Burden of haemodialysis catheter-related bloodstream infections in Australia: A national data-linkage study

Benjamin Lazarus, Kevan Polkinghorne, Martin Gallagher, Sarah Coggan, Nicholas Gray, Girish Talaulikar, and Sradha Kotwal
on behalf of the REDUCCTION Investigators
Background

• > 12,000 Australians received chronic HD in 2021 and trend is rising \(^1\)
  • Haemodialysis catheters are widely used \(^1\)

• Infections are 3\(^{rd}\) leading cause death among patients receiving HD\(^1\)

• Patients using a HD-CVC had a higher risk of infection\(^2\)
  • Not all excess infections are directly attributable to the catheter \(^2\)
  • Types of infections in Australia, and relative contribution of CVC-related infections is unknown

References: 1. ANZDATA 45\(^{th}\) Report 2022;  2. Ravani, JASN 2013
Haemodialysis catheter related bloodstream infections

• Burden in Australia
  • Incidence during REDUCTION: 0.27 events per 1000 catheter days\(^1\)

  • Western Australia\(^2\): 111 infections from 2005-18, 92% required hospitalisation, hospitalization more likely with Gram positives

  • Outcomes of hospitalisation with HDCRBSI in Australia are unknown

References
1. Kotwal BMJ 2022;
2. Phillips Nephrology 2022;
Aims

• To quantify the burden of different types of infections among chronic haemodialysis patients that used a HD-CVC in Australia, and

• To estimate the effect of HDCRBSI on hospital length of stay and patient outcomes in Australia
Data sources and linkage

REDUCTION COHORT

1. Exclude patients enrolled in WA and not in ANZDATA

2016-2020
>6000 patients

LINKED ANZDATA

LINKED STATE HOSPITALIZATIONS

References 1. Kotwal BMJ 2022
Cohort follow up

Catheter follow-up for chronic haemodialysis patients who started HD via a CVC during REDUCTION.

- **CATHETER PERIOD**
  - Enrolment into REDUCTION (first catheter during trial)
  - Last catheter removed (or end of trial if catheter not removed)

- **POST CATHETER PERIOD**

  - End of the trial (March 2020)
Classification of hospitalisations

Excluded same day admissions
Patient transfers to other facility included in the individual admission

Hospitalisation that precipitated HD catheter insertion

CATHETER PERIOD
Hospitalisations during the catheter period

POST CATHETER PERIOD
Hospitalisations after the catheter period

Enrolment into REDUCTION (first catheter during trial)

Last catheter removed (or end of trial if catheter not removed)

End of the trial (March 2020)

TIME
## Infectious hospitalisations

<table>
<thead>
<tr>
<th>Classification</th>
<th>Principal ICD-10-AM diagnostic code</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sepsis or bacteraemia</td>
<td>A02.1 A03.7 A20.7 A21.7 A22.7 A23.7 A24.7 A26.7 A28.01 A28.21 A32.7 A39.7 A40.0 A40.1 A40.2* A40.3 A40.8 A40.9 A41.0 A41.1 A41.2 A41.4 A41.5* A41.8 A41.9 A42.7 A54.7 B00.71 B37.7 R65.1 A32.8 A39.2 A39.4 R65.0 A49.0* A49.1 A49.9</td>
</tr>
<tr>
<td>Vascular access infection</td>
<td>T80.2 T82.7 T82.74 T82.75 T82.76 T82.77 T82.79 T85.7 T85.78</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>A20.2 A21.2 A31.0 A37* A43.0 A48.1 B01.2 B05.2 B20.6 B25.0 B37.1 B38.0 B38.2 B39.0 B39.2 B58.3 B59 B95.3 B96.0 B96.1 J09/J18.9 J20/J22 B44.0</td>
</tr>
<tr>
<td>Intra-abdominal</td>
<td>A00* A02.0 A03* A04* D73.3 K35.2 K35.3 K35.8 K36 K37 K38.9 K57.0* K57.12 K57.13 K57.2 K57.32 K57.33 K57.4* K57.52 K57.53 K57.8* K57.92 K57.93 K63.0 K65.0 K67* K75.0 K77.0 K81.0 K81.9 K80.3* A08* A09.0 A09.9 B17.9 T85.71</td>
</tr>
<tr>
<td>Cellulitis</td>
<td>A31.1 A36.3 A43.1 A46 A48.0 H00.0 H05.0 H60.0/H60.3 I73.0 I34.0 K12.2 K61* L01.0 L01.1 L02* L03* L05.0 L05.9 L08* M72.6 N73.0 N73.2</td>
</tr>
<tr>
<td>Bone or joint</td>
<td>M46.2* M46.3* M86* M00* M01*</td>
</tr>
<tr>
<td>Urinary tract</td>
<td>N10 N16.0 N39.0 N41.0 N41.1 N41.2</td>
</tr>
<tr>
<td>Endocarditis</td>
<td>A39.5 B33.2 B37.6 I30.1 I32.0 I32.1 I33* I39* I40.0 I41.0/I41.2</td>
</tr>
<tr>
<td>CNS infection</td>
<td>A17.0 A20.3 A27.8 A32.1 A39.0 A87* B00.3 B01.0 B02.1 B05.1 B06.0 B26.1 B37.5 B38.4 B45.1 B57.4 G00* G01* G02* G03.8 G03.9 G06* G07 G08 B02.0</td>
</tr>
<tr>
<td>Other infections</td>
<td>A* or B* codes not otherwise classified above</td>
</tr>
</tbody>
</table>

