



## REVIEW ARTICLE

# The impact of catheter-based bladder drainage method on urinary tract infection risk in spinal cord injury and neurogenic bladder: A systematic review

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## Abstract

**Aims:** To systematically compare the impact of catheter-based bladder drainage methods on the rate of urinary tract infections (UTIs) amongst patients with neurogenic bladder.

**Methods:** A search of Cochrane Library, Embase, Medline, and Grey literature to February 2019 was performed using methods prepublished on PROSPERO. Reporting followed the Preferred Reporting Items for Systematic Review and Meta-analysis guidelines. Eligible studies were published in English and compared UTI incidence between neurogenic bladder patients utilizing bladder drainage methods of the indwelling urethral catheter (IUC), suprapubic catheter (SPC) or intermittent self-catheterization (ISC). The odds ratio of UTI was the sole outcome of interest.

**Results:** Eight nonrandomized observational cohort studies were identified, totaling 2321 patients who utilized either IUC, SPC, or ISC. Studies enrolled patients with neurogenic bladder due to spinal cord injury (seven studies) or from any cause (one study). UTI rates were compared between patients utilizing IUC vs SPC (four studies), IUC vs ISC (six studies), and SPC vs ISC (four studies). Compared with IUC, five of six studies suggested ISC use was associated with lower rates of UTI. Studies comparing IUC vs SPC and SPC vs ISC gave mixed results. Meta-analysis was not appropriate due to study methodology heterogeneity.

**Conclusions:** Low-level evidence suggests amongst patients with neurogenic bladder requiring catheter-based drainage, the use of ISC is associated with lower rates of UTI than IUC. Comparisons of IUC vs SPC and SPC vs ISC gave mixed results. Future randomized trials are required to confirm these findings.

## KEYWORDS

bladder drainage, bladder management, catheter, neurogenic bladder, spinal cord injury, urinary tract infection

## 1 | INTRODUCTION

Urinary tract infections (UTIs) are a common cause of morbidity and mortality in patients with neurogenic bladder,<sup>1,2</sup> and frequent related to catheter use. Subsequently, a primary management goal in patients with the neurogenic bladder is the facilitation of bladder drainage by the least invasive means.<sup>3</sup> However, many patients, including more than 60% of those with a spinal cord injury (SCI), will need some form of catheterization to urinate.<sup>4</sup> For these patients, the three key options are intermittent self-catheterization (ISC), an indwelling urethral catheter (IUC) or a suprapubic catheter (SPC). ISC is thought to represent the gold standard, as the bladder volumes cycle in close approximation to normal, and the lack of constant urethral foreign body is thought to preserve the urethral sphincter and reduce UTI rates.<sup>5</sup> This stance is led by guidelines of both the European Association of Urology (EAU) and the American Urological Association (AUA), which describe ISC and IUC as most- and least-preferred, respectively, with regard to UTI risk.<sup>3,6</sup> However, the literature cited by these guidelines is weak. Comparison of UTI rates between cohorts utilizing distinct catheter options (IUC, SPC, or ISC) was provided by only a single retrospective study,<sup>7</sup> while a separate Cochrane review of randomized trials of bladder management in neurogenic bladder found no eligible studies.<sup>8</sup> Therefore, this study aims to systematically analyze the literature on the relationship between catheter-based bladder drainage and UTIs. We hypothesize that ISC use will be associated with lower UTI rates than other methods.

## 2 | MATERIALS AND METHODS

### 2.1 | Search strategy

A comprehensive search was performed in February 2019 of Medline, Embase, the Cochrane Central Register of Controlled Trials, and Grey literature. The search strategy and list of the reviewed articles are provided separately (Appendices 1 and 2).

### 2.2 | Inclusion criteria

This study followed the Preferred Reporting Items for Systematic Reviews and Meta-analyses method<sup>9</sup> (Figure 1), including preregistration of the intended approach on PROSPERO (CRD42019124211). Search results were screened independently by two authors (NK and DH) with the elimination of ineligible studies occurring successively after reviewing of titles, then abstracts, then full-text articles.

Data extraction was performed independently by two authors (NK and DH) utilizing a standardized form and undertaken twice for accuracy (Appendix 3). Disagreements were resolved by a third author (DB).

