Dialysis Catheter–Related Bloodstream Infections: A Cluster-Randomized Trial of the ClearGuard HD Antimicrobial Barrier Cap

Jeffrey L. Hymes, MD,[1] Ann Mooney, MSN, RN, CNN,[2] Carly Van Zandt, MS,[2] Laurie Lynch, PhD,[3] Robert Ziebol, BS,[3] and Douglas Killion, MBA[3]

Background: The rate of bloodstream infections (BSIs) is disproportionately high in hemodialysis (HD) patients with central venous catheters (CVCs) versus those with permanent accesses, contributing to poorer outcomes, such as increased rates of death and hospitalizations.

Study Design: 12-month, prospective, cluster-randomized, multicenter, open-label trial.

Setting & Participants: 40 Fresenius Medical Care North America dialysis facilities were matched and paired by positive blood culture rate and number of patients with CVCs and then cluster-randomized with 20 in each study group. 2,470 patients participated in the study (1,245, intervention group; 1,225, control group), accruing approximately 350,000 CVC-days.

Intervention: Use of ClearGuard HD Antimicrobial Barrier Caps versus use of standard CVC caps; assigned at the facility level.

Outcome: Primary end point was positive blood culture rate as an indicator of BSI rate.

Measurements: Positive blood cultures, hospital admissions for BSI, hospitalization-days for BSI, intravenous antibiotic starts, and CVC-days.

Results: Baseline positive blood culture rates were similar ($P = 0.8$) between groups. Use of ClearGuard HD caps for 12 months was associated with a 56% lower BSI rate versus use of standard CVC caps (0.26 vs 0.59/1,000 CVC-days, respectively; $P = 0.01$). When considering sustained use (defined as last 6 months of the study), the intervention versus the control was associated with a 69% lower BSI rate (0.22 vs 0.72/1,000 CVC-days, respectively; $P = 0.01$), 43% fewer hospital admissions for BSI (0.28 vs 0.48/1,000 CVC-days, respectively; $P = 0.04$), and 51% fewer hospitalization days for BSI (2.42 vs 4.94/1,000 CVC-days, respectively; $P = 0.04$). No device-related adverse events were reported.

Limitations: Study was open label; patients occasionally received HD at nonresearch facilities; patients did not receive the intervention when hospitalized.

Conclusions: The findings show that use of ClearGuard HD Antimicrobial Barrier Caps, when compared with standard CVC caps, significantly lowers rates of catheter-related BSIs and hospital admissions for BSI in HD patients using CVCs.

Am J Kidney Dis. 69(2):220-227. © 2016 The Authors. Published by Elsevier Inc. on behalf of the National Kidney Foundation, Inc. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

INDEX WORDS: Hemodialysis; central venous catheter (CVC); chlorhexidine acetate; bloodstream infection (BSI); positive blood culture; infection prevention; end-stage renal disease (ESRD); ClearGuard HD antimicrobial barrier cap; antimicrobial lock; catheter-related bloodstream infection (CRBSI); central line–associated bloodstream infection (CLABSI); cluster-randomized trial.

Significant efforts have been made over the past 25 years to reduce the number of bloodstream infections (BSIs) that are caused by use of hemodialysis (HD) central venous catheters (CVCs) in patients with end-stage renal disease. These efforts include the Centers for Medicare & Medicaid Services Fistula First initiative,[1] Centers for Disease Control and Prevention (CDC) guidelines including Scrub-the-Hub protocol,[2] education and training of health care personnel,[3] and using antimicrobial locks.[3-8] Despite these efforts, the use of CVCs for HD continues to be a leading contributor to higher rates of BSI, hospitalization, morbidity, and mortality, as well as increased health care costs.[9,10]

This study reports results of a novel device, the ClearGuard HD Antimicrobial Barrier Cap (Pursuit Vascular, Inc), hereinafter also referred to as the ClearGuard HD cap, which was recently cleared for market by the US Food and Drug Administration. As shown in Fig 1, it is similar to a standard CVC cap, except the ClearGuard HD cap contains a rod coated with the antimicrobial agent chlorhexidine acetate. The rod extends into the CVC hub and has been shown to reduce the presence of pathogenic organisms in the CVC lock solution proximal to the clamp by >99.99%.[11] Chlorhexidine is a nonantibiotic antimicrobial agent; thus, the risk for developing resistant organisms is minimal compared to the use of antibiotics.[12] In addition, it is effective against antibiotic-resistant organisms.[11] The ClearGuard HD cap is used in the same manner as a standard CVC cap, without a change to procedural workflow.