Confirmed HD-CRBSI events during REDUCCTION

• Staff at each participating site reported any infectious events that may be related to the HD-CVC and uploaded de-identified clinical information

• Central adjudication by a blinded committee

• Modified IDSA definition for HD-CRBSI
  • Culture of the same organism from catheter tip and at least one peripheral percutaneous blood culture
  • Culture of the same organism from at least two blood samples (catheter hub and peripheral vein), or
  • Bacteraemia in the absence of another (non-haemodialysis catheter) source
Hospitalisations attributable to HDCBRSI

• If both of the following 2 criteria were met:

1. Principal diagnostic code for admission was compatible with sepsis or vascular access infection AND

2. Trial confirmed HDCBRSI was reported within 3 days before or 2 days after admission date¹

References 1. Wasik Ped Neph 2022
Other study measures

• Patient and catheter data
  • Age, gender, ethnicity, diabetes, immunosuppressant use (REDDUCTION)
  • Primary kidney disease, other comorbidities, KRT vintage (ANZDATA)
  • Indication for patient first catheter, total duration catheters in situ (REDDUCTION)

• Hospitalisation data
  • Length of stay, ICU admission, modality of separation
  • Metastatic infection (IE, osteomyelitis, septic arthritis, epidural abscess) 1-4

Study flowchart

6248 patients in REDUCCTON

Exclude
295 patients enrolled in WA
1949 patients without linked ANZDATA
61 patients with first CVC for either PLEX or unknown reasons

3943 chronic HD patients (outside WA)
Chronic HD patients in REDUCCTION

- 3943 Patients
- 60 Years old ± 15 years
- 40% Female
- 15% First Nations (60% White)
- 50% DM or HTN as 1° kidney disease
- 20% Glomerular disease as 1° kidney disease
- 10% Immunosuppressed
- 2633 Years of follow up during catheter period
Indications for first HD-CVC

Number of patients

- Prior KRT
- New to KRT
Among patients new to KRT, 1/3 had their transition to HD with a CVC precipitated by AKI.
Among patients new to KRT, 1/3 had their transition to HD with a CVC precipitated by AKI.

2/3 transitioned to chronic HD via a CVC without AKI precipitant.
Ethnicity of patients who started chronic HD via a CVC

![Chart showing the percentage of patients by ethnicity for those who started HD precipitated by AKI and those who started maintenance HD. The chart includes categories such as Other, Pacific Island, Asian, First Nations, and White.]
**Classification of hospitalisations**

Excluded same day admissions
Patient transfers to other facility included in the individual admission

- Hospitalisation that precipitated HD catheter insertion
- Enrolment into REDUCTION (first catheter during trial)
- Last catheter removed (or end of trial if catheter not removed)
- End of the trial (March 2020)

**CATHETER PERIOD**
- Hospitalisations during the catheter period

**POST CATHETER PERIOD**
- Hospitalisations after the catheter period
Burden of infectious admissions

10,096 admissions during the catheter period (3707 patients)

1831 admissions (18%) due to infection

8265 admissions without infection as principal diagnosis (incl. many admissions with infection as a secondary diagnosis)
Burden of infectious admissions among chronic HD patients

Admissions (N = 1,831)

Bed days (N = 18,839)
Burden of admissions due to HDCRBSI

10,096 admissions during the catheter period (3707 patients)

1831 admissions due to infection

8265 admissions without infection as principal diagnosis (incl. many admissions with infection as a secondary diagnosis)

764 admissions due to sepsis (n = 390) or vascular access infection (n = 374)

1067 other infectious admissions

91 other trial confirmed HDCRBSI events
25 other admits with HDCRBSI within 2d but without sepsis or VAI as principal Dx code
34 confirmed HDCRBSI events occurred >2d into admit
32 confirmed HDCRBSI without linked admit

121 admissions (10% of sepsis and 25% of VAI admissions) with trial confirmed HDCRBSI within 3d before or 2d after admission