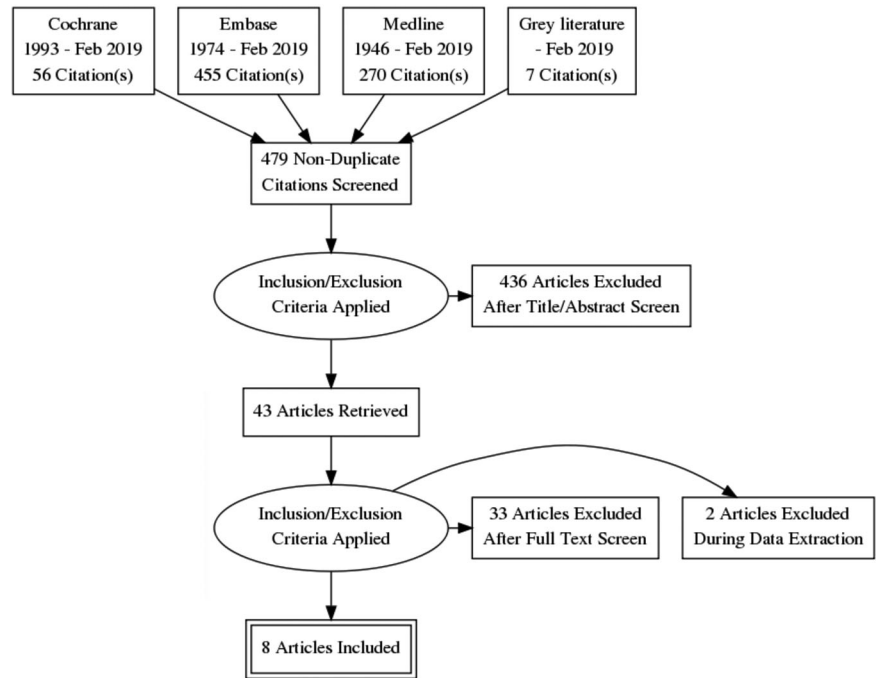
### 2.3 | Study eligibility

The patient population, intervention, comparator, outcome, and study type approach was used to define eligible studies.<sup>9</sup> These were required to include only patients with neurogenic bladder (P), present a cohort receiving catheter-based bladder drainage (I), a comparator cohort utilizing a different catheter-based bladder drainage option (C), and report UTI rates for each method in raw numbers (O). Eligible studies were written in English language, original, published before 1 February 2019, comparative in nature, and clearly described their observation period (S). The presence of patient randomization or did not affect study eligibility.

Amongst patients utilizing frequent or permanent urinary catheters, asymptomatic bacteriuria is common, not clinically meaningful and does not require treatment. The most widely accepted definition of catheter-associated UTI is the presence of signs or symptoms of UTI with no other identified source, supported by a culture of  $\geq 10^3$  CFU/mL of  $\geq 1$  bacterial species in a catheter urine specimen, or a midstream-voided urine sample less than 48 hours after catheter removal.<sup>10</sup> However, definitions have changed over time, accompanied by a growing acceptance of the relevance of patient-reported UTIs.<sup>11,12</sup> Hence, eligible studies defined UTIs as either symptoms or signs suggestive of UTI and any of (a) positive urine culture, (b) UTI requiring antibiotics or hospitalization or (c) patient-reported UTI. Studies were excluded if they failed to report UTI rates for at least two cohorts containing only patients with neurogenic bladder who used different bladder drainage methods. Variations within a single drainage method were not considered distinct management options, such as studies of ISC comparing catheters of different materials.

### 2.4 | Intended analyses

The sole outcome of interest was a comparison of the incidence of UTI with each different bladder drainage method, to be presented as odds ratios with confidence intervals. The descriptive summary was intended for all data, presenting studies comparing IUC vs SPC, IUC vs ISC, or SPC vs ISC. If studies of sufficiently similar methodology were found, then meta-analyses were intended using Review Manager Software version 5.3 (the Nordic Cochrane



**FIGURE 1** Preferred Reporting Items for Systematic Reviews and Meta-analyses flow diagram

Centre, the Cochrane Collaboration, Copenhagen, Denmark). Fixed effects analysis was to be used throughout. Funnel plots were used to assess publication bias for each of the three comparisons above. All analyses were two-tailed, and significance was assessed at the 5%  $\alpha$ -level.

