Supplementary Material

Lazarus B, Kotwal S, Gallagher M, Gray N, Coggan S, Rogers K, Talaulikar G, Polkinghorne K. **Effect of a multifaceted intervention on the incidence of haemodialysis catheter dysfunction in a national stepped-wedge cluster randomized trial**. Kidney International Reports, 2023

Supplementary Appendix. List of trial investigators.

Service	First name	Last name
Alice Springs Hospital	Senthil Kumar	Balakrishnan
Alice Springs Hospital	David	Fernandes
Armadale Hospital	Hemant	Kulkarni
Armadale Hospital	Casey	Light
Armadale Hospital	Jo	Ryan
Auckland Hospital	Emma	Marsh
Auckland Hospital	David	Semple
Auckland Hospital	Jason	Wei
Alfred Health	Omar	Tombocon
Alfred Health	Rowan	Walker
Alfred Health	Scott	Wilson
Austin Health	Vilma	Lleva
Austin Health	Lucy	Mwangi
Austin Health	Peter	Mount
Austin Health	Maree	Ross-Smith
Austin Health	Marieke	Veenendaal
Barwon Health	Vicki	Smith
Barwon Health	Christine	Somerville
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Cairns Hospital	Natalie	Grainer
Cairns Hospital	Stella	Green
Cairns Hospital	Murty	Mantha
Cairns Hospital	Kati	Thiessen
Canberra Hospital	Girish	Talaulikar
Canberra Hospital	Alison	Winsbury
Canberra Hospital	Irene	Yao
Canberra Hospital	Emily	Neville
Concord Hospital	Khalilah	Marquez
Concord Hospital	Mona	Razavian
Concord Hospital	Lisa	Tienstra
Concord Hospital	Glenn	Stewart
Eastern Health	Cathy	Chan
Eastern Health	Peta	McLean
Eastern Health	Lawrence	McMahon
Eastern Health	Matthew	Roberts
Eastern Health	Dong	Wang
Fiona Stanley Hospital	Monika	Chang
Fiona Stanley Hospital	Anna	Chiam
Fiona Stanley Hospital	Duncan	Wright
Fiona Stanley Hospital	Orla	O'Brien
Fiona Stanley Hospital	Ramyasuda	Swaminathan
Fiona Stanley Hospital	Samadhi	Wimalasena
Fiona Stanley Hospital	Harish	Puttagunta
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Flinders Medical Centre	Amanda	Luke
Flinders Medical Centre	Margaret	Pummeroy
Flinders Medical Centre	Kim	Torpey
Gold Coast Hospital and Health Service	Gemma	Nicholls
Gold Coast Hospital and Health Service	Amy	Swinbank
Gold Coast Hospital and Health Service	Thomas	Titus
John Hunter Hospital	Peter	Choi
John Hunter Hospital	Ginger	Chu
John Hunter Hospital	Leanne	Garvey
John Hunter Hospital	Alastair	Gillies
Liverpool Hospital	Josephine	Chow

