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# Bladder emptying method is the primary determinant of urinary tract infections in patients with spinal cord injury: results from a prospective rehabilitation cohort study

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## Objective

To understand the occurrence of and risk factors for urinary tract infections (UTIs) in patients with spinal cord injury (SCI) undergoing specialized SCI rehabilitation in Switzerland.

## Patients and Methods

This study used data collected from 369 patients, who participated in a nationwide rehabilitation cohort for SCI in Switzerland between 2013 and 2017. Information on UTIs as well as their potential determinants, including demographics, lesion characteristics, and time-updated data on functional independence and bladder management, was used. Multivariable regression methods were applied to perform a time-updated evaluation of determinants of UTI risk.

## Results

The crude incidence rate (IR) of UTIs was 0.55 UTIs per 100 person-days (95% confidence interval [CI] 0.49–0.62), the cumulative IR was 43%, and the median length of stay was 122 days. The bladder emptying method at discharge was largely determined by 28 days after admission. Among those using indwelling or assisted intermittent catheterization (IC), the likelihood of self-IC at discharge was positively related to the level of self-care independence, negatively related to age at injury, and lower in women than men. Catheter users consistently had higher adjusted IRs for UTI than spontaneous voiders. The IR ratios were: indwelling catheter: 5.97 (95% CI 2.63–13.57); assisted IC: 6.05 (95% CI 2.63–13.94); self-IC: 5.16 (95% CI 2.31–11.52); test for differences across catheter groups: $P = 0.82$. Lesion severity and previous UTI had additional but smaller effect sizes.

## Conclusions

Bladder emptying method was identified as the main risk factor for UTI in patients with SCI. As spontaneous voiders had the lowest UTI rate, further research is warranted to reduce voiding dysfunction, for instance using neuromodulation procedures.

## Keywords

urinary tract infections, urinary bladder, neurogenic, urinary catheters, spinal cord injuries, neurological rehabilitation

## Introduction

Urinary tract infections (UTIs) are a commonly reported source of morbidity in patients with spinal cord injury (SCI) undergoing specialized rehabilitation [1–3]. One prospective study reported an overall incidence rate (IR) of 0.68 UTIs per 100 person-days with a cumulative IR of 78% during hospitalization after acute SCI [4]. An estimated 80% or more of the SCI population has chronic neurogenic lower urinary tract dysfunction [4,5], which may lead to high post-void residual urine volume and chronic catheter use [3], contributing to a high susceptibility to UTIs in the SCI population [1,3,6]. UTIs can have serious consequences, most notably, acute kidney damage [7], septicaemia or renal failure [8]. Historically, renal damage was the leading cause of death among individuals with SCI, and it is still associated with a diminished life expectancy [2,9,10]. UTI reduction is further a patient priority among community-dwelling people with SCI;

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for example, in a representative survey for Switzerland, 59% of individuals with SCI reported problems with UTIs, with 41% categorizing UTIs as a moderate or significant problem [11].

It is commonly assumed that UTIs interfere with rehabilitation because they often increase spasticity and may even necessitate bed rest and prolong admission times, a hypothesis with preliminary support in the literature [3,12]. Other infections have also been associated with impaired functional recovery [13]; therefore, besides the aforementioned impact on patients' health, a reduction in the number of UTIs during the rehabilitation period could offer the further benefit of increasing the efficiency of the rehabilitation process and thereby reduce unnecessary healthcare costs. Better insights into the characteristics of UTIs in this patient group could inform health policy decisions that target clinical cost reduction. A recent shift in European SCI patient demographics towards older individuals who are more vulnerable to non-traumatic SCI further supports an updated epidemiological analysis [14,15]. Finally, a better understanding of UTI development and pathophysiology in patients with SCI would aid healthcare professionals, caregivers and patients to make informed clinical decisions, especially given the complexity of UTIs in this group and the ongoing debate regarding UTI treatment guidelines [1,8,16]. The objective of the present study was therefore to gain a better understanding of UTI occurrence and the risk factors for UTIs in the context of specialized inpatient SCI rehabilitation in Switzerland. The specific aims were: (i) to describe the IR of UTIs in this study population; (ii) to identify predictors of bladder emptying method at discharge; and (iii) to evaluate the incidence of UTIs in relation to bladder emptying method.

## Patients and Methods

The STROBE (Strengthening of Reporting of Observational Studies in Epidemiology) guidelines were used to ensure quality reporting [17].

### Data Source

#### Patient Population and Study Design

Data were derived from the longitudinal, multicentre inception cohort of the Swiss Spinal Cord Injury Cohort Study (SwiSCI) [18]. This national, prospective cohort includes Swiss residents aged ≥16 years, newly diagnosed with a traumatic or non-traumatic SCI, and admitted to inpatient rehabilitation at one of the four Swiss centres providing specialized rehabilitation for SCI. Individuals with an SCI attributable to a congenital condition, neurodegenerative disorder, or Guillain–Barré syndrome, or who had a new SCI in the context of palliative care, were excluded from the study. Data were collected at four time points after the date of SCI diagnosis: at 28 days (range 16–40 days), 84 days (70–98 days), 168 days (150–186 days), and at discharge (10–0 days before discharge). Data collection occurred exclusively during inpatient stays at one of the participating rehabilitation centres; therefore, not all patients were expected to have available data from all four time points. This study used data from patients admitted and discharged between May 2013 and June 2017.