## 2.5 | Assessment of bias

On the basis of the negative searches of a recent Cochrane review,<sup>8</sup> Randomised controlled trials (RCTs) were not expected to be identified. In compliance with the Cochrane Handbook, the Newcastle-Ottawa Quality Assessment Scale was therefore used to evaluate the risk of bias.<sup>13,14</sup> Each study was independently scored by two authors (NK and DH) using a standardized form (Appendix 4). Disagreements were resolved by a third author (DB). Studies scoring 0 to 3, 4 to 6, and 7 to 9 points were identified as high, medium, and low quality, respectively. Funnel plots were used to assess the risk of publication bias.

## 3 | RESULTS

Database searches identified 781 manuscripts, with an additional seven titles located from Grey literature. After the elimination of duplicate and irrelevant results, 43 full-text articles were retrieved. Of these, eight articles met eligibility criteria, comprising 2321 patients with neurogenic bladder utilizing either IUC, SPC, or ISC (Table 1 and Figure 1).<sup>7,11,12,15,16,19,21,22</sup> All studies were

observational and nonrandomized, constituting level III-2 evidence per the National Health and Medical Research Council.<sup>7,11,12,15-17,19,21,22</sup> Seven studies enrolled only patients with SCI, while one study assessed patients with neurogenic bladder from any cause.<sup>12</sup> Mean observation period ranged from 29 days to 11.5 years. Mean subgroup age and percentage female varied widely, from 36 to 63 years and 0% to 100%, respectively (Table 1). None of the studies which included an ISC subgroup reported the self-catheterization frequency per day or protocols to maximize aseptis.

There was great variability in the definitions used to diagnose UTI. These included the presence of signs or symptoms and positive urine culture,<sup>15,16,21</sup> UTI requiring antibiotics or hospitalization,<sup>11,22</sup> symptomatic UTI not further defined<sup>7,19</sup> or patient-reported UTI.<sup>11,12,21</sup> Some studies used multiple definitions. Due to this heterogeneity in study design, incomplete data reporting, patient population, and UTI definition a meta-analysis was not appropriate. Hence, comparisons between bladder drainage methods were presented qualitatively in subsections below, and in forest plots with the summary statistic suppressed, as recommended by the Cochrane Handbook<sup>13</sup> (Table 2 and Figure 2).

### 3.1 | Indwelling urethral catheterization vs SPC

Four studies totaling 586 patients assessed UTI rates in patients with neurogenic bladder utilizing either IUC or

**TABLE 1** Characteristics of eligible studies

Year and first author	Country	Prosp	Patient cohort	Exclusion criteria & no.	Out-pt.	Single center	UTI definition	Mean observation period, d	Mean age, y	% Female	Cervical level SCI	Level of evidence	NOS
1986 McGuire et al <sup>15</sup>	USA	No	SCI	Males (no. unknown)	Yes	Yes	"Febrile urinary tract infections" not further defined	IUC: 2555 ISC: 2190	-	All: 100%	IUC: 62% ISC: 27%	III-2	2
1987 Cardenas et al <sup>16</sup>	USA	No	SCI	Nil & none lost to f/up	Yes	Yes	Fever >101.4°F and bacteriuria >10 <sup>5</sup> CFU/mL, or patient-reported UTI	All: 365	-	All: 21%	IUC: 70% SPC: 75% ISC: 21%	III-2	5
2000 Mitsui et al <sup>10</sup>	Japan	No	SCI	F/up <3 y (no. unknown)	Yes	Yes	"Symptomatic genitourinary tract infection" not further defined	SPC: 3139 ISC: 3614	SPC: 53 ISC: 44	SPC: 3% ISC: 11%	SPC: 100% ISC: 15%	III-2	5
2010 Katsumi et al <sup>17</sup>	USA	No	SCI	Use of IUC or SPC for <1 y, or incomplete data (102 pts)	Yes	Yes	Fever >101.2°F and infection requiring antibiotics	IUC: 4271 SPC: 3979	IUC: 63 SPC: 60	IUC: 1% SPC: 0%	IUC: 45% SPC: 65%	III-2	5
2014 Togan et al <sup>18</sup>	Turkey	Yes	SCI	Nil & none lost to f/up	Yes	Yes	Bacteriuria >10 <sup>5</sup> CFU/mL and signs or symptoms of UTI	All: 29	All: 36	All: 16%	-	III-2	5
2016 Krebs et al <sup>19</sup>	Switzer	No	N.B. > 12 mo	F/up <3 y or incomplete data (220 pts)	Yes	Yes	Patient-reported UTI	All: 1095	All: 48	All: 26%	-	III-2	5
2018 Elliott et al <sup>14</sup>	USA	No	SCI	Congenital N.B. or poor written English	Yes	No	Patient-reported UTIs requiring hospitalization	All: 365	IUC: 46 ISC: 44	IUC: 40% ISC: 33%	IUC: 70% ISC: 31%	III-2	6
2019 Hennessey et al <sup>20</sup>	Australia	No	SCI	Nil & none lost to f/up	No	Yes	Bacteriuria (>10 <sup>2</sup> CFU/mL [ISC] or any [SPC or IUC]) and signs or symptoms of UTI	IUC 1st period: 58 IUC 2nd period: 102 SPC: 105 ISC: 44	All: 42 <sup>a</sup>	All: 25%	-	III-2	6