Liverpool Hospital	Imelda	De Guzman
Liverpool Hospital	Jeanny	Gando
Liverpool Hospital	Jeffrey	Wong
Liverpool Hospital	Richard	Nguyen
Mackay Hospital	Roy	Cherian
Mackay Hospital	Raye	Gillard
Mackay Hospital	Rachel	James
Mater Hospital	Michael	Burke
Mater Hospital	Leanne	Glancy
Mater Hospital	Shimbie	Lewis
Mater Hospital	Richard	Baer
Mater Hospital	Sophie	Wade
Monash Health	Kate	Fitt
Monash Health	Peter	Kerr
Monash Health	Kevan	Polkinghorne
Monash Health	Mechelle	Seneviratne
Nepean Hospital	Muralikrishna	Komala
Nepean Hospital	Junie	McCourt
Nepean Hospital	Craig	Lawlor
Ipswich Hospital	Julia	Bell
Ipswich Hospital	David W	Johnson
Prince of Wales Hospital	Michaela	Kelleher
Prince of Wales Hospital	Sradha	Kotwal
Metro South Hospital and Health Service	Amanda	Coburn
Metro South Hospital and Health Service	Sarah	Guo
Metro South Hospital and Health Service	David W	Johnson
Metro South Hospital and Health Service	Joanna	Sudak
Metro South Hospital and Health Service	Diana	Leary
Rockhampton Hospital	Jenny	Anderson
Rockhampton Hospital	Thin	Han
Rockhampton Hospital	Tresna	Titmarsh
Royal Adelaide Hospital	Emily	Adam
Royal Adelaide Hospital	Bronwyn	Hockley
Royal Adelaide Hospital	Jenny	Latte
Royal Adelaide Hospital	Yvonne	Matthew
Royal Adelaide Hospital	Stephen	McDonald
Royal Adelaide Hospital	Chen Au	Peh
Royal Adelaide Hospital	Rebecca	Taylor
Royal Brisbane Hospital	David	McIntyre
Royal Brisbane Hospital	Sharadchandra	Ratanjee
Royal Darwin Hospital	Karolynn	Maurice
Royal Darwin Hospital	Fiona	Rettie
Royal Darwin Hospital	Madhivanan	Sundaram
Royal Darwin Hospital	Naomi	Grimshaw
Royal Hobart Hospital	Matthew	Jose
Royal Hobart Hospital	Gail	Read
Royal Melbourne Hospital	Jayne	Amy
Royal Melbourne Hospital	Patricia	Coutts
Royal Melbourne Hospital	Maria	Presno
Royal Melbourne Hospital	Nigel	Toussaint
Royal North Shore Hospital	Debbie	Knagge
Royal North Shore Hospital	Colleen	Van Senden
Royal North Shore Hospital	Linh	Pham
Royal North Shore Hospital	Muh Geot	Wong
Royal Prince Alfred Hospital	Jane	Nicholson
Royal Prince Alfred Hospital	Paul	Snelling
Sir Charles Gairdner Hospital	Neil	Boudville
Sir Charles Gairdner Hospital	Alison	Farmer

Sir Charles Gairdner Hospital	Ingrid	Holmes
Sir Charles Gairdner Hospital	Victoria	Link
Sir Charles Gairdner Hospital	Vivien	Perreau
Sir Charles Gairdner Hospital	Nicole	Warnecke
St George Hospital	Sunil	Badve
St George Hospital	Yanella	Martinez-Smith
St George Hospital	Jayson	Catiwa
St Vincent's Hospital	Frank	Ierino
St Vincent's Hospital	Emmet	O'flaherty
Sunshine Coast Hospital and Health Service	Nicholas	Gray
Sunshine Coast Hospital and Health Service	Gerald	Hilder
Sunshine Coast Hospital and Health Service	Kaylene	Wadd
Sunshine Coast Hospital and Health Service	Andrea	Pollock
Sunshine Coast Hospital and Health Service	Stanley	Searle
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Tamworth Hospital	Stephen	May
Tamworth Hospital	Jill	Telfer
The George Institute for Global Health	Martin	Gallagher
The George Institute for Global Health	Sradha	Kotwal
The George Institute for Global Health	Sarah	Coggan
The George Institute for Global Health	Casey	Yates
The George Institute for Global Health	Kathryn	Higgins
The George Institute for Global Health	Earl	James
The George Institute for Global Health	Alison	Coenen
The George Institute for Global Health	Kris	Rogers
The George Institute for Global Health	Gian Luca	Di Tanna
The George Institute for Global Health	Jayanthi	Mysore
The George Institute for Global Health	Joseph	Alvin Santos
The George Institute for Global Health	Benjamin	Talbot
The George Institute for Global Health	Katrina	Thistlethwaite
Toowoomba Hospital	Elizabeth	Coroneos
Toowoomba Hospital	Shannon	Nugent
Toowoomba Hospital	Ian	Fox
Toowoomba Hospital	Sree	Venuthurupalli
Western Health	Jennifer	Connor
Western Health	Ruth	Thachaw
Western Health	Sandra	Crikis
Wollongong Hospital	Pauline	Byrne
Wollongong Hospital	Karumathil	Murali
Wollongong Hospital	Hicham	Cheikh Hassan
Western Sydney Local Health District	Lin	Huang
Western Sydney Local Health District	Romiereeza	Dizon
Western Sydney Local Health District	Deepika	Joshi
Western Sydney Local Health District	Jon	Mendoza
Western Sydney Local Health District	Bishi	Augustine
Western Sydney Local Health District	Disha	Balraj
Western Sydney Local Health District	Vincent	Lee
Western Sydney Local Health District	David	O'Donnell

