# The Hydrocephalus Clinical Research Network quality improvement initiative: the role of antibiotic-impregnated catheters and vancomycin wound irrigation

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**OBJECTIVE** Two previous Hydrocephalus Clinical Research Network (HCRN) studies have demonstrated that compliance with a standardized CSF shunt infection protocol reduces shunt infections. In this third iteration, a simplified protocol consisting of 5 steps was implemented. This analysis provides an updated evaluation of protocol compliance and evaluates modifiable shunt infection risk factors.

**METHODS** The new simplified protocol was implemented at HCRN centers on November 1, 2016, for all shunt procedures, excluding external ventricular drains, ventricular reservoirs, and subgaleal shunts. Procedures performed through December 31, 2019, were included (38 months). Compliance with the protocol, use of antibiotic-impregnated catheters (AICs), and other variables of interest were collected at the index operation. Outcome events for a minimum of 6 months postoperatively were recorded. The definition of infection was unchanged from the authors' previous report.

**RESULTS** A total of 4913 procedures were performed at 13 HCRN centers. The overall infection rate was 5.1%. Surgeons were compliant with all 5 steps of the protocol in 79.4% of procedures. The infection rate for the protocol alone was 8.1% and dropped to 4.9% when AICs were added. Multivariate analysis identified having  $\geq$  2 complex chronic conditions (odds ratio [OR] 1.76, 95% confidence interval [CI] 1.26–2.44, p = 0.01) and a history of prior shunt surgery within 12 weeks (OR 1.84, 95% CI 1.37–2.47, p < 0.01) as independent risk factors for shunt infection. The use of AICs

ABBREVIATIONS AIC = antibiotic-impregnated catheter; CCC = complex chronic condition; EVD = external ventricular drain; HCRN = Hydrocephalus Clinical Research Network; IV = intravenous; QI = quality improvement. SUBMITTED January 12, 2022. ACCEPTED February 2, 2022.

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(OR 0.70, 95% CI 0.50–0.97, p = 0.05) and vancomycin irrigation (OR 0.36, 95% CI 0.21–0.62, p < 0.01) were identified as independent factors protective against shunt infection.

**CONCLUSIONS** The authors report the third iteration of their quality improvement protocol to reduce the risk of shunt infection. Compliance with the protocol was high. These updated data suggest that the incorporation of AICs is an important, modifiable infection prevention measure. Vancomycin irrigation was also identified as a protective factor but requires further study to better understand its role in preventing shunt infection.

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KEYWORDS cerebrospinal fluid; shunt infection; quality improvement; protocol; hydrocephalus; pediatric

EDIATRIC CSF shunt infection remains a common complication and carries significant patient morbidity. Additionally, treatment for shunt infections is costly, with estimates as high as \$50,000 per occurrence.1 The Hydrocephalus Clinical Research Network (HCRN) has adopted quality improvement (QI) initiatives and implemented standardized surgical protocols to reduce shunt infection. We first reported our 11-step protocol in 2011 (protocol 1; Fig. 1) and successfully reduced network-wide shunt infection from 8.8% to 5.7%.<sup>2</sup> Our second report simplified the protocol to 5 core steps plus antibiotic-impregnated catheters (AICs) and postoperative antibiotics (protocol 2; Fig. 1). That protocol resulted in a similar infection rate as the original protocol.<sup>3</sup> In this third iteration of the process, we chose to further simplify the protocol, using only the 5 core steps. Other interventions that were intended to reduce infection (including AICs) were recorded but not required. The purpose of the current analysis is to assess the impact of this simplified protocol on shunt infection rates and to identify other potentially modifiable risk factors for shunt infection.

# Methods

# HCRN

The HCRN is a collaborative group of 14 pediatric neurosurgical centers and 22 investigators conducting clinical research in pediatric hydrocephalus. Thirteen centers contributed data to this study. From its inception, the HCRN has used QI methodology in an effort to reduce shunt infection. Data collection at each site was approved by the local IRB. Data analysis was approved by the University of Utah IRB.

