influence cancer recurrence and thus survival. Clearly the situation is far more complex than the headline; I do hope when prospective research is undertaken, it takes these wide-ranging aspects of perioperative care into account.

Competing Interests
The author declares no competing interests.

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References

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Long-term Survival, All-cause Mortality, and Propensity Score Matching

To the Editor:
We read with great interest the article by Wigmore et al.1 The authors have produced one of the largest studies published looking at cancer survival and anesthetisa.

In an era where new cancer therapies are becoming ever more expensive to develop, their primary study finding, increase in mortality associated with inhalational anesthesia compared to intravenous anesthesia with an adjusted hazard ratio of 1.46 (1.29 to 1.69) after propensity score matching and multivariate analysis, is one of huge potential significance.

There are three points arising from the study we would like to discuss.

First, we agree with the authors that long-term survival is a key outcome measure in cancer surveillance. However, we noticed this study analyzed patients over a 3-yr period, with a further 18-month follow-up period, giving a maximum total potential follow-up time of 4.5 yr.

Widely accepted measures of long-term cancer survival are 5 and 10 yr.2,3 We feel that the use of the phrase “long term” in the study title could mislead some readers. Perhaps it would have been more appropriately titled, simply, “survival rates for patients undergoing volatile versus intravenous anesthesia for surgery.”

Second, we would like to highlight issues around the use of propensity scoring analyses and all-cause mortality data.

All-cause mortality is typically used as an outcome measure in prospective trials. Randomization helps account for unknown confounding factors affecting the outcome, thus facilitating the use of all-cause mortality as a primary outcome.

Usefulness of propensity scoring matching in retrospective studies is limited by the fact that remaining unmeasured confounding may still be present.4 This makes the all-cause mortality data presented in this study more difficult to evaluate.

Preclinical studies in the literature suggest some form of immunomodulatory effects related to propofol or volatiles5,6 during the intraoperative period affect the likelihood of recurrence of cancer.

Given this potential for causality combined with the limitations of propensity score matching, we suggest the study could be further refined by looking at cancer-related deaths only as opposed to all-cause mortality.

A possible suggestion would be obtaining mortality data from national cancer registries where cause of death would also be available, as an alternative to the National Health Service demographics service.

Finally, we noticed the Kaplan–Meier survival curves were for unmatched data only. We think that comparing the survival curves for the unmatched groups to those of the groups matched for known variables would add something to the study.

We acknowledge the authors recognized some of the inevitable shortcomings of retrospective studies and support their calls for urgent prospective work to corroborate their findings.

Competing Interests
The authors declare no competing interests.


References
1. Wigmore TJ, Mohammed K, Jhanji S: Long-term survival for patients undergoing volatile versus IV anesthesia for...
As far as including cancer types in either the propensity model or the multivariate analysis (beyond the broad groups that have already been included in the analysis, see tables 1 and 2), the major issue is the numbers of different types and subtypes, with consequent substantial implications for outcome. A look through the data reveals more than 20 broad cancer types. Within those types are further subdivisions, for example, triple-negative breast cancer has a very different

In Reply:
Many thanks for your comments on our recent retrospective study.1 With regard to the first point posed by Drs. Ali and Ghori, concerning the use of the term “long-term cancer survival,” we agree that together with 1-yr survival, 5- and 10-yr survival rates are commonly used when reporting cancer survival. However, contextually, mortality rates for perioperative interventions are commonly reported as either 30 days or length of stay, and as such the reported follow-up of between 18 months and 4.5 yr would qualify as long term.

With regard to the use of the propensity model and all-cause mortality data, we agree that a better approach would have been to consider cancer-attributable mortality. However, these data are not reliably available in the United Kingdom. National cancer registries do not cover the broad span of cancers we considered, and in addition often have incomplete data for the early years covered by the study.

We agree that Kaplan–Meier curves for the propensity-matched groups should have been included in the study. These are now included in figure 1, A–C, and as you can see are very similar to those for the nonmatched groups.

Drs. Doleman, Lun, and Williams raise interesting queries regarding our analysis, much of which we are in agreement with.

There is little doubt that cancer type and stage have a profound effect on outcome, and the lack of accurate data within our study for the latter in particular is a potential major confounder. However, as we state in the discussion, the very lack of availability of staging data to the practitioners administering the anesthesia lessens this fact since it could not have been a deciding factor in the choice of anesthetic.

James C. Eisenach, M.D., served as Editor-in-Chief for this exchange.


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