

## REDUCing the burden of dialysis Catheter ComplicaTIONs: a National approach (REDUCCTION) – design and baseline results

Sradha Kotwal<sup>1,2</sup>, Sarah Coggan<sup>1</sup>, Stephen McDonald<sup>3</sup>, Girish Talaulikar<sup>4</sup>, Alan Cass<sup>5</sup>, Stephen Jan<sup>1</sup>, Kevan R. Polkinghorne<sup>6,7</sup>, Nicholas A. Gray<sup>8,9</sup>, Martin Gallagher<sup>1,10</sup> on behalf of the REDUCCTION project investigators (detailed in Appendix)

1. The George Institute for Global Health, UNSW, Sydney, Australia
2. Department of Nephrology, Prince of Wales Hospital, Sydney, Australia
3. ANZDATA Registry, Adelaide, South Australia
4. Renal Services, ACT Health, Canberra, ACT
4. Concord Clinical School, University of Sydney, Sydney, Australia
5. Menzies School of Health Research, Charles Darwin University, Darwin, Northern Territory, Australia
- 6 Department of Epidemiology and Preventive Medicine, Monash University, Prahran, Victoria
7. Departments of Nephrology & Medicine, Monash Medical Centre, Monash University, Clayton, Victoria, Australia
- 8 Sunshine Coast University Hospital, Birtinya, Australia
9. University of the Sunshine Coast, Sippy Downs, Australia
10. Concord Clinical School, University of Sydney, NSW

### Corresponding author

Dr. Sradha Kotwal  
The George Institute for Global Health  
Renal and Metabolic Division  
Level 5, 1 King Street  
Newtown  
Sydney, N/A 2041  
Australia  
skotwal@georgeinstitute.org.au

## Abstract

### Background

Patients with hemodialysis central venous catheters (HD CVC) are susceptible to health care associated infections, particularly hemodialysis catheter related blood stream infection (HD-CRBSI), which is associated with high mortality and health care costs. There have been few systematic attempts to reduce this burden and clinical practice remains highly variable. This manuscript will summarize the challenges in preventing HD-CRBSI and describe the methodology of the REDUCing the burden of dialysis Catheter ComplicaTIONS – a National approach (REDUCCTION) trial.

### Methods

The REDUCCTION trial is a stepped wedge cluster randomized trial of a suite of clinical interventions aimed at reducing HD-CRBSI across Australia. It clusters the intervention at the renal service level with implementation randomly timed across three tranches. The primary outcome is the effect of this intervention upon the rate of HD-CRBSI.

Patients who received a HD CVC at a participating renal service are eligible for inclusion. A customized data collection tool allows near to real-time reporting of the number of active catheters, total exposure to catheters over time and rates of HD-CRBSI in each service.

The interventions are centered around the insertion, maintenance and removal of HD CVC, informed by the most current evidence at the time of design (mid-2018).

### Results

A total of 37 renal services are participating in the trial. Data collection is ongoing with results expected in the last quarter of 2020. The baseline phase of the study has collected provisional data on 5385 catheters in 3615 participants, representing 603,506 days of HD CVC exposure.

### Conclusion

The REDUCCTION trial systematically measures the use of HD CVCs at a national level in Australia, accurately determines the rate of HD-CRBSI and tests the effect of a multifaceted, evidence-based intervention upon the rate of HD-CRBSI. These results will have global relevance in nephrology and other specialties commonly using CVCs.

## Introduction

Patients receiving hemodialysis are highly susceptible to healthcare-associated infections. Most prominent among these infections is hemodialysis catheter-related bacteremia (HD-CRBSI), which is associated with high mortality and high health care costs.(1) Hemodialysis central venous catheters (HD CVC) are ubiquitous in modern nephrology; used in up to 80% of incident maintenance hemodialysis patients, 20% of prevalent hemodialysis patients and universally in patients requiring hemodialysis for acute kidney injury.(2-5)

HD-CRBSI is associated with risks beyond the primary event, such as endocarditis, major organ abscesses, recurrent sepsis and mortality. A 2013 meta-analysis concluded that the healthcare cost per episode of all CVC-related bacteremia, including HD-CRBSI, in the USA was \$45,814 (95% CI \$30,919- \$65,245), constituting 18.9% of the total national cost of healthcare-associated infections or \$1.85b per annum.(1) These costs exclude the impact on the patient's quality of life from additional catheters, hospital admissions and medical procedures.

There have been few systematic attempts to reduce this burden in dialysis services, and clinical practice remains highly variable.(6) Many interventions have been studied with the aim of reducing HD-CRBSI, and the nature of this literature has likely contributed to practice variation.(6-9) The recent Making Dialysis Safer for Patients Coalition initiative, led by the Centers for Disease Control and Prevention (CDC), is testament to the need for standardized approaches to infection prevention in dialysis services as was the success of the Keystone Michigan Project.(10, 11) Herein, we review the research that formed the basis of the design and protocol of the REDUCing the burden of dialysis Catheter ComplicaTIONS – a National approach (REDUCCTION) trial, a stepped-wedge cluster randomized clinical trial of a suite of clinical interventions aimed at reducing the rate of HD-CRBSI across Australian renal services.