## **Five-Step Protocol**

The 5-step protocol (protocol 3; Fig. 1) was implemented at the HCRN centers from November 1, 2016, through December 31, 2019. The 5 core steps of protocol 3 included intravenous (IV) antibiotic administration before incision, use of chlorhexidine as final preparation, hand scrub by all participants, double gloves by all participants, and application of an iodine-impregnated incision drape (Ioban, 3M) to the surgical field. Patients were monitored for at least 6 months after shunt insertion or revision. During this follow-up, any surgical and/or infectious events were recorded.

# **Study Sample**

The entry and outcome criteria for the study were identical to those used previously.<sup>3</sup> All children  $\leq$  18 years of age who underwent shunt insertion or revision operation at each HCRN center were entered into the study. Operations for ventriculoperitoneal, ventriculoatrial, ventriculopleural, arachnoid cyst, and subdural-peritoneal shunts were included. If a patient first presented with a shunt infection, they were entered into the study cohort at the time of shunt replacement after treatment of their infection. Children who were undergoing external ventricular drain (EVD), Ommaya reservoir, ventricular access device, or subgaleal shunt placement were not eligible for inclusion at the time of those procedures, but these children were eligible if they subsequently underwent a shunt procedure listed above.

## **Primary Endpoint**

Each patient included in the study was evaluated for infection during routine clinical follow-up or if they visited the emergency room or were admitted to the hospital. Evaluation was performed according to the surgeons' usual clinical practice. As in our previous study,<sup>3</sup> the primary endpoint for the study was shunt infection. An identical definition for infection was used: 1) identification of organisms on culture or Gram stain from CSF, wound swab, or pseudocyst fluid; 2) shunt erosion, defined as wound breakdown with visible shunt hardware; 3) abdominal pseudocyst, even in the absence of positive cultures; or 4) positive blood cultures in a child with a ventriculoatrial shunt.<sup>3</sup>

## **Shunt Procedures**

The shunt procedures were classified based on timing and presence of infection. The four classifications were 1) shunt insertion in a child who had not had one previously (insertion); 2) shunt revision in which a child entered the operating room with all previously implanted shunt equipment and left with all shunt equipment implanted (i.e., they had no externalized components or drains before or after surgery; revision); 3) shunt insertion after external ventricular drainage (not infected); and 4) shunt insertion after infection treatment. All repeat procedures were recorded regardless of type.

## **Protocol Compliance**

Protocol compliance with all steps was assessed in a prospective manner by HCRN coordinators and the surgeons, fellows, and residents. Several surgeon-specific nonprotocol steps that might reduce infection were also recorded if performed. These steps included AICs, preoperative bathing/shampoo (with or without chlorhexidine products), chlorhexidine body wipes, skin preparation,

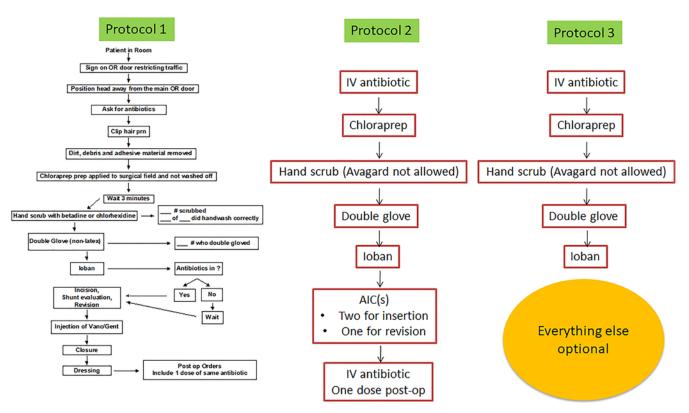


FIG. 1. HCRN shunt surgery protocols. The results associated with protocols 1 and 2 were described previously.<sup>2.3</sup> Gent = gentamycin; OR = operating room; prn = as needed; Vanc = vancomycin. Figure is available in color online only.

intraoperative guidance (stereotaxis, ultrasound, endoscopy), changing the outer gloves after draping, using a "notouch" technique in which the shunt equipment is only handled with surgical instruments, injection of antibiotics into the shunt, irrigating wounds before closure with bacitracin solution, and leaving bacitracin powder in the wounds. In addition, an open text field was used to collect "other steps intended to reduce infection."

