A Cost-Effectiveness Analysis of Bladder Management Strategies in Neurogenic Lower Urinary Tract Dysfunction after Spinal Cord Injury: A Publicly Funded Health Care Perspective

Samer DA Shamout

Department of Experimental Surgery

McGill University, Montreal

Quebec, Canada

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Dedication

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Table of Contents

ACKNOWLEDGMENTS **2**

DEDICATION **3**

TABLE OF CONTENTS **4**

LIST OF FIGURES **6**

LIST OF TABLES **6**

PREFACE AND CONTRIBUTION OF AUTHORS **7**

ABSTRACT **8**

RÉSUMÉ **10**

ABBREVIATIONS **13**

CHAPTER 1: INTRODUCTION AND LITERATURE REVIEW **14**

1.1 Overview of Spinal Cord Injury (SCI) 14
1.2 Pathophysiology of Spinal Cord Injury 14
1.3 Epidemiology and Demographics 15
1.3.1 Incidence and prevalence of SCI in Canada *15*
1.3.2 The global map for spinal cord injury epidemiology *15*
1.4 Etiology 16
1.5 Neurologic Level at Discharge 17
1.6 Overview on Clinical Classification 17
1.7 Age at Injury 18
1.8 SCI is Gender-specific 18
1.9 Life expectancy and mortality 18

CHAPTER 2: NEUROGENIC LOWER URINARY TRACT DYSFUNCTION (NLUTD) **21**

2.1 Introduction 21
2.2 Patterns of NLUTD and classification system 22
2.3 Genitourinary sequelae of NLUTD 23
2.3.1 UTIs *24*
2.3.2 Risk of upper urinary tract deterioration *25*
2.3.3 Urolithiasis *25*
2.3.4 Urethral Complications *26*
2.4 Management of NLUTD 27
2.4.1 Assisted bladder drainage *27*
2.4.2 Indwelling catheterization (urethral or suprapubic) *27*
2.4.3 Intermittent catheterization *28*

CHAPTER 3: ECONOMIC BURDEN OF SCI AND ASSOCIATED BLADDER MANAGEMENT **30**

3.1 Economic burden of SCI in Canada 30
3.2 Costs of secondary complications 31
3.3 Health technology assessment (Comparative Economic Studies) 32

CHAPTER 4: RESEARCH QUESTIONS AND STUDY RATIONALE **34**

4.1 Research questions 34
4.2 Study rationale 35

CHAPTER 5: HYPOTHESIS AND OBJECTIVES **36**

5.1 Hypothesis 36

5.2 Objectives 36
5.1.1 Objective 1...*36*
5.1.2 Objective 2...*36*
5.1.2 Objective 3...*37*

CHAPTER 6: A COST-EFFECTIVENESS ANALYSIS OF BLADDER MANAGEMENT STRATEGIES IN NLUTD AFTER SCI: A PUBLICLY FUNDED HEALTH CARE PERSPECTIVE 38

6.1 Abstract 38
6.2 Introduction...40
6.3 Materials and Methods 42
6.3.1 Model design and population of patients *42*
6.3.2 Model structure...*42*
6.3.3 Definition of health states *43*
6.3.4 Data input *44*
6.3.5 Utility values...*47*
6.3.6 Costs assignments..*47*
6.3.7 Model output *49*
6.3.8 Sensitivity analysis *49*
6.4 Results..50
6.5 Discussion 52
6.6 Conclusions 57
6.7 Tables and Figures...59

CHAPTER 7: OVERALL DISCUSSION 71

7.1 Contribution to the literature 71
7.2 Summary of the major findings 73
7.3 Overall limitations and strength 75
7.4 Future research 77
7.5 Conclusions 78

REFERENCES.. 79

List of Figures

Chapter 1:

Figure 1.1 Patterns of NLUTD based on the level of neurologic insult……………………….… 19

Chapter 2:

Figure 2.1 International standards for neurological classification of SCI …………………….…43

Chapter 6:

Figure 6.1 Markov model with four different health states.……………………………….…... 44

Figure 6.2a Tornado diagram, One-Way sensitivity analyses: CIC Versus UC…………...….45

