Authors’ Reply

We thank Zhao et al.\textsuperscript{1} and Wei\textsuperscript{2} for their interest in our manuscript, “Long-term kidney outcomes following childhood acute kidney injury receiving dialysis: A population-based cohort study,”\textsuperscript{3} and for providing thoughtful feedback. The letter from Zhao et al.\textsuperscript{1} correctly highlights that outcomes after AKI differ significantly depending on the cause of AKI. AKI caused by isolated, brief insults, where removal of the offending agent is feasible (e.g., hypovolemia or isolated nephrotoxic medication exposure) typically have better outcomes than those with prolonged or recurrent insults (e.g., prolonged ischemia or repeated nephrotoxin exposure in patients with cancer).

On the basis of available data within the Ontario healthcare administrative databases, we cannot precisely identify the etiology of dialysis-treated AKI in our participants. Instead, we included all children with dialysis-treated AKI within Ontario between 1996 and 2017. We performed subgroup analyses evaluating children that underwent cardiac surgery during their hospitalization and those that had prior cardiac surgery or malignancy. Cardiac surgery during hospitalization may be a proxy indicator of cardiac surgery–associated AKI, but we acknowledge that other factors may have caused or contributed to AKI. We found the incidence of kidney failure or death after dialysis-treated AKI was similar between children that did or did not undergo cardiac surgery.\textsuperscript{3} Whether pediatric cardiac surgery–associated AKI is associated with adverse long-term kidney outcomes remains unclear. Recent prospective studies, including Translational Research Investigating Biomarker Endpoints in Acute Kidney Injury (TRIBE-AKI)\textsuperscript{4} and Assessment, Serial Evaluation, and Subsequent Sequelae in Acute Kidney Injury (ASSESS-AKI),\textsuperscript{5} have not found significant associations between cardiac surgery–associated AKI and CKD or hypertension by 4–5 years. Overall CKD and hypertension incidence in pediatric cardiac surgery populations is high.\textsuperscript{4,5} We hypothesize that other factors—such as underlying heart disease, residual postoperative deficits leading to recurrent surgeries, and other comorbidities—may be stronger mediators of long-term kidney outcomes than postoperative AKI occurrence.

We also evaluated a number of other potential etiologic factors (e.g., sepsis, shock, extracorporeal membrane oxygenation, stem cell transplantation, hemolytic uremic syndrome, and various preexisting comorbidities). Although this provided clues to the potential etiology of each AKI, we cannot fully establish causality using administrative data, which we acknowledge as a study limitation.

Additional large, prospective studies focused on long-term kidney outcomes after pediatric AKI are needed to improve the risk stratification of survivors of AKI. Most current studies have focused on initial AKI hospitalization risk factors. However, a number of postdischarge factors may also significantly contribute to long-term CKD risk and warrant further exploration. Improved risk-stratification tools would help establish criteria for targeted follow-up and CKD prevention strategies (such as dedicated post-AKI follow-up clinics).

As Wei\textsuperscript{2} highlights, laboratory data were not available in our study, preventing us from further validating the dialysis-treated AKI exposure. However, the administrative codes we used to define acute dialysis have been previously validated with a high positive predictive value (94%).\textsuperscript{6} In Ontario, accurate billing is required for physician and facility reimbursement, making these codes reliable for identifying acute dialysis. We excluded children with inborn errors of metabolism or poisoning, given that they may have received acute dialysis without an AKI. We believe the vast majority of the included cohort that received acute dialysis in our study had associated AKI.

We did not use a combination of AKI and dialysis codes to define dialysis-treated AKI, given that administrative codes for AKI have a low sensitivity (<15%) in children.\textsuperscript{7} This would significantly reduce the size of our dialysis-treated AKI cohort. Although understanding differences in long-term kidney outcomes after dialysis-treated versus less severe forms of AKI is important, this was not our focus. For that reason, we used hospitalized patients (without dialysis-treated AKI) as comparators to determine the adverse kidney outcomes attributable to an episode of dialysis-treated AKI. Further, administrative database codes are better at detecting stage 3 AKI than stage 1–2 AKI, which would create selection bias.\textsuperscript{7}

We acknowledge Wei’s\textsuperscript{2} comment on the greater number of deaths versus kidney failure events contributing to our composite end point. However, the incidence of both kidney failure and death were also separately higher in the dialysis-treated AKI cohort. Due to the absence of laboratory data, change in serum creatinine could not be determined. With regards to adjustment and matching, we matched cases and comparators on the basis of age, sex, and index.
hospitalization year, and adjusted our Cox models using variables selected a priori. These variables were selected on the basis of their reported associations with long-term kidney outcomes and the reliability of their administrative coding.

DISCLOSURES

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REFERENCES


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