Clinical Adjudication of Hemodialysis Catheter-Related Bloodstream Infections: Findings from the REDUCCTION Trial

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Key Points

- The inter-rater reliability of reporting hemodialysis catheter-related infectious events between site investigators and trial adjudicators in Australia and New Zealand was substantial.
- The high concordance level in reporting catheter infections improves confidence in using site-level bacteremia rates as a clinical metric for quality benchmarking and future pragmatic clinical trials.
- A rigorous adjudication protocol may not be needed if clearly defined criteria to ascertain catheter-associated bacteremia are used.

Abstract

Background Hemodialysis catheter-related bloodstream infection (HD-CRBSI) are a significant source of morbidity and mortality among dialysis patients, but benchmarking remains difficult because of varying definitions of HD-CRBSI. This study explored the effect of clinical adjudication process on HD-CRBSI reporting.

Methods The REDUcing the burden of Catheter ComplicaTIOns: a National approach trial implemented an evidence-based intervention bundle using a stepped-wedge design to reduce HD-CRBSI rates in 37 Australian kidney services. Six New Zealand services participated in an observational capacity. Adult patients with a new hemodialysis catheter between December 2016 and March 2020 were included. HD-CRBSI events reported were compared with the adjudicated outcomes using the end point definition and adjudication processes of the REDUcing the burden of Catheter ComplicaTIOns: a National approach trial. The concordance level was estimated using Gwet agreement coefficient (AC_1) adjusted for service-level effects and implementation tranches (Australia only), with the primary outcome being the concordance of confirmed HD-CRBSI.

Results A total of 744 hemodialysis catheter-related infectious events were reported among 7258 patients, 12,630 catheters, and 1.3 million catheter-exposure days. The majority were confirmed HD-CRBSI, with 77.9% agreement and substantial concordance (AC_1=0.77; 95% confidence interval [CI], 0.73 to 0.81). Exit site infections have the highest concordance (AC_1=0.85; 95% CI, 0.78 to 0.91); the greatest discordance was in events classified as other (AC_1=0.33; 95% CI, 0.16 to 0.49). The concordance of all hemodialysis catheter infectious events remained substantial (AC_1=0.80; 95% CI, 0.76 to 0.83) even after adjusting for the intervention tranches in Australia and overall service-level clustering.

Conclusions There was a substantial level of concordance in overall and service-level reporting of confirmed HD-CRBSI. A standardized end point definition of HD-CRBSI resulted in comparable hemodialysis catheter infection rates in Australian and New Zealand kidney services. Consistent end point definition could enable reliable benchmarking outside clinical trials without the need for independent clinical adjudication.

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See related editorial, "Preventing Sepsis in Maintenance Dialysis: Is Adjudication of CRBSI Necessary?" on pages 485–486.

Introduction

Dialysis central venous catheters are ubiquitous in clinical practice and are central to the delivery of hemodialysis globally.[1,2] However, hemodialysis catheter-related bloodstream infection (HD-CRBSI) remains a significant access-related complication and is a major source of morbidity and mortality among patients with ESKD.[3–5]

Accurate identification and measurement of HD-CRBSI is crucial for reducing infection rates.[4,6] Because of its association with poor patient outcomes, various health care institutions are required by state health departments to monitor catheter infection data and make HD-CRBSI measurement an important safety and quality indicator of patient care.[7–9] However, there is considerable heterogeneity in the presentation of bacteremia rates because of the lack of a widely agreed upon definition of HD-CRBSI. In the United States, a number of clinical and surveillance definitions for catheter-related infections were described in different practice guidelines prepared by the Healthcare Infection Control Practices Advisory Committee of the Centers for Disease Control and Prevention,[10] Kidney Disease Outcomes Quality Initiative,[11] and the Infectious Diseases Society of America (IDSA).[12] The variations in HD-CRBSI definitions and their interpretations make it challenging to compare infection rates and understand the harms associated with their use.[7,13] There also exists a disparity in reporting of infection burden that adds to the ambiguity of the true rate of HD-CRBSI for interhospital and interstate benchmarking.[14–16] In Australia, there is no national system to collect and report HD-CRBSI rates. Compounding the methodological difficulties in measuring HD-CRBSI is the poverty of literature describing the feasibility and accuracy of service-based reporting of infectious events associated with hemodialysis catheter use.

A consistent approach for the measurement of HD-CRBSI events is pivotal to the reliability of reporting key performance indicators and good clinical management. There is growing interest in the value of adjudication of study outcomes in clinical trials to ensure the collection and reporting of highly robust data.[17] The REDUcing the burden of dialysis Catheter ComplicaTIOns: a National approach (REDUCCTION) trial (ACTRN 12616000830493) was a cluster randomized trial that studied the impact of evidence-based intervention bundles in reducing the rate of HD-CRBSI in participating kidney services and used a standardized process in reporting and validating catheter-related infectious events.[18] Although the previous findings from the REDUCCTION trial revealed that the implementation of the intervention bundles did not yield a significant reduction in HD-CRBSI rates in Australia,[18] this study is built on the trial's established reporting structure for catheter-related infections to assess the concordance between service-reported HD-CRBSI events and the corresponding adjudicated outcomes across Australia and New Zealand. We hypothesized that there would be a high level of agreement between the outcomes defined by kidney services and those confirmed by the adjudicators.