## **Complex Chronic Conditions**

The following patient complex chronic conditions (CCCs) were recorded: neuromuscular (brain and spinal cord malformations, mental retardation, CNS degeneration and disease, infantile cerebral palsy, muscular dystrophies and myopathies), cardiovascular (heart and great vessel malformations, cardiomyopathies, conduction disorders, dysrhythmias), respiratory (respiratory malformations, chronic respiratory disease, cystic fibrosis), renal (congenital anomalies, chronic renal failure), gastrointestinal (congenital anomalies, chronic liver disease and cirrhosis, inflammatory bowel disease), hematological or immunological (sickle cell disease, hereditary anemias or immunodeficiency, acquired immunodeficiency), metabolic (amino acid, carbohydrate, or lipid metabolism; storage disorders; other metabolic disorders), other congenital or genetic defect (chromosomal, bone and joint, diaphragm and abdominal wall, or other congenital anomalies), and malignancy (malignant neoplasms).4 Data were entered in the HCRN Registry using OpenClinica, a clinical trials management software. A "compliant" procedure was one in which all 5 protocol steps were performed.

At the time of data analysis, we identified one site and one surgeon at another site who consistently used a vancomycin solution as irrigation during the surgery or left it in the wound at the end of surgery. These participants had very low infection rates. We therefore contacted the HCRN principal investigator at each site to ask about the use of vancomycin irrigation at their site. Their responses were added to the data set for analysis.

#### **Statistical Analysis**

Infection rates were summarized with frequencies and proportions by shunt procedure type and by center. Protocol and nonprotocol infection risk factors were summarized by infection rate for compliant and noncompliant procedures. Univariate analysis of infection risk factors was conducted with Pearson chi-square tests. Risk factors showing an association of p < 0.2 in univariate analysis were entered into a logistic regression model that adjusted for within-patient correlation (patients often have multiple procedures) using generalized estimating equations. Two multivariate logistic regression models were constructed via backward stepwise selection using all potentially significant variables associated with shunt infection. In one model, the compliance category was simplified into a binary variable based on whether all 5 protocol steps were completed or not and was forced into the model. In a second model, the 5 protocol steps were considered individu-

TABLE 1. Procedure-specific infection rates

Shunt Procedure Type	No. of Procedures	No. of Infections (%)
Insertion	1442	63 (4.4)
Revision	2844	145 (5.1)
Insertion after EVD (not infection)	195	16 (8.2)
Insertion after infection	432	28 (6.5)
Total	4913	252 (5.1)

ally for inclusion using a criterion of statistical significance ( $p \le 0.05$  in the multivariable model). Statistical analysis was performed using SAS (version 9.4, SAS Institute).

# Results

A total of 4913 shunt procedures were completed at 13 HCRN centers from November 1, 2016, through December 31, 2019. The most common procedure type was shunt revision (n = 2844, 57.9%), followed by shunt insertion (n = 1442, 29.4%), shunt insertion after infection (n = 432, 8.8%), and shunt insertion after EVD (n = 195, 4.0%; Table 1). The overall infection rate was 5.1% (n = 252), and there was no difference in infection rate among procedure types (p = 0.07). HCRN site-specific infection rates ranged from 2.2% to 9.3% (p ≤ 0.01; Table 2).