Abbreviations: °F, degrees Fahrenheit; -, not stated; %, percentage; 1st, first; 2nd, second; CFU/mL, colony-forming units per milliliter; F/up, follow up; ISC, intermittent self-catheterization; IUC, indwelling urethral catheter; mo, months; N.B., neurogenic bladder; no., number of patients; NOS, Newcastle-Ottawa Scale; Out-pt., outpatient; Prosp, prospective; Pts., patients; SCI, spinal cord injury; SPC, suprapubic catheter; Switzer, Switzerland; USA, United States of America; UTI, urinary tract infection; Y, years.

<sup>a</sup>Median, not mean.

**TABLE 2** Outcomes of eligible studies

Year and first author	IUC		SPC		ISC		IUC vs SPC		IUC vs ISC		SPC vs ISC	
	Pts.	UTI	Pts.	UTI	Pts.	UTI	Odds ratio	95% CI	Odds ratio	95% CI	Odds ratio	95% CI
1986 McGuire et al <sup>15</sup>	13	12			22	7			25.71	2.90 - 238.8 <sup>a</sup>		
1987 Cardenas et al <sup>16</sup>	57	25	16	9	62	33	0.61	0.20 - 1.90	0.69	0.33 - 1.42	1.13	0.37 - 3.42
2000 Mitsui et al <sup>10</sup>			34	4	27	7					0.3810	0.09850 - 1.473
2010 Katsumi et al <sup>17</sup>	133	21	46	7			1.05	0.41 - 2.65				
2014 Togan et al <sup>18</sup>	57	17			24	4			2.13	0.63 - 7.16		
2016 Krebs et al <sup>19</sup>	18	15	120	70	427	301	3.57	0.98 - 13.00	2.09	0.60 - 7.36	0.59	0.40 - 0.89 <sup>a</sup>
2018 Elliott et al <sup>14</sup>	271	59			753	92			2.00	1.39 - 2.87 <sup>a</sup>		
2019 Hennessey et al <sup>20</sup>	172	67	24	7	45	12	1.55	0.61 - 3.94	1.76	0.847 - 3.64	1.13	0.340 - 3.40

Note: Shaded cell, no data reported.

Abbreviations: CI, confidence interval; ISC, intermittent self-catheterization; IUC, indwelling urethral catheter; Pts., patients; SCI, spinal cord injury; SPC, suprapubic catheter; UTI, urinary tract infection; vs, versus.

<sup>a</sup>Statistically significant result.

SPC.<sup>12,16,21,22</sup> In all studies, the odds ratio of UTI was not significantly different between bladder drainage methods.

### 3.2 | Indwelling urethral catheterization vs ISC

Six studies comprising 1921 patients compared IUC vs ISC.<sup>11,12,15,16,19,21</sup> ISC use was associated with a lower odds ratio of UTI in five studies, although in only two were these results significant.<sup>11,19</sup>

### 3.3 | SPC vs ISC

Four studies representing 755 patients reported rates of UTI in patients with neurogenic bladder managed with either ISC or SPC.<sup>7,12,16,21</sup> The odds ratio of UTI was lower amongst patients using SPC in one study,<sup>12</sup> and not significantly different in the remainder.