Methods

Study Design

This is a *post hoc* analysis of the data collected during the REDUCCTION trial. The REDUCCTION trial design and primary results from the Australian cohort have previously been published.[18,19] In brief, the study was a stepped-wedge cluster-randomized trial of an evidence-based intervention package aimed at reducing HD-CRBSI which included all hemodialysis patients who had a new catheter inserted in 37 participating Australian kidney services between December 20, 2016 and March 30, 2020. Six New Zealand kidney services contributed patient and catheter data to the dataset but did not implement the study intervention because of local regulatory requirements. The trial and data collection were approved by the respective ethics committee in all regions across the two countries.[19]

Setting

A kidney service was defined as a hospital-based service or site within a local health district that operates under the same clinical governance and uses a single framework to manage hemodialysis catheters. The REDUCCTION trial implemented a suite of interventions throughout Australia in a series of three intervention implementation tranches commencing in April 2018 (with 12 kidney services), September 2018 (with a further 12 kidney services), and April 2019 (with 13 kidney services).[19]

Participants

Adult patients in a participating kidney service who had a hemodialysis catheter inserted at any time after the commencement of the trial, or in whom the kidney service assumed the care of such a catheter, were included. Hemodialysis catheters inserted before the start of the trial were excluded.

Data Sources

Data were collected on all catheters under the care of the participating kidney services until the hemodialysis catheter was either removed, no longer under the care of the kidney service, or when the trial was completed. Local site investigators *e.g.*, nephrologists and vascular access nurses/coordinators from each kidney service were supported by REDUCCTION trial resources (online instructional videos, dedicated iPad, and trial-specific case report forms) to document all catheter-related infectious events. The standardized Infectious Event Proforma (Supplemental Appendix A) captured the date and type of infection and the circumstances around the development and management of the infection. The site investigators submitted the anonymized forms to the trial adjudication team and entered events into a central database.

End Point Definitions of Catheter-Related Infection

We used end points of catheter-related infection as defined using a modified version of the IDSA definition and reported previously in the REDUCCTION trial design and results[18,19] (Supplemental Appendix B).

The primary end points of catheter-related infections in this study were (*1*) confirmed HD-CRBSI, (*2*) suspected or possible HD-CRBSI, and (*3*) events categorized as other

(Table 1). Confirmed HD-CRBSI was defined as fulfilling one of the following criteria: (*1*) positive culture of the same organism from both the catheter tip and at least one peripheral blood, (2) isolation of the same organism from at least two blood samples (one from a catheter hub and the other from a peripheral vein), or (*3*) bacteremia without apparent source of infection except the catheter. Suspected or possible HD-CRBSI referred to clinical symptoms of bacteremia without laboratory-confirmed positive blood cultures. Catheter-related infectious events that were classified as other were identified on the basis of the presence of elements that indicated a hemodialysis catheter-related infection that did not meet the criteria for confirmed or suspected/possible HD-CRBSI or of a tunnel-related or exit site–related origin.

In addition, our study included secondary end points of catheter-related infection, including tunnel-related and exit site infections. A few infectious events recorded as a combination of primary and secondary end points were reported only for complete data representation but were excluded from the analysis because these did not constitute the main outcomes of interest.

Adjudication of HD-CRBSI Events

Throughout the study period, the outcome adjudication process (Figure 1) was consistently followed for all services, regardless of their randomization status. The adjudication process involved nephrologists who were independent of each other and external from the REDUCCTION trial team. The adjudication began with the first/lead adjudicator reviewing all catheter-related infection reports and supporting information using a standard infectious event adjudication form (Supplemental Appendix C). Events reported as confirmed HD-CRBSI, suspected/possible HD-CRBSI, or other catheter-related bacteremia events uncharacteristic of tunnel or exit site infection source were reviewed by a second blinded adjudicator to ensure consistent classification. Infectious event reports that remained inconclusive after the first two adjudications were then reviewed by the third adjudicator. Any infectious event that did not have consensus after the third adjudication was reviewed by the REDUCCTION trial Steering Committee to reach a final classification.

Statistical Method

Dichotomous variables were measured by counts and percentages. The concordance between the kidney services and the REDUCCTION trial adjudicators for the primary catheter end points was evaluated using the Gwet agreement coefficient (AC_1).[20,21] The Gwet AC_1 offers an alternative inter-rater reliability measure to circumvent the paradoxes observed in the traditional kappa (κ) statistic, where κ tend to assume low values despite a high degree of agreement and produce high values in the presence of unequal marginal distribution of ratings.[21,22] The extent of inter-rater agreement was interpreted using the benchmarking model proposed by Gwet,[21] which involves computing for the cumulative interval membership probability. Interval membership probability represents the likelihood of a given AC_1 value falling into each category of the selected benchmark scale, such as Landis and Koch criteria.[23] The Gwet probabilistic approach fits the benchmarking for this study to account for the level of disagreement and accommodate the inherent margin of error associated with AC_1, a consideration overlooked by the conventional approach of directly applying the criteria of Landis and Koch to the agreement coefficient.[24] The concordance was reported according to the Guidelines for Reporting Reliability and Agreement Studies.[25]