Figure 6.2b Tornado diagram, One-Way sensitivity analyses: CIC Versus SPC…………..……45

Figure 6.3a Probabilistic analysis. Scatterplot of the 1000 (ICUR): CIC Versus UC ……….…47

Figure 6.3b Probabilistic analysis. Scatterplot of the 1000 (ICUR): CIC Versus SPC ………...47

List of Tables

Chapter 6:

Table 6.1 Characteristic of the hypothetical patient population and assumptions.………... 44

Table 6.2 Key input parameters to the model………………………………..…………...….45

Table 6.3 Health utility associated with key health states……………………..……….……45

Table 6.4 Main cost inputs ……………………………………………………………….….47

Table 6.5 Base-case scenario (lifetime horizon) ………………………………...………...47

Table 6.5 Deterministic sensitivity analysis……………………………………...………..47

Preface and contribution of authors

The order of the contributors is in descending order of participation. This is a manuscript-based thesis which is drafted, prepared by me and revised by my supervisor Dr. Lysanne Campeau and co-supervisor Dr. Alice Dragomir. Abstract French translation was performed by Nawar Touma. The present thesis consists of 7 chapters. The first chapter is introduction and literature review of relevant topics done completely by me. The contribution to other chapters is as follows:

Chapter 2: This chapter includes literature that has recently been published on NLUTD and related bladder management strategies. The conception of this chapter was proposed by Lysanne Campeau. Text writing by Samer Shamout.

Chapter 3: This chapter summarizes available evidence with regard to economic burden of SCI and health technology assessment. The conception of this chapter was proposed by Alice Dragomir. Text writing by Samer Shamout.

Chapter 4 and 5: Both chapters present data related to study design, objectives and rationale. Along with Drs. Lysanne Campeau and Alice Dragomir I contributed to the conception of the study. Drafting was done by Samer Shamout.

Chapter 6: This chapter presents a manuscript which includes detailed analysis, interpretation and discussion of study results. Along with Drs. Lysanne Campeau, Alice Dragomir and Sara Nazha, I contributed to the conception of the study and acquisition of the results presented here. The interpretation of the results in this chapter are entirely my own. Markov model analysis done by Alice Dragomir and Sara Nazha. All tables and figures in the manuscript prepared by Samer Shamout and Sara Nazha. Text writing by Samer Shamout.

Chapter 7: Discussion and conclusions by Samer Shamout

Abstract

Neurogenic lower urinary tract dysfunction (NLUTD) is a prevalent unavoidable lifelong complication, commonly observed in patients as early as the first year after spinal cord injury (SCI). Management of neurogenic bladder dysfunction represents an incredible economic burden on the health care system and quality of life. Various approaches have been described to manage impaired bladder emptying in SCI population including clean intermittent catheterization (CIC), indwelling urethral catheters (UC), suprapubic catheterization (SPC) along with pharmacotherapy. Intermittent catheterization is accepted worldwide as a standard of care for NLUTD related to SCI. Indwelling urethral or suprapubic catheters have been frequently used in SCI patients where self-catheterization is difficult, impossible or inconvenient. Reviews have shown variability in terms of urological complications, quality of life and compliance rates with the use of CIC, UC or SPC. Despite the complications related to chronic use of indwelling catheters, many SCI individuals switch to these catheters over time, which adds more economical burden on the health care system.[1,2] Current evidence is limited, and the clinical impact of the different bladder management strategies has been debated. Thus, we performed a cost-utility analysis with a lifetime perspective of intermittent catheterization compared to indwelling urethral or suprapubic catheters in an adult SCI population from a Canadian publicly funded health care system perspective. The work in this study was divided into two parts:

(1) A comprehensive literature search that involved PubMed/Medline, Embase and Cochrane Library databases. After screening potentially relevant studies and publications focusing on SCI patients using different bladder management approaches, we created our database including all relevant details which were utilized in the development of the economic evaluation model.

(2) A Markov model with Monte Carlo simulation was developed with a cycle length of one year and lifetime horizon to estimate the incremental cost per quality-adjusted life years (QALYs). We conducted this analysis from the perspective of the Canadian provincial public healthcare system. Transition probabilities, efficacy data, and utility values were derived from published literature and expert opinion. Costs were obtained from provincial health care system and hospital data in 2019 Canadian Dollars. Probabilistic and one-way deterministic sensitivity analyses were performed to evaluate the robustness of the model.