Surgical teams were compliant with all 5 steps of the protocol in 79.4% of procedures (Table 3). Compliance with individual protocol steps was variable. The use of chlorhexidine as final preparation had the lowest compliance rate (83.3%), while Ioban application and surgical scrubbing had the highest (98.8%). Additional nonprotocol factors were also recorded (Table 3). AICs were used in 81.3% of cases and were associated with an infection rate of 4.9%, compared with 6.3% when AICs were not used (p = 0.08). The use of vancomycin irrigation of wounds had a statistically significant effect on infection rate (2.2%)compliant vs 5.7% noncompliant, p < 0.01), but it was only used in 15.7% of cases. Conversely, bacitracin irrigation of wounds had a significant and paradoxical increase in infection rate (5.4% compliant vs 3.0% noncompliant, p = 0.01). A similar negative effect was seen when vancomycin and gentamicin were injected into the shunt (7.1%) compliant vs 4.9% noncompliant, p = 0.04).

Univariate analysis of additional risk factors is shown in Table 4. Compliance category, number of CCCs, and prior shunt surgery were found to be statistically significant. Within compliance category, completion of the 5 steps alone yielded an infection rate of 8.1%. The addition of vancomycin and gentamicin did not significantly change the infection rate (7.8%). The infection rate of 5 steps with the addition of AICs was 4.9%, a relative risk reduction of approximately 40% when compared with the 5 steps alone. The lowest infection rate was observed when the 5 steps were used in combination with AICs and vancomycin wound irrigation (2.0%).

A multivariate logistic regression model was constructed using all potentially significant variables associated with shunt infection (Table 5). The compliance category was simplified into a binary variable based on whether all

	1	
Center No.	Case Volume (n)	Infection Rate (%)
1	86	9.3
2	279	3.6
3	315	3.8
4	455	6.6
5	465	7.1
6	308	7.8
7	330	5.8
8	608	4.3
9	116	5.2
10	281	6.4
11	652	4.3
12	561	5.0
13	457	2.2
Overall	4913	5.1

TABLE 2. Center-specific case volume and infection rates

5 protocol steps were completed or not. Significant risk factors that were independently associated with shunt infection included having  $\geq 2$  CCCs (odds ratio [OR] 1.76, 95% confidence interval [CI] 1.26–2.44, p = 0.01) and history of prior shunt surgery < 12 weeks (OR 1.84, 95% CI 1.37–2.47, p < 0.01). Significant risk factors that were protective against shunt infection were use of AICs (OR 0.70, 95% CI 0.50–0.97, p = 0.05) and use of vancomycin irrigation (OR 0.36, 95% CI 0.21–0.62, p < 0.01). A second model (Table 6) included the same variables, but the 5 protocol steps were considered individually. In this model, none of the individual steps met the criterion for statistical significance (p < 0.05). The same risk factors were identified in both models (Tables 5 and 6).

# Discussion

The implementation of standardized protocols for infection prevention has become increasingly popular among pediatric neurosurgeons. Adherence to a standardized preoperative preparation protocol reduced surgical site infection risk by 79% for all pediatric neurosurgical procedures at a tertiary care institution.<sup>5</sup> Desai et al.<sup>6</sup> reported a 50% relative risk reduction in pediatric baclofen pump infections after an infection prevention surgical checklist was implemented. Similarly, Tipper et al. noted a significant reduction in pediatric scoliosis surgery infection rates (from 8.6% to 2.2%) when a standardized perioperative protocol was used.<sup>7</sup>

This report further reinforces the HCRN's previous findings that compliance with a standardized protocol reduces shunt infection rate.<sup>2,3</sup> Since our last article, the HCRN has expanded from 8 centers to 14 centers, and the total number of procedures has increased more than two-fold compared with the previous study. The overall protocol compliance was similar to that previously reported (79.4% vs 77.0%), and we observed a similar infection rate (5.1% vs 6.0%). Furthermore, the standardization of our shunt infection protocol over multiple HCRN centers enabled us to identify other independently associated risk