## Challenges in reducing HD-CRBSI

### 1. Reporting and comparison of rates of HD-CRBSI

A crucial requirement for the implementation and evaluation of strategies to reduce HD-CRBSI is the ability to accurately measure and report the disease burden. While measurement has been done well in RCTs and prospective studies, sustainable, system-wide measurement in clinical practice can be difficult. Historically, HD-CRBSI rates have used different definitions and denominators, with the numerator usually being HD-CRBSI events and denominators using variable measures of catheter exposure, making comparisons difficult.(12, 13) Furthermore, the lack of clinical adjudication of BSI also adds uncertainty around the true rate of HD-CVC BSI. Our survey of ANZ renal services found 84% of services were collecting data on HD-CRBSI rates but only 51% could report a rate.(6) The reported HD-CRBSI rates in the literature vary widely, with published rates of 1.1 - 5.5 episodes per 1000 days of catheter exposure at the time of design of the REDUCCTION trial.(14-17) Studies published from USA and Canada subsequently have published much lower rates of between 0.19-0.84 per 1000 catheter days, making it difficult for clinicians to ascertain appropriate targets.(13, 18)

## 2. Complex care

There are many components to catheter care, with breakdown in any element likely to influence the risk of HD-CRBSI. Published research has focused upon the use of prophylactic antimicrobial agents, either applied topically to the catheter exit site, or as solutions to 'lock' the catheter lumen after insertion and between dialysis treatments, as well as non-microbial agents such as citrate taurolidine, and chlorhexidine.(8, 19, 20) Other interventions include catheter dressing types (21), catheter dressing frequency (22), catheters with subcutaneous tunnels (23) and, more recently, antimicrobial catheter lumen caps that form a physical and antimicrobial barrier at the closure of the dialysis catheter.(24) A recent review highlighted the complexity of this literature, presenting challenges for clinicians in untangling the evidence to decide upon optimal catheter care.(25) In addition, various hospital departments may play a role in managing any single HD CVC complicating care and making standardization difficult.(6)

## 3. Evidentiary limitations

The difficulties posed by the literature examining HD-CRBSI are perhaps best illustrated by the differing and often outdated recommendations from guideline groups. The Australia/New Zealand (ANZ) guideline, published in 2012, made a single recommendation based upon high grade (level 1) evidence, and the Canadian guidelines from 2006 made two recommendations with high level evidence.(26, 27) The US guidelines published in April 2020 make multiple recommendations around the use, insertion, management and removal of HD-CVC's most of which remain based on expert opinion or at best moderate level of evidence.(28) .(29) The limited recommendations, whilst reflecting the available literature at the time of guideline production, is a notable contrast to the myriad elements of catheter insertion, management and care. The guidelines also highlight the gaps in this literature, most notably the paucity of head-to-head studies comparing differing treatments and approaches, such that their relative benefits remain unclear. (23)

In contrast, the CDC guidelines for the prevention of intravascular catheter-related infections updated in 2017 cover 20 sub-topic areas, illustrating the complexity of what most clinicians would consider a relatively routine part of clinical nephrology care.(30) The final recommendation, that of using collaborative performance improvement initiatives and multi-faceted strategies to improve practice, has been central to the development of the REDUCTION trial.

Many other elements such as insertion site, showering/bathing, use of sterile techniques at insertion and when accessing the catheter, frequency of dressing changes and patient factors (such as socioeconomic status, comorbidities, residence characteristics and patients' understanding of catheter care) could also influence HD-CRBSI, but are not readily studied. Furthermore, much of the current evidence arises from small studies, many of low quality, testing differing interventions with variable outcome reporting. These characteristics make the distillation of findings into a coherent and implementable practice change at a service level difficult and allow variability in clinical practice to flourish.(25, 31-33)

#### 4. Practice variation

A survey of ANZ renal services demonstrated wide variation in the processes around catheter care, such as prophylactic antibiotic use, exit site dressings and catheter insertion personnel.(6, 34) This showed that prophylactic antibiotics were used at 21% of renal services and eight different combinations of exit site dressing were in use, with an antibiotic patch being most common (35%).(6)

Reducing such variation has, had some success in reducing CVC-related bacteremia. The Keystone ICU project used a suite of interventions to address healthcare-associated infections, most notably CVC-associated bacteremia, and showed significant reductions in this outcome.(11)

The REDUCTION trial aims to systematically measure the use of HD CVCs for dialysis access at a national level in Australia, to accurately determine the rate of HD-CRBSI and test the effect of a multifaceted, evidence-based intervention upon the rate of HD-CRBSI.

## Methods

### Design

REDUCTION uses a stepped-wedge cluster design (Figure 1) (35), clustering the intervention at the renal service level, ensuring that all participating services receive the intervention and serve as their own control. The application of such an intervention at the individual patient level was impractical due to the requirement of having two (or more) systems of HD CVC management within each service and the risk of “contamination” of the intervention practices into the control group. This approach implements the entire suite of interventions at a service level, minimizing contamination, uses the benefits of randomization in the timing of the application of the intervention, and accommodates for changes in practice that occur with time. The trial was registered on the Australia New Zealand clinical trials registry on the 23 June 2016 (ACTRN12616000830493).

### Setting

The trial is being conducted at 37 renal services across Australia which, collectively, manage 75% of the Australian prevalent dialysis population (Table 1). Many services oversee multiple dialysis facilities, such that a service is defined as a site, or sites (usually hospital-based in Australia), under the same clinical governance as it pertains to clinical decision making around HD CVC management. Australia has a universal health insurance system, covering the costs of inpatient public hospital care and varying proportions of outpatient health services. Dialysis is largely provided in public hospitals and is covered by the national insurance scheme, and private facilities manage a small proportion of dialysis patients.

### Participant inclusion criteria

All Australian renal services were approached to participate in the trial in 2016, with 37 proceeding to enrolment. Adult patients who have a HD CVC inserted after the start of the trial at a participating renal service are eligible for inclusion in the data collection. Prevalent dialysis catheters inserted

prior to the start of the trial are excluded. Data are collected from the time of HD CVC insertion, or the time the HD CVC comes under the care of the renal service, until the HD CVC is removed, no longer under the care of the renal service, or end of the trial.

### Informed Consent

Ethics approval was obtained according to institutional processes across 8 states and territories (Supplemental Table 1). The trial uses two approaches to consent; an 'opt-out' approach or a 'waiver of consent' approach, as decided by local research governance. (Table 1) Renal services using the 'opt-out' approach allow patients to opt-out of the data collection following provision of a trial information sheet, but the renal service continues to treat such patients as per the service's participation in the trial. Services with approval to use the 'waiver of consent' approach are not required to perform any study-related consent activities. Any participant is able to decline participation in the data collection at any point in the trial.