A clustered data analysis of the hemodialysis catheter infectious events was performed at the service level to account for any interdependence of observations within kidney services. The Gwet AC_1 value was estimated from 1000 bootstrap samples to establish independence of

Table 1. Hemodialysis catheter-related infection end point definition

Hemodialysis Catheter-Related Infection End Point	Definition
Primary end points	
Confirmed HD-CRBSI	One of the following • Culture of the same organism from both the catheter tip and at least one peripheral vein; or • Culture of the same organism from at least two blood samples (one from a catheter hub and the other from a peripheral vein); or • Bacteremia in the absence of another source
Suspected or possible HD-CRBSI	Treatment of a patient because of suspected infection with negative blood cultures, with or without subsequent catheter removal
Other hemodialysis catheter-related infection	Treatment of a patient based on the presence of composite elements suggesting a catheter-related infection uncharacteristic of confirmed or suspected/possible bacteremia nor of a tunnel-related or exit site–related source
Secondary end points	
Tunnel-related infection	Presence of signs of inflammation (erythema, tenderness, exudate, induration) extending >2 cm from the catheter exit site along the subcutaneous tract of a tunneled catheter, may or may not be associated with bacteremia
Exit site infection	Presence of signs of inflammation (erythema, tenderness, exudate, induration) within 2 cm of the catheter exit site, may or may not be associated with bacteremia

HD-CRBSI, hemodialysis catheter-related bloodstream infection.

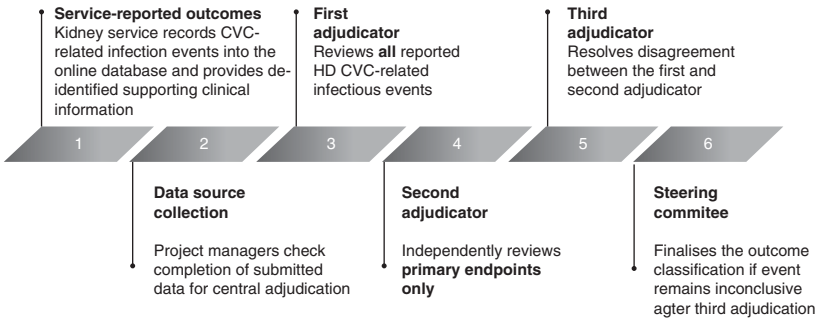

Figure 1. Outcome adjudication process in the REDUCCTION trial. REDUCCTION, REDUcing the burden of Catheter ComplicaTIOns: a National approach.

observations and account for the positive correlation between observations within clustered data.[26] We conducted a sensitivity analysis excluding kidney service clustering to evaluate the relative influence of the different phases of the study on the overall level of agreement. The concordance levels and percentage of agreement among individual services that reported more than ten hemodialysis catheter-related infectious events were also examined to ascertain any correlation between the number of events reported and the level of concordance. All analyses were performed using STATA 17.[27]

Results

Participants

The REDUCCTION trial collected data on 6364 patients and 11,293 catheters in both the baseline and intervention phases of the study period in Australia, which represented 1.14 million days of exposure to hemodialysis catheters.[18] In New Zealand, 894 patients and 1337 catheters were reported with 157,142 catheter exposure days. Overall, the REDUCCTION trial included a cumulative of 7258 patients and 12,630 catheters with 1.3 million catheter exposure days during the 40-month data collection period.

Primary Outcome

A total of 744 hemodialysis catheter-related infectious events were reported between December 2016 and March 2020 at 42 participating services across Australia and New Zealand. One kidney service in Australia did not report any HD-CRBSI event and was excluded. Of the 744 hemodialysis catheter infectious events, confirmed HD-CRBSI comprised the majority of both service-reported events (n=367) and adjudicated outcomes (n=382) congruent to the end point definition (Table 2).

Among the primary catheter-related infection end points, HD-CRBSI was suspected in 175 and 156 of the total catheter infectious events reported by the kidney services and adjudicated by the REDUCCTION trial adjudicators, respectively. Thirty-six events were reported by the services and 54 were assessed by the adjudicators as meeting the criteria of other hemodialysis catheter-related infections.

The service investigators and trial adjudicators agreed on 328 confirmed infectious events reported, resulting in a crude agreement of 77.9% and an AC_1 value of 0.77 (95% confidence interval [CI], 0.73 to 0.81) (Table 3). Across the primary and secondary end points, the highest concordance level between investigator-reported and adjudicator-assessed outcomes was observed from catheter infectious events that were of exit site source (AC_1, 0.85; 95% CI, 0.78 to 0.91). The most discordant events across all end points were hemodialysis catheter-related infectious events classified as other, with an AC_1 index of 0.33 (95% CI, 0.16 to 0.49). Overall, the estimated agreement percentage from the adjudication of all hemodialysis catheter-related infectious events was 82.3% and a Gwet AC_1 of 0.80 (95% CI, 0.76 to 0.85), which represents a substantial concordance level between service-reported and adjudication-assessed outcomes (Table 3).

