

**Study Protocol**  
**Patient Reported Outcomes for Bladder Management Strategies in young adults with spina bifida**

**(Adult Bladder and quality of Life Evaluation in Spina Bifida [ABLE-SB])**

*Cross-sectional, multi-center, questionnaire-based pelvic centric/bladder-bowel functional assessment of young people living with spina bifida.*

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## **Lay summary**

Spina bifida (SB) is a birth defect that affects the spine, often causing paralysis in the legs and problems with bladder and bowel control. Managing these bladder issues is important, but different methods, like using a catheter or surgery, can impact a person's quality of life. This study looks at how different bladder management methods affect the quality of life for young people with SB. Researchers will ask people with SB to complete a survey about how they manage their bladder and how it impacts their daily lives. The main goal is to find out if certain bladder management methods are associated with a better quality of life. This information could help doctors make better treatment decisions and counsel young people living with SB.

## **Background**

Spina bifida is a congenital defect of the spine where some of the spinal cord and its covering (meninges) are exposed through a gap in the lower back or sacrum; this often results in paralysis of the lower limbs. The majority of spina bifida (SB) patients also have pelvic floor dysfunction (bladder, bowel, prolapse, sexual function) because of neurologic damage to this portion of the spinal nerves, and this increases the risk of their long-term morbidity.<sup>1</sup> These problems place a substantial burden on patients' physical health and quality of life (QoL). Serious urological complications, such as urosepsis, skin breakdown, and renal failure, can occur in this patient population due to bladder dysfunction.<sup>2</sup> Approximately 50% of young adults with SB have renal dysfunction<sup>3</sup>, 50% have urinary incontinence<sup>4</sup>, and they are nine times more likely to present with urinary tract infections<sup>5</sup>. The "gold standard" bladder management strategy when a person with SB is unable to void spontaneously is to perform clean intermittent catheterization (CIC). Alternatives to CIC include spontaneous voiding (if possible), incontinence products, an indwelling catheter (IDC), or reconstructive surgery (to create a urinary diversion or to enable CIC). However, IDC and surgery have increased risks of specific complications, including the risk of bladder cancer, urethral damage, urinary infections, and surgical morbidity.<sup>6</sup> People with SB usually discuss bladder management options with their urologist, however they may prioritize a variety of factors around bladder management that directly affect their QOL, and these may not be as apparent to urologists. This is further complicated when patients reach adolescence and young adulthood; at this age they transition from pediatric to adult care providers, all while transitioning in other areas of their life (such as increasing responsibility, cognitive growth, and a wish for more independence). These factors may all impact thoughts about bladder management. Few studies have addressed QoL in relation to different bladder/bowel management methods in this SB age group, and most have not considered things like health literacy and cognitive function.

## Objective

To conduct a cross-sectional, multi-center, questionnaire-based pelvic centric/bladder-bowel functional assessment of young people living with spina bifida, with a primary analysis goal of examining factors that are related to different methods of bladder management (indwelling catheter, urologic reconstruction, CIC without reconstruction, or spontaneous voiding/incontinence).

## Study Design

This study is a multi-institutional cross-sectional study consisting of patient questionnaires completed at a single time point.

## Study Location

The primary study location is: Western University. Additional sites may also participate. Institutional review board approval will be obtained from each study site prior to recruitment.

## Study Population and Recruitment

Inclusion and exclusion criteria are as follows:

Inclusion criteria	<ol style="list-style-type: none"><li>1. Diagnosis of SB</li><li>2. Age <math>\geq 13</math> years of age</li><li>3. Able to effectively communicate in English or Spanish</li><li>4. Willing to provide informed consent for participation and answer a set of questionnaires</li></ol>
Exclusion criteria	<ol style="list-style-type: none"><li>1. Reconstructive surgery or urinary diversion in the last 3 months</li><li>2. Hospital admission in the last 1 month</li><li>3. Inconsistent or newly changed (within the last month) method of bladder management</li></ol>

While the protocol allows for centers to recruit in Spanish, and recruit the age group of 13-18, each center can choose whether or not it is appropriate to include these populations in their individual ethics applications based on their practice patterns.