### Data collection methods

A web-based data collection tool was custom designed for the study and data entered by each participating service. Renal services can see, in real-time, all dialysis catheters currently in use, and the total exposure of patients to dialysis catheters over various time periods. Services are able to see their own rates of HD-CRBSI during the baseline phase and, during the trial intervention phase, can also see the HD-CRBSI rate across the entire trial.

The data collection includes baseline patient and catheter characteristics and classifies catheters by their reason for insertion: initiation of maintenance hemodialysis, acute kidney injury requiring hemodialysis (HD CVC is managed by the renal service), interim hemodialysis due to failure of an existing dialysis access e.g. failure of peritoneal dialysis, or thrombosis of an existing arterio-venous fistula. Data on interventions upon the dialysis catheter (e.g. rewiring, re-suturing), surgery for creation or revision of permanent dialysis access, the reasons for catheter removal, and the results of any blood or catheter tip cultures are also collected. (Supplemental Table 3) In addition, service-level data on existing practices around catheter care and dialysis activity within each renal service at trial initiation and prior to implementation is collected. Services were discouraged from making changes to the processes of care for HD CVCs during the baseline phase of the trial.

Reporting of HD-CRBSI uses a standardized definition (Table 2) and a central blinded adjudication process. All possible HD-CRBSI events are reviewed by two adjudicators (clinicians who are independent from the research team). Disagreement between the two adjudicators requires review from the third adjudicator. If agreement is not reached by the third adjudication, the Trial Management Committee reviews the de-identified event.

Data linkage to state-specific hospitalization and death datasets will complete at the end of the intervention phase, after all trial data collection has ceased, allowing analyses of long-term patient outcomes and economic impacts of catheter complications.

## Interventions and Implementation

The suite of evidence-based interventions, designed by a sub-committee of the REDUCTION Steering Committee in consultation with the Australasian renal guidelines group (36) and the Australian consumer body (Kidney Health Australia), was endorsed by the Trial Management Committee. The interventions were informed by the most current evidence at the time of design, including the Keystone Project in Michigan ICUs (15, 16), expert opinion across ANZ and were finalised in January 2018. The components of the intervention were separated into three timepoints in catheter use – insertion, maintenance and removal and were deemed as guiding rather than prescriptive (Figure 2).

All services implemented the entire suite of interventions at their randomly assigned time point, overseen by local physician and nursing leaders. The delivery of the intervention training was in the form of three short videos (one for each component of the intervention) delivered to the service 6 weeks prior to the implementation of the interventions as well as a pre-intervention teleconference. Upon intervention implementation, the data collection tool was modified to allow each service to compare the primary outcome, HD-CRBSI, at their service with the study-wide rate, and additional data prompts and fields were added to remind service staff of the intervention components and allow monitoring. (Supplemental Table 4)

## Blinding

Blinding of the trial intervention is not possible, but the timing and nature of the trial interventions was kept confidential and revealed prior to implementation at each service. Services were asked to keep the intervention confidential until all services had implemented the intervention.

## Outcomes

The primary outcome of the trial is the comparative rate of HD-CRBSI per 1000 catheter days of exposure, between the baseline and intervention trial periods (Table 2). A modified version from the the Infectious Diseases Society of America definition was used to define HD-CRBSI as detailed in Table 2.(37) The secondary outcomes are suspected or possible HD-CRBSI; total suspected and possible bacteremia (Table 2).

## Statistical methods

A covariate-based constrained randomization determined the division of participating services into three balanced tranches and the commencement of the intervention over the trial period.(35, 38) The allocation sequence was informed by the total number of catheters inserted in the baseline phase of the trial (December 2016 - January 2018). One hundred thousand random allocation sequences were generated, and those that achieved a degree of balance of no more than a 10% different from the average number of dialysis catheters in the trial (between 73.2-89.8 average catheters per arm) were retained. Of the original sequences generated, 6865 met our balance criteria, and the final randomization allocation was chosen randomly from this subset.

Pilot data collected from a Sydney service (unpublished) allowed us to estimate that an average of 100 dialysis catheter insertions (100 observations) occurred per year at a medium sized Australian

renal service (defined based on number of dialysis patients as per ANZDATA), with each catheter lasting for a mean of 46 days. The expected rate of baseline HD-CRBSI was 2.5 per 1000 catheter days, derived from a combination of pilot data and the published literature at the time.(17) Further considerations included the inter-cluster correlation co-efficient (ICC) which we estimated at 0.07 when the rate seen in a large US study from 2014 was 0.03, (9) and the number of intervention points (number of steps) planned was three. The powering was based upon the intervention resulting in a 50% reduction in the risk of catheter-related bacteremia which was a conservative estimate based on the Key Michigan project outcomes.(11, 39)

On the basis of these figures, the trial was estimated to have a power of over 0.9 to detect a 50% reduction in the bacteremia rate using a proposed sample of 30 renal services following 100 patients per 'step' in the stepped-wedge design. This is likely a conservative figure as the ICC in other studies has been substantially lower, the number of patients per 'step' is likely to be more than 100 as the duration of follow-up post-intervention is longer for some services, and the trial has included 37 renal services to ensure that 100 patients per 'step' during implementation is met. A formal statistical analysis plan has been derived for the trial and will be published on the REDUCTION study site. (URL to be confirmed).