Sensitivity Analysis

The crude agreement for between-group classification of hemodialysis catheter-related infectious events from baseline to the final tranche of intervention was above 75% (Table 4). The highest proportion of agreement between service-reported events and final adjudicated outcomes was in the first tranche (86.6%), reflecting a substantial concordance level (AC_1, 0.85; 95% CI, 0.80 to 0.89).

Repeating the analysis without service-level clustering resulted in narrower 95% CIs, suggesting greater certainty and precision of the point estimates of the observations when compared with the clustered data. The inter-rater reliability of hemodialysis catheter-related infectious events did not vary (Table 4).

Across 42 Australian and New Zealand services, 30 reported more than ten hemodialysis catheter-related infectious events (Figure 2). Of the 30 services, 17 had more than 80% inter-rater reliability agreement on hemodialysis catheter infectious events with the trial adjudicators, corresponding to moderate and perfect levels of concordance (Gwet AC_1 values between 0.81 and 1.0).

Discussion

This *post hoc* analysis of the data from the REDUCCTION trial's prospective cohort design is the first to analyze the interobserver agreement in the reporting of infection-related catheter complications among hemodialysis patients. In this study, we found a substantial level of concordance in the reporting of catheter-related

Table 2. Contingency table of the classification of service-reported versus adjudicated hemodialysis catheter-related infection

Service-Reported Outcomes	Adjudication Outcomes						
	Confirmed HD-CRBSI	Suspected or Possible HD-CRBSI	Other Hemodialysis Catheter-Related Infection	Tunnel-Related Infection	Exit Site Infection	Combined Infections[a]	Total
Confirmed HD-CRBSI	328	26	9	0	3	1	367
Suspected or possible HD-CRBSI	41	119	13	0	2	0	175
Other hemodialysis catheter-related infection	4	4	27	0	1	0	36
Tunnel-related infection	2	3	0	13	3	0	21
Exit site infection	1	3	5	1	125	0	135
Combined infections[a]	6	1	0	0	3	0	10
Total	382	156	54	14	137	1	744

HD-CRBSI, hemodialysis catheter-related bloodstream infection.
[a]Combined infections reported for comprehensive data representation but not part of the primary or secondary outcomes.

infections between the participating kidney services and the independent adjudication team, suggesting that the classification of catheter-related infectious events was largely consistent at the service level.

The lack of a national system to collect and report HD-CRBSI events in Australian dialysis units has led to wide variation in surveillance and management practices of hemodialysis catheter-associated infections,[28] likely increasing the ambiguity of the true reported HD-CRBSI rate. A recent cross-sectional survey of health care–associated infection screening practices in Australia revealed that nearly half of infection prevention staff lack formal training on infection surveillance and reporting thereby, raising concerns of underreporting.[16] The large variation in the collection of catheter-related infection data partly explains why hemodialysis-specific CRBSI surveillance may lack consistency, which highlights the complexities in communicating results for benchmarking health service performance.

Misclassification of outcomes in large, multicenter trials is common because of the subjectivity of end point definitions.[29] The strong correlations between the risk of misclassification and the characteristics of the outcomes have been explored in several studies. De Grooth *et al.*[4] analyzed the most common end points used to capture infectious complications of catheters in clinical trials and acknowledged the considerable incongruence in the surveillance definition of CRBSI. A cross-sectional study in 692 infectious-diseases specialists in the United States illustrated the sizable disagreement on the identification of primary central-line infection,[5] which represented the impact of the clinicians' subjective interpretation of the end point definitions on the misclassification of catheter-related bacteremia. As HD-CRBSI events are likely misdiagnosed or misreported,[30] the adoption of a modified IDSA definition in the REDUCCTION trial minimized misclassification and added confidence in the identification of HD-CRBSI by kidney service investigators. It is noteworthy that the consensus on catheter-related infections in the different tranches of the study rarely differed, which highlights the consistency in reporting catheter-related infectious events across the participating kidney services and is partly due to the application of an objective end point definition. Our results compared favorably with those seen in a Canadian multicenter cohort study, where the implementation of well-defined criteria and an adjudication process of catheter outcomes reduced the likelihood of erroneous diagnosis of catheter-associated bacteremia.[30]

Advocates for clinical outcome adjudication highlight that the introduction of this validation method into outcome reporting can improve the classification of clinical events and limit reporting biases.[31,32] Despite this, newer evidence suggests that outcome classification on the basis of predefined end points rarely differ between local investigators and independent, blinded adjudicators. For example, a recent systematic review by Godolphin *et al.*[33] concluded, after reviewing primary, composite, and functional stroke outcomes in 12 methodological studies, that central adjudication had no substantial influence on the main trial outcomes. Similarly, a previous Cochrane review examined the usefulness of an end point adjudication committee in 47 randomized clinical trials and found that masked validation of investigator-reported events had no discernible impact on the treatment effect estimates.[17]

