First, we disagree with the exclusion of studies in which the control subjects had taken clopidogrel until 5 to 7 days before coronary artery bypass grafting. This excluded group is exactly the important group that must be assessed, because it will contain many patients with recent acute coronary syndrome, patients with stent placement, and higher risk patients requiring ongoing clopidogrel therapy. Because those undergoing operation while they are receiving clopidogrel are likely a similar cohort, inclusion of patients who received clopidogrel to that point would make the comparison more valid.

Second, Biancari and colleagues¹ predominantly used a fixed-effects model and only used the random-effects model when statistical heterogeneity was greater than a predefined cutoff. We believe that a random-effects model is more appropriate when reviewing surgical cohorts, which by their nature have significant clinical heterogeneity. Furthermore, nonsignificant results of tests of heterogeneity do not guarantee homogeneity between studies included in the meta-analysis, and sources of methodologic or clinical heterogeneity should be explored.³

The more conservative nature of the random-effects model provides more realistic confidence intervals for groups that can differ wildly between surgical centers as a result of surgical experience, the percentage of urgent cases, and the cornucopia of different adjunct medical therapies used.

Finally, the debate between fixed- and random-effects models is not new. The general consensus remains that it is unreasonable to assume that even with adjustment of multiple covariates all between-trial variation can be accounted for, and thus the random-effects model is preferable.^{4,5}

From a scientific point of view, reporting the results of both models allows readers to judge more objectively through sensitivity analysis the robustness of the meta-analytic

findings. This is particularly relevant when the fixed-effects model for postoperative death demonstrates a lower 95% confidence interval, just marginally above the 1-null effect. On reassessment with a random-effects model, we find that their effect size becomes statistically nonsignificant, with risk ratio of 1.28 (95% confidence interval, 0.99–1.66).

The findings regarding reduced postoperative myocardial infarction and increased blood product use and reoperation remain valid.

Although the statistical change in mortality may appear small, it reflects the importance of appropriate methodologic rigor and accurate reporting. The original choice of model may have been influenced by the *P* value generated.

We conclude that with a change in the statistical model from fixed to random effects, the conclusion of Biancari and colleagues¹ that observational studies show significantly increased mortality no longer holds true.

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Reply to the Editor:

On the basis of their own recent meta-analysis on this topic,¹ Nijjer and colleagues commented on the results of our meta-analysis about the effects of preoperative exposure to clopidogrel before coronary artery bypass grafting.² Nijjer and colleagues raised concerns regarding our methodology, which could have affected the results of our meta-analysis. In our study, we used a fixed-effects model when heterogeneity was considered unimportant. We do agree with Nijjer and colleagues that a random-effects model is more appropriate when analyzing nonrandomized studies. In fact, we used the latter method in our most recent meta-analyses. Here, we report the results of using a random-effects model in all outcome end points (Table 1). The use of this method provided similar results to those published, but according to random-effects analysis, the increased risk of immediate postoperative mortality for patients exposed to clopidogrel only tended to be significant (risk ratio, 1.28; 95% confidence interval, 0.99–1.66; *P* = .06).

Nijjer and colleagues disagreed about our decision to exclude from the analysis those studies including control subjects exposed to clopidogrel for whom the drug was discontinued 5 to 7 days before surgery. Even if Nijjer and colleagues argue that these control subjects would include

TABLE 1. Risk of postoperative adverse events in patients who received clopidogrel versus control subjects before coronary artery bypass grafting

Outcome end points	No. of studies	Subjects	Statistical method	Effect estimate	95% CI
Immediate postoperative mortality	13	12,129	Risk ratio (M-H, random, 95% CI)	1.28	0.99–1.66
Reoperation for bleeding	14	10,944	Risk ratio (M-H, random, 95% CI)	1.78	1.28–2.48
Stroke	7	4422	Risk ratio (M-H, random, 95% CI)	1.28	0.61–2.70
Myocardial infarction	11	4084	Risk ratio (M-H, random, 95% CI)	0.64	0.49–0.83
Postoperative blood loss	10	3186	Mean difference (IV, random, 95% CI)	157.77	61.91–253.63
Red blood cell transfusion	9	10,026	Risk ratio (M-H, random, 95% CI)	1.23	1.10–1.37
Transfused red blood cells (units)	7	2369	Mean difference (IV, random, 95% CI)	0.77	–0.05 to 1.59
Transfused fresh-frozen plasma (units)	7	2369	Mean difference (IV, random, 95% CI)	0.31	0.12–0.50
Transfused platelets (units)	6	741	Mean difference (IV, random, 95% CI)	2.41	–0.03 to 4.86

CI, Confidence interval; M-H, Mantel-Henzel method; IV, inverse variance method.

many patients with recent acute coronary syndrome and those in whom percutaneous coronary interventions were likely performed, we believe that patients for whom it was possible to discontinue clopidogrel 5 to 7 days before surgery were those who were in stable condition permitting delay of surgery and therefore not requiring urgent or emergency surgery. Their inclusion would have been a potential source of bias.

Here we take also the opportunity to comment briefly on the differences and similarities of these 2 meta-analyses to get more conclusive results on this controversial issue. In addition to excluding studies in which control subjects were exposed to clopidogrel, we excluded from our analysis those studies in which aprotinin was used in most or all patients, because its use could have had a major effect in reducing the risk of major postoperative bleeding. Importantly, we excluded studies that included patients who underwent valve surgery, which may have significantly affected the results of meta-analysis. The study by Nijjer and colleagues¹ did not share these important exclusion criteria. Despite these methodologic differences, our studies reached similar conclusions. In fact, it seems rather clear that recent exposure to clopidogrel before coronary surgery is associated with increased risk of excessive bleeding and need for reexploration. Furthermore, in both meta-analyses we observed a trend toward increased mortality with recent exposure to

clopidogrel, which is consistent in most of the included studies.

Because excessive bleeding is a major determinant of postoperative outcome,³ we conclude that continuing clopidogrel until the time of coronary artery bypass grafting may expose patients to an increased risk of excessive bleeding and its related complications. These results must be viewed, however, in the light of suboptimal design and analysis of the included studies.

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EFFICACY OF AWAKE THORACIC SURGERY To the Editor:

We greatly appreciated reading the simple but clear case report by Noda and colleagues¹ of awake thoracoscopic surgery for intractable pneumothorax. Noda and colleagues¹ demonstrated the benefits of local and epidural anesthesia in treating a particular patient who had right pneumothorax after left pneumonectomy for cancer. The procedure was both well tolerated and successful in completely controlling the air leakage.

We agree with Noda and colleagues¹ that lesions situated next to the hilum may present some difficulties in approach when operating on a breathing lung. Nevertheless, we would first contend that pulmonary tears causing air leakage are more frequently situated in the peripheral surface of the lung and are therefore very well suited to approaches performed with epidural anesthesia. Second, we advocate that even hilar lesions can be reached and treated in an awake modality after adequate training.

Noda and colleagues¹ also stated that total lung collapse cannot be obtained in patients who have limited contralateral pulmonary function. In our own awake series,² however, lung collapse was most of the time equivalent to that achieved with single-lung ventilation. In addition, we found that awake video-assisted thoracoscopic management of pneumothorax is particularly feasible for and well tolerated by elderly patients and those with poor