The following model of the cause of catheter-related BSI is useful for understanding the Clear-Guard HD cap mode of action.[8,13] Pathogenic organisms are present in the environment surrounding the CVC hub. Organisms may be transferred into the hub during use and at the end of the dialysis procedure. The planktonic organisms tend to be flushed into the bloodstream, whereas the sessile organisms tend to remain in the hub. Between dialysis sessions, any organisms in the hub are confined between the CVC cap and clamp within the lock solution, where they can multiply and form a biofilm. The clamp is typically repositioned after each dialysis session, which eventually results in biofilm distal to the clamp. Organisms within the biofilm can then multiply and colonize the entire length of the CVC, enter the bloodstream in increasing quantity, and eventually overwhelm the immune system, causing a BSI.

The ClearGuard HD cap is intended to prevent this intraluminal cascade from occurring by killing the organisms within the lock solution proximal to the clamp, thus preventing the subsequent steps that lead to BSI. The ClearGuard HD cap does not eradicate organisms in a previously colonized CVC and does not address extraluminal sources of BSI.

The aim of the study was to investigate whether use of ClearGuard HD caps in HD patients is associated with improvements in rates of BSIs, hospital admissions for BSI, hospitalization-days for BSI, and intravenous (IV) antibiotic starts as compared with facilities using standard CVC caps.

METHODS

Design

This study was a prospective cluster-randomized comparative-effectiveness trial intended to evaluate the assigned facilities' use of the ClearGuard HD cap. A cluster was defined as a pair of facilities that were matched for prestudy BSI rate and number of patients with CVCs using data obtained from March through August 2014.

Only Fresenius Medical Care North America (FMCNA) facilities not currently participating in another study were eligible to participate. Forty facilities were matched and paired based on positive blood culture rate and number of patients with CVCs, then one of each matched facility pair was randomly assigned using a computer-generated random number to either begin using Clear-Guard HD caps (intervention group) or continue using standard CVC caps (MPC-125 end caps; Molded Products, Inc; control group). Facility staff members were trained on device use via a group webinar.

The study was conducted by Frenova Renal Research, with data collection through FMCNA's electronic records. The study was approved by New England Independent Review Board (IRB# 14-321), which also granted a patient informed consent waiver (TBP reference TB14-032). The informed consent waiver resulted in broad inclusion and ease of conducting the study. All HD patients with a tunneled CVC within each facility were eligible to participate unless they had a known allergy to chlorhexidine. All patients with CVCs in all facilities were treated using the same FMCNA standard best-practice policies and procedure throughout the study.[14] The only difference in intervention was the type of cap used.

Standard policies and procedures require that clean gloves, gown, and full face shield with mask were worn during access procedures. Prior to accessing the CVC, the exit site was routinely inspected, the dressing was changed, and the site was cleaned using 2% chlorhexidine with 70% alcohol swab sticks. The hub threads were wiped for 15 seconds using a 70% sterile alcohol pad any time the blood lines were disconnected. Heparinized saline lock solution was used unless modified by physician order. After each dialysis session, a new pair of ClearGuard HD caps (intervention) or standard CVC caps (control) were placed on the CVC hubs (typically 3 times per week). When clinical indications for BSI were present (eg, fever, chills, and

Figure 1. Attaching ClearGuard HD Caps to a central venous catheter.

hypotension), blood cultures were collected from the CVC and/or peripheral vein.

In order to avoid counting pre-existing BSIs, patients were censored for the first 21 days after entering the study. To avoid double-counting the same BSI, patients were censored using the CDC's National Healthcare Safety Network−recommended 21-day rule[15]: a positive blood culture is counted only if it occurred 21 days or more after a previously reported positive blood culture in the same patient, new positive blood culture events are based on blood cultures drawn as an outpatient or within 1 calendar day after a hospital admission, and following a positive blood culture, hospitalization for BSI, or IV antibiotic start, additional same-type events are not counted for 21 days following the initial event (CVC-days are counted during this period). Patients were censored at CVC removal, death, withdrawal from intervention, or loss to follow-up.