The high crude agreement and the substantial inter-rater reliability of the catheter infectious event reporting in this study provide confidence in the diagnosis made by the participating kidney services. Our findings, therefore, suggest that a rigorous adjudication protocol may not be necessary, particularly if standardized outcome definition and clear guidance on the collection and reporting of hemodialysis catheter infection data exist. Performing independent outcome adjudication in HD-CRBSI surveillance outside of the clinical trial remains challenging and not sustainable. Recent evidence suggests that outcome adjudication comes not only with a considerable cost related to time and staffing but the additional administrative requirements are also a sizable hurdle because of its iterative process.[17,34–37] Given the limited resources for research, it is crucial that processes are designed to deliver

Table 3. Pairwise agreement between kidney services and trial adjudicators

Hemodialysis Catheter-Related Infection End Point		Site Yes; Adjudicators No	Site No; Adjudicators Yes	Site Yes; Adjudicators Yes	Agreement, %	AC_1	95% CI	Agreement Category[a]
		n	*n*	*n*				
Primary end points	Confirmed HD-CRBSI	39	54	328	77.9	0.77	0.73 to 0.81	Substantial
	Suspected or possible HD-CRBSI	56	37	119	56.1	0.53	0.45 to 0.60	Moderate
	Other hemodialysis catheter-related infection	9	27	27	42.9	0.33	0.16 to 0.49	Poor
Secondary end points	Tunnel-related infection	8	1	13	59.1	0.54	0.26 to 0.82	Fair
	Exit site infection	10	12	125	85.0	0.85	0.78 to 0.91	Substantial
All hemodialysis catheter-related infections		122	131	612	82.3	0.80	0.76 to 0.83	Substantial

AC, agreement coefficient; CI, confidence interval; HD-CRBSI, hemodialysis catheter-related bloodstream infection.
[a]Based on probabilistic benchmarking model proposed by Gwet.

Table 4. Concordance level according to implementation tranches and clustering of kidney services

Implementation Tranches[a]	Hemodialysis Catheter-Related Infection, *n*	Agreement, %	Clustered Data		Non-Clustered Data		Agreement Category[b]
			AC_1	95% CI	AC_1	95% CI	
Baseline[c]	419	81.1	0.78	0.72 to 0.84	0.78	0.74 to 0.83	Substantial
Tranche 1[d]	157	86.6	0.85	0.80 to 0.89	0.85	0.79 to 0.91	Substantial
Tranche 2[e]	99	84.8	0.82	0.68 to 0.95	0.82	0.72 to 0.90	Substantial
Tranche 3[f]	69	75.4	0.70	0.54 to 0.86	0.70	0.58 to 0.83	Moderate
Overall	744	82.3	0.80	0.75 to 0.84	0.80	0.76 to 0.83	Substantial

AC, agreement coefficient; CI, confidence interval.
[a]Implementation tranches for Australian kidney services only.
[b]Based on probabilistic benchmarking model proposed by Gwet.
[c]Forty-two services.
[d]Twelve services.
[e]Twelve services.
[f]Thirteen services.

adequate value to the relevant end-users to prevent research waste[38] and ensure that available resources are used efficiently on methodologies that are systematic, meaningful, and feasible.

One of the notable strengths of this analysis lies in the systematic collection of catheter-related infectious complications with the utilization of a bespoke online database created for the REDUCCTION trial. The web-based format of the central database facilitated real-time monitoring of catheter exposure, including the number of active catheters, the duration of placement, and HD-CRBSI rates for each kidney service. A further strength was the adoption of a standardized infectious event reporting form, which enabled consistent application of the hemodialysis catheter infection end point definition. Deidentified clinical information, such as imaging studies, blood cultures, other pathology results, and clinical notes, aided the classification process.

Our study has several limitations. First, the number of infection-related hemodialysis catheter events was limited to the data collected in the REDUCCTION trial because of the trial's pragmatic nature. Our analyses were highly dependent on the data submitted by the participating kidney services, which may have led to underreporting if the service investigators failed to record and report the event or if insufficient clinical information was presented for adjudication. Second, the inter-rater reliability agreement per tranche of intervention implementation could only be pooled from the participating Australian kidney services as New Zealand services did not participate in the intervention period. Third, we were unable to evaluate the sensitivity and specificity of the CRBSI definition used in the REDUCCTION trial. Because there is no existing harmonized national definition for HD-CRBSI in Australia and the general hemodialysis population,[15,39] we modified the IDSA definition to make surveillance pragmatic and feasible for this cohort. Fourth, this study did not measure the downstream effects of the concordance of event reporting with hospitalization or the propensity to future bloodstream infection. However, our study will inform future studies once linkage to administrative data becomes available. Finally, we did not collect data on the cost estimate related to the clinical adjudication process, yet the resources used during the REDUCCTION trial remained similar.