Over the study period, 52% of the patients who met the SwiSCI study eligibility criteria provided written consent to full data collection, meaning data collection both from the clinical record and from additional examinations. As the additional examinations included assessments that procured relevant urological data, full data consent was necessary for inclusion in the present study. Older patients and those with a higher comorbidity load were less likely to consent to full data collection (unpublished analysis; available upon request). All appropriate ethical approvals were obtained (Ethics Committee northwest/central Switzerland (EKNZ): PB_2016-00183, Ethics Committee Vaud (CEVD): 032/13 (CEVS), Ethics Committee Zurich (KEKZH): 2013-0249).

#### Neuro-Urological Management

The neuro-urological management was patient-tailored according to the European Association of Urology Guidelines on Neuro-Urology [8]. Asymptomatic bacteriuria was not screened for or treated.

### Study Measures

#### Demographic and General Clinical Information

Demographic, general clinical information, and rehabilitation characteristics were extracted from the clinical record. Demographic information included sex and age at injury. Relevant clinical information included lesion aetiology and diabetes. Rehabilitation characteristics such as overnight rehospitalization and study centre were also collected.

#### Neurological Category

Neurological status was collected as part of the clinical assessment at all four time points. A variable, 'neurological category', was created that combined information from the American Spinal Injury Association (ASIA) Impairment Scale (AIS) [19] – a measure of lesion completeness – and lesion level information, which was divided into the groups: C1–C8, AIS categories A,B and C; T1–S5, AIS categories A,B and C; and all AIS category D. The International Spinal Cord Society

(ISCoS) recommendations for grouping reflect common characteristics of bladder emptying [20].

### Functional Independence

Spinal cord independence measure (SCIM) III scores were collected as part of the clinical assessment at all time points. The SCIM subscales were psychometrically validated for interval use as in regression analysis [21].

### Bladder Management

Bladder emptying method was chosen as the primary exposure variable for the UTI analysis [2,3,22], with time-updated information taken from both the ISCoS Lower Urinary Tract Function Basic Data Set (ISCoS dataset) [23] – collected 28 days after admission and at discharge, and the SCIM III examination [21] – collected at all four time points. In case both measurements were available on the same day, priority was given to the SCIM score ($n$ = 7). The scores from SCIM item six ('sphincter management – bladder') were classified into four categories: indwelling catheter (score = 0); assisted intermittent catheterization (IC; score = 3–6); self-IC (score = 9–13); and spontaneous voiding (score = 15). This classification is supported by a Rasch validation of the SCIM III [21]. ISCoS results were translated to the categories outlined above. People using exclusively reflex voiding, condom catheters, or bladder expression ($n$ < 10 at any given time point) were combined with the self-IC group. Patients using multiple emptying methods according to the ISCoS dataset were classified as using the more invasive method.

Analyses where bladder emptying method was the main outcome were informed by the ISCoS dataset only, thus facilitating discrimination of transurethral and suprapubic catheterization methods. People who used exclusively reflex voiding, condom catheters, or bladder expression were grouped in a separate category for the bladder emptying analysis.

### Urinary Tract Infections

Urine samples were collected and UTIs were defined in accordance with the ISCoS Urinary Tract Infection Basic Data Set [24] in the main analysis. This UTI definition requires both a positive bacterial culture and the presence of a new sign or symptom; these criteria are consistent with guidelines from other medical societies [8,25]. Fever was defined as a rectal or tympanic temperature >37.8 °C. The diagnoses were made by neuro-urology or SCI specialists. Data on UTIs were taken directly from clinical records. UTIs recorded in acute care patient discharge reports or diagnosed on the first day of rehabilitation were excluded from analysis ($n$ = 19) because of the lack of diagnostic information as well as uncertainty regarding start dates, which precluded a proper calculation of UTI risk. In line with international guidelines, a UTI was considered unique if at least 7 days had elapsed since the previous reported UTI [8,16,25].

## Statistical Analyses

### Modelling Considerations

Potential confounders for the association of interest included: demographic characteristics (gender and age); lesion characteristics, including time since injury, lesion level, lesion aetiology and lesion severity; and functional independence [1,2,4,8]. Overnight hospitalization was used as an indicator to account for time spent outside of observation in an environment with a potentially different risk of UTI and bladder management norms, but was never the result of a UTI. Diabetes was identified as an independent risk factor for UTI [26]. Study centre was included as a control variable in all analyses to account for between-centre heterogeneity, but comparative results will not be shown. Time-updated information (based on repeated measures) for neurological category, functional independence, and bladder emptying method was used in the longitudinal analysis of UTI risk.

As bladder management involves multifaceted decision-making that could also encompass some of the risk factors for a UTI [8], it was not possible to fully understand the relationship between bladder emptying method and UTIs without recognizing which factors motivate the choice of bladder emptying method. As detailed bladder emptying method data were only available 28 days after admission and at discharge, patient status 28 days after admission was used as a predictor for patient bladder emptying status at discharge, and this model did not include time-updated covariates. Demographic characteristics, lesion characteristics, and functional independence were all identified as factors that might influence bladder management decisions [8,27]. Diabetes was included because, in some cases, it can lead to peripheral neuropathy that is severe enough to warrant catheterization [28]. The variable 'UTI before first bladder emptying assessment' was used to control for whether an early UTI had already influenced bladder emptying method at the first measurement point. It was also necessary to control for the time between injury and admission as patients who are in rehabilitation for a longer period of time have more opportunity to start an IC programme.

