also be considered. Their suggestion regarding assessment of the rate of adverse events during the first 6 weeks as a potential indicator of response is interesting. Their point regarding correlation of response with immune-related adverse events is supported by data showing that patients receiving the combination who discontinued treatment owing to toxic effects had a higher objective response rate (58%) than those who did not discontinue treatment (50%).[1] We also agree that identification of biomarkers for response to monotherapy would be helpful in treatment decision making.

In addition, we appreciate the comments by Alegre-del Rey et al. regarding careful interpretation of subgroup analyses. It is not clear that statistical testing for the presence of treatment-by-subgroup interactions would add value here; the trial was not powered for a comparison between the nivolumab-containing groups, so the analyses were descriptive in nature. Interaction testing of subgroups would have even less power. The subgroup analyses were all exploratory, but preplanned, to help assess which populations might have better outcomes; *BRAF* mutation status was also a stratification factor for randomization. The presentation of *BRAF* subgroups was not intended to imply a treatment recommendation but to represent two clinically relevant subgroups of patients with melanoma. As for biologic plausibility, the survival curves for the nivolumab-containing groups in the population with *BRAF* mutations show delayed separation, suggesting the effect of subsequent therapy, and are hypothesis-generating regarding a possible association of adaptive resistance mechanisms with *BRAF* mutations.[2] The published hazard ratio for this subgroup shows the 95% confidence interval crossing 1.0. The factors determining the likelihood of response are numerous, and treatment decisions should be made after careful consideration of adverse events, response rates, and survival rates.

Jedd D. Wolchok, M.D., Ph.D.
Memorial Sloan Kettering Cancer Center
New York, NY
wolchokj@mskcc.org

Linda Rollin, Ph.D.
Bristol-Myers Squibb
Princeton, NJ

James Larkin, F.R.C.P., Ph.D.
Royal Marsden NHS Foundation Trust
London, United Kingdom

Since publication of their article, the authors report no further potential conflict of interest.

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Hospital-Readmission Risk — Isolating Hospital Effects

TO THE EDITOR: The hospital-specific effects on readmission rates seen by Krumholz and colleagues were small (Sept. 14 issue).[1] Despite thousands of patients in the sample, the only significant difference was for the most extreme comparison (hospitals in the highest quartile of readmission rates vs. those in the lowest quartile), and the differences were smaller than what would have been expected on the basis of publicly available adjusted hospital-wide readmission rates. According to the authors' data, the relative per-quartile differences in readmission rates ranged from 0.78 to 3.46%. In contrast, by our calculations, the relative per-quartile differences seen in publicly available adjusted hospital-wide readmisison data are higher: 2.69 to 5.79% (https://data.medicare.gov/Hospital-Compare/Hospital-Returns-Hospital/632h-zaca). This suggests that nonhospital factors account for an important component of variance in hospital performance on the hospital-wide readmission measure. Rather than reassuring us about the robustness of the hospital-wide readmission metric as a quality measure, the data by Krumholz and colleagues suggest that the hospital-wide readmission measure has limited ability to detect or quantify meaningful between-hospital differences in care processes, except at the extremes of performance, and may be too dependent on nonhospital factors to be a valid measure of hospital quality.

Daniel J. Brotman, M.D.
Erik Hoyer, M.D.

Johns Hopkins University
Baltimore, MD
brotman@jhmi.edu

Amy Deutschendorf, R.N.

Johns Hopkins Hospital
Baltimore, MD

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1. Krumholz HM, Wang K, Lin Z, et al. Hospital-readmission risk — isolating hospital effects from patient effects. N Engl J Med 2017;377:1055-64.

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TO THE EDITOR: Krumholz et al. studied readmission rates of elderly Medicare recipients and concluded that hospital quality determines readmission rates independently of patient factors. Their methods are valid, but we challenge the premise that the lowest readmission rates reflect the best quality of hospital care. Uncertainty whether discharge will be successful is inherent in clinical care for elderly patients. In every patient, this decision should involve not just the risk of readmission, but also risks associated with further prolongation of the hospital stay (e.g., loss of self-supportiveness, hospital-acquired infection, delirium, and social deprivation). Rather than minimizing readmission risk, physicians should balance this risk against the benefit of early discharge. In other words, timely discharge comes at the price of some readmissions.

The study does not allow final conclusions regarding quality of care. Can the authors present data on length of stay and overall health outcomes — including self-supportiveness and quality of life — in the different strata of readmission rates?

Yvo M. Smulders, M.D.
Prabath W.B. Nanayakkara, M.D.

VU University Medical Center
Amsterdam, the Netherlands
y.smulders@vumc.nl

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THE AUTHORS REPLY: Brotman et al. use relative differences in publicly available data to suggest that hospital effects are less than what we found. In our article, we reported that in the performance-classification sample the absolute difference in mean risk-standardized readmission rates between the top and bottom quartiles was 1.3 percentage points. The question was whether this difference is the result of case-mix differences or the result of factors, such as quality of care, that may be related to the hospital. When we evaluated the difference in risk for the same patients admitted to top and bottom hospitals, we found an absolute difference of 2.0 percentage points, even greater than that found in the adjusted analysis from the performance-classification sample. If unmeasured patient factors were responsible for some hospitals being labeled as worse than others, then we would have expected no or less difference when we evaluated the same patients admitted to hospitals classified as performing differently. We focused on the absolute difference in readmission risk, which is often more meaningful than a relative difference given that small base rates tend to make the relative differences large. Moreover, publicly available hospital-wide readmission data cannot be used to implement our design, because the samples are not comparable.

Smulders and Nanayakkara question whether lower readmission rates may be equated with higher-quality care. Deficits in transitional care are well documented. Readmission rates do appear amenable to improvements in care transitions, and rates have declined without evidence of apparent harms during the period that national incentives were instituted in the Hospital Readmissions Reduction Program.[1-3]

Harlan M. Krumholz, M.D.
Kun Wang, Ph.D.

Yale School of Medicine
New Haven, CT
harlan.krumholz@yale.edu

Sharon-Lise T. Normand, Ph.D.

Harvard Medical School
Boston, MA

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