Evaluation Periods

A 1-month preintervention baseline period occurred in November 2014. Subsequently, all facilities participated in the 12-month follow-up from December 1, 2014, through November 30, 2015. Every patient with a CVC who came into a study facility for dialysis received the facility's assigned intervention.

Primary and Secondary End Points

The primary end point was comparison of the overall rate of BSIs (represented by positive blood culture episodes divided by CVC-days) between patients in the intervention group (Clear-Guard HD cap facilities) and the control group (standard CVC cap facilities). Greater than 93% of blood cultures were analyzed by a single central laboratory.

Secondary end points were rates of hospital admissions and hospitalization-days for BSI (Item S1) and IV antibiotic starts.

Statistical Analysis

Because randomization was performed with the facility as the cluster, incidence rate ratios (IRRs) and corresponding 95% confidence intervals (CIs) were calculated using a Poisson regression model with a log link function and the natural logarithm of patient-years at risk for offset and adjusted for the facility cluster effect, where each matched facility pair was considered a cluster. All statistical analyses were performed using SAS, version 9.3 or higher (SAS Institute Inc).

RESULTS

Cohort Population and Trends

Characteristics of the groups at baseline and throughout the follow-up period are summarized in Table 1. Outcomes were analyzed within the subgroups of white and nonwhite participants and were found to be comparable.

All facilities started the study simultaneously on December 1, 2014; existing HD patients with a tunneled CVC (hereafter referred to as patients with CVCs) received the facility's assigned intervention at their first dialysis session after the study start date, and new patients with CVCs coming into the facility were added as appropriate throughout the study. During the study period, there were 2,912 patients with CVCs at all 40 participating facilities. Of these, 2,470 patients with CVCs dialyzed for longer than the 21-day censor period were included in the analysis. A breakdown of patient disposition is shown in Fig 2.

In the 1-month baseline period prior to the start of the study, there were 1,229 patients (618 intervention and 611 control) who accrued approximately 30,000 CVC-days. This was calculated without imposing 21-day censoring at the beginning of the baseline period because the intent was to understand the attributes of the baseline population prior to the start of the study.

During the 12-month follow-up period, the 2,470 patients in the analysis accrued approximately 350,000 CVC-days. Data are shown by quarters in Fig 3. The first quarter is lower than the other quarters due to a greater number of patients censored for the 21-day period as they first entered the study.

All patients who dialyzed for more than 21 days and had a standard tunneled CVC were entered into the study. Additionally, no patients with an

Table 1. Facility and Patient Characteristics at Baseline and Follow-up

Characteristic	Baseline (Nov 2014)			Follow-Up (Dec 2014-Nov 2015)	
	All	Intervention Group	Control Group	Intervention Group	Control Group
No. of facilities	40	20	20	20	20
No. of CVC patients	1,229	618	611	1,245	1,225
Age, y	61.1 ± 15.5	61.5 ± 15.6	60.7 ± 15.3	61.5 ± 15.1	60.6 ± 15.1
Male sex	624 (51)	321 (52)	303 (50)	654 (53)	666 (54)
Race					
White	591 (48)	295 (48)	296 (48)	609 (49)	631 (52)
Black	587 (48)	306 (50)	281 (46)	566 (46)	495 (40)
Other	24 (2)	6 (1)	18 (3)	17 (1)	40 (3)
Missing	27 (2)	11 (2)	16 (3)	53 (4)	59 (5)
Diabetes	722 (59)	363 (59)	359 (59)	705 (57)	698 (57)
Dialysis vintage, y	3.2 ± 4.2	3.0 ± 4.0	3.4 ± 4.3	2.2 ± 3.7	2.6 ± 4.0

Note: Values for categorical variables are given as number (percentage); values for continuous variables, as mean ± standard deviation.