Supplementary Methods. Details of trial methods.

Details of the covariate-constrained randomization method.

In this trial 37 nephrology services were randomized, and each service varied in size. Some services had fewer haemodialysis patients, others had more, and the number of catheters used in each service therefore also varied. If randomization of services was performed without considering these differences in catheter use, it is possible that substantial imbalance in the average number of catheters in each of the three tranches could occur by chance, which would reduce the power of the study. To mitigate this possibility, baseline data on the number of catheters used at each service (from Dec 2016 – Jan 2018) was incorporated into the randomization process. Specifically,100,000 random allocation sequences were generated and those sequences in which the average number of catheters per service in each tranche were balanced (within 10% of the overall trial average) were retained. Of the original sequences generated, 6865 met the balance criteria, and the final randomization allocation was randomly chosen from this subset.

Details of the trial intervention.

The catheter management interventions were developed by a trial Sub-committee following an independent evidence-based review and were finalized in January 2018. Haemodialysis catheter-related bloodstream infections were the primary consideration in designing the interventions, however non-infectious catheter complications were also considered as secondary outcomes of interest. Two local champions, consisting of one physician and one nurse, were identified at each nephrology service, and were tasked with implementing the intervention at their service.

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

2. Catheter maintenance
   - 2.1. Hand hygiene, sterile gloves, a plastic apron, and aseptic technique (hand hygiene, gloves) **MUST** be applied at all occasions of catheter access
     - 2.1.1. An antiseptic solution using a minimum of 2% chlorhexidine with 70% alcohol must be used
     - 2.1.2. For those unable to tolerate chlorhexidine, povidone–iodine or 70% alcohol may be used
   - 2.2. Dressing must be changed at least every 7 days and each time the dressing appears visibly soiled or loose
   - 2.3. We do **NOT** recommend the routine use of mupirocin ointment or medicated honey at the catheter exit site.
   - 2.4. All units **MUST** use **at least one** of the following specific interventions aimed at prophylaxis against catheter related bacteraemia*
     - 2.4.1. Impregnated dressings (such as chlorhexidine impregnated patch or sponge) at the catheter exit site and/or
     - 2.4.2. Anti-microbial (e.g. citrate or taurolidine based) or anti-bacterial (e.g. gentamicin) catheter locking solutions #
   - 2.5. 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.
   - 2.6. All patients should receive a copy of the REDUCCTION catheter care sheet as above
   - 2.7. All patients must receive education on the following topics
     - 2.7.1. Vascular access care
     - 2.7.2. Hand hygiene
     - 2.7.3. Risks related to catheter use
     - 2.7.4. Recognizing signs of infection
     - 2.7.5. Instructions for access management when away from the dialysis unit
   - 2.8. 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

3. Catheter removal
   - 3.1. 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.
   - 3.2. 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.
   - 3.3. Catheters must be removed when there are signs of catheter related infections except in extenuating cases
   - 3.4. Re-wiring of catheters is **NOT** recommended in the setting of any catheter related infection

Supplementary Table S1. Baseline characteristics of tunnelled catheters during baseline, intervention or both phases.

