Although treating pCR as a binary variable defined only by residual invasive disease is appealing from the standpoint of simplicity for planning analyses for future studies and for the purposes of clinical management, we feel that the reported findings do not support this. The results suggest that pCR with residual in situ disease may have prognostic utility and that this outcome should be included as an independent end point for efficacy of neoadjuvant regimens, representing an inferior response to pCR with the absence of DCIS but a superior response compared with the absence of pCR. The authors note that pCR is considered an end point for accelerated drug approval in neoadjuvant trials. The maintenance of a status of pCR with DCIS would allow for further stratification of the associations of novel agents with outcomes and possibly allow for the establishment of differential effects by breast cancer subtype.

In Reply We thank O’Keefe and Wallace for reading our study. In our analysis of data from I-SPY2, a prospective, randomized, neoadjuvant trial with prespecified pathological assessment of specimens according to the Residual Cancer Burden method, we found a nonsignificant difference in 3-year event-free survival (EFS) and distant recurrence-free survival (DRFS) among those with pathologic complete response (pCR) with or without residual ductal carcinoma in situ (DCIS). Those with pCR without residual DCIS had 3-year EFS and DRFS of 95.6% and 96%, respectively; those with pCR plus residual DCIS had 3-year EFS and DRFS of 89.2% and 90.6%, respectively. While the observed EFS and DRFS differed between groups, our study was underpowered to detect differences of this magnitude. Indeed, for these findings to have reached statistical significance in our study would have required over 5000 patients. Such a large sample size reflects the small absolute difference between groups, with nearly 90% of patients in both groups having excellent 3-year outcomes. While response to therapy is on a continuum and cut points will continue to be refined, we do not feel that there are currently sufficient data to support designating pCR with vs without DCIS as 2 distinct prognostic groups.

The mixed findings in the literature reflect the challenges of answering this question definitively. Differences in specimens evaluation including the number of sections examined, which can vary by type of surgery performed, may influence the detection rates of residual in situ or invasive carcinoma; additionally, residual invasive disease could be reported as in situ disease depending on pathologist interpretation. While our study lacks the statistical power of larger studies, it has the advantage of prospective centralized pathology training and assessment by a small group of pathologists with a standardized approach. We too are intrigued by the differences in rates of residual DCIS by tumor receptor subtype, and perhaps with accumulating data, prognostic groups by subtype and therapy response will be refined. However, given the excellent outcomes of both groups in our study, we do not feel that our findings as currently reported provide sufficient data to alter the definition of pCR at this time.

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CORRECTION

Errors in Figure 3: The Original Investigation titled “Effect of Multimodal Prehabilitation on Reducing Postoperative Complications and Enhancing Functional Capacity Following Colorectal Cancer Surgery: the PREHAB Randomized Clinical Trial,” published on March 29, 2023, had errors in Figure 3D. Footnote a should also be indicated for before surgery and at 4 weeks for the prehabilitation group. This article was corrected online


Error in Text: The Invited Commentary titled “The Benefits of Surgery for Diverticular Disease—Have We Met the Burden of Proof?” published online April 19, 2023, was corrected to fix the recurrence rate in the surgery arm in the text. It now reads, “It is also critical to note that 1 of 4 recurrences in the surgery arm…” instead of “the entire 11% recurrence rate (n = 2) in the surgery arm…” This article was corrected online.