#### Additional analyses

There are two planned sub-group analyses of the primary outcome. The first examining for differences in the primary outcome on the basis of renal service size, and the second on the basis of whether renal services were using either an impregnated dressing or an antimicrobial catheter lock, as per the KHA-CARI guidelines (27), at baseline. A prospective process evaluation is being conducted during the baseline and intervention phases of the trial to better understand the factors that influence the implementation of evidence-based practices around dialysis catheter management.(40)

In addition, this uniquely large prospective cohort of patients receiving dialysis catheters will allow future exploration of the effects of a variety of factors, including renal service, patient, clinical and HD CVC characteristics upon important patient outcomes such as HD-CRBSI, hospitalization, and mortality. These analyses will use trial data and linkage to administrative (hospitalization and death) datasets, allowing assessments of the healthcare costs of catheter practice.

#### Key Limitations

A limitation of the trial and its design is that the completeness of data collection is not known, and there is a risk that this could change between baseline and intervention phases. Potentially the risk of the primary outcome across services may also have varied between the two study phases, but the absence of tools to guide clinicians in such patient selection makes this unlikely. Most importantly, the Hawthorne effect may impact the trial outcomes: the phenomenon whereby individuals change their behavior as a result of their knowledge of being observed.(41) To mitigate this, services are discouraged from changing to their clinical practices around catheter care during the trial, beyond those changes arising from the trial intervention. The risk of under-reporting of HD-CRBSI remains but is mitigated by the requirement to centrally report all possible infectious events and the central adjudication of these events.



## Results

### Participant characteristics

Data collection commenced on the 20<sup>th</sup> of December 2016 and is ongoing. A provisional extract from the trial dataset, encompassing the intervention phase at all services, includes data on 5385 HD CVCs in 3615 participants, representing 603,506 days of HD CVC exposure.

The average age of the participants was 63.0 years (IQR 50-73.0 years), 60.1% (n=2174) were male, and 43.7% (n=1578) had diabetes (Table 3). The majority of HD CVCs inserted were tunneled catheters with a median catheter duration of 90.0 days (IQR 28-207 days). Non-tunneled HD CVC had a median catheter duration of 6 days (IQR 3-8 days).

The major indications for HD CVC insertion were for acute kidney injury (n=1896, 35.0%), or for initiation of maintenance hemodialysis without permanent access (n=1703, 31.6%) (Table 4). The majority of tunneled catheters were inserted by interventional radiology services (n=2699; 67%) while the non-tunneled catheters were inserted predominantly by intensive care units (n=753; 55.8%). The internal jugular vein was the most popular site for HD CVC insertion (total 4619; tunneled =3780 (81.8%); non-tunneled= 838 (18.1%)) with femoral being the second most popular site (total 577; tunneled =83 [14.4%]; non-tunneled= 494 [85.6%]).

## Conclusion

REDUCTION is a large stepped wedge cluster randomized trial which systematically measures the use of dialysis catheters across 37 Australian renal services in real-time. It will study the effect of a standardized suite of evidence-based interventions around catheter care upon the rate of HD-CRBSI at the service level and, by virtue of its scale and robust design, will provide novel insights into dialysis catheter care and its impacts upon patients.

## Disclosures

N. Gray reports personal fees from Baxter Healthcare and non-financial support from Amgen Australia outside the submitted work. M. Gallagher reports grants from Australian National Health and Medical Research Council, non-financial support from Multiple partner hospitals, grants from Victorian Department of Health, and grants from Queensland Depart of Health during the conduct of the study; and 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 Dr Gallagher is not aware of any possible conflicts arising from this work. All remaining authors have nothing to disclose.

## Funding

The REDUcing the burden of dialysis Catheter ComplicaTIONS: a National approach (REDUCTION) trial is supported by NHMRC Partnership grant (APP1103241), Department of Health Victoria, Queensland Health. The ANZDATA Registry, Kidney Health Australia, Kidney Health Australia – Caring for Australasians with Renal Impairment, Alice Springs Hospital, Royal Darwin Hospital, Royal

Adelaide Hospital, Austin Hospital, Alfred Hospital, Eastern health, Monash Medical Centre, Royal Melbourne Hospital, Western Health, Royal Hobart Hospital, Cairns Hospital, Princess Alexandra Hospital, Royal Brisbane Hospital, Sunshine Coast Hospital and health Service, Toowoomba Hospital, ACT/NSWSHLD Renal Network, Concord Repatriation General Hospital, Royal Prince Alfred Hospital, Liverpool Hospital, Nepean Hospital, and the Western Sydney LHD provided in-kind support. S. Kotwal is supported by a MRFF Next Generation TRIP Fellowship (MRF1150335)

### Author Contributions

S Kotwal: Conceptualization; Formal analysis; Methodology; Project administration; Validation; Writing - original draft; Writing - review and editing

S Coggan: Project administration; Writing - review and editing

N Gray: Conceptualization; Funding acquisition; Writing - review and editing

K Polkinghorne: Conceptualization; Funding acquisition; Methodology; Writing - review and editing

S Jan: Funding acquisition; Methodology; Writing - review and editing

S McDonald: Conceptualization; Funding acquisition; Methodology; Writing - review and editing

G Talaulikar: Conceptualization; Funding acquisition; Methodology; Writing - review and editing

A Cass: Funding acquisition; Writing - review and editing

M Gallagher: Conceptualization; Funding acquisition; Methodology; Project administration; Resources; Supervision; Writing - review and editing

### Supplemental Materials

List of REDUCCTION Partnership Project contributors

Table 1 – Ethics committee and services covered

Table 2 – Allocation schedule

Table 3 - Data collected in the trial/CRF

Table 4 – New questions added in the intervention phase

### References

1. Zimlichman E, Henderson D, Tamir O, Franz C, Song P, Yamin CK, Keohane C, Denham CR, Bates DW: Health care-associated infections: a meta-analysis of costs and financial impact on the US health care system. *JAMA internal medicine*, 173: 2039-2046, 2013
2. United States Renal Data System: 2018USRDS annual data report: Epidemiology of kidney disease in the United States. Bethesda, MD, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, 2018
3. Byrne C CF, Castledine C, Davenport A, Dawnay A, Fraser S, Maxwell H, Medcalf JF, Wilkie M, Williams AJ: UK Renal Registry - 20th Annual Report of the Renal Association. Bristol, UK, UK Renal Registry, 2017