Length of stay and admission outcomes analysed for these admissions which were "solely" attributable to HDCRBSI
Hospitalisations due to HDCRBSI: length of stay

121 admissions caused by HDCBRSI (113 patients)
Median (IQR) length of stay = 9 days (5 – 15)
In-hospital deaths = 3
Results consistent for each patient’s first HDCRBSI admission
Microbiology

• Available for 120 out of 121 admissions caused by HDCRBSI
  • 64 *Staphylococcus aureus* (50 MSSA, 14 MRSA)
  • 10 *Staphylococcus epidermidis*
  • 1 *Escherichia coli*
  • 1 *Klebsiella pneumoniae*
  • 38 Other
  • 6 Polymicrobial
HDCRBSI admissions caused by *S. aureus* were longer

<table>
<thead>
<tr>
<th></th>
<th><em>S. aureus</em></th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of admissions</td>
<td>64</td>
<td>56</td>
</tr>
<tr>
<td>Median length of stay, days (IQR)</td>
<td>12 (5 – 22)</td>
<td>7.5 (4 – 16)</td>
</tr>
</tbody>
</table>

\[ p = 0.027 \]
ICU admissions

- 19 out of 121 admissions (15.7%) required stay in ICU
- Median days in ICU (IQR) = 2.7 (1.1 – 4.6)
Metastatic infection

• 10 out of 121 admissions (8.3%) complicated by metastatic infection
  • 4 infective endocarditis
  • 4 septic joint
  • 2 osteomyelitis
Summary

• Disparities in patients transitioning to chronic HD via a catheter in Aus

• Sepsis and vascular access infections were leading causes of infectious hospitalization among chronic HD patients using a CVC

• 10% of sepsis and 25% of VAI admissions were able to be linked to a confirmed HDCRBSI event

• Morbidity from hospitalization due to HDCRBSI is substantial
Next steps

• Examine precipitants of HD-CVC use and disparities
  • Aim to reduce unnecessary exposure to CVCs for dialysis

• Predictors of length of stay and other hospital outcomes

• Economic costs

• Promote surveillance for HDCRBSI
Acknowledgements

• Supervisors
  • Kevan Polkinghorne
  • Sradha Kotwal
  • Martin Gallagher

• REDUCTION team

• Funding sources

• Patients and carers
Classification of hospitalisations

Excluded same day admissions
Patient transfers to other facility included in the individual admission

Hospitalisation that precipitated HD catheter insertion

2/3 of patients had initial CVC inserted during an admission

2/3 of patients had initial CVC inserted during an admission

Enrolment into REDUCCTION (first catheter during trial)

Last catheter removed (or end of trial if catheter not removed)

End of the trial (March 2020)

TIME

CATHETER PERIOD

Hospitalisations during the catheter period

POST CATHETER PERIOD

Hospitalisations after the catheter period
## Admissions that precipitated HD catheter insertion

<table>
<thead>
<tr>
<th></th>
<th>Precipitated by AKI</th>
<th>Start maintenance HD</th>
<th>Transfer from PD</th>
<th>AVF or AVG complication</th>
<th>Failing transplant</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>802</td>
<td>1541</td>
<td>602</td>
<td>729</td>
<td>33</td>
<td>3707</td>
</tr>
<tr>
<td>First HD catheter precipitated by admission, n (%)</td>
<td>627 (78.2)</td>
<td>966 (62.7%)</td>
<td>405 (67.3)</td>
<td>491 (67.4)</td>
<td>22 (66.7)</td>
<td>2511 (67.7)</td>
</tr>
<tr>
<td>Leading principal diagnoses (ICD-10AM)</td>
<td>AKI, multiple myeloma, acute MI</td>
<td>CKD stage 5, fluid overload, prep for dialysis</td>
<td>PD catheter infection or malfunction</td>
<td>Vascular thrombosis or mechanical</td>
<td>CKD stage 5, transplant rejection</td>
<td>NA</td>
</tr>
<tr>
<td>Median duration of admission, days (IQR)</td>
<td>20 (10-41)</td>
<td>10 (5-21)</td>
<td>11 (6-24)</td>
<td>7 (3-15)</td>
<td>7.5 (4 – 22)</td>
<td>11 (6-25)</td>
</tr>
</tbody>
</table>
Infectious admissions: median length of stay