### Longitudinal Data Considerations

The data analysis of longitudinal UTI risk is subject to left truncation given that the majority of patients spent time in acute care prior to admittance to specialized rehabilitation. In order to reduce left truncation bias, all times used in the study for UTIs and time-updated covariates were referenced to the date of SCI. Additionally, two indicator variables, one marking whether a UTI was recorded on or before the date of admission to rehabilitation and another indicating a stay in acute care of >1 week before the SCI was formally diagnosed using the AIS, were included in the multivariable analysis. A further time-updated variable, 'UTI during rehabilitation', recorded whether someone had previously experienced a UTI during rehabilitation so as to account for UTIs that occurred before the measurement of the other time-updated covariates. All patients entered rehabilitation with a baseline value of 0 (no previous UTI), which changed to 1 (previous UTI) when a UTI occurred, and remained at 1 for the rest of the rehabilitation stay. We assumed that UTIs had a minimal duration of 1 week and, accordingly, adjusted the time at risk for a new UTI. Results of the time-updated analysis were compared with those of an analysis using baseline values for covariates only.

## Handling Missing Data

The complete case analysis was presented as the primary analysis because missing data in time-updated covariates in a rehabilitation setting are typically affected by unanticipated changes in the patient health status that prevent data collection as scheduled. Consequently, the condition of 'missing at random', an assumption made for common missing data methods, including multiple imputation, is unlikely to be fulfilled. The extent of missing data was limited: 6% for the SCIM assessment and 12% for the AIS score (Table S1). The complete case analysis included cases with data collection for SCIM and bladder emptying method within 40 days of admission to rehabilitation. For the neurological assessment, any initial measurement was taken, but giving priority to the measurement at the first time point (28 days). Neurological characteristics were generally stable over time (correlation between four successive AIS measurements: 0.84, 0.92 and 0.96), as previously reported [29]. There were only 11 cases with a single neurological assessment from the very acute period (<14 days after SCI).

## Data Analysis

All analyses were conducted using STATA version 14.2 for Windows (College Station, TX, USA). Between-group differences in the univariable analyses were evaluated using chi-squared or Fisher's exact tests for categorical variables. Because all the continuous variables had non-normal distributions, non-parametric Kruskal–Wallis tests were chosen. Kaplan–Meier curves were generated for the entire population, and for each categorical variable, a Wilcoxon–Breslow–Gehan test was performed to identify statistical differences between the groups.

Since spontaneous bladder emptying and self-IC bladder emptying 28 days after admission were both close to deterministic bladder emptying method at discharge (Table S2), these cases were excluded from the regression modelling of bladder emptying method at discharge. Likewise, users of condom catheters, bladder expression, urostomy bags, and reflex triggering ($n$ = 8) were also excluded. The present analysis was, thus, targeted at whether or not individuals achieved self-IC, using a logistic regression model (coding use of self-IC at discharge as 1 and indwelling transurethral or suprapubic catheter, assisted IC, and condom catheter use at discharge as 0). Non-linearity of continuous variables was evaluated by modelling multivariable fractional polynomials [30].

Crude IRs (with binomial 95% CIs) for UTIs were calculated using time-updated covariates. The method of episode splitting was implemented by prospectively using the date of a new UTI or the date of a change in any predictor variable as the condition for temporal splitting and stacking of data. A time-updated indicator for a previous UTI, which also accounted for UTIs prior to the first clinical assessment of covariates, was also included. To obtain unadjusted and adjusted IR ratios (IRRs) for UTI (with 95% CIs), corrected for within- and between-person differences (repeated measures), a mixed-effects negative binomial regression with robust standard errors was used to account for overdispersion. Scores on the SCIM self-care and mobility subscales were used to obtain adjusted odds ratios for bladder management outcomes and IRRs for UTI. Significance was tested using the Wald test. For categorical variables with more than two levels that showed global significance, post-estimation was used to evaluate between-level differences, applying a Bonferroni adjustment to account for multiple testing. $P$ values <0.05 were taken to indicate statistical significance.

## Sensitivity Analysis

In sensitivity analyses, we used a broad, operational definition of UTIs, which included all treated UTIs (suspected UTIs).

Multiple imputation was used to evaluate the impact of any missing data in AIS score (assuming that high correlations for successive AIS scores reliably inform the imputation process) and bladder emptying method (ISCoS dataset) at the first measurement time point as well as for the variables 'overnight hospitalization' and 'time in acute care'. Multiple imputation using chained equations was chosen to impute values missing at random, and 20 imputed datasets were created [31,32].

Sensitivity analyses used identical statistical testing to the main analysis, with one exception, due to convergence issues, and a mixed-effects Poisson regression with QR decomposition of the variance components matrix was used to calculate unadjusted and adjusted IRRs in the multiple imputation dataset [33].