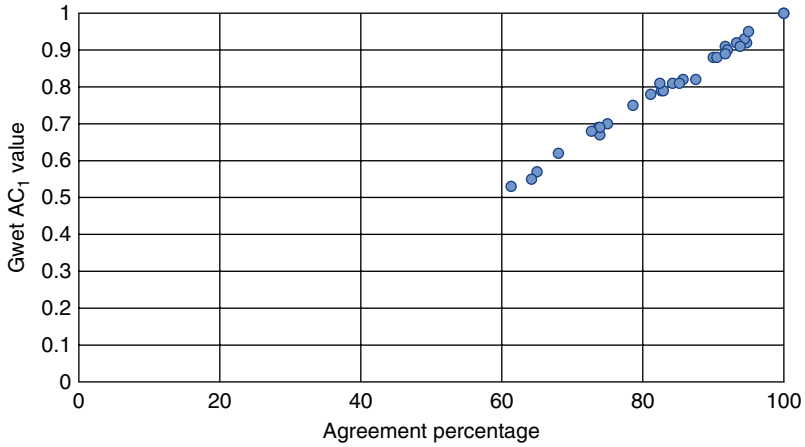

Figure 2. Concordance and agreement percentage among kidney services with >10 reported hemodialysis catheter infections.

In conclusion, our analysis of the cluster-randomized trial revealed a substantial level of concordance in the reporting of catheter-related infections between the participating kidney services and the adjudication team. This supports a high degree of confidence in service-reported HD-CRBSI and other catheter-related infection rates in Australia and New Zealand without the need for independent outcome adjudication. Given the ongoing prevalence of hemodialysis catheter utilization in clinical practice, the need for reliable measurement and reporting of HD-CRBSI rates through the standardization of end point definitions and catheter outcome evaluation for health care performance benchmarking remain imperative. Independent outcome adjudication may provide some benefit to clinical studies where differential reporting of outcomes is likely to exist, but its overall practicality outside of clinical trials may need to be evaluated on a case-by-case basis to fully understand its true prognostic significance.

Disclosures

A. Cass reports the following: Advisory or Leadership Role: Menzies School of Health Research. M. Gallagher reports the following: Consultancy: George Clinical; Research Funding: Bayer Pharmaceuticals; Advisory or Leadership Role: Alexion Pharmaceuticals (unpaid), Ellen Medical Devices Pty Ltd. (unpaid), and George Clinical (paid); and Other Interests or Relationships: The George Institute for Global Health. N.A. Gray reports the following: Ownership Interest: CSL; and Honoraria: AstraZeneca, Baxter Healthcare, Eli Lilly Boehringer Ingelheim, and GSK. P.G. Kerr reports the following: Honoraria: AstraZeneca, Australia, CSL-Seqiris, and Roche, Singapore; and Advisory or Leadership Role: ISN Oceania Committee and ISN Transplant Sister Centre Committee—both unpaid. S. Kotwal reports the following: Consultancy: Chinook Pharmaceuticals and Dimerix Pharmaceuticals; Ownership Interest: Google; Research Funding: The George Institute and its affiliated entities work with numerous health and pharmaceutical companies in the design, implementation and analyses of clinical research and clinical trials. It is possible that some of these companies have products relevant to the clinical space covered in this analysis, but S. Kotwal is not aware of any possible conflicts arising from this work.; and Advisory or Leadership Role: Chinook Pharmaceuticals (steering committee member) and Dimerix Pharmaceuticals. M.A. Roberts reports the following: Honoraria: AstraZeneca, and Boehringer Ingleheim; In both instances, honoraria was for speaking at educational activities; and Advisory or Leadership Role: Australasian Kidney Trials Network Scientific Committee, Cochrane Renal Group Advisory Board and Editorial Board, Subject Editor, *BMC Trials*, Subject Editor, *Nephrology*; No income is received from these roles. D.J. Semple reports the following: Advisory or Leadership Role: ANZDATA Haemodialysis Working Group. G. Talaulikar reports the following: Consultancy: Spouse—Amgen, Beigene, Eusa, Janssen-Cilag, and Roche; Ownership Interest: Avita Medical and Immutep, Research Funding: Spouse—Janssen and Roche; Honoraria: Spouse—as listed above; Advisory or Leadership Role: Member Finance Committee, Australia NZ Society of Nephrology; Spouse—Scientific Board—Beigene, Janssen, and Roche; and Speakers Bureau: Spouse—Celgene and Roche. B. Talbot reports the following: Ellen Medical Devices and George Clinical; Consultancy: Scientific Leadership role at George Clinical; Ownership Interest: Ellen Medical Devices; Research Funding: Ellen Medical Devices; Advisory or Leadership Role: Scientific Leadership role at George Clinical; and Other Interests or Relationships: Affiliated with The George Institute, Sydney, Australia; Previously in receipt of a Scientia scholarship from the University of New South Wales, Sydney, Australia to complete a PhD in medical education; Clinical Adviser to Ellen Medical Devices (a subsidiary of The George Institute leading the Affordable Dialysis Program). All remaining authors have nothing to disclose.

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Data Sharing Statement

Previously published data were used for this study. The REDUcing the burden of dialysis Catheter ComplicaTIOns: a National approach (REDUCCTION) trial (ACTRN 12616000830493).

Supplemental Material

This article contains the following supplemental material online at http://links.lww.com/KN9/A443.