<table>
<thead>
<tr>
<th>Principal diagnosis</th>
<th>Number of admissions</th>
<th>Median LOS, days (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sepsis or bacteraemia</td>
<td>390</td>
<td>8 (4 - 16)</td>
</tr>
<tr>
<td>Vascular access infection</td>
<td>374</td>
<td>6 (3 – 11)</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>360</td>
<td>4 (2 – 7)</td>
</tr>
<tr>
<td>Intra-abdominal infection</td>
<td>338</td>
<td>5 (2 – 10)</td>
</tr>
<tr>
<td>Cellulitis</td>
<td>139</td>
<td>4 (2 – 10)</td>
</tr>
<tr>
<td>Bone or joint infection</td>
<td>93</td>
<td>10 (3 – 26)</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>79</td>
<td>4 (2 – 6)</td>
</tr>
<tr>
<td>Endocarditis</td>
<td>13</td>
<td>14 (6 – 31)</td>
</tr>
</tbody>
</table>

*Admissions for sepsis and vascular access infection were longer than pneumonia, abdominal infections, and cellulitis, p < 0.0001 for all 6 comparisons using t-test of log-transformed mean length of stay.
Service size and total number of reported HDCRBSI

[Graph showing the relationship between the number of chronic HD patients on 31 Dec 2016 and the total number of reported HDCRBSI, with various hospitals plotted on the graph.]
Aim: To quantify the health burden of haemodialysis catheter-related bloodstream infection (HDCRBSI) among chronic haemodialysis patients in Australia.

Background: Haemodialysis catheters are widely used and prone to infection. The health impact of catheter infections in Australia is unknown.

Methods: Patients who commenced chronic haemodialysis via a catheter in the REDUCCTION trial (Dec 2016-Mar 2020) were followed from first catheter insertion to last catheter removal, or end of the trial if a catheter remained. Hospitalizations in all States and Territories (except WA) were probabilistically linked and classified using the principal ICD10-AM diagnostic code. Hospitalizations for vascular access infection (VAI) or bacteraemia, with concurrent HDCRBSI reported at time of admission, were characterized.

Results: 3436 patients commenced chronic haemodialysis via a catheter and were followed for 873,433 days. Baseline characteristics were comparable with the Australian haemodialysis population. 1502 (17.6%; 15,217 bed days) of 8545 multiple-day admissions (65,851 bed days) were due to infection. Hospitalizations for VAI (n=316; 2990 bed days) and bacteraemia (n=309; 4844 bed days) were longer than for pneumonia or cellulitis (all p<0.01), accounted for 42% of infectious admissions, and 51.5% of infectious bed days. Concurrent HDCRBSI at time of hospitalization was reported in 124 admissions, 98 (79%) with primary code for VAI or bacteraemia. The median length of stay was 9 days (IQR 5-14), 16 (16.3%) required intensive care (median 57.5 hours, IQR 30 – 98.5), 9 (9.2%) had metastatic endocarditis, osteomyelitis, or septic arthritis, and 3 patients died in hospital. 27 HDCRBSI occurred more than 2 days into admission. Conclusion: Catheter-related infections are a major source of infectious hospitalization among Australians receiving chronic haemodialysis via a catheter. The burden of HDCRBSI is substantial.
Strengths and Limitations

**Strengths**

- Large study
- Extensive data
- Perspective

**Limitations**

- Not all infections may have been reported
Baseline patient characteristics at time of enrolment to REDUCTION

<table>
<thead>
<tr>
<th></th>
<th>AKI</th>
<th>Start HD</th>
<th>Tf PD</th>
<th>Tf AVF/AVG</th>
<th>Failing Tx</th>
</tr>
</thead>
<tbody>
<tr>
<td># catheters per pt, median (IQR)</td>
<td>1 (1-2)</td>
<td>1 (1-2)</td>
<td>1 (1-2)</td>
<td>1 (1-2)</td>
<td>1 (1-2)</td>
</tr>
<tr>
<td># vas caths per pt, median (IQR)</td>
<td>1 (0-1)</td>
<td>0 (0-0)</td>
<td>0 (0-0)</td>
<td>0 (0-1)</td>
<td>0 (0-0)</td>
</tr>
<tr>
<td>Total catheter days per pt during trial period, median (IQR)</td>
<td>24.75 (12.5 – 72)</td>
<td>175.5 (73.5 – 314.5)</td>
<td>117.5 (42.5 – 289.5)</td>
<td>105.5 (20 – 291.5)</td>
<td>175.5 (117.5 – 266.6)</td>
</tr>
<tr>
<td>Total catheter free days BETWEEN catheters during the trial, mean (sd) [all median and IQR are 0, 0-0]</td>
<td>6.0 (42.2)</td>
<td>16.7 (79.8)</td>
<td>11.9 (63.2)</td>
<td>31.8 (108.4)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Total catheter free days AFTER last catheter removed during the trial, median (IQR)</td>
<td>376.5 (32 – 681.5)</td>
<td>207 (0 – 538)</td>
<td>335 (0 – 623)</td>
<td>189 (0 – 647)</td>
<td>525 (70 – 690)</td>
</tr>
</tbody>
</table>