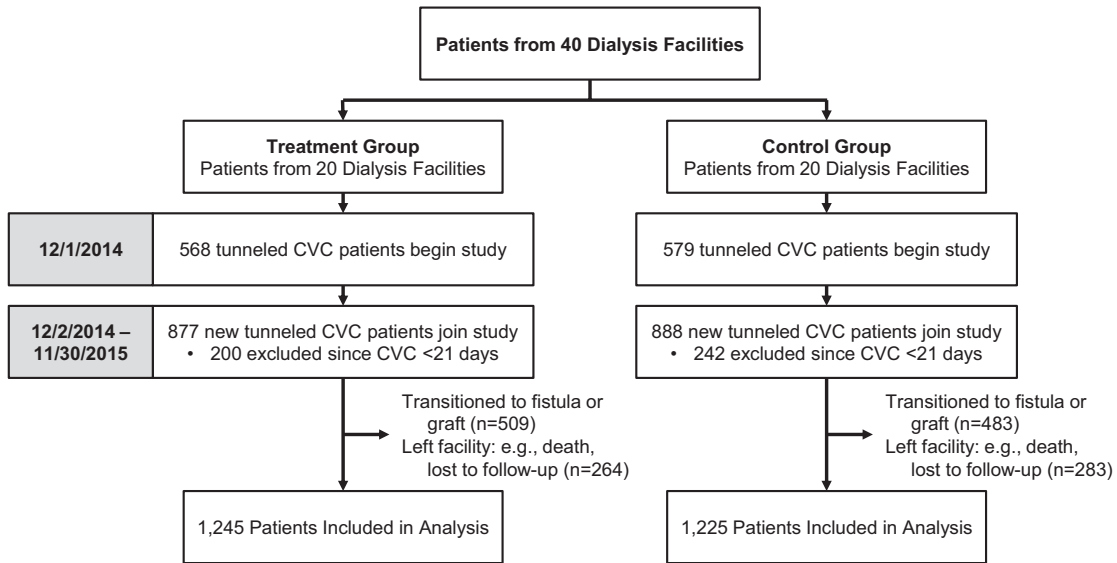Abbreviation: CVC, central venous catheter.

Figure 2. Patient count during follow-up period for the intervention and control groups. Abbreviation: CVC, central venous catheter.

appropriate CVC were excluded from study (ie, no chlorhexidine allergies), and no device-related adverse events were reported. There were no protocol changes during the study.

Primary Outcome: Positive Blood Cultures

During the baseline period, there was no significant difference between the intervention and control groups (0.56 vs 0.60/1,000 CVC-days; $P = 0.8$). During the follow-up period, there were 153 positive blood cultures, with 46 in the intervention group and 107 in the control group. There were 346,946 CVC-days during the follow-up period, with 169,609 CVC-days in the intervention group and 177,337 CVC-days in the control group. The resultant follow-up positive blood culture rate (adjusted for facility cluster effect) was 0.26/1,000 CVC-days in the

intervention group versus 0.59/1,000 CVC-days in the control group (56% less in the intervention group; $P = 0.01$), as shown in Table 2. The positive blood culture IRR of the intervention compared to the control was 0.44 (95% CI, 0.23-0.83).

Quarterly results are shown in Fig 4. The rate of positive blood cultures between groups during the last 6 months of the study (Fig 5) indicated a significant difference: 0.22/1,000 CVC-days in the intervention group versus 0.72/1,000 CVC-days in the control group (69% less in the intervention group; $P = 0.01$).

In addition, subgroup analysis of de novo CVCs, defined as patients who entered the study with a new CVC, demonstrated a significantly lower positive blood culture rate: 0.16/1,000 CVC-days in the intervention group versus 0.50/1,000 CVC-days in
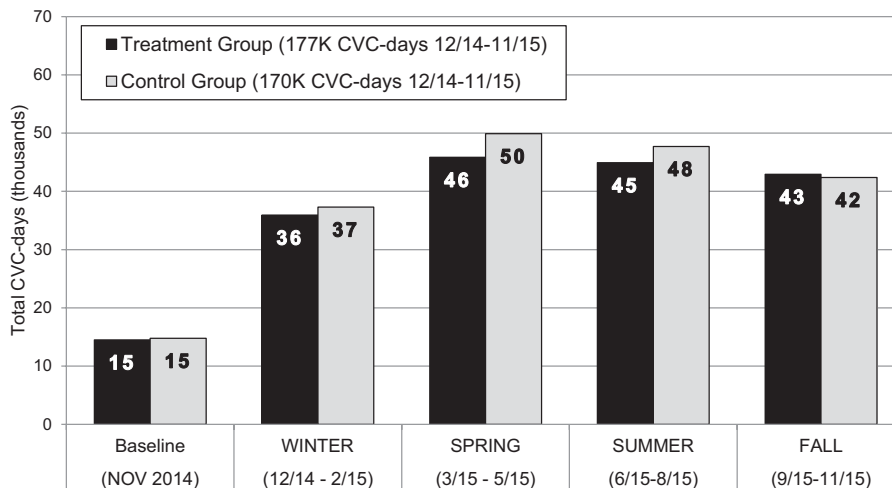

Figure 3. Central venous catheter (CVC)-days each period for the intervention and control groups.