4. Robinson BM, Akizawa T, Jager KJ, Kerr PG, Saran R, Pisoni RL: Factors affecting outcomes in patients reaching end-stage kidney disease worldwide: differences in access to renal replacement therapy, modality use, and haemodialysis practices. *Lancet*, 388: 294-306, 2016
5. Registry A: 41st Report, Chapter 4: Haemodialysis. Australia and New Zealand Dialysis and Transplant. Adelaide, Australia, ANZDATA, 2018
6. Smyth B, Kotwal S, Gallagher M, Gray NA, Polkinghorne K, REDUCCTION Partnership Study: Dialysis catheter management practices in Australia and New Zealand. *Nephrology*, 24: 827-834, 2019
7. Aslam S, Vaida F, Ritter M, Mehta RL: Systematic Review and Meta-Analysis on Management of Hemodialysis Catheter-Related Bacteremia. *Journal of the American Society of Nephrology*, 25: 2927-2941, 2014
8. Jaffer Y, Selby NM, Taal MW, Fluck RJ, McIntyre CW: A meta-analysis of hemodialysis catheter locking solutions in the prevention of catheter-related infection. *Am J Kidney Dis*, 51: 233-241, 2008
9. Rosenblum A, Wang W, Ball LK, Latham C, Maddux FW, Lacson E, Jr.: Hemodialysis catheter care strategies: a cluster-randomized quality improvement initiative. *Am J Kidney Dis*, 63: 259-267, 2014
10. Patel PR, Brinsley-Rainisch K: The Making Dialysis Safer for Patients Coalition. *A New Partnership to Prevent Hemodialysis-Related Infections*, 13: 175-181, 2018
11. Pronovost P, Needham D, Berenholtz S, Sinopoli D, Chu H, Cosgrove S, Sexton B, Hyzy R, Welsh R, Roth G, Bander J, Kepros J, Goeschel C: An Intervention to Decrease Catheter-Related Bloodstream Infections in the ICU. *New England Journal of Medicine*, 355: 2725-2732, 2006
12. Klevens RM, Edwards JR, Andrus ML, Peterson KD, Dudeck MA, Horan TC, Surveillance atNPIOD: Special Report: Dialysis Surveillance Report: National Healthcare Safety Network (NHSN)—Data Summary for 2006. *Seminars in Dialysis*, 21: 24-28, 2008
13. Thompson S, Wiebe N, Klarenbach S, Pelletier R, Hemmelgarn BR, Gill JS, Manns BJ, Tonelli M, for the Alberta Kidney Disease N: Catheter-related blood stream infections in hemodialysis patients: a prospective cohort study. *BMC Nephrology*, 18: 357, 2017
14. Nguyen DB, Shugart A, Lines C, Shah AB, Edwards J, Pollock D, Sievert D, Patel PR: National Healthcare Safety Network (NHSN) Dialysis Event Surveillance Report for 2014. *Clinical Journal of the American Society of Nephrology*, 12: 1139-1146, 2017
15. Aitken E, Thomson P, Bainbridge L, Kasthuri R, Mohr B, Kingsmore D: A randomized controlled trial and cost-effectiveness analysis of early cannulation arteriovenous grafts versus tunneled central venous catheters in patients requiring urgent vascular access for hemodialysis. *Journal of Vascular Surgery*, 65: 766-774, 2017
16. Al-Solaiman Y, Estrada E, Allon M: The Spectrum of Infections in Catheter-Dependent Hemodialysis Patients. *Clinical Journal of the American Society of Nephrology*, 6: 2247-2252, 2011

17. Miller LM, Clark E, Dipchand C, Hiremath S, Kappel J, Kiaii M, Lok C, Luscombe R, Moist L, Oliver M, MacRae J: Hemodialysis Tunneled Catheter-Related Infections. *Canadian Journal of Kidney Health and Disease*, 3: 2054358116669129, 2016
18. Zhang HH, Cortés-Penfield NW, Mandayam S, Niu J, Atmar RL, Wu E, Chen D, Zamani R, Shah MK: Dialysis Catheter-related Bloodstream Infections in Patients Receiving Hemodialysis on an Emergency-only Basis: A Retrospective Cohort Analysis. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America*, 68: 1011-1016, 2019
19. Landry DL, Braden GL, Gobeille SL, Haessler SD, Vaidya CK, Sweet SJ: Emergence of Gentamicin-Resistant Bacteremia in Hemodialysis Patients Receiving Gentamicin Lock Catheter Prophylaxis. *Clinical Journal of the American Society of Nephrology*, 5: 1799-1804, 2010
20. Arechabala MC, Catoni MI, Claro JC, Rojas NP, Rubio ME, Calvo MA, Letelier LM: Antimicrobial lock solutions for preventing catheter-related infections in haemodialysis. *Cochrane Database of Systematic Reviews*, 2018
21. McCann M, Moore Z: Interventions for preventing infectious complications in haemodialysis patients with central venous catheters. *Cochrane Database of Systematic Reviews*: CD006894, 2010
22. Daisy Kosa S, Lok CE: The economics of hemodialysis catheter-related infection prophylaxis. *Seminars in dialysis*, 26: 482-493, 2013
23. Atapour A, Shahidi S, Sairafian S: Does tunneling the temporary vascular access extend its lifetime? *J Res Med Sci*, 11: 41-47, 2006
24. Brunelli SM, Van Wyck DB, Njord L, Ziebol RJ, Lynch LE, Killion DP: Cluster-Randomized Trial of Devices to Prevent Catheter-Related Bloodstream Infection. *Journal of the American Society of Nephrology*, 29: 1336-1343, 2018
25. Fisher M, Golestaneh L, Allon M, Abreo K, Mokrzycki MH: Prevention of Bloodstream Infections in Patients Undergoing Hemodialysis. *Clinical Journal of the American Society of Nephrology*, 15: 132-151, 2020
26. Jindal K, Chan CT, Deziel C, Hirsch D, Soroka SD, Tonelli M, Culleton BF: CHAPTER 4: Vascular Access. *Journal of the American Society of Nephrology*, 17: S16-S23, 2006
27. Polkinghorne KR, Chin GK, MacGinley RJ, Owen AR, Russell C, Talaulikar GS, Vale E, Lopez-Vargas PA: KHA-CARI Guideline: vascular access - central venous catheters, arteriovenous fistulae and arteriovenous grafts. *Nephrology*, 18: 701-705, 2013
28. Lok CE, Huber TS, Lee T, Shenoy S, Yevzlin AS, Abreo K, Allon M, Asif A, Astor BC, Glickman MH, Graham J, Moist LM, Rajan DK, Roberts C, Vachharajani TJ, Valentini RP: KDOQI Clinical Practice Guideline for Vascular Access: 2019 Update. *American Journal of Kidney Diseases*, 75: S1-S164, 2020
29. KDOQI N: Clinical practice guidelines for vascular adequacy, update. 2006
30. O'Grady N AM, Burns L, Dellinger P, Garland J, Heard S, Lipsett P, Masur H, Mermel L, Pearson M, Raad I, Randolph A, Rupp M, Saint S and the Healthcare Infection Control Practices Advisory Committee: Guidelines for the Prevention of Intravascular Catheter-Related Infections. 2011