## Results

Out of the 369 full dataset records available for analysis in June 2017, 159 (43%) of the patients experienced a total of 263 UTIs, and 62 of those patients (17% of the total population), had two or more UTIs (Table 1). In 94% (247) of the UTIs, the concentration of bacteria in the urine culture was at least $10^5$ CFU/mL. Fever and cloudy urine were the most commonly reported symptoms, with each occurring in 36% (95) of the UTIs, while 45% (118) of the UTIs presented with more than one symptom (Table S3). The crude IR for UTI was 0.55 per 100 person-days (95% CI 0.49–0.62), and this increased to 0.68 per 100 person-days (95% CI 0.61–0.76) when all suspected UTIs were included. The median (interquartile range [IQR]) time to the first UTI was 44 (25–88) days. The median (IQR) length of stay was 122 (64–187) days, patients were admitted to first rehabilitation a median (IQR) of 13 (8–24) days after injury, and 95% of the population was admitted within 51 days of injury ($n$ = 351). Female sex, AIS category D lesion, non-traumatic SCI, shorter length of stay, spontaneous bladder voiding, and higher SCIM scores were associated with fewer UTIs in univariable analysis (Table 1).

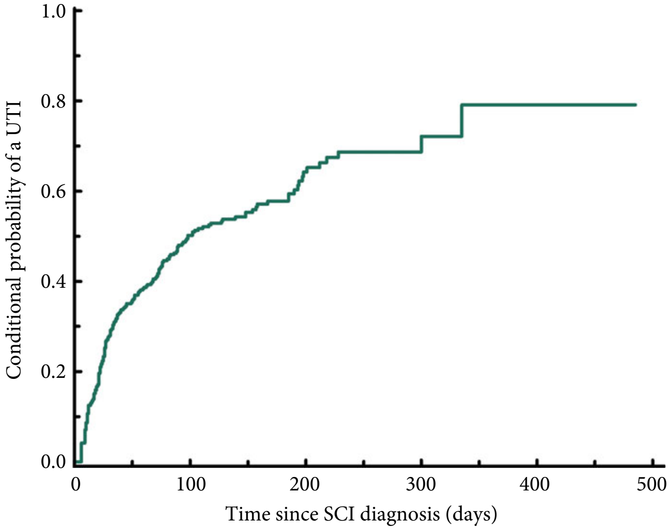
**Table 1** Basic characteristics of the study population.

| Characteristic [Missing]<br>Indicator variable | Overall<br>*n* (%) | Patients with 0 UTIs<br>*n* (%) | Patients with 1 UTI<br>*n* (%) | Patients with ≥2 UTIs<br>*n* (%) | *P* |
|---|---|---|---|---|---|
| **Study population** | 369 (100) | 210 (56.9) | 97 (26.3) | 62 (16.8) | |
| **Age at injury [0]** | | | | | 0.17 |
| 16–30 | 45 (12.2) | 20 (9.5) | 14 (14.4) | 11 (17.7) | |
| 31–45 | 65 (17.6) | 38 (18.1) | 19 (19.6) | 8 (12.9) | |
| 46–60 | 120 (32.5) | 78 (37.1) | 21 (21.6) | 21 (33.9) | |
| 61–75 | 104 (28.2) | 57 (27.1) | 30 (30.9) | 17 (27.4) | |
| 76+ | 35 (9.5) | 17 (8.1) | 13 (13.4) | 5 (8.1) | |
| **Gender [0]** | | | | | <0.01 |
| Female | 121 (32.8) | 78 (37.1) | 35 (36.1) | 8 (12.9) | |
| Male | 248 (67.2) | 132 (62.9) | 62 (63.9) | 54 (87.1) | |
| **Neurological category, 28 days after admission* [3]** | | | | | <0.0001 |
| C1–C4, AIS A,B,C | 24 (6.5) | 8 (3.8) | 7 (7.2) | 9 (14.5) | |
| C5–C8, AIS, A,B,C | 21 (5.7) | 4 (1.9) | 5 (5.2) | 12 (19.4) | |
| T1–S5, AIS A,B,C | 105 (28.5) | 42 (20.0) | 39 (40.2) | 24 (38.7) | |
| All AIS D | 216 (58.5) | 155 (73.8) | 44 (45.4) | 17 (27.4) | |
| **Lesion aetiology [0]** | | | | | <0.01 |
| Non-traumatic SCI | 155 (42.0) | 103 (49.0) | 37 (38.1) | 15 (24.2) | |
| Traumatic SCI | 214 (58.0) | 107 (51.0) | 60 (61.9) | 47 (75.8) | |
| **Length of stay, days [0]** | | | | | <0.0001 |
| 1–60 | 83 (22.5) | 71 (33.8) | 11 (11.3) | 1 (1.6) | |
| 61–120 | 96 (26.0) | 61 (29.0) | 32 (33.0) | 3 (4.8) | |
| 121–180 | 87 (23.6) | 50 (23.8) | 18 (18.6) | 19 (30.6) | |
| 180+ | 103 (27.9) | 28 (13.3) | 36 (37.1) | 39 (62.9) | |
| **Overnight hospitalization [5]** | | | | | 0.13 |
| No | 310 (84.0) | 182 (86.7) | 79 (81.4) | 49 (79.0) | |
| Yes | 54 (14.6) | 24 (11.4) | 17 (17.5) | 13 (21.0) | |
| **Bladder emptying method, 28 days after admission [5]** | | | | | <0.0001 |
| Indwelling catheter | 192 (52.0) | 83 (39.5) | 70 (72.2) | 39 (62.9) | |
| IC – assisted | 41 (11.1) | 16 (7.6) | 12 (12.4) | 13 (21.0) | |
| IC – self | 32 (8.7) | 18 (8.6) | 8 (8.2) | 6 (9.7) | |
| Spontaneous voiding | 99 (26.8) | 91 (43.3) | 5 (5.2) | 3 (4.8) | |
| **SCIM III score, 28 days after admission [14]** | | | | | <0.0001 |
| 0–24 | 97 (26.3) | 33 (15.7) | 37 (38.1) | 27 (43.5) | |
| 25–49 | 106 (28.7) | 45 (21.4) | 36 (37.1) | 25 (40.3) | |
| 50–74 | 83 (22.5) | 65 (31.0) | 13 (13.4) | 5 (8.1) | |
| 75–100 | 69 (18.7) | 61 (29.0) | 7 (7.2) | 1 (1.6) | |
| **Diabetes [0]** | | | | | 0.38 |
| No | 335 (90.8) | 190 (90.5) | 86 (88.7) | 59 (95.2) | |
| Yes | 34 (9.2) | 20 (9.5) | 11 (11.3) | 3 (4.8) | |