TABLE 3. Protocol and nonprotocol factor compliance	TABLE 3.	Protocol	and	nonprotocol	factor	compliance
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	Compliance	Infection Rate (%)		
Factor	Rate (%)	Compliant	Noncompliant	p Value
Protocol factors				
IV antibiotics requested before incision	97.8	5.1	4.7	0.83
Chlorhexidine as final prep	83.3	5.4	3.8	0.06
All team members performed formal surgical scrub (no antiseptic cream)	98.8	5.1	3.5	0.58
All team members wore double gloves	98.5	5.1	4.2	0.71
loban applied	98.8	5.2	1.7	0.23
All 5 steps completed	79.4	5.4	4.0	0.06
Additional nonprotocol factors				
AIC	81.3	4.9	6.3	0.08
Vancomycin & gentamicin injected into shunt	10.0	7.1	4.9	0.04
Outer gloves changed after draping	87.4	5.0	6.1	0.26
No touch technique	30.1	5.9	4.9	0.15
Bacitracin irrigation of wounds	87.1	5.4	3.0	0.01
Vancomycin irrigation of wounds	15.7	2.2	5.7	<0.01

factors for shunt infection: greater number of CCCs, prior shunt surgery within 12 weeks, use of AICs, and use of vancomycin irrigation. From a QI standpoint, the use of AICs and vancomycin irrigation represent two modifiable risk factors.

Although the data in Table 3 for "chlorhexidine as final prep" and "all 5 steps completed" seem to suggest an increased infection risk, these are univariate comparisons. When evaluated in the multivariable regressions (Tables 5 and 6), none of the 5 steps, individually or as a group, impacted the infection risk. This does not mean that the 5 steps are irrelevant. Compliance with these steps was high (79.4%). In fact, of the noncompliant cases, 90% completed 4 of 5 steps, and in 92% of the 4-step cases, the one missing component was antibiotic compliance. That may mean a different antibiotic or dose, but we believe it is unlikely that no prophylactic antibiotics would have been used in those cases. We therefore believe that any benefit of AICs and vancomycin irrigation is seen when they are used in addition to the 5 protocol steps.

#### AICs

Several systematic reviews and meta-analyses have indicated that AICs can reduce shunt infection as well as provide a cost savings advantage, but the primary studies have been limited to lower-quality levels of evidence.<sup>8-10</sup> Recently, the British Antibiotic and Silver Impregnated Catheters for Ventriculoperitoneal Shunts (BASICS) trial, a multicenter, single-blind randomized controlled trial conducted in the United Kingdom and Ireland, provided high-quality evidence in support of AICs.<sup>11</sup> The investigators sought to determine the clinical efficacy and costeffectiveness of antibiotic- and silver-impregnated catheters at reducing shunt infection. A total of 1605 patients with hydrocephalus (both adult and pediatric) undergoing first-time shunt insertion were randomized to receive a standard shunt catheter, an AIC, or a silver-impregnated catheter. Their primary endpoint was time to shunt failure due to infection. Patients who received AICs had a significantly lower rate of infection compared with both standard and silver-impregnated catheters (2% for AICs vs 6% for both standard and silver-impregnated shunts). Furthermore, the authors expected a cost savings of £135,753 per shunt infection prevented with AICs, despite an inherently higher upfront equipment cost. The authors recommended that AICs should be used for all patients undergoing firsttime ventriculoperitoneal shunt insertions.

Our current data and the results of our multivariate analysis support a protective effect of AICs against shunt infection. Since our last report, the use of AICs has become increasingly popular among HCRN surgeons, and they were used in more than 80% of our procedures. In practice, we observed a 40% relative risk reduction in infection when AICs were used in conjunction with our shunt infection protocol. The injection of antibiotics into the shunt reservoir did not convey additional benefit toward infection rate when compared with the shunt infection protocol alone. The comparison between AICs and antibiotic injection could not be made in our last study, but our current data demonstrate an advantage of AICs against shunt infection. Interestingly, when both AIC and antibiotic injection were used, a paradoxical increase in infection rate was observed. Our current study was not designed to address the underlying reason for these findings, which may be subject to future investigations. Overall, our data strongly favor the use of AICs for CSF shunts. We recommend AICs be used for all pediatric shunt procedures. This step has now been included in the HCRN shunt infection protocol.