	Study Phase					
	Baseline only		Both phases		Intervention only	
	N	%	N	%	N	%
Number of catheters	2889		1038		3476	
Venous insertion site, n (%)						
R internal jugular	2,226	(77.1%)	834	(80.3%)	2,731	(78.6%)
L internal jugular	469	(16.2%)	149	(14.4%)	558	(16.1%)
R femoral	43	(1.5%)	11	(1.1%)	71	(2.0%)
L femoral	26	(0.9%)	5	(0.5%)	31	(0.9%)
R subclavian	63	(2.2%)	26	(2.5%)	44	(1.3%)
L subclavian	37	(1.3%)	6	(0.6%)	15	(0.4%)
Other	25	(0.9%)	7	(0.7%)	26	(0.7%)
Reason for catheter insertion, n (%)						
Acute kidney injury	910	(31.5%)	173	(16.7%)	993	(28.6%)
Commence maintenance HD	1,001	(34.6%)	478	(46.1%)	1,415	(40.7%)
AV access complication	546	(18.9%)	201	(19.4%)	623	(17.9%)
Transfer from PD	373	(12.9%)	165	(15.9%)	377	(10.8%)
Failing transplant	21	(0.7%)	14	(1.3%)	22	(0.6%)
Other	38	(1.3%)	7	(0.7%)	46	(1.3%)
Catheter proceduralist, n (%)						
Interventional radiology	1,957	(67.7%)	634	(61.1%)	2,434	(70.0%)
Nephrology	341	(11.8%)	172	(16.6%)	393	(11.3%)
Surgery	484	(16.8%)	182	(17.5%)	469	(13.5%)
Critical care	52	(1.8%)	21	(2.0%)	89	(2.6%)
Not known	55	(1.9%)	29	(2.8%)	91	(2.6%)

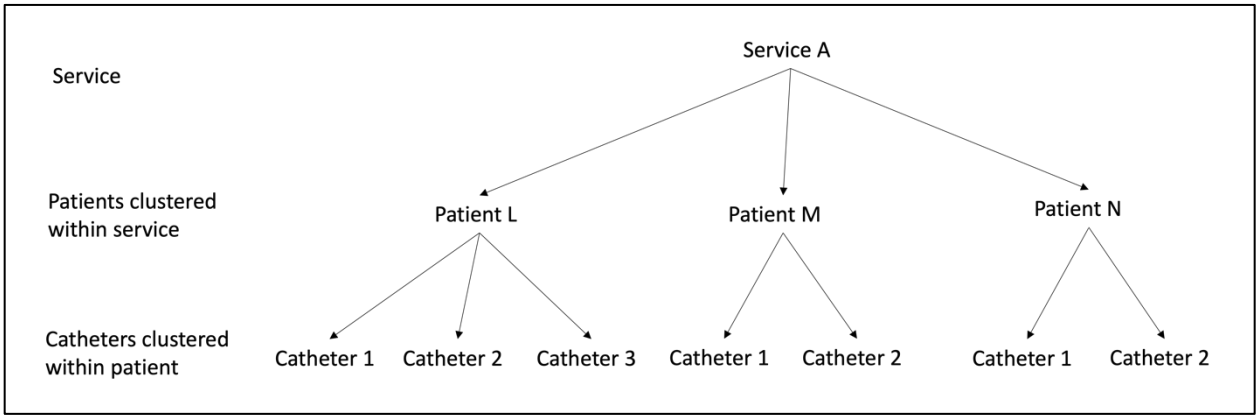
Abbreviations: AV = arteriovenous, HD = hemodialysis, PD = peritoneal dialysis, L = Left, R = Right

Supplementary Table S2. Relationship between patient-level and catheter-level covariates and the incidence of catheter dysfunction among tunnelled catheters from three-level Poisson regression models.

