



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

Wayne Kondro.¹ There is indeed fragmentation in the organization of the organ and tissue donation and transplantation system in Canada, and Canadian donation rates are a concern.

We know that the Canadian organ and tissue donation and transplantation system is complex and the optimal made-in-Canada solution to improving patient outcomes and quality of life needs to be found through collaboration, consensus and coordination. As a national nonprofit organization with a mandate to provide advice to the Conference of Deputy Ministers of Health on improving the organ and tissue donation and transplantation system, the CCDT is a catalyst for change in this system.

Measures such as donation rates can be informative. We have learned, though, that international donation rates are not measured in the same way. Thus, comparing Canadian donation rates to those in other countries may not be a useful way to mark Canadian progress.

Kondro cites the United Network for Organ Sharing in the United States as a model to solve the current problems in the Canadian system. There are some things that we can learn from this model, but it may be significantly less applicable in our country because of the different health care context in Canada. The United Network for Organ Sharing is a regulatory body that specializes in organ allocation, but, according to our stakeholders, efficiency in allocation is not the only issue that needs to be addressed to improve patient outcomes.

The CCDT, physicians and other health care providers involved in donation and transplantation seek to ensure that people requiring transplantation have access to the care they need at the earliest opportunity. The creation of a made-in-Canada system is already evolving through national dialogue and deliberation about best practices in donation and transplantation.²⁻⁴ We look forward to further consensus recommendations from experts in the field and trust that regional authorities will implement them, as they have done in the past.

Canada has centres of excellence

with high donation rates, and the role of the CCDT is to support the transfer of this excellence throughout our country. All stakeholders in the organ and tissue donation and transplantation system want to move more quickly because lives are being lost.

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Wayne Kondro's recent article on organ donation programs¹ highlights some of the challenges that the Canadian transplant community faces as it responds to the changes that have occurred in the transplantation landscape over the last 3 or 4 decades. Although a national organ donation agency may be beneficial, it is inaccurate to suggest, as Kondro does, that a nationwide wait-list does not exist and that organ sharing is somehow an afterthought.

For more than 20 years, the liver

transplant community has had a nationwide agreement on wait-list priority for both urgent and nonurgent cases. This allocation system includes a consensus on organ sharing for urgent cases right across the country. A list is updated weekly by each regional organ procurement agency and is disseminated to the transplant centres. About half of the 50–60 urgent liver transplantations each year are performed using organs that come from another region. Although it is informal and operates with limited funding, the “liver study group” meets annually, has achieved consensus on many difficult issues and continues to find ways to optimize liver allocation and transplantation outcomes across Canada.

The driving forces behind changes in organ allocation policy in the United States are not exactly the same as those in Canada; solutions should be sought that reflect our reality. Where a national agency may be most beneficial is in providing the infrastructure to gather the statistics that will be most useful in tracking trends in transplantation. This will permit stakeholders to implement the necessary modifications in practice in a timely manner.

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Wayne Kondro has pointed out the weaknesses in our organ donation programs in Canada.¹ In the United States, the Department of Health and Human Services vigorously took up the challenge of increasing organ donation rates. It established the Organ Donation Breakthrough Collaborative to increase the likelihood that initiatives to improve organ donation rates will be successful. The Centers for Medicare and Medicaid Services established conditions of participation designed to enhance organ donation in all hospitals