Supplemental Table 1. List of REDUCCTION trial investigators.

Supplemental Table 2. List of other contributing partner organizations.

Supplemental Appendix A. Infectious event proforma.

Supplemental Appendix B. REDUCCTION trial outcomes.

Supplemental Appendix C. Infectious event adjudication form.

References

1. Pisoni RL, Zepel L, Port FK, Robinson BM. Trends in US vascular access use, patient preferences, and related practices: an update from the US DOPPS practice monitor with international comparisons. *Am J Kidney Dis.* 2015;65(6):905–915. doi:10.1053/j.ajkd.2014.12.014

2. Thurlow JS, Joshi M, Yan G, et al. Global epidemiology of end-stage kidney disease and disparities in kidney replacement therapy. *Am J Nephrol.* 2021;52(2):98–107. doi:10.1159/000514550
3. Fisher M, Golestaneh L, Allon M, Abreo K, Mokrzycki MH. Prevention of bloodstream infections in patients undergoing hemodialysis. *Clin J Am Soc Nephrol.* 2020;15(1):132–151. doi:10.2215/CJN.06820619
4. de Grooth H, Timsit J, Mermel L, et al. Validity of surrogate endpoints assessing central venous catheter-related infection: evidence from individual- and study-level analyses. *Clin Microbiol Infect.* 2020;26(5):563–571. doi:10.1016/j.cmi.2019.09.022
5. Beekmann SE, Diekema DJ, Huskins WC, et al. Diagnosing and reporting of central line–associated bloodstream infections. *Infect Control Hosp Epidemiol.* 2012;33(9):875–882. doi:10.1086/667379
6. Verberk JD, Van Der Kooi TI, Derde LP, Bonten MJ, De Greeff SC, Van Mourik MS. Do we need to change catheter-related bloodstream infection surveillance in The Netherlands? A qualitative study among infection prevention professionals. *BMJ Open.* 2021;11(8):e046366. doi:10.1136/bmjopen-2020-046366
7. Herzig CT, Reagan J, Pogorzelska-Maziarz M, Srinath D, Stone PW. State-mandated reporting of health care–associated infections in the United States: trends over time. *Am J Med Qual.* 2015;30(5):417–424. doi:10.1177/1062860614540200
8. Liu H, Herzig CTA, Dick AW, et al. Impact of state reporting laws on central line-associated bloodstream infection rates in U.S. Adult intensive care units. *Health Serv Res.* 2017;52(3):1079–1098. doi:10.1111/1475-6773.12530
9. Australian Commission on Safety and Quality in Health Care. *National Safety and Quality Health Service Standards*; 2021. Accessed May 10, 2022. https://www.safetyandquality.gov.au/sites/default/files/2021-05/national_safety_and_quality_-health_service_nsqhs_standards_second_edition_-_updated_may_2021.pdf
10. O'Grady NP, Alexander M, Burns LA, et al. Guidelines for the prevention of intravascular catheter-related infections. *Clin Infect Dis.* 2011;52(9):e162–e193. doi:10.1093/cid/cir257
11. Lok CE, Huber TS, Lee T, et al. KDOQI clinical practice guideline for vascular access: 2019 update. *Am J Kidney Dis.* 2020;75(4 suppl 2):S1–S164. doi:10.1053/j.ajkd.2019.12.001
12. Mermel LA, Allon M, Bouza E, et al. Clinical practice guidelines for the diagnosis and management of intravascular catheter-related infection: 2009 Update by the Infectious Diseases Society of America. *Clin Infect Dis.* 2009;49(1):1–45. doi:10.1086/599376
13. Aswani MS, Reagan J, Jin L, Pronovost PJ, Goeschel C. Variation in public reporting of central line–associated bloodstream infections by state. *Am J Med Qual.* 2011;26(5):387–395. doi:10.1177/1062860611399116
14. Kotwal S, Webster AC, Cass A, Gallagher M. Comorbidity recording and predictive power of comorbidities in the Australia and New Zealand dialysis and transplant registry compared with administrative data: 2000-2010. *Nephrology.* 2016;21(11):930–937. doi:10.1111/nep.12694
15. Russo PL, Barnett AG, Cheng AC, Richards M, Graves N, Hall L. Differences in identifying healthcare associated infections using clinical vignettes and the influence of respondent characteristics: a cross-sectional survey of Australian infection prevention staff. *Antimicrob Resist Infect Control.* 2015;4(1):29. doi:10.1186/s13756-015-0070-7
16. Russo PL, Cheng AC, Richards M, Graves N, Hall L. Variation in health care-associated infection surveillance practices in Australia. *Am J Infect Control.* 2015;43(7):773–775. doi:10.1016/j.ajic.2015.02.029
17. Ndounga Diakou LA, Trinquart L, Hróbjartsson A, et al. Comparison of central adjudication of outcomes and onsite outcome assessment on treatment effect estimates. *Cochrane Database Syst Rev.* 2016;3(3):MR000043. doi:10.1002/14651858.mr000043.pub2