| Continuous variable | Median (IQR) | Median (IQR) | Median (IQR) | Median (IQR) | *P* |
|---|---|---|---|---|---|
| **Age at injury [0]** | 55 (42–68) | 56 (43–66) | 56 (39–72) | 54 (38–66) | 0.58 |
| **Length of stay (days) [0]** | 122 (64–187) | 90 (49–144) | 141 (80–208) | 205 (161–244) | <0.0001 |
| **SCIM III score, 28 days after admission [14]** | 40 (23–70) | 58 (34–81) | 30 (18–46) | 26 (15–34) | <0.0001 |

*IC, intermittent catheterization; IQR, interquartile range; SCI, spinal cord injury; SCIM, spinal cord independence measure. *In cases with missing data in the first measurement window, neurological status information from the next available examination was used. P values are based on a chi-squared test for categorical variables, or on a Kruskal–Wallis test for continuous variables.*

**Fig. 1** Kaplan–Meier failure curve of time until the first UTI for the study population. SCI, spinal cord injury.




The population Kaplan–Meier curve revealed an elevated risk of first UTI early in rehabilitation (Fig. 1). Kaplan–Meier curves for bladder emptying, categorized SCIM score, and neurological category were statistically different ($P < 0.001$ for all), while categorized age, sex, lesion aetiology, overnight hospitalization, and diabetes were not (Fig. 2). The conditional probability of a UTI over time since diagnosis varied according to AIS category score ($P < 0.001$), with AIS categories A, B and C showing an elevated UTI probability, but not according to lesion level ($P = 0.64$).

Bladder emptying method was analysed using the ISCoS questionnaire data, and 315 cases were available for analysis. A cross-tabulation of bladder emptying methods at 28 days and at discharge showed that bladder emptying method at 28 days was predictive of discharge status, particularly in the self-IC and spontaneous voiding groups ($P < 0.001$ [Table S2]). In the subgroup of patients ($n = 146$) using indwelling catheterization or assisted IC at 28 days after rehabilitation admission, the adjusted odds for self-IC at discharge were elevated in those initially using assisted IC, increased with SCIM self-care subscale score, were elevated in men, and declined with increasing age at injury (Table 2). In a sensitivity analysis using multiple imputation of missing AIS values and bladder emptying at 28 days that included further seven cases (total $n = 151$), results were identical (not shown).

Spontaneous voiding, AIS category D lesion, female sex, and higher SCIM self-care and mobility subscale scores were also associated with lower unadjusted IRs of UTI (Table 3). In the adjusted model including time-updated covariates ($n = 344$), bladder emptying method was identified as an important risk factor for UTIs, with an IRR for indwelling catheter use of 5.97 (95% CI 2.63–13.57), for assisted IC of 6.05 (2.63–13.94) and for self-IC of 5.16 (2.31–11.52) in comparison with individuals who were able to void spontaneously. There were similar IRs of UTI among catheter users (*post hoc* test, $P = 0.82$). Those with AIS category D lesions also had significantly lower rates of UTIs than those with C1–C8 AIS category A, B or C lesions (IRR 2.79 [95% CI 1.25–6.22]) and T1–S5 AIS category A,B or C lesions (IRR 1.25 [95% CI 0.80–1.94]); there was no statistically significant difference between the last two groups. Additionally, IRs were significantly lower among people who had already had a UTI during rehabilitation (IRR 0.48 [95% CI 0.29–0.79]).