#### Vancomycin Irrigation

There is clinical equipoise regarding the use of intraoperative antibiotic wound irrigation, with significant heterogeneity in the literature about its use as an anti-infec-

TABLE 4. Univariate analysis of additional risk factors

Risk Factor	No. of Procedures	No. of Infections (%)	p Value
Compliance category		(,)	<0.01
5 steps alone	443	36 (8.1)	<b>VU.UT</b>
5 steps + vancomycin	218	17 (7.8)	
& gentamicin	210	17 (7.0)	
5 steps + AIC	2760	136 (4.9)	
5 steps + vancomycin,	185	17 (9.2)	
gentamicin, & AIC		(0.1_)	
5 steps + AIC & vancomycin	297	6 (2.0)	
irrigation			
Other combination	1010	40 (4.0)	
CCCs			<0.01
0	2693	117 (4.3)	
1	1505	78 (5.2)	
≥2	715	57 (8.0)	
Corrected age at time of procedure			0.66
<0 wks	352	19 (5.4)	
0 to <4 wks	11	0 (0.0)	
4 to <26 wks	39	4 (10.3)	
26 to <52 wks	38	2 (5.3)	
52 to <104 wks	63	2 (3.2)	
≥104 wks	4377	224 (5.1)	
Unknown	33	1 (3.0)	
Cause of hydrocephalus			0.98
Post-infectious	186	10 (5.4)	
Post-IVH secondary to	1365	76 (5.6)	
prematurity			
Myelomeningocele	682	29 (4.3)	
Aqueductal stenosis	300	15 (5.0)	
Spontaneous ICH/IVH/SAH	161	9 (5.6)	
Posterior fossa tumor	267	12 (4.5)	
Supratentorial tumor	286	15 (5.2)	
Midbrain tumor or other midbrain lesion	93	4 (4.3)	
Post-head injury	148	7 (4.7)	
Encephalocele	57	3 (5.3)	
Posterior fossa cyst, including Dandy-Walker	171	13 (7.6)	
Other intracranial cyst (e.g., arachnoid cyst)	137	6 (4.4)	
Communicating congenital hydrocephalus	207	12 (5.8)	
Other congenital (e.g., schizencephaly)	126	7 (5.6)	
Craniosynostosis	47	4 (8.5)	
Other cause	255	13 (5.1)	
Unknown cause	46	1 (2.2)	
Unknown	379	16 (4.2)	

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TABLE 4. Univariate analysis of additional risk factors

Risk Factor	No. of Procedures	No. of Infections (%)	p Value
Prior shunt surgery			<0.01
None	2439	98 (4.0)	
<12 wks	1132	90 (8.0)	
12 to <26 wks	322	22 (6.8)	
26 to <52 wks	262	9 (3.4)	
>52 wks	758	33 (4.4)	
Prior shunt infection			0.36
None	4584	228 (5.0)	
<12 wks	192	14 (7.3)	
12 to <26 wks	58	3 (5.2)	
26 to <52 wks	21	2 (9.5)	
>52 wks	58	5 (8.6)	

ICH = intracerebral hemorrhage; IVH = intraventricular hemorrhage; SAH = subarachnoid hemorrhage.

tive measure.12 Nonetheless, all participating HCRN sites included antibiotic wound irrigation before skin closure. Specific details regarding antibiotic irrigation were not included in our protocol and were left to the discretion of the surgeon. Vancomycin irrigation was used in 15% of the procedures, while the remaining 85% used bacitracin irrigation. One site that used vancomycin irrigation consistently had a very low infection rate (2.2%) and one surgeon who used it consistently at another site had no infections. These results prompted us to assess the impact of vancomvcin irrigation across the network. Our multivariate analysis demonstrated that vancomycin irrigation had a significant protective effect, whereas bacitracin irrigation was ineffective. We also observed a synergistic effect when vancomycin irrigation was used in combination with the shunt infection protocol and AICs, as this resulted in the lowest shunt infection rate (2.0%) across the network.