18. Kotwal S, Cass A, Coggan S, et al. Multifaceted intervention to reduce haemodialysis catheter related bloodstream infections: REDUCCTION stepped wedge, cluster randomised trial. *BMJ* 2022;377:e069634. doi:10.1136/bmj-2021-069634
19. Kotwal S, Coggan S, McDonald S, et al. REDUcing the burden of dialysis Catheter ComplicaTIOns: a National approach (REDUCCTION)-design and baseline results. *Kidney360.* 2020;1(8):746–754. doi:10.34067/KID.0001132020
20. Gwet KL. Computing inter-rater reliability and its variance in the presence of high agreement. *Br J Math Stat Psychol.* 2008;61(Pt 1):29–48. doi:10.1348/000711006X126600
21. Gwet KL. *Handbook of Inter-rater Reliability: The Definitive Guide to Measuring the Extent of Agreement Among Raters.* Advanced Analytics, LLC; 2014.
22. Feinstein AR, Cicchetti DV. High agreement but low kappa: I. The problems of two paradoxes. *J Clin Epidemiol.* 1990;43(6):543–549. doi:10.1016/0895-4356(90)90158-L
23. Landis JR, Koch GG. The measurement of observer agreement for categorical data. *Biometrics.* 1977;33(1):159–174. doi:10.2307/2529310
24. Vach W, Gerke O. Gwet's AC1 is not a substitute for Cohen's kappa – a comparison of basic properties. *MethodsX.* 2023;10:102212. doi:10.1016/j.mex.2023.102212
25. Kottner J, Audigé L, Brorson S, et al. Guidelines for reporting reliability and agreement studies (GRRAS) were proposed. *J Clin Epidemiol.* 2011;64(1):96–106. doi:10.1016/j.jclinepi.2010.03.002
26. Field CA, Welsh AH. Bootstrapping clustered data. *J R Stat Soc Ser B: Stat Methodol.* 2007;69(3):369–390. doi:10.1111/j.1467-9868.2007.00593.x
27. *StataCorp. Stata Statistical Software: Release 17*. StataCorp LLC; 2021.
28. Smyth B, Kotwal S, Gallagher M, Gray NA, Polkinghorne K.; REDUCCTION Partnership Project. Dialysis catheter management practices in Australia and New Zealand. *Nephrology.* 2019;24(8):827–834. doi:10.1111/nep.13507
29. Hróbjartsson A, Thomsen ASS, Emanuelsson F, et al. Observer bias in randomised clinical trials with binary outcomes: systematic review of trials with both blinded and non-blinded outcome assessors. *BMJ.* 2012;344:e1119. doi:10.1136/bmj.e1119
30. Thompson S, Wiebe N, Klarenbach S, et al. Catheter-related blood stream infections in hemodialysis patients: a prospective cohort study. *BMC Nephrol.* 2017;18:357–358. doi:10.1186/s12882-017-0773-5
31. McArthur KS, Johnson PCD, Quinn TJ, et al. Improving the efficiency of stroke trials: feasibility and efficacy of group adjudication of functional end points. *Stroke.* 2013;44(12):3422–3428. doi:doi:10.1161/strokeaha.113.002266
32. Olivier CB, Bhatt DL, Leonardi S, et al. Central adjudication identified additional and prognostically important myocardial infarctions in patients undergoing percutaneous coronary intervention. *Circ Cardiovasc Interv.* 2019;12(7):e007342. doi:10.1161/circinterventions.118.007342
33. Godolphin PJ, Bath PM, Montgomery AA. Should we adjudicate outcomes in stroke trials? A systematic review. *Int J Stroke.* 2023;18(2):154–162. doi:10.1177/17474930221094682
34. Van Der Ende NAM, Roozenbeek B, Berkhemer OA, et al. Added value of a blinded outcome adjudication committee in an open-label randomized stroke trial. *Stroke.* 2022;53(1):61–69. doi:10.1161/strokeaha.121.035301
35. Hata J, Arima H, Zoungas S, et al. Effects of the endpoint adjudication process on the results of a randomised controlled trial: the ADVANCE trial. *PLoS One.* 2013;8(2):e55807. doi:10.1371/journal.pone.0055807
36. Petrie MC, McMurray JJV. Do we need clinical events committees to adjudicate end points? *Circ Heart Fail.* 2020;13(7):e007209. doi:10.1161/circheartfailure.120.007209
37. Godolphin PJ, Montgomery AA, Woodhouse LJ, et al. Central adjudication of serious adverse events did not affect trial's safety results: data from the Efficacy of Nitric Oxide in Stroke (ENOS) trial. *PLoS One.* 2018;13(11):e0208142. doi:10.1371/journal.pone.0208142
38. Tong A, Chando S, Crowe S, et al. Research priority setting in kidney disease: a systematic review. *Am J Kidney Dis.* 2015;65(5):674–683. doi:10.1053/j.ajkd.2014.11.011

39. Quittnat Pelletier F, Joarder M, Poutanen SM, Lok CE. Evaluating approaches for the diagnosis of hemodialysis catheter–related bloodstream infections. *Clin J Am Soc Nephrol*. 2016;11(5): 847–854. doi:10.2215/CJN.09110815

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