### 3.4 | Assessment of bias

The Newcastle-Ottawa Quality Assessment Scale indicated that the risk of bias was moderate or high for all included publications (Appendix 5). Most did not statistically compare age, sex, or other demographic characteristics between cohorts, nor utilize approximately equal follow-up durations. Only two studies used the most robust UTI diagnostic approach of exclusively requiring positive urine culture and signs or symptoms of infection. In addition, only a small number of studies reported ethics approval,<sup>11,12,16</sup> conflicts of interest,<sup>12,16</sup> or funding.<sup>16,21</sup>

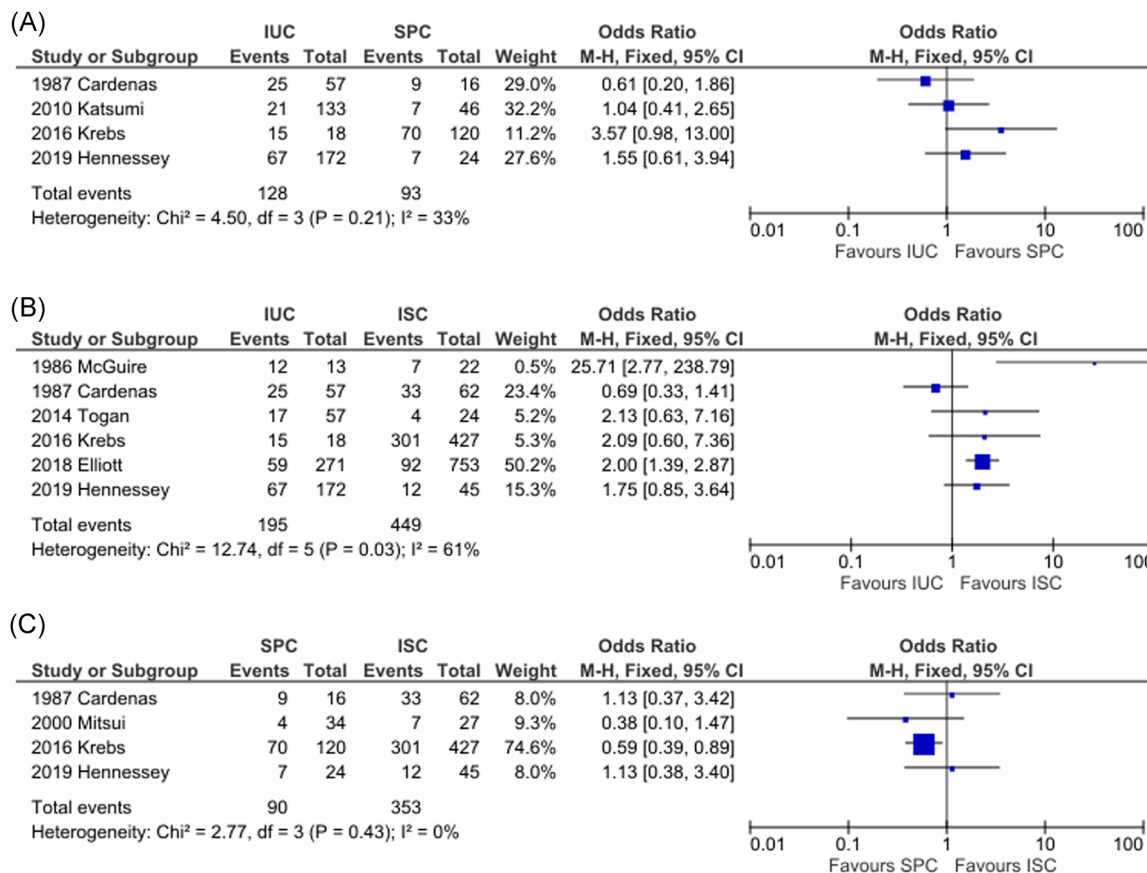
All studies were nonrandomized and therefore, at increased risk of selection bias. Reporting bias may have

been present in the three studies that did not describe the number of patients lost to follow-up.<sup>7,11,19</sup> Funnel plots for each of the three comparisons did not indicate publication bias (Figure 3).