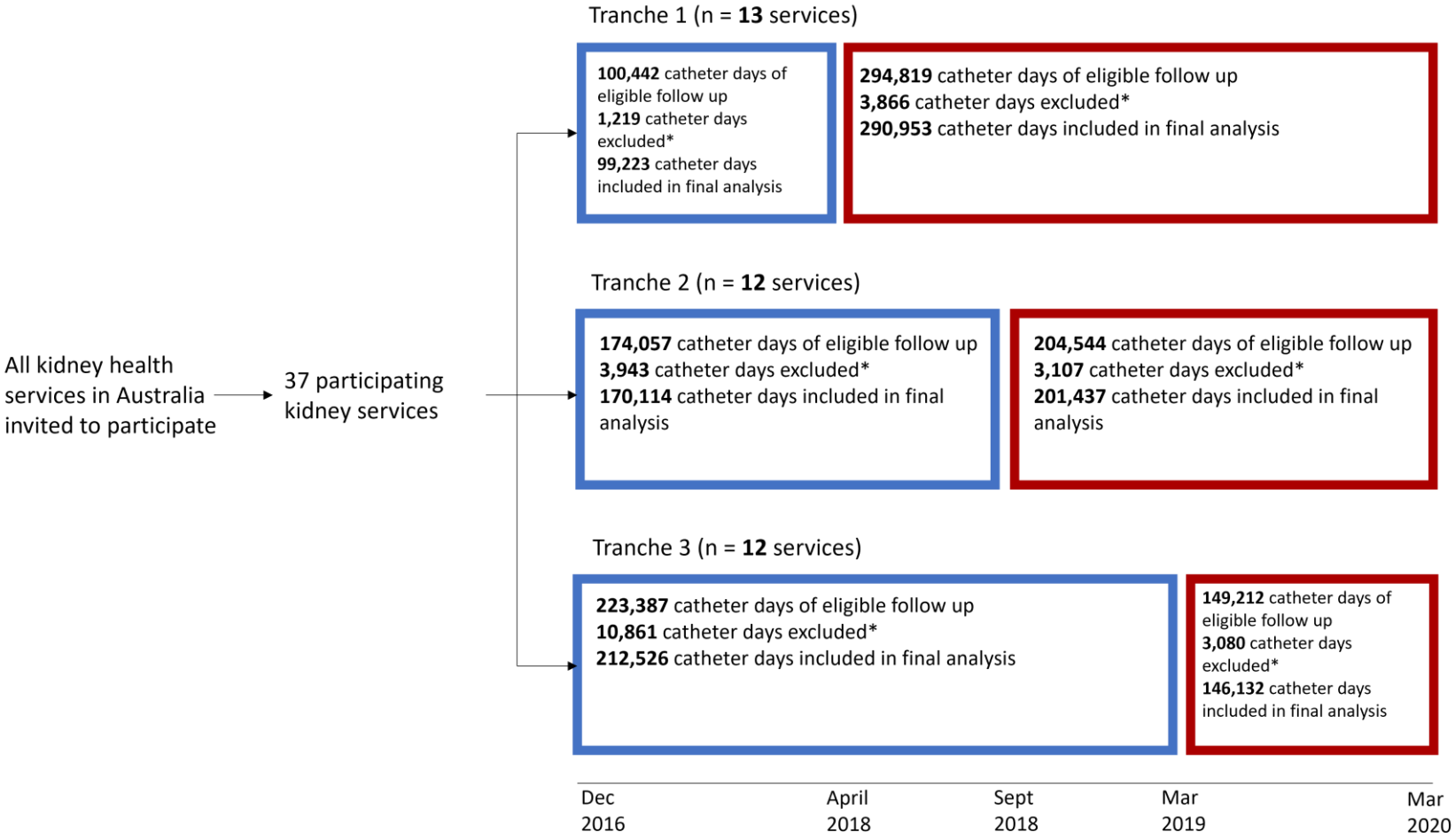
	Model 1		Model 2		Model 3	
	IRR	(95% CI)	IRR	(95% CI)	IRR	(95% CI)
Intervention						
Baseline	1.00	(ref)	1.00	(ref)	1.00	(ref)
Intervention	0.65	(0.47, 0.90)	0.68	(0.49, 0.94)	0.68	(0.49, 0.94)
Time period						
1	1.00	(ref)	1.00	(ref)	1.00	(ref)
2	0.94	(0.73, 1.21)	0.93	(0.72, 1.20)	0.93	(0.72, 1.20)
3	1.06	(0.77, 1.46)	1.04	(0.76, 1.42)	1.03	(0.75, 1.42)
4	1.25	(0.85, 1.83)	1.16	(0.79, 1.70)	1.14	(0.78, 1.67)
Insertion site						
R internal jugular			1.00	(ref)	1.00	(ref)
L internal jugular			2.15	(1.76, 2.64)	2.09	(1.70, 2.57)
R femoral			3.30	(1.93, 5.66)	3.30	(1.93, 5.66)
L femoral			4.77	(2.39, 9.49)	4.73	(2.37, 9.44)
R subclavian			1.54	(0.85, 2.78)	1.44	(0.80, 2.61)
L subclavian			3.02	(1.31, 6.99)	2.90	(1.26, 6.66)
Other			1.71	(0.78, 3.74)	1.57	(0.72, 3.43)
Age category, years						
<50					1.04	(0.78, 1.38)
50-60					1.34	(1.01, 1.77)
60-70					1.00	(ref)
70-80					1.27	(0.98, 1.64)
>80					1.06	(0.73, 1.53)
Gender						
Male					1.00	(ref)
Female					1.38	(1.14, 1.67)
Diabetes mellitus						
Absent					1.00	(ref)
Diet controlled					1.06	(0.74, 1.50)
Medication required					1.02	(0.84, 1.25)
Catheter indication						
Kidney failure					1.00	(ref)
Acute kidney injury					0.86	(0.68, 1.08)
Proceduralist department						
Interventional radiology					1.00	(ref)
Nephrology					0.72	(0.42, 1.26)
Surgery					1.01	(0.66, 1.54)
Critical care					1.26	(0.45, 3.50)
Other					0.97	(0.53, 1.76)