Table 2. Twelve-Month Comparison of Rates for Bloodstream Infections, Cause-Specific Hospitalizations, and IV Antibiotics

	Episodes/1,000 CVC-Days		Poisson Regression	
	Intervention Group	Control Group	IRR (95% CI)	*P*
Primary end point: positive blood culture episodes	0.26	0.59	0.44 (0.23-0.83)	0.01
Secondary end points				
No. of hospital admissions for BSI	0.28	0.47	0.60 (0.37-0.97)	0.04
No. of hospitalization-days for BSI	3.24	4.68	0.69 (0.41-1.16)	0.2
No. of IV antibiotic starts	1.68	1.78	0.94 (0.74-1.19)	0.6

Abbreviations: BSI, bloodstream infection; CI, confidence interval; IRR, incidence rate ratio; IV, intravenous.

the control group (68% less in the intervention group; $P = 0.02$; n = 678 patients).

Secondary Outcomes

Hospital Admissions for BSI

During the baseline period, there was no significant difference between the intervention and control groups ($P = 0.6$) for hospital admissions for BSI. During the follow-up period, the rate of hospital admissions for BSI between groups (Table 2) demonstrated a significant improvement: 0.28/1,000 CVC-days in the intervention group versus 0.47/ 1,000 CVC-days in the control group (40% less in intervention group; $P = 0.04$).

Comparing rates between groups during the last 6 months of the study (Fig 5) indicated a significant difference: 0.28/1,000 CVC-days in the intervention group versus 0.48/1,000 CVC-days in the control group (43% less in intervention group; $P = 0.04$).

Hospitalization-Days for BSI

During the baseline period, there was no significant difference between the intervention and control groups ($P = 0.7$) for hospitalization-days for BSI. During the follow-up period, there were nominally fewer hospitalization-days in the intervention group (3.24/1,000 CVC-days) compared to the control

group (4.68/1,000 CVC-days), but the difference was not statistically significant (31% less in the intervention group; $P = 0.2$; Table 2).

Comparing the rates between groups during the last 6 months of the study (Fig 5) indicated a significant difference: 2.42/1,000 CVC-days in the intervention group versus 4.94/1,000 CVC-days in the control group (51% less in intervention group; $P = 0.04$).

IV Antibiotic Starts

During the baseline period, there was no significant difference between the intervention and control groups ($P = 0.4$) for new IV antibiotic starts. During the follow-up period, there were nominally fewer IV antibiotic starts in the intervention group (1.68/1,000 CVC-days) compared to the control group (1.78/ 1,000 CVC-days), but the difference was not statistically significant (6% less in intervention group; $P = 0.6$; Table 2).

DISCUSSION

This prospective cluster-randomized comparative-effectiveness study demonstrated that use of Clear-Guard HD caps for 12 months was associated with a 56% lower BSI rate versus use of standard CVC caps. We also observed a 69% lower rate of BSI ($P = 0.01$), 43% fewer hospital admissions for BSI
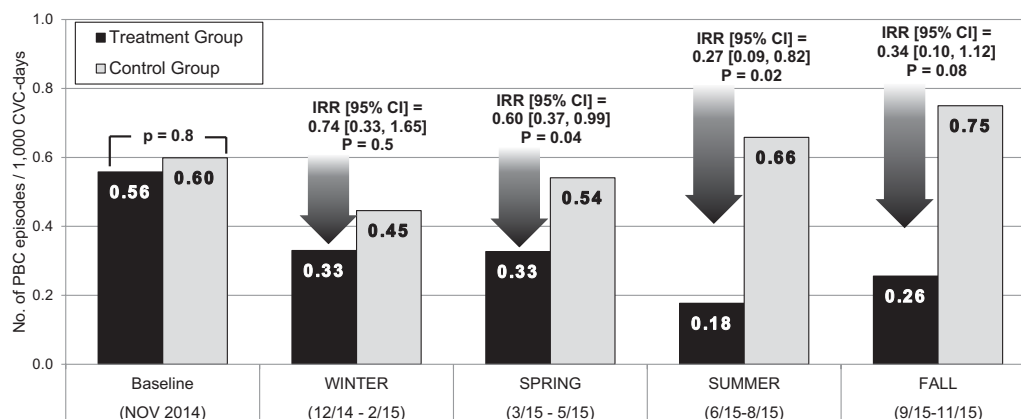