## 4 | DISCUSSION

The number of patients affected by neurogenic bladder continues to grow. Annually in the United States of America, neurogenic bladder will affect 80% of the 11 000 patients with new spinal cord injuries,<sup>1,18</sup> more than 70% of the 10 000 patients diagnosed with multiple sclerosis,<sup>20,23</sup> more than 40% of the 60 000 patients who develop Parkinson's disease,<sup>24</sup> and 15% of the 800 000 who suffer a stroke.<sup>25</sup> In addition, 2.1 million Americans are diagnosed annually with diabetes mellitus, of whom half will develop some degree of neurogenic bladder dysfunction.<sup>26-29</sup> A large minority of this heterogenous cohort patients with neurogenic bladder will require catheter-based drainage. Common noninfectious sequelae of catheter use include urethral erosion, catheter obstruction, hematuria, bladder stones, more frequent health care visits and decreased quality of life.<sup>30,31</sup> However, given its high frequency and impact, a chief consideration in the selection of the drainage method will be the prevention of UTIs.

Catheter-associated UTIs are the most common healthcare-associated infection worldwide.<sup>10</sup> They are associated with increased hospital admissions, cost, morbidity, and mortality.<sup>1,2,10,32,33</sup> Asymptomatic bacteriuria, the prerequisite, is almost universal after 30 days.<sup>10</sup> Catheters bypass host defense mechanisms, impair complete bladder emptying and facilitate bacterial entry to the bladder. Bacteria may be inoculated at the time of insertion from the patient or health care provider's skin, ascend on the mucosal-catheter interface or spread intraluminally if the drainage bag is contaminated.



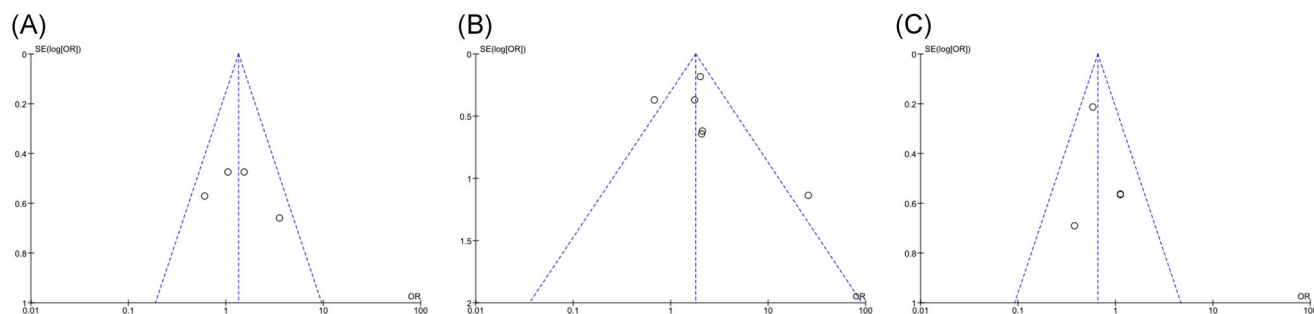
**FIGURE 2** Forest plots of urinary tract infection odds ratios between (A) indwelling urethral catheter vs suprapubic catheter, (B) indwelling urethral catheter vs intermittent self-catheterization, and (C) suprapubic catheter vs intermittent self-catheterization, with suppression of the pooled estimate. CI, confidence interval; ISC, intermittent self-catheterization; IUC, indwelling urethral catheter; SPC, suprapubic catheter

Previous reviews comparing bladder drainage methods have sought only randomized or quasirandomized trials, and found none.<sup>34,35</sup> This study represents the first systematic review to include nonrandomized studies and the strongest literature to date on the topic, although still constituting only level III evidence. The review's scope extended to include comparative cohort studies. Eight such publications were identified, representing low-level evidence. While meta-analysis was not possible, the strongest findings were in the comparison of IUC vs ISC, with IUC use associated with higher odds ratios for UTI in five of six studies (two significantly). This supports the stance of the current EAU and AUA guidelines, which favors ISC over other catheter-based options.<sup>3,6</sup> The nature of ISC may explain why its use appears least conducive to developing UTIs. Cyclical emptying replicates normal bladder function, and it does not provide the constant foreign body bacterial pathway of IUC or SPC. In patients with neurogenic bladder managed by IUC yet who are appropriate candidates for ISC, such a change may be offered only after a great delay, or never. These findings should encourage urologists treating such

patients to aim for an early trial of void or conversion to ISC.