Our results showed that CIC uncoated catheters (single-use) had a lifetime mean total cost of $ 29,161 for 20.91 QALYs. While UC had a mean total cost of $31,657 for 18.95 QALYs, SPC mean cost was $ 29,491 for 19.14 QALYs. The model predicted that a 40-year-old patient with SCI would gain an additional 1.72 QALYs if CIC were utilized instead of SPC at an incremental cost savings of $330. CIC confer 1.96 QALYs and 3 discounted life-years gained compared to UC at an incremental cost savings of $2496.

This economic analysis demonstrates that CIC is the dominant treatment strategy (offering increased benefits at lower cost) to manage SCI patients with NLUTD compared to indwelling urethral or suprapubic catheters over lifetime horizon, from a Canadian publicly funded health care system perspective. Despite high ongoing cost of using hydrophilic coated intermittent catheters; it was perceived as a cost-effective technology. Given these findings, we offer a new insights and broader evaluation of economic burden over the public health care system that, with further research, may be of value to health care decision making and government advocacy.

Résumé

La dysfonction neurogène des voies urinaires inférieures (NLUTD), couramment appelée « vessie neurogène », est une complication inévitable observée principalement au cours de la première année suivant une blessure à la moelle épinière. La gestion de la vessie neurogène affecte la qualité de vie et représente un fardeau financier au système de santé. Plusieurs approches ont été décrites pour gérer la vidange altérée chez les blessés médullaires, notamment les cathétérismes intermittent (CIC), les cathéters à demeure urétraux (UC) et sus-pubien (SPC), ainsi que la pharmacothérapie. Le cathétérisme intermittent est accepté globalement comme étant la norme pour gérer la vessie neurogène secondaire à une blessure médullaire. Les cathéters à demeure urétraux et sus-pubien sont aussi fréquemment utilisés chez ces patients lorsque l'auto-cathétérisme est inconvénient, voire parfois impossible. Certaines revues ont montré une variabilité des complications urologiques, de la qualité de vie et de l'observance des patients avec l'usage des cathétérismes intermittent, à demeure et sus-pubien. Malgré les complications observées avec l'usage chronique du cathétérisme à demeure, plusieurs blessés médullaires optent pour cette stratégie au cours de leurs vies, ce qui contribue au fardeau financier déjà existant sur le système de santé public. Étant donnée les connaissances actuelles limitées, l'impact clinique des différentes stratégies de gestion de la vessie reste à établir. C'est pourquoi nous avons effectué une analyse de coût-utilité comparant le cathétérisme intermittent aux cathéters à demeure urétraux et sus-pubien chez une population canadienne adulte de blessés médullaires en adoptant la perspective du ministère de la santé provincial. Le travail démontré dans cette étude est divisé en deux parties :

(1) Une revue compréhensive de la littérature est effectuée à partir des bases de données PubMed/Medline, Embase et Cochrane. Suite à la sélection d'études et de publications axées sur la gestion de la vessie neurogène chez les blessés médullaires, nous avons créé notre banque de données incluant tous les détails pertinents afin de développer le modèle économique.

(2) Une simulation Monte Carlo appliquée au modèle de Markov a été générée avec une durée de cycle d'un an et un horizon temporel d'une vie entière pour estimer les coûts supplémentaires par année de vie pondérée par la qualité (QALY). Nous avons mené cette analyse avec une perspective du système de santé provincial. Les probabilités de transition, les données d'efficacité et les valeurs d'utilité ont été tirées de la littérature existante et des opinions d'experts. Les coûts, en dollars canadiens (2019), ont été obtenus à partir de données du système de santé provincial et des registres d'hôpitaux. Des analyses de sensibilités probabiliste et déterministe à un seul facteur ont été produites afin d'évaluer la stabilité de nos résultats et la qualité du model Markov.