Figure 4. Baseline and quarterly follow-up comparison of positive blood culture (PBC) rates for the intervention and control groups. Abbreviations: CI, confidence interval; CVC, central venous catheter; IRR, incidence rate ratio.
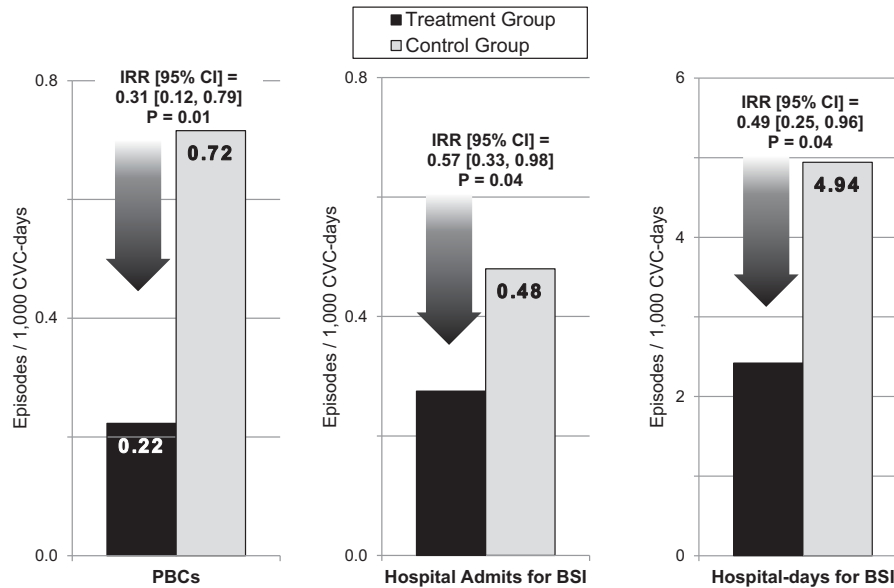
Figure 5. Comparison of sustained rates (last 6 months) for positive blood cultures (PBCs), hospital admissions for bloodstream infection (BSI), and hospitalization-days for BSI for the intervention and control groups. Abbreviations: CI, confidence interval; CVC, central venous catheter; IRR, incidence rate ratio.

($P = 0.04$) and 51% fewer hospitalization-days for BSI ($P = 0.04$) associated with facilities with sustained use of the ClearGuard HD cap versus facilities with sustained use of standard CVC caps, where sustained use was defined as the last 6 months of the study.

The baseline BSI rate at facilities participating in this study was better than the national average (0.58/1,000 vs 0.71/1,000 CVC-days). In addition, the BSI rate during the 12-month follow-up period at the control facilities (0.59/1,000 CVC-days; Table 2) was also better than the national average. Therefore, results of this study are representative of what would be expected in better-than-average facilities. The national average BSI rate is from the 2014 national aggregate National Healthcare Safety Network Dialysis Event Surveillance data for "any CVC" of 0.71/1,000 CVC-days.[16] This national rate represents the aggregate pooled mean values from more than 6,000 outpatient HD facilities throughout the United States. It may be noted that the BSI rate in the control facilities increased during the follow-up period (Fig 4). Because the study started in the winter, one possible explanation for the control arm's increasing positive blood culture rate over time is the seasonal trend for the "summer bloom" of bacteremias during the warmer months.[14]

This study accepted all patients regardless of CVC vintage; thus, many CVCs were likely precolonized with organisms at the beginning of the study.[17] Because the mode of action of the ClearGuard HD cap is to prevent colonization and not eradicate organisms in a previously colonized CVC, it was anticipated that the ClearGuard HD cap might be less effective with CVCs that had previously used standard CVC caps. Based on the mode of action, efficacy was expected to improve over time as old CVCs are replaced with new CVCs. Therefore, an analysis was performed in quarterly increments, as shown in Fig 4. Consistent with the mode of action, there was a lower positive blood culture rate in the intervention versus control group during the first quarter, which improved further during the second quarter and was greatest during the third and fourth quarters. During the last 6 months of the study, the positive blood culture decrease had reached a sustained level (IRR, 0.31 for the intervention vs control group; $P = 0.01$).