A recent study by Goswami et al.<sup>13</sup> demonstrated superior antimicrobial activity of vancomycin irrigation over bacitracin irrigation. The authors conducted an in vitro study on the antimicrobial ability of frequently used irrigation solutions, including bacitracin (50,000 U/L) plus polymyxin (500,000 U/L), vancomycin (1 g/L), gentamicin (80 mg/L), 0.9% saline, 0.3% povidone-iodine, 0.05% chlorhexidine, 0.45% Castile soap, and 0.125% sodium hypochlorite, on cultures of Staphylococcus aureus and Escherichia coli. Bacterial colony-forming units were counted after 1 and 3 minutes of exposure to each solution. The authors found that vancomycin irrigation was effective at eradicating S. aureus but had no effect on E. coli, whereas bacitracin-polymyxin solution had no effect on either S. aureus or E. coli. Interestingly, the povidoneiodine solution was found to have the best antimicrobial activity against both S. aureus and E. coli. Nonetheless, these findings may provide a possible explanation of our results because Staphylococcus species are the most common organisms in pediatric shunt infections.14

In January 2020, the US FDA voluntarily withdrew

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Variable	OR (95% CI)	p Value
All 5 protocol steps completed	1.09 (0.77–1.56)	0.62
CCCs		0.01
1 CCC	1.15 (0.86–1.54)	
≥2 CCCs	1.76 (1.26–2.44)	
History of prior shunt surgery		<0.01
<12 wks	1.84 (1.37–2.47)	
12–26 wks	1.54 (0.95-2.48)	
26 to <52 wks	0.76 (0.38-1.52)	
>52 wks	0.95 (0.63-1.44)	
AIC	0.70 (0.50-0.97)	0.05
Vancomycin irrigation	0.36 (0.21-0.62)	<0.01

#### TABLE 5. Multivariable analysis

Boldface type indicates statistical significance.

bacitracin for injection from the market because of risks of nephrotoxicity and anaphylactic reactions. As a result, several HCRN sites have transitioned to the use of vancomycin irrigation for their shunt procedures. This will be a significant variable of interest for the next analysis of our shunt infection protocol.

#### Nonmodifiable Factors: CCCs and Recent Shunt Surgery

The presence of  $\geq 2$  CCCs as a risk factor associated with shunt infection is also a novel finding. The relationship between increasing medical complexity and shunt infection has often been a spoken tenet in neurosurgery, but our previous work did not demonstrate that having  $\geq 2$ CCCs was associated with CSF shunt infection.<sup>15</sup> One possibility for this difference is that the prior study included only first-time shunts, before CCCs became apparent. Additionally, the current study analyzed significantly more patients, increasing our power to identify risk factors. Although the presence of  $\geq 2$  CCCs is a nonmodifiable factor, these patients should be counseled that they are at an increased risk of infection with shunt surgery.

We also found that patients who had undergone a recent shunt operation (within 12 weeks) were at risk for infection. This finding aligns with previous HCRN work showing that shunt revisions are a risk factor for shunt infection.<sup>16</sup> We observed a nonstatistically significant trend of declining ORs for infection with increasing time from the index shunt operation (Table 5). These data are consistent with the current literature that most shunt infections present within weeks of surgery and the infection risk decreases over time.<sup>14,17</sup> Of course, the best way to avoid this risk factor is to minimize the need for shunt revision, but when early revisions are necessary, attention to infection prevention measures are particularly important.

