



Bias in revascularization study

We believe that the survival benefit of revascularization in patients with heart failure was probably overestimated in the study by Ross Tsuyuki and colleagues¹ because of time-dependent bias.² Time-dependent bias can occur whenever patients are assigned to treatment groups after the start of observation. Patients who experience an event early in the observation period will not receive the treatment being studied. As a result, the outcome risk in the untreated group is inflated and the relative benefit of treatment is exaggerated.

It is possible that this phenomenon occurred in the present study.

Patients were assigned to the revascularization group if they received treatment during the first year of observation. If patients had died at any time during the first year of observation before treatment, they would have been assigned to the control group. Also, if patients had experienced any other significant event (e.g., stroke) during the first year of observation, they would have been less likely to undergo revascularization. Either of these events would have made outcomes appear to be worse in the group of patients who did not undergo revascularization.

That the survival curves of the treatment groups appear to separate primarily during the initial year of observation suggests that a time-dependent bias might have played a strong role in the study's results. We strongly suggest that the analysis be repeated using

time-dependent covariates to account for this potential bias.³

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[Two of the authors respond:]

Carl van Walraven and Alan Forster are correct. In our study,¹ the medical treatment group included patients who were truly selected for medical management and those for whom revascularization was planned initially but not carried out owing to early death or patient or provider preference. Thus, some of the patients in the medical treatment group would have been in the revascularization group if information on their initial therapy plan had been available. The bias, then, is perhaps more correctly labelled misclassification bias rather than time-dependent bias.

Thompson and colleagues have elegantly demonstrated the potential effect of such a misclassification in observational studies.² In this work, 4 groups were analyzed: patients who received coronary artery bypass grafting as recommended, patients who received percutaneous coronary intervention as recommended, patients who received medical management as recommended, and patients who received medical management although percutaneous coronary intervention or coronary artery bypass grafting had been recommended (this group is com-

parable to the group misclassified in our work). Indeed, this final group had the poorest survival rate.

Unfortunately, in our study we were unable to differentiate between patients who received medical therapy as a chosen therapy and patients who were treated medically, although the initial plan was for revascularization. Thus, early deaths in the medical management group may have been events that occurred while patients were waiting for a planned revascularization procedure that did not occur. In this case, the issue is not one of time-dependent covariates but rather one of knowing the true intention at $t = 0$, an issue not easily addressed using observational data. In our case, the separation between the survival curves does occur early on, when this bias would be at play. However, our curves continue to separate over time, indicating a longer term survival advantage that is possibly attributable to revascularization. We thank Walraven and Forster for shedding light on this important issue.

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Improving organ donation in Canada

The Canadian Council for Donation and Transplantation (CCDT) agrees with some of the issues raised by