31. Lok CE, Mokrzycki MH: Prevention and management of catheter-related infection in hemodialysis patients. *Kidney international*, 79: 587-598, 2011
32. Allon M: Vascular Access for Hemodialysis Patients. *New Data Should Guide Decision Making*, 14: 954-961, 2019
33. Niyar VD: Catheter dysfunction and lock solutions: are we there yet? *Nephrology Dialysis Transplantation*, 2019
34. Smyth B, Kotwal S, Gallagher M, Gray NA, Polkinghorne KR: Arteriovenous access practices in Australian and New Zealand dialysis units. *The Journal of Vascular Access*, 0: 1129729819851061, 2019
35. Hussey MA, Hughes JP: Design and analysis of stepped wedge cluster randomized trials. *Contemporary clinical trials*, 28: 182-191, 2007
36. KHA-CARI: Kidney Health Australia - Caring for Australasians with Renal Impairment. 2020
37. Mermel LA, Allon M, Bouza E, Craven DE, Flynn P, O'Grady NP, Raad, II, Rijnders BJ, Sherertz RJ, Warren DK: Clinical practice guidelines for the diagnosis and management of intravascular catheter-related infection: 2009 Update by the Infectious Diseases Society of America. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America*, 49: 1-45, 2009
38. Moulton LH: Covariate-based constrained randomization of group-randomized trials. *Clinical Trials*, 1: 297-305, 2004
39. Nuckols TK, Keeler E, Morton SC, Anderson L, Doyle B, Booth M, Shanman R, Grein J, Shekelle P: Economic Evaluation of Quality Improvement Interventions for Bloodstream Infections Related to Central Catheters: A Systematic Review. *JAMA Internal Medicine*, 176: 1843-1854, 2016
40. Craswell A, Massey D, Wallis M, Sriram D, Gray NA, Kotwal S, Investigators R: Current practice in dialysis central venous catheter management: Multi-disciplinary renal team perspectives. *Nephrology*, 2019
41. Landsberger H: *HAWTHORNE REVISITED.*, Ithaca, New York, The New York State School of Industrial and Labor Relations, 1958

## Tables and Figures

Table 1 – Renal services participating in the trial

Service Name	State	Number of Satellite Services	Urban/Regional *	Consent model	HD patient numbers from ANZDATA as on 31/12/2016
Alice Springs	NT	2	Regional	Opt-out	358
Armadale Health Service	WA	0	Regional	Opt-out	53
Austin Health	VIC	4	Urban	Waiver	243
Cairns Hospital	QLD	5	Regional	Waiver	266
Concord Hospital	NSW	2	Urban	Waiver	126
Eastern Health	VIC	5	Urban	Opt-out	179
Fiona Stanley Hospital	WA	7	Urban	Opt-out	469
Flinders Medical Centre	SA	4	Urban	Waiver	218
Geelong Hospital (Barwon Health)	VIC	4	Urban	Waiver	156
Gold Coast Hospital and Health Service	QLD	2	Urban	Waiver	151
John Hunter Hospital	NSW	5	Urban	Waiver	222
Liverpool Hospital	NSW	5	Urban	Waiver	424
Mackay Hospital	QLD	1	Regional	Waiver	55
Mater Hospital, Brisbane	QLD	2	Urban	Waiver	30
Monash Health	VIC	5	Urban	Waiver	507
Sunshine Coast University Hospital and Health Service	QLD	3	Urban	Waiver	128
Nepean Hospital	NSW	1	Urban	Waiver	119
Prince of Wales Hospital	NSW	1	Urban	Waiver	80
Metro South Hospital and Health Service (including Princess Alexandra Hospital, Redlands and Logan Hospital)	QLD	3	Urban	Waiver	328