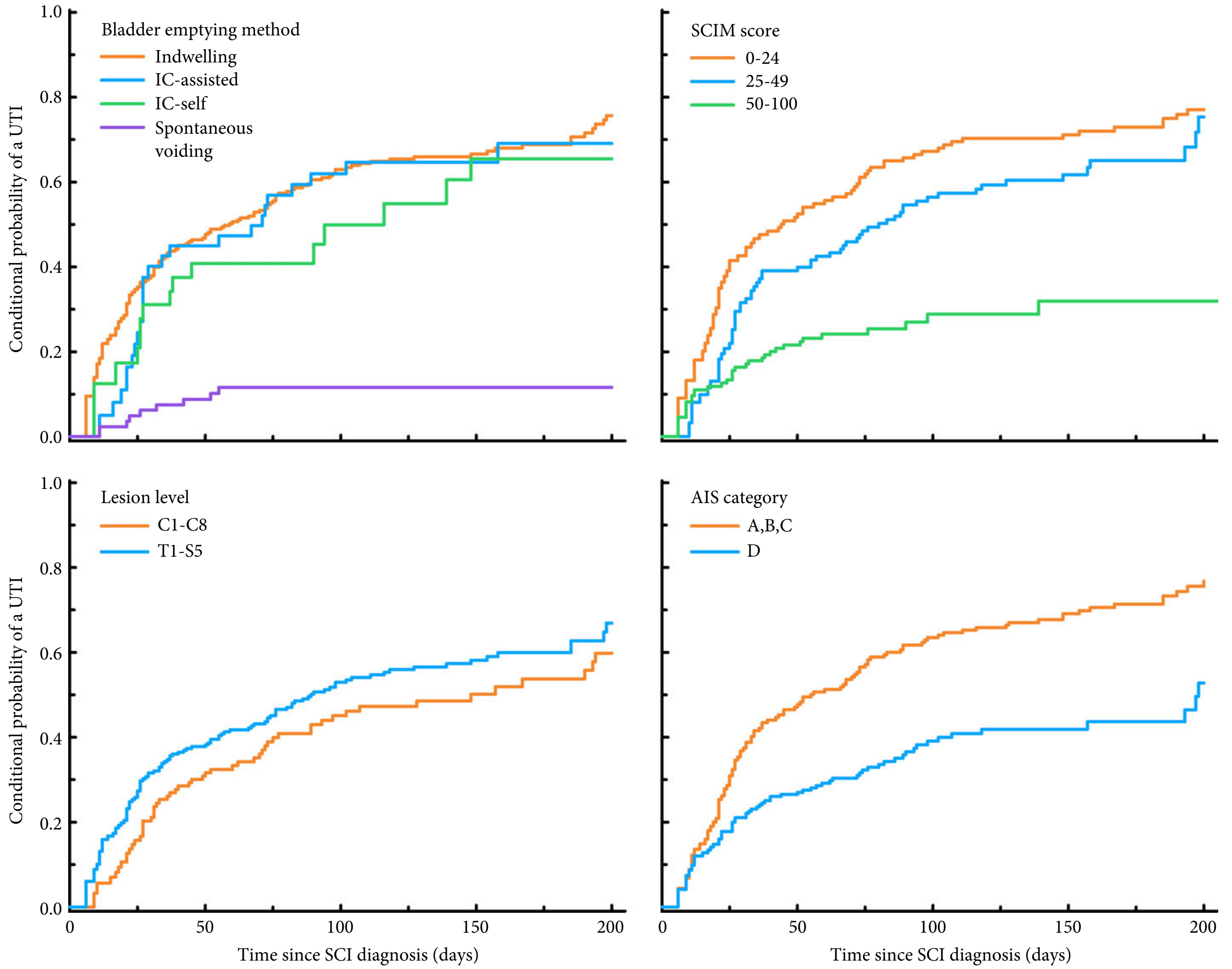
Sensitivity analyses including all suspected UTIs and using multiple imputation, both separately (available on request) and combined (Table S4), were similar to the results from the complete case analysis (i.e. the effect sizes were within the limits of the main analysis).

## Discussion

The present population-based study showed that the use of any method of catheterization as opposed to spontaneous voiding appears to be the main determinant of elevated UTI risk in the context of specialized inpatient SCI rehabilitation in Switzerland. A contemporary time-updated covariate analysis showed that adjusted IRs of UTIs in all groups of catheter users were consistently five to six times higher than those of people who were able to void spontaneously. Determinants of bladder emptying method include age, sex and SCIM self-care subscale score. These results further underline that bladder management plays a central role in moderating UTI risk in patients with SCI.

Contrary to expectations, there was no difference in UTI risk between indwelling catheterization and IC in our population. Clinical guidelines consistently indicate that patients with indwelling catheters are expected to have a significantly higher rate of UTIs than those using IC [2,8,25]. A prospective study which also used time-updated bladder emptying status presented IRs of 2.72 UTIs per 100 person-days among men with indwelling transurethral catheters, vs 0.41 in men using clean IC and 0.34 in women with suprapubic catheters [4]. However, two recent systematic reviews have shown that the evidence base regarding catheterization strategy and UTI risk is inconclusive [1,3]. We confirm that UTI risk was similarly and consistently elevated with use of catheterization, when correlating the risk of UTI to the baseline bladder management status, irrespective of whether other variables were time-updated. Furthermore, a sensitivity analysis showed that these findings were not sensitive to changes in the criteria used for defining a UTI. Notably, unlike other studies, our study was prospective and population-based and

**Fig. 2** Kaplan–Meier failure curves of time until the first UTI for bladder emptying method, spinal cord independence measure (SCIM) score, lesion level, and American Spinal Injury Association Impairment Scale (AIS) category, 28 days after admission to rehabilitation. Curves were truncated at 200 days because of insufficient observations beyond that point. Bladder emptying method, SCIM score, and AIS groups were all significantly different according to a Wilcoxon test (all $P < 0.001$), and lesion level groups were not ($P = 0.64$). IC, intermittent catheterization; SCI, spinal cord injury.




therefore not subjected to the selective measurement of either catheter use or UTI risk. Thus, between-study variation in sampling bias cannot be excluded as an explanation for the contradictory findings.