Abbreviations: IRR = Incidence Rate Ratio, R = Right, L = Left, ICU = Intensive care unit, ref = reference category

Supplementary Figure S1. Illustration of multiple levels of clustering when catheter-level characteristics are included in assessing the intervention effect in a stepped wedge cluster randomized trial.



Supplementary Figure S2. Participant flow diagram for the post-hoc analysis of the REDUCCTION national stepped-wedge cluster randomized trial. *Catheter days were excluded due to unknown reason for catheter removal (n= 310 catheters, 198 participants) or unknown tunnel status (n = 2 catheters, 2 participants).



Supplementary materials 3: Checklist of information to include when reporting a stepped wedge cluster randomised trial (SW-CRT)

Topic	Item no	Checklist item	Page no
Title and abstract			
	1a	Identification as a SW-CRT in the title.	1
	1b	Structured summary of trial design, methods, results, and conclusions (see separate SW-CRT checklist for abstracts).	3
Introduction			
Background and objectives	2a	Scientific background. Rationale for using a cluster design and rationale for using a stepped wedge design.	5-7
	2b	Specific objectives or hypotheses.	5
Methods			
Trial design	3a	Description and diagram of trial design including definition of cluster, number of sequences, number of clusters randomised to each sequence, number of periods, duration of time between each step, and whether the participants assessed in different periods are the same people, different people, or a mixture.	7-9,sup
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons.	NA
Participants	4a	Eligibility criteria for clusters and participants.	7
	4b	Settings and locations where the data were collected.	7
Interventions	5	The intervention and control conditions with sufficient details to allow replication, including whether the intervention was maintained or repeated, and whether it was delivered at the cluster level, the individual participant level, or both.	7-9
Outcomes	6a	Completely defined prespecified primary and secondary outcome measures, including how and when they were assessed.	9
	6b	Any changes to trial outcomes after the trial commenced, with reasons.	9
Sample size	7a	How sample size was determined. Method of calculation and relevant parameters with sufficient detail so the calculation can be replicated. Assumptions made about correlations between outcomes of participants from the same cluster. (see separate checklist for SW-CRT sample size items).	NA
	7b	When applicable, explanation of any interim analyses and stopping guidelines.	NA
Randomisation			
Sequence generation	8a	Method used to generate the random allocation to the sequences of treatments.	7, sup
	8b	Type of randomisation; details of any constrained randomisation or stratification, if used.	7, sup
Allocation concealment mechanism	9	Specification that allocation was based on clusters; description of any methods used to conceal the allocation from the clusters until after recruitment.	7-8
Implementation	10a	Who generated the randomisation schedule, who enrolled clusters, and who assigned clusters to sequences.	7
	10b	Mechanism by which individual participants were included in clusters for the purposes of the trial (such as complete enumeration, random sampling; continuous recruitment or ascertainment; or recruitment at a fixed point in time), including who recruited or identified participants.	7
	10c	Whether, from whom and when consent was sought and for what; whether this differed between treatment conditions.	7-8
Blinding	11a	If done, who was blinded after assignment to sequences (eg, cluster level participants, individual level participants, those assessing outcomes) and how.	NA
	11b	If relevant, description of the similarity of treatments.	NA
Statistical methods	12a	Statistical methods used to compare treatment conditions for primary and secondary outcomes including how time effects, clustering and repeated measures were taken into account.	9-11
	12b	Methods for additional analyses, such as subgroup analyses, sensitivity analyses, and adjusted analyses.	9-11

(*Continued*)

Supplementary materials 3 (*Continued*)

Topic	Item no	Checklist item	Page no
Results			
Participant flow (a diagram is strongly recommended)	13a	For each treatment condition or allocated sequence, the numbers of clusters and participants who were assessed for eligibility, were randomly assigned, received intended treatments, and were analysed for the primary outcome (see separate SW-CRT flow chart).	supp
	13b	For each treatment condition or allocated sequence, losses and exclusions for both clusters and participants with reasons.	supp
Recruitment	14a	Dates defining the steps, initiation of intervention, and deviations from planned dates. Dates defining recruitment and follow-up for participants.	7
	14b	Why the trial ended or was stopped.	7
Baseline data	15	Baseline characteristics for the individual and cluster levels as applicable for each treatment condition or allocated sequence.	13, T1
Numbers analysed	16	The number of observations and clusters included in each analysis for each treatment condition and whether the analysis was according to the allocated schedule.	13-14
Outcomes and estimation	17a	For each primary and secondary outcome, results for each treatment condition, and the estimated effect size and its precision (such as 95% confidence interval); any correlations (or covariances) and time effects estimated in the analysis.	13-14, T:
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended.	13-14
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing prespecified from exploratory.	14-15
Harms	19	Important harms or unintended effects in each treatment condition (for specific guidance see CONSORT for harms).	NA
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses.	18-19
Generalisability	21	Generalisability (external validity, applicability) of the trial findings. Generalisability to clusters or individual participants, or both (as relevant).	18
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence.	16-19
Other information			
Registration	23	Registration number and name of trial registry.	2
Protocol	24	Where the full trial protocol can be accessed, if available.	2
Funding	25	Sources of funding and other support (such as supply of drugs), and the role of funders.	20-21
Research ethics review	26	Whether the study was approved by a research ethics committee, with identification of the review committee(s). Justification for any waiver or modification of informed consent requirements.	8

This checklist has been taken from table 3 in *BMJ* 2018;363:k1614, as a standalone document for readers to print out or fill in electronically.