Analyses of IUC vs SPC and SPC vs ISC were less compelling, from which no definitive conclusions can be drawn. This lack of statistical significance is possibly due to unmeasured confounders and sampling bias, with none of these comparisons involving two groups of more than 200 patients. In addition, UTI rates during early ISC use may have been affected by the learning curve, as patients become familiar with the procedure and aseptic technique. In the absence of clear findings from the identified literature, patients should continue to be managed in accordance with current guidelines. For patients managed by an IUC, this involves an early transition to non-IUC based bladder management, while for those with an SPC remains little evidence that ISC offer significantly different UTI risk.<sup>3,6,10</sup>

The included publications spanned a broad publication period, from 1986 to 2019. To the best of the authors' knowledge, to date, no studies have objectively described trends over time in the proportion of patients with neurogenic bladder prescribed either IUC, SPC, or ISC.



**FIGURE 3** Funnel plots of urinary tract infection odds ratios between (A) indwelling urethral catheter vs suprapubic catheter, (B) indwelling urethral catheter vs intermittent self-catheterization, and (C) suprapubic catheter vs intermittent self-catheterization

Looking at the seminal policy papers, the EAU and AUA delivered their first guidelines on neurourology or catheter-related UTIs in 2003 and 2009, respectively.<sup>10,36</sup> From their debut until present day, the EAU guidelines have supported ISC as the “gold standard” catheter-based drainage option in neurogenic bladder to reduce UTI.<sup>36</sup> In contrast, the inaugural 2009 AUA catheter-associated UTI guidelines were more conservative in their support of ISC, describing it as a viable alternative to IUC but not clearly preferable to SPC, and it was not until their 2014 updates that ISC became the preferred method.<sup>6,10</sup> This shift in policy may have led to increased consideration of ISC in patients with neurogenic bladder.

Separate trends in the management of neurogenic bladder include a shift towards less invasive therapies, including increasing uptake of intradetrusor onabotulinum toxin A (OBTA) and less frequent utilization of augmentation cystoplasty.<sup>37</sup> OBTA has been associated with a significant reduction in UTI incidence in patients with neurogenic bladder.<sup>12</sup> However, while there is a well-known risk for some initially catheter-free patients to require short-term IUC or ISC following OBTA treatment, the therapy’s long-term effect on the prevalence of different catheter-based drainage options is unclear.

Several excluded studies also assessed the effect of different catheter-based bladder drainage methods on UTI rates in patients with neurogenic bladder but were ineligible for a variety of reasons. These included less robust definitions of UTI,<sup>2,38–42</sup> unclear follow-up durations,<sup>43,44</sup> and inability to extract a raw number of UTI events per patient days.<sup>45,46</sup>

This review’s strengths are its sound methodology and comprehensive curation of the literature. It is limited by the lack of randomized trials, the identified studies’ heterogeneous methodology, wide variation in UTI definition and inclusion of patients both with and without SCI. Nonrandomized studies are more prone to bias, so these results should be interpreted with caution. Also, the included studies span a broad 30-year period, over which time the understanding and management of neurogenic bladder and UTI have

evolved substantially. In addition, seven of the eight studies included only patients with SCI. These patients have additional risk factors for UTI including reduced mobility and frequent renal and bladder stones. This may limit the generalizability of these findings to patients without SCI. Prospective trials are needed to confirm these findings.

## 5 | CONCLUSION

Low-level evidence suggests that compared with IUC, the use of ISC may be associated with lower rates of UTI in patients with neurogenic bladder. Comparisons of UTI rates between patients utilizing IUC or SPC, and SPC or ISC, were inconclusive. Future randomized trials are needed to better establish the impact of catheter-based drainage methods on UTI incidence in patients with neurogenic bladder.

## CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

## AUTHOR CONTRIBUTIONS

NK created the report concept and wrote the initial manuscript. NK and DB screened searches, conducted data extraction, and assessed risk of bias. MOC performed statistical analysis and created the figures. All authors refined the final manuscript, and agree to be accountable for all aspects of the work.

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## SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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