The crude IR of ~0.55 UTIs per 100 person-days with a cumulative IR of 43%, found in Swiss specialized rehabilitation, is in line with previous reports from similar settings over the past 15 years [1,4]. Studies that reported lower cumulative UTI IRs tended to use more restrictive definitions for UTIs, such as the presence of a fever in addition to a positive bacterial culture or a higher threshold for a positive bacterial culture [1,34,35]. Swiss rehabilitation centres follow the European Association of Urology Guidelines on Neuro-Urology [8]; therefore, bladder management decisions revolve around urodynamic factors, hand function, continence, and patient quality of life [8,27,36]. The systematic variation of catheter use with age, sex, and functional independence accordingly reflects up-to-date and personalized neuro-urological patient management. Yet, best practice catheterization techniques have not changed fundamentally over the last decade [3], which is probably the critical reason that the UTI risk on a population level has stabilized at an elevated rate.

Any type of catheterization should be avoided, if voiding without a catheter can be achieved without jeopardizing patient safety or upper urinary tract function. Furthermore,

**Table 2** Predictors of voiding method at discharge in patients using indwelling or assisted intermittent catheterization as bladder emptying method 28 days after admission.

| Predictor | Adjusted odds ratio (95% CI) | *P* |
|---|---|---|
| **Bladder emptying method, 28 days after admission** | | <0.01 |
| Indwelling – transurethral | ref | |
| Indwelling – suprapubic | 0.30 (0.09–0.97) | |
| IC – assisted | 3.67 (1.11–12.17) | |
| **UTI before first bladder emptying assessment** | | 0.19 |
| No | ref | |
| Yes | 2.05 (0.70–5.98) | |
| **SCIM self-care subscale, 28 days after admission** | 1.25 (1.09–1.44) | <0.01 |
| **SCIM mobility subscale, 28 days after admission** | 0.97 (0.90–1.03) | 0.30 |
| **Age at injury** | 0.95 (0.92–0.99) | <0.01 |
| **Gender** | | <0.01 |
| Female | 0.21 (0.07–0.69) | |
| Male | ref | |
| **Neurological category, 28 days after admission*** | | 0.11 |
| C1–C8 AIS A,B,C | 0.45 (0.10–2.07) | |
| T1–S5 AIS A,B,C | 2.00 (0.67–5.96) | |
| All AIS D | ref | |
| **Lesion aetiology** | | 0.40 |
| Non-traumatic SCI | 0.64 (0.22–1.84) | |
| Traumatic SCI | ref | |
| **Diabetes** | | 0.32 |
| No | ref | |
| Yes | 2.19 (0.47–10.15) | |
| **Time between injury and admission (per 10 days)** | 1.31 (0.89–1.93) | 0.17 |

*IC, intermittent catheterization; SCI, spinal cord injury; SCIM, spinal cord independence measure; *In cases of missing data in the first measurement window, neurological status information from the next available examination is used. Results from a multivariable logistic regression analysis, use of self-IC at discharge is coded to 1, assisted IC, indwelling catheterization, and condom catheterization are coded to 0. Study centre was included in this analysis as a control variable, results not shown.*

awareness that UTI is only one complication of catheter use is essential as there may be important differences in other factors, which justify the use of IC instead of indwelling catheters. Clinicians therefore must not only base their decisions regarding method of bladder management on the current evidence, but also need to take urodynamic results into consideration, as urodynamics are the most important investigation for predicting upper urinary tract damage and monitoring treatment [37–39].

A strength of the present study is that it is population-based and thus representative of urological management and UTI risk in Swiss specialized rehabilitation centres; however, we acknowledge that the SwiSCI inception cohort is subject to moderate under-representation with regard to older people and those with a higher comorbidity load (Cumulative Illness Rating Scale score) [40]. Contemporary modelling techniques were employed that facilitated an unbiased assessment of the association between UTI risk and the predictor variables over the time course of specialized rehabilitation. Yet, the panel data study design with a fixed updating schedule provided limited granularity to fully capture the dynamics of changes in SCIM score and bladder emptying status. Additionally, the inclusion of a time-updated indicator of previous UTI during specialized rehabilitation as a predictor variable accounted for confounding by previous UTIs. It was not possible, however, to determine whether the reduction in UTIs among the group that had already experienced one had a biological cause (adaptive immunity), or resulted from an identification problem (diagnosis based on a previous pattern), or was a combination of these and potentially other factors.

A further strength of the present study was the strategic use of sensitivity analyses to evaluate the robustness of results in the face of uncertainty regarding UTI definition, missing data, and handling of time-updated information. Yet, we acknowledge that some of the sequential UTIs may represent single infection events as the effectiveness of treatment of the initial UTI was not systematically confirmed with a sterile repeat urine culture. We also acknowledge, given the evidence suggesting that suprapubic indwelling catheters are superior to transurethral indwelling catheters with regard to UTI risk [1,3], that use of data from the SCIM bladder item did not allow discrimination between the two catheter types in the longitudinal analysis of UTI risk. Finally, considering that bladder management decisions are patient-tailored and influenced by many factors such as evolution of bladder function, manual dexterity, cognitive function, general health condition and comorbidities, it is not possible in the present study to draw conclusions on bladder management changes made specifically because of UTIs.

In conclusion, in the Swiss specialized inpatient SCI rehabilitation setting, bladder emptying method is the main relevant risk factor for UTIs. Although the present study showed that UTI risk with indwelling catheterization was similar to that in IC users, UTIs are only a single outcome. Bladder management decisions should of course incorporate other considerations, such as protection of upper urinary tract function [27], bladder stone prevention [3,41,42], and quality of life [8,43,44]. Considering that people who void spontaneously have the lowest IRs for UTI, promotion of spontaneous micturition (if it can be achieved without jeopardizing patient safety or upper urinary tract function) should be a priority. Furthermore, research into alternative methods of reducing voiding dysfunction, for example, through neuromodulative procedures such as transcutaneous electrical nerve stimulation [45], tibial nerve stimulation [46], and sacral neuromodulation [47], could provide clinicians with additional tools with which to reduce UTIs in patients with SCI.