The mode of action also predicts that the device will be most effective on new CVCs that are only capped using the ClearGuard HD cap (de novo CVCs). Results in the de novo CVC subgroup were comparable to results during the last 6 months of the study (IRR, 0.32 for the intervention vs control group; $P = 0.02$). These results provide the best indication of expected sustained performance if ClearGuard HD caps were fully implemented as standard of care across all dialysis centers.

Use of ClearGuard HD caps resulted in 6% fewer IV antibiotic starts in the intervention group versus the control group, but the difference was not statistically significant. The reason for the smaller than expected decrease is not fully understood, but it is known that IV antibiotics are often administered when a BSI is suspected but might not be present. In addition, IV antibiotics are administered for other types of infections, which are often present in this

population. Finally, in the baseline period prior to the study, the intervention group had a 25% higher rate of new IV antibiotic starts versus the control group (3.32 vs 2.66/1,000 CVC-days, respectively; $P = 0.4$).

In addition to the important patient-related benefits resulting from reduced BSIs and hospitalizations, the resulting economic savings for providers and payers are substantial. Reducing catheter-related BSIs may save dialysis providers $2,400 per BSI episode[18] and save Medicare $16,000 per BSI episode,[19] primarily due to reducing missed interventions, medication use, and hospitalization costs. This equates to a combined per-member-per-month cost savings of $274 based on the national average BSI rate (0.71/1,000 CVC-days) and sustained use of the ClearGuard HD cap (IRR, 0.31). If extended to all HD patients with CVCs in the United States,[20] the estimated combined savings are conservatively $300 million annually.

This study has many strengths. It was prospective and randomized and used best-practice methods for infection prevention in the control arm. All facilities followed standard clinical policies and procedures throughout the study, except for using the ClearGuard HD cap at intervention group facilities; therefore, results are representative of use in current clinical practice. Also, it was of 12 months' duration, so seasonal variations and sustainability were assessed. In addition, it was larger than any reported antimicrobial lock meta-analysis study to date.[4,5,21,22]

The study also has limitations. It was open label, and intervention patients occasionally received dialysis at nonparticipating facilities, which likely diminished the effectiveness of the intervention. Not all positive blood culture measurements were captured, such as during hospitalization; therefore, BSI rates are under-reported. In addition, diagnosis-specific hospitalizations are not always accurately coded and were likely underestimated due to barriers preventing complete access to hospital discharge records[23,24]; however, there was no indication that potential biases were unbalanced between groups. In consideration of these issues, the study is likely generalizable to other dialysis facilities with similar patient populations and intervention practices.

In summary, our findings show that the ClearGuard HD cap, when compared to a standard CVC cap, significantly lowers rates of catheter-related BSI and hospital admissions for BSI, representing an important breakthrough for HD patient care in the United States.

ACKNOWLEDGEMENTS

SUPPLEMENTARY MATERIAL

Item S1: Codes for hospital admission.

Note: The supplementary material accompanying this article (http://dx.doi.org/10.1053/j.ajkd.2016.09.014) is available at www.ajkd.org

REFERENCES

1. Centers for Medicare & Medicaid Services. The Fistula First breakthrough initiative. http://www.fistulafirst.org. Accessed May 25, 2016.

2. Centers for Disease Control and Prevention. Hemodialysis central venous catheter Scrub-the-Hub protocol. www.cdc.gov/dialysis/PDFs/collaborative/Hemodialysis-Central-Venous-Catheter-STH-Protocol.pdf. Accessed May 25, 2016.

3. 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.

4. Maki DG, Ash S, Winger RK, Lavin P. A novel antimicrobial and antithrombotic lock solution for hemodialysis catheters: a multi-center, controlled, randomized trial. *Crit Care Med.* 2011;39(4):613-620.

5. 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.* 2008;51(2):233-241.

6. Böhlke M, Uliano G, Barcellos FC. Hemodialysis catheter-related infection: prophylaxis, diagnosis and treatment. *J Vasc Access.* 2015;16(5):347-355.