## Study procedures

Participating centers will recruit patients from regular clinical care encounters. They will identify people that meet the relevant inclusion/exclusion criteria and ask them if they are interested in hearing more about the study. The initial identification of participants will be done by the study physician (or other clinical staff within the circle of care). The potential participant will then have an opportunity to hear about the study from the research staff at that center. The study information will be reviewed with the participant, and they will be allowed as much time as they wish to consider participation. If they are agreeable to participating in the study, the

research staff will obtain a signature on the informed consent form (not necessary if IRB provides a consent waiver), and will then go through the data collection and questionnaires. Some participants may be willing to do this during the same visit, and some may wish to reach out at a later timepoint if they wish to participate. The participant will be asked several questions about their life, socioeconomic situation, some general SB questions, and what they do for general functional, bladder and bowel management by the research assistant. The participant will then complete several questionnaires (neurogenic bladder symptom score-short form<sup>7</sup>, the quality of life assessment in spina bifida (with either the teenage or adult version used based on the patients age)<sup>8</sup>, the BRIEF health literacy assessment<sup>9</sup>, a newly developed sexual health function questionnaire, and the cognitive function portion of the Neuro-QOL<sup>10</sup>). The answers will be recorded either with a paper-based version of the redcap database (to be later entered into redcap), or directly entered into the redcap database. Optional information about previous tests for renal function, renal anatomy, and bladder function (urodynamics-a type of bladder test) may be entered by the study physician. The full data collection document from redcap is shown in appendix 1.

We anticipate recruiting patients over approximately 12-18 months, depending on enrollment, and the speed of study opening across the different sites.

### **Data handling**

We will use the secure Lawson Redcap system for all data collection. As an added safeguard, we will collect minimal personal health information (limited to sex, gender, age, race, and Ethnicity, all collected in order to describe our study population; postal code/zip code will be collected so that we can calculate socioeconomic status based on area of residence) in this dataset. Each site will keep a paper-based key linking study ID, and participant name. This will be kept in a locked file cabinet in the hospital office of the relevant site. Paper-based informed consent forms will be kept in a locked file cabinet in the hospital office of the relevant site.

### **Data Analysis**

We will consider bladder management the primary exposure. The question “Primary Bladder management-what best describes how you usually manage your bladder?” will be used to classify patients into one of the four following groups:

Answer value	Answer text	Classification for analysis
1	voiding into toilet	Voiding/incontinent
2	voiding most of my urine into diapers/pads/condom catheter	Voiding/incontinent
3	Voiding and CIC	CIC
4	CIC	CIC

5	Indwelling catheter-suprapubic/in channel	Indwelling catheter
6	indwelling catheter-urethral	Indwelling catheter
7	incontinent urinary diversion	Diversion
8	continent urinary diversion	Diversion
9	Other	*

\*Patients will be classified into one of the 4 above groups based on a review by two study investigators based on the free text answer to the “other” option.

Demographics will be summarized overall and by bladder management category. Continuous variables will be reported as medians and interquartile ranges. Categorical variables will be reported as frequencies and percentages.

We will consider the quality of life assessment in spina bifida (QALAS) questionnaire bowel and bladder domain score the primary outcome<sup>8</sup>. It is a continuous measure scored from 0-100, with a higher score suggesting a worse SB related QOL. In prior SB populations, it has a mean of 62 (standard deviation 25). The primary exposure is bladder management category. The association between bladder management category and QALAS score will be evaluated using multivariable linear regression, with bladder management treated as a categorical variable. Potential confounders such as age, sex, ambulatory status, cognitive function, prior urinary reconstruction, and bowel management will be included in the adjusted analysis

### Sample size

We will power our study to evaluate differences in the QALAS bowel and bladder QOL score between the primary bladder management categories: voiding/incontinent, CIC, indwelling catheter, and diversion. Sample size was estimated using a one-way fixed-effects ANOVA omnibus test (G\*Power version 3.1.9.7<sup>22</sup>).

$H_0: \mu_{\text{voiding}} = \mu_{\text{CIC}} = \mu_{\text{indwelling catheter}} = \mu_{\text{diversion}}$

$H_A$ : At least one group mean differs

We set the alpha to 0.05, and the power to 0.95. We estimated group means of 55, 65, 40, and 65 in the four respective bladder management groups, a shared standard deviation of 25, and a group weighting of 5:5:2:1 based on the expected frequency of those 4 groups in clinical practice. The weighted mean is 59.2, the between group standard deviation is 7.3, and the effect size  $f = 7.3/25 = 0.29$ . Our final calculated sample size is 208 participants. We increased our target sample size to 300 participants to account for uncertainty in group distributions, missing variables, and covariate adjustment in the planned multivariable models.

**Adverse events**

As this is a survey/questionnaire study, we do not anticipate any serious adverse events. As with any study, questions may trigger negative reactions/feelings in the participants. If this happens, the study investigator will be informed, and will assess the need for intervention based on regular clinical care standards. There is a small chance of a data breach, however this is mitigated with the use of a secure online platform, and the minimally personal health information that is collected as part of the study.

## References

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