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**Table 3** Crude UTI incidence rate, unadjusted and fully adjusted UTI incidence rate ratios.

| Predictor | Crude IR per 100 person-days (95% CI) | Unadjusted IRR (95% CI) | P | Adjusted IRR (95% CI) | P |
|---|---|---|---|---|---|
| **Bladder emptying method** | | | <0.0001 | | <0.001 |
| Indwelling catheter | 0.62 (0.51–0.76) | 5.96 (3.17–11.20) | | 5.97 (2.63–13.57) | |
| IC – assisted | 0.68 (0.52–0.90) | 6.16 (3.04–12.50) | | 6.05 (2.63–13.94) | |
| IC – self | 0.53 (0.39–0.71) | 4.50 (2.25–9.01) | | 5.16 (2.31–11.52) | |
| Spontaneous voiding | 0.13 (0.07–0.22) | ref | | ref | |
| **SCIM self-care subscale** | na | 0.95 (0.93–0.97) | <0.001 | 1.02 (0.96–1.08) | 0.56 |
| **SCIM mobility subscale** | na | 0.96 (0.94–0.99) | <0.01 | 1.00 (0.96–1.04) | 0.88 |
| **Age at injury – 10 year increase** | na | 0.98 (0.90–1.07) | 0.72 | 1.03 (0.90–1.17) | 0.70 |
| **Gender** | | | 0.033 | | 0.27 |
| Female | 0.41 (0.31–0.54) | 0.67 (0.47–0.97) | | 0.76 (0.47–1.23) | |
| Male | 0.59 (0.51–0.68) | ref | | ref | |
| **Neurological category** | | | <0.0001 | | 0.042 |
| C1–C8 AIS A,B,C | 0.87 (0.69–1.10) | 3.32 (2.19–5.02) | | 2.79 (1.25–6.22) | |
| T1–S5 AIS A,B,C | 0.68 (0.55–0.83) | 2.25 (1.56–3.25) | | 1.25 (0.80–1.94) | |
| All AIS D | 0.35 (0.28–0.43) | ref | | ref | |
| **Lesion aetiology** | | | 0.10 | | 0.54 |
| Non-traumatic SCI | 0.46 (0.36–0.58) | 0.75 (0.53–1.06) | | 1.17 (0.71–1.91) | |
| Traumatic SCI | 0.58 (0.50–0.68) | ref | | ref | |
| **Overnight hospitalization** | | | 0.83 | | 0.26 |
| No | 0.54 (0.47–0.62) | ref | | ref | |
| Yes | 0.53 (0.39–0.72) | 1.05 (0.69–1.59) | | 0.74 (0.43–1.25) | |
| **Diabetes** | | | 0.16 | | 0.21 |
| No | 0.56 (0.49–0.64) | ref | | ref | |
| Yes | 0.38 (0.23–0.62) | 0.65 (0.35–1.18) | | 0.59 (0.26–1.35) | |
| **Time in acute care before SCI diagnosis** | | | 0.86 | | 0.51 |
| <1 week | 0.54 (0.48–0.61) | ref | | ref | |
| >1 week | 0.56 (0.25–1.25) | 1.07 (0.51–2.25) | | 1.38 (0.53–3.59) | |
| **UTI reported during acute care** | | | 0.31 | | 0.94 |
| No | 0.55 (0.48–0.62) | ref | | ref | |
| Yes | 0.45 (0.24–0.83) | 0.75 (0.44–1.30) | | 0.97 (0.42–2.21) | |
| **UTI during rehabilitation** | | | <0.01 | | <0.01 |
| No previous UTI | 0.53 (0.45–0.63) | ref | | ref | |
| Previous UTI | 0.55 (0.45–0.68) | 0.47 (0.27–0.81) | | 0.48 (0.29–0.79) | |
| **Time until rehabilitation admission – per 10 days** | na | 0.93 (0.85–1.02) | 0.14 | 0.89 (0.78–1.02) | 0.08 |

*IC, intermittent catheterization; IR, incidence rate; IRR, incidence rate ratio; SCI, spinal cord injury; SCIM, spinal cord independence measure. Adjusted and unadjusted incidence rate ratios are from negative binomial regression analyses. Study centre was included in this analysis as a control variable, results not shown. Complete case analysis, n = 344.*

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## Conflict of Interest

None declared.

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Abbreviations: AIS, American Spinal Injury Association Impairment Scale; IC, intermittent catheterization; IR, incidence rate; IRR, incidence rate ratio; ISCoS, International Spinal Cord Society; SCIM, spinal cord independence measure; SCI, spinal cord injury; SwiSCI, Swiss Spinal Cord Injury Cohort Study.

## Supporting Information

Additional Supporting Information may be found in the online version of this article:

**Table S1.** Summary of missing data in time-updated covariates.
**Table S2.** Cross-tabulation of bladder emptying methods at discharge and 28 days after admission.
**Table S3.** UTI signs and symptoms.
**Table S4.** Sensitivity analysis of Table 3.

 