7. Liu J, Wang C, Zhao H, et al. Anticoagulant therapies versus heparin for the prevention of hemodialysis catheter-related complications: systematic review and meta-analysis of prospective randomized controlled trials. *Int J Clin Exp Med.* 2015;8(8):11985-11995.

8. Soi V, Moore CL, Kumbar L, Yee J. Prevention of catheter-related bloodstream infections in patients on hemodialysis: challenges and management strategies. *Int J Nephrol Renovasc Dis.* 2016;9:95-103.

9. Ravani P, Palmer SC, Oliver MJ, et al. Associations between hemodialysis access type and clinical outcomes: a systematic review. *J Am Soc Nephrol.* 2013;24:465-473.

10. Malas MB, Canner JK, Hicks CW, et al. Trends in incident hemodialysis access and mortality. *JAMA Surg.* 2015;150(5):441-448.

11. K131060 ClearGuard HD Hemodialysis Catheter Luer End Cap. www.accessdata.fda.gov/cdrh_docs/pdf13/k131060.pdf. Accessed August 4, 2016.

12. Horner C, Mawer D, Wilcox M. Reduced susceptibility to chlorhexidine in staphylococci: is it increasing and does it matter? *J Antimicrob Chemother*. 2012;67(11):2547-2559.

13. Mermel LA. What is the evidence for intraluminal colonization of hemodialysis catheters? *Kidney Int*. 2014;86(1):28-33.

14. Rosenblum A, Wang W, Ball LK, et al. Hemodialysis catheter care strategies: a cluster-randomized quality improvement initiative. *Am J Kidney Dis*. 2014;63(2):259-267.

15. Centers for Disease Control and Prevention. National Healthcare Safety Network. http://www.cdc.gov/nhsn. Accessed May 25, 2016.

16. CDC. Guide to the NHSN dialysis event surveillance bloodstream infection (BSI) standardized infection ratio (SIR) measure, August 2015. http://www.cdc.gov/nhsn/pdfs/dialysis/understanding-the-de-bsi-sir.pdf. Accessed May 30, 2016.

17. Raad I, Costerton W, Sabharwal U, et al. Ultrastructural analysis of indwelling vascular catheters: a quantitative relationship between luminal colonization and duration of placement. *J Infect Dis*. 1993;168(2):400-407.

18. Brunelli SM, Turenne W, Sibbel S, et al. Economic burden to dialysis providers of central venous catheter-related blood stream infections and occlusions among incident hemodialysis patients. Poster. http://www.davitaclinicalresearch.com/publication/economic-burden-dialysis-providers-central-venous-catheter-related-blood-stream-infection-occlusions-among-incident-hemodialysis-patients/. Accessed September 28, 2016.

19. Sibbel S, Brunelli SM, Hunt A, et al. Economic burden to Medicare of central venous catheter-related blood stream infections and occlusions among hemodialysis patients. Poster. http://www.davitaclinicalresearch.com/publication/economic-burden-medicare-central-venous-catheter-related-blood-stream-infections-occlusions-among-hemodialysis-patients/. Accessed September 28, 2016.

20. Saran R, Li Y, Robinson B, et al. US Renal Data System 2015 Annual Data Report: epidemiology of kidney disease in the United States. *Am J Kidney Dis*. 2016;67(3)(suppl 1):S1-S434.

21. Yahav D, Rozen-Zvi B, Gafter-Gvili A, et al. Antimicrobial lock solutions for the prevention of infections associated with intravascular catheters in patients undergoing hemodialysis: systematic review and meta-analysis of randomized, controlled trials. *Clin Infect Dis*. 2008;47(1):83-93.

22. Labriola L, Crott R, Jadoul M. Preventing haemodialysis catheter-related bacteremia with an antimicrobial lock: a meta-analysis of prospective randomized trials. *Nephrol Dial Transplant*. 2008;23(5):1666-1672.

23. Krishnan M, Wilfehrt HM, Lacson E Jr. In data we trust: the role and utility of dialysis provider databases in the policy process. *Clin J Am Soc Nephrol*. 2012;7(11):1891-1896.

24. Reilly JB, Marcotte LM, Berns JS, Shea JA. Handoff communication between hospital and outpatient dialysis units at patient discharge: a qualitative study. *Jt Comm J Qual Patient Saf*. 2013;39(2):70-76.