reply:

We thank Ishii et al (1) for their insightful comments. They raise pertinent questions about the use of Diagnostic Error Evaluation and Research (DEER) taxonomy, cohort selection, and evaluation of errors occurring after the first 24 hours of ICU stay.

First, the DEER taxonomy is primarily intended to delineate where process failures occur in the diagnostic evaluation (2). For example, in our recently published article (3) in Critical Care Medicine, we were able to identify that cognitive failures, such as failure to consider the ultimate diagnosis or giving too much weight to a competing diagnosis, were most often implicated in diagnostic errors among the critically ill. We agree that the most appropriate next steps are to detail the origins of cognitive errors; to explore how breakdowns in systems and other processes, such as handovers, contribute to error; to devise real time systems to detect diagnostic error; and to create closed-loop feedback with referring providers, which might enhance future cognitive performance and diagnostic calibration (4). Given the retrospective nature of our study (3), we were unable to accomplish these tasks.

Obtaining more granular data to parse critically ill patients into more specific cohorts, such as by the source of admission, could enrich our understanding of diagnostic errors in the ICU. However, we found that on multivariable analysis, the patient’s antecedent location (i.e., emergency department vs ward) did not impact the risk of diagnostic error (3). Nevertheless, our sample size may have been insufficient. Further, we may not have accounted for all pertinent variables such as the number of diagnostic tests performed, prolonged ICU length of stay, or reversals in management (5).

Finally, we focused our attention on the transition period around ICU admission because, logically, establishing the correct diagnosis at admission is most likely to reduce morbidity and mortality. Akin to the “golden hour” of trauma, many medical ICU admission diagnoses, such as sepsis, pulmonary embolism, and vascular emergencies, require rapid recognition to avoid downstream harm. Nonetheless, we recognize that critically ill patients are susceptible to many iatrogenic harms, including diagnostic error, during a prolonged ICU stay. We hope our work incites the greater patient safety community to examine other forms of diagnostic error among the critically ill.

Dr. Singh disclosed government work. The remaining authors have disclosed that they do not have any potential conflicts of interest.
We read with great interest the systematic review by Santacruz et al (1) over 242 randomized controlled trials (RCTs) performed in critically ill patients, recently published in Critical Care Medicine. They found that only 13% of the RCTs they analyzed demonstrated a significant reduction in mortality from the new/tested intervention. We would like to make some points based on our feeling about the interpretation the authors made of their results.

First, we were feeling that the authors found disappointing the observed rate of beneficial trials, which was perceived as too low. Why should any RCT systematically end up with a significant benefit from using the new intervention? Basically, a trial should be done to refute the null hypothesis, as it is the case for any research which is done to disregard the a priori hypothesis we had, according to the 1974 Nobel Prize in Medicine Christian de Duve (2). Ioannidis (3) used the same argument in daily clinical practice as the routine in a given ICU. This would reinforce the clinicians not to use this cost-effective (5) and proven intervention, as research showed.

Fourth, other endpoints than mortality are relevant. The Fluids and Catheters Treatment Trial in ARDS patients found that fluid restrictive strategy increased the ventilator-free days, with no change in mortality, as compared with a liberal use fluids. This beneficial strategy should then be adopted in the daily clinical practice as the routine in a given ICU. This would contribute to make the practice of care more homogeneous 24 hours a day 7 days a week.

The authors have disclosed that they do not have any potential conflicts of interest.

Claude Guérin, MD, Laurent Argaud, MD, Médecine Groupement Hospitalier Centre, Hôpital Edouard Herriot, Department of Médecine Intensive-Réanimation Pavillon H, and University of Lyon, Faculté de Médecine Lyon-Est, Lyon, France

REFERENCES

1. Santacruz CA, Pereira AJ, Celis E, et al: Which Multicenter Randomized Controlled Trials in Critical Care Medicine Have Shown Reduced Mortality? A Systematic Review. Crit Care Med 2019; 47:1680–1691
2. de Duve C: Sept vies en une: Mémoires d’un prix Nobel. Paris, Odile Jacob, 2015
3. Ioannidis JPA: The importance of predefined rules and prespecified statistical analyses do not abandon significance. JAMA 2019; 321:2067–2068
4. Guérin C, Reignier J, Richard JC, et al; PROSEVA Study Group: Prone positioning in severe acute respiratory distress syndrome. N Engl J Med 2013; 368:2159–2168
5. Baston CM, Coe NB, Guerin C, et al: The cost-effectiveness of interventions to increase utilization of prone positioning for severe acute respiratory distress syndrome. Crit Care Med 2019; 47:e198–e205

The authors reply:

We thank Guérin and Argaud (1) for their interesting comments on our recent article (2), published in Critical Care Medicine. We agree that randomized controlled trials are conducted to refute the null hypothesis.