Service Name	State	Number of Satellite Services	Urban/Regional *	Consent model	HD patient numbers from ANZDATA as on 31/12/2016
Rockhampton	QLD	3	Regional	Waiver	89
Royal Adelaide Hospital	SA	17	Urban	Waiver	591
Royal Brisbane Hospital	QLD	3	Urban	Waiver	229
Royal Darwin Hospital	NT	4	Urban	Waiver	287
Royal Hobart Hospital	TAS	1	Urban	Waiver	87
Royal Melbourne Hospital	VIC	25	Urban	Waiver	483
Royal North Shore Hospital	NSW	2	Urban	Opt-out	225
Royal Prince Alfred Hospital	NSW	1	Urban	Waiver	223
Sir Charles Gairdner Hospital	WA	6	Urban	Opt-out	362
St George Hospital	NSW	1	Urban	Waiver	213
St Vincent's Hospital, Melbourne	VIC	6	Urban	Waiver	225
Tamworth Hospital	NSW	3	Rural	Waiver	74
The Alfred Hospital	VIC	2	Urban	Opt-out	237
The Canberra Hospital	ACT	8	Urban	Waiver	259
Toowoomba Hospital	QLD	3	Regional	Waiver	81
Western Health	VIC	3	Urban	Waiver	231
Western Sydney Local Health District (including Westmead, Auburn and Blacktown Hospitals)	NSW	0	Urban	Opt-out	320
Wollongong Hospital	NSW	4	Regional	Waiver	170

\*Urban was defined as being located in an area with a population of 100,000 and over. All other services were categorised as regional/rural.

Table 2 – Trial outcomes

Primary outcome	Definition
Dialysis catheter related bacteremia per 1000 catheter days	One of the following – <ul style="list-style-type: none"> <li>• Culture of the same organism from both the catheter tip AND at least one percutaneous blood culture;</li> <li>• OR culture of the same organism from at least two blood samples (one from a catheter hub and the other from a peripheral vein</li> <li>• OR bacteremia in the absence of another source.</li> </ul>
<b>Secondary outcomes</b>	
Suspected or possible catheter related bacteremia	Catheter removal for the reason of suspected infection with negative blood cultures
Total suspected and possible bacteremia	Catheter removal for the reason of suspected infection with positive or negative blood cultures



Table 3 – Participant characteristics of all participants with data entered during the baseline phase .

Patient Characteristics n (%)	(n=3615 (%))
<b>Males</b>	2174 (60.1)
<b>Age (Median, IQR) years</b>	63.0 (50-73)
<b>Ethnicity/ Ancestry</b>	
Asian (including Chinese, Malay, Filipino, Vietnamese, Indonesian)	292 (8.1)
Indigenous Australian (including Aboriginal & Torres Strait Islander)	350 (9.7)
Caucasian	2331 (64.5)
Māori	31 (0.9)
Pacific Islander (including Tongan, Samoan and Cook Islander)	91 (2.5)
Other	112 (3.1)
Medical records did not indicate ethnicity/ancestry	408 (11.3)
<b>State of enrolment</b>	
ACT	96 (2.7)
NSW	1232 (34.1)
QLD	877 (24.3)
NT	194 (5.4)
SA	245 (6.8)
VIC	758 (21.1)
WA	165 (4.6)
TAS	48 (1.3)
<b>Location of Enrolling Renal service</b>	
Urban	3111 (86.1)
Regional/Rural	504 (13.9)
<b>Diabetes Mellitus-</b>	
Yes, diet controlled	309 (8.6 %)
Yes, medication controlled	1268 (35.1 %)
<b>Immunosuppressant use</b>	<b>477 (13.2%)</b>

Table 4 – Reasons for Catheter Insertion

Reason for CVC Insertion	N=5385 (100%)
AKI	1896 (35.0%)
Initiation of maintenance dialysis with no functioning access	1703 (31.6%)
Transfer from peritoneal dialysis	632 (11.7%)
AVF/AVG Problems	706 (13.1%)
Other	446 (8.3%)