#### Limitations

Although we have a large sample size and prospectively collected data, there may be residual confounding effects due to variables that could not be recorded. For example, there may be site- and surgeon-specific nuances that have not been documented. Capturing every detail during surgery can be a significant challenge; however, the purpose

#### TABLE 6. Stepwise multivariable analysis

Variable	OR (95% CI)	p Value
CCCs		0.01
1 CCC	1.15 (0.85–1.54)	
≥2 CCCs	1.76 (1.26–2.44)	
History of prior shunt surgery		<0.01
<12 wks	1.84 (1.37–2.48)	
12–26 wks	1.54 (0.95–2.51)	
26 to <52 wks	0.77 (0.38-1.54)	
>52 wks	0.96 (0.63-1.45)	
AIC	0.70 (0.50-0.97)	0.05
Vancomycin irrigation	0.35 (0.21–0.60)	<0.01

Boldface type indicates statistical significance.

of our protocol was to create common, standardized steps that all HCRN surgeons could follow to reduce shunt infection. Second, we identified strong associations between AICs and vancomycin wound irrigation against shunt infection, but this does not prove causality and these data must be confirmed in our future QI studies or randomized trials. Finally, our vancomycin data were collected retrospectively and represented a minority of patients from a few HCRN centers; thus, it is possible that our observed effect may be due to type I error and/or center effect. As several HCRN sites have transitioned to vancomycin irrigation exclusively, our sample size for this group will increase in the next iteration of our QI analysis.

# Conclusions

We report the third iteration of our QI protocol to reduce the risk of shunt infection. Compliance with the protocol was high. Patients who have  $\geq 2$  CCCs and those undergoing recent shunt surgery within 12 weeks are at higher risk for shunt infection. From a QI standpoint, our updated data suggest that use of AICs and vancomycin irrigation of wounds are important infection prevention measures during CSF shunt surgery.

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# Appendix

Hydrocephalus Clinical Research Network Members The HCRN currently consists of the following clinical centers and investigators: Primary Children's Hospital, University of Utah (J. Kestle); Children's Hospital of Alabama, University of Alabama at Birmingham (C. Rozzelle, B. Rocque); Hospital for Sick Children, University of Toronto (J. Drake, A. Kulkarni); Texas Children's Hospital, Baylor College of Medicine (W. Whitehead); Seattle Children's Hospital, University of Washington (S. Browd, J. Hauptman); Children's Hospital of Pittsburgh, University of Pittsburgh (I. Pollack); St. Louis Children's Hospital, Washington University in St. Louis (D. Limbrick); Monroe Carell Jr. Children's Hospital at Vanderbilt, Vanderbilt University Medical Center (J. Wellons, R. Naftel); British Columbia Children's Hospital, University of British Columbia (M. Tamber); Alberta Children's Hospital, University of Calgary (J. Riva-Cambrin); The Johns Hopkins Hospital (E. Jackson); Children's Hospital of Los Angeles (M. Krieger, J. Chu, T. Simon); Children's Hospital Colorado (T. Hankinson); Nationwide Children's Hospital (J. Pindrik); HCRN Data Coordinating Center, Department of Pediatrics, University of Utah (R. Holubkov); and no affiliated clinical center (P. McDonald).

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Conception and design: all authors. Acquisition of data: Kestle, Chu, Krieger, Kulkarni, Riva-Cambrin, Rozzelle, Limbrick, Wellons, Browd, Whitehead, Pollack, Simon, Tamber, Hauptman, Pindrik, Naftel, McDonald, Hankinson, Jackson, Rocque, Drake. Analysis and interpretation of data: Kestle, Chu, Jensen, Holubkov, Reeder. Drafting the article: Kestle, Chu. Critically revising the article: Kestle, Chu, Jensen, Holubkov, Krieger, Kulkarni, Riva-Cambrin, Rozzelle, Limbrick, Wellons, Browd, Whitehead, Pollack, Simon, Tamber, Hauptman, Pindrik, Naftel, McDonald, Hankinson, Jackson, Reeder, Drake. Reviewed submitted version of manuscript: Kestle, Rocque. Approved the final version of the manuscript on behalf of all authors: Kestle. Statistical analysis: Kestle, Jensen, Holubkov, Reeder. Administrative/technical/material support: Kestle.

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