Figure 1 – Trial timelines

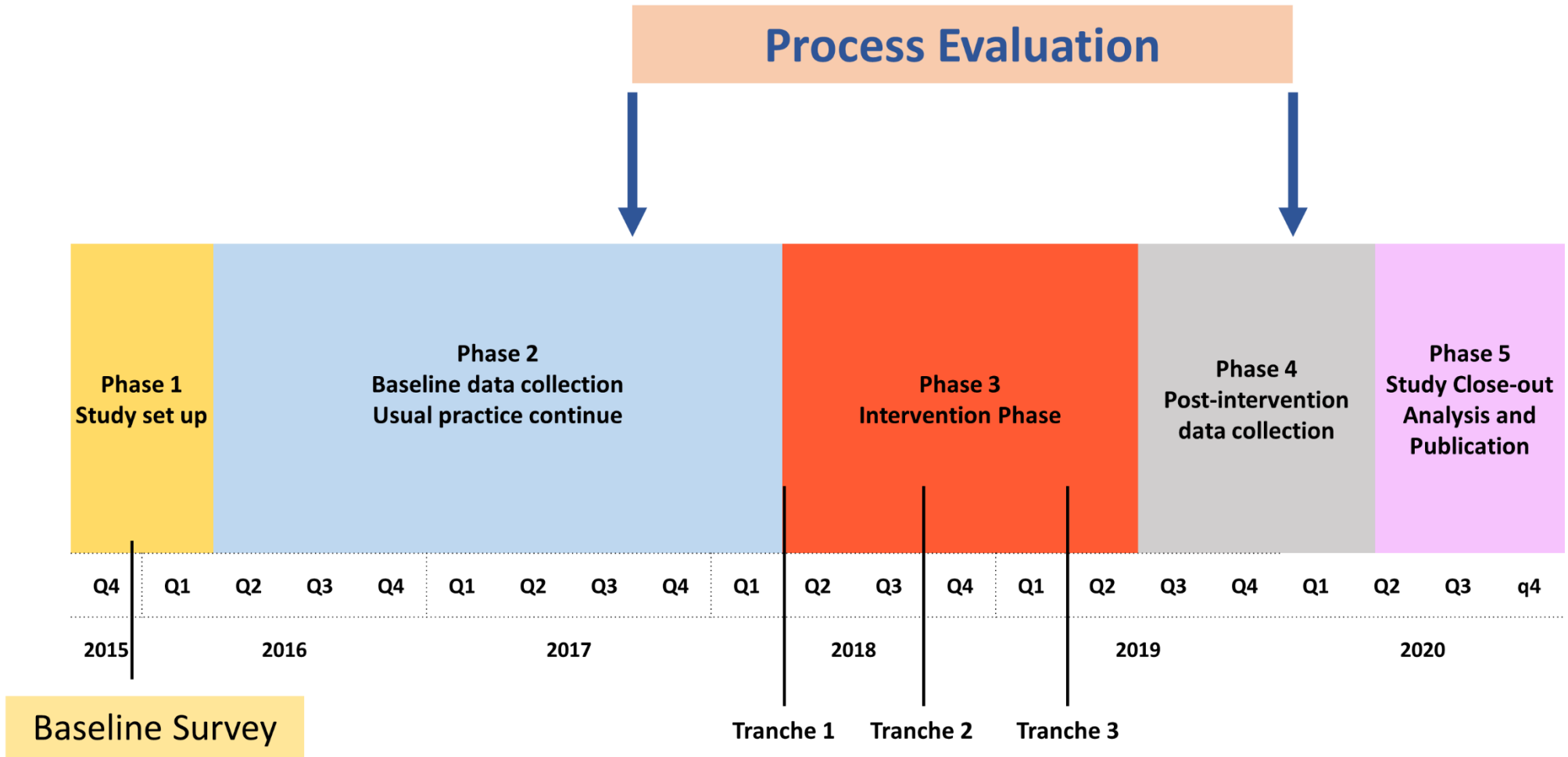


Figure 2 – Interventions Information sheet

1. At the time of catheter insertion
  - 1.1. Surgical aseptic technique (hand hygiene, sterile gloves, surgical mask, eye protection and gown), and a sterile environment (sterile surgical field on the patient) and/or a sterile room as per unit availability **MUST** be applied.
  - 1.2. An antiseptic solution using a minimum of 2% chlorhexidine with 70% alcohol **MUST** be used
    - 1.2.1. For those who cannot tolerate chlorhexidine, povidone–iodine or 70% alcohol may be used
  - 1.3. Site of insertion
    - 1.3.1. The right internal jugular vein is the best site for catheter insertion
    - 1.3.2. Catheters in the subclavian vein should be avoided due to incidence of central vein stenosis.
    - 1.3.3. Avoid femoral catheters where possible
  - 1.4. We do not recommend any specific catheter type
  - 1.5. Ultrasound guided catheter placement is recommended if the resources are available
  - 1.6. Semi permeable transparent dressing **MUST** be applied to the line. If a patient is allergic to these dressings, then an alternative appropriate dressing may be used.
  - 1.7. All patients **MUST** receive education on the following topics
    - 1.7.1. Vascular access care
    - 1.7.2. Hand hygiene
    - 1.7.3. Risks related to catheter use
    - 1.7.4. Recognizing signs of infection
    - 1.7.5. Instructions for access management when away from the dialysis unit
    - 1.7.6. To ensure that their catheter and exit site are kept dry.
    - 1.7.7. To seek assistance from dialysis should a dressing become wet, soiled or leak, or if the catheter itself begins to slip out
    - 1.7.8. To **NOT** shower in the first 72 hours after catheter insertion. After 72 hours, in order to have a shower, the catheter site must be covered with waterproof material.
  - 1.8. All patients **SHOULD** receive a copy of the REDUCCTION catheter care sheet

1. Catheter maintenance
  - 1.1. Hand hygiene, sterile gloves, a plastic apron, and aseptic technique (hand hygiene, gloves) **MUST** be applied at all occasions of catheter access
    - 1.1.1. An antiseptic solution using a minimum of 2% chlorhexidine with 70% alcohol must be used
    - 1.1.2. For those unable to tolerate chlorhexidine, povidone–iodine or 70% alcohol may be used
  - 1.2. Dressing must be changed at least every 7 days and each time the dressing appears visibly soiled or loose
  - 1.3. We do **NOT** recommend the routine use of mupirocin ointment or medicated honey at the catheter exit site.
  - 1.4. All units **MUST** use **at least one** of the following specific interventions aimed at prophylaxis against catheter related bacteraemia\*
    - 1.4.1. Impregnated dressings (such as chlorhexidine impregnated patch or sponge) at the catheter exit site and/or
    - 1.4.2. Anti-microbial (e.g. citrate or taurolidine based) or anti-bacterial (e.g. gentamicin) catheter locking solutions #
  - 1.5. All patients must be advised to ensure that their catheter and exit site are kept dry. Patients must be advised to seek assistance from dialysis should a dressing become wet, soiled or leak, or if the catheter itself begins to slip out.
  - 1.6. All patients should receive a copy of the REDUCCTION catheter care sheet as above
  - 1.7. All patients must receive education on the following topics
    - 1.7.1. Vascular access care
    - 1.7.2. Hand hygiene
    - 1.7.3. Risks related to catheter use
    - 1.7.4. Recognizing signs of infection
    - 1.7.5. Instructions for access management when away from the dialysis unit
  - 1.8. All patients must be advised **NOT** to shower in the first 72 hours after catheter insertion. After 72 hours, in order to have a shower, the catheter site must be covered with waterproof material.

\*check manufacturer's instructions when choosing the intervention to ensure compatibility with catheters

#with the use of gentamicin locks, monitoring of antibiotic resistance should be considered as per hospital policy

2. Catheter removal
  - 2.1. Catheters **MUST** be removed as soon as it is clinically identified that they are no longer needed and within a maximum of 2 weeks of their last use.
  - 2.2. Non-Tunnelled catheters should be changed to tunnelled catheters as soon as possible. Non-tunnelled femoral catheters should not be in place for more than 5 days, and non-tunnelled upper limb catheters– should not be in place for more than 7 days.
  - 2.3. Catheters must be removed when there are signs of catheter related infections except in extenuating cases
  - 2.4. Re-wiring of catheters is **NOT** recommended in the setting of any catheter related infection