Nos résultats montrent que le cathétérisme intermittent a un coût total moyen de $29 161 pour 20,91 QALY. Alors que le cathéter urétral à demeure a un coût total moyen de $31 657 pour 18,95 QALY, le coût total moyen attribué au cathéter sus-pubien est de $29 491 pour 19,14 QALY. Le modèle prédit qu'un blessé médullaire de 40 ans bénéficiera de 1,72 QALY additionnel si le cathétérisme intermittent est employé au lieu du sus-pubien avec une économie de coûts supplémentaires de $330. Le cathétérisme intermittent confère 1,96 QALY et 3 années de vie gagnées actualisées comparé au cathéter urétral à demeure avec une économie de $2496.

Cette analyse économique démontre que le cathétérisme intermittent est une stratégie dominante pour gérer la vessie neurogène de ces patients. Autrement dit, c'est celle qui confère le plus de bénéfices observés avec le moindre coût, comparativement aux cathéters à demeure urétraux ou sus-pubiens dans l'horizon temporel de la vie entière en adoptant la perspective d'un ministère de la santé provincial. Malgré les coûts élevés associés à l'usage des cathéters intermittents enduits d'un revêtement hydrophile, ils sont perçus comme une technologie rentable. Compte tenu de ces résultats, on offre ainsi un nouvel aperçu et une évaluation plus large du fardeau économique sur le système de santé public pouvant être utile à la prise de décisions et à la promotion des soins de santé auprès du gouvernement.

Abbreviations

SCI: Spinal Cord Injury
RHSCIR: Rick Hansen Spinal Cord Injury Registry
tSCI: Traumatic Spinal Cord Injury
ntSCI: Non-traumatic Spinal Cord Injury
ASIA: American Spinal Injury Association Impairment Scale
UTI: Urinary Tract Infection
UTIs: Urinary Tract Infections
NLUTD: Neurogenic Lower Urinary Tract Dysfunction
LUTS: Lower Urinary Tract Symptoms
LUTD: Lower Urinary Tract Dysfunction
NDO: Neurogenic Detrusor Overactivity
DSD: Detrusor-Sphincter Dyssynergia
VUR: Vesico-Ureteric Reflux
CIC: Clean Intermittent Catheterization
SPC: Suprapubic Catheterization
UTT: Upper Urinary Tract
QoL: Quality of Life
CKD: Chronic Kidney Disease
IC: Intermittent Catheterization
UC: Urethral Catheterization
PU: Pressure Ulcers
CAD: Canadian Dollars
RCTs: Randomized Controlled Trials
LYG: Life Year Gained
QALYs: Quality-Adjusted Life Years
RAMQ: Régie de l'assurance maladie du Québec
MSSS: Ministere de la Sante et des Services Sociaux
ICUR: Incremental Cost Utility Ratio
ICs: Intermittent Catheters
CUA: Canadian Urology Association
HRQoL: Health-Related Quality Of Life
PVC-Catheter: Polyvinyl Chloride Catheter

Chapter 1: Introduction and Literature review

1.1 Overview of Spinal Cord Injury (SCI)

Spinal cord injury (SCI) is defined as an insult to the spinal cord with subsequent neuronal dysfunction, resulting in temporary or permanent impairment in motor, sensory, or autonomic function. Impairment and disability occur due to primary damage to neural elements and vasculature, accompanied by secondary physiological insults including a complex cascade of cellular and systemic destructive events that contribute to ongoing tissue damage and death of neurons and glial cells. [3]

1.2 Pathophysiology of Spinal Cord Injury

When referring to pathophysiology of SCI, there are two complex phases, that give rise to a set of long-lasting and irreversible deficits. Primary injury refers to the initial traumatic forces delivered to the spinal cord due to laceration/ transection, compression, distraction and contusion. This mechanical insult results in damage to the cord architecture, disruption of the vascular structures and interrupt the descending and ascending pathways to the spinal cord, which contributed to hemorrhage and secondary ischemia. Consequently, an interdependent cascade of cellular and molecular changes that occur from hours to weeks and may persist to years after injury, termed secondary injury. It is postulated that hypotension, hypoxia, vasospasm and loss of autoregulation results in progressive tissue damage through sequence of pathological events such as inflammation, oxidative cellular stress, excitotoxicity, lipid peroxidation, all of which can induce apoptosis and cell death. [4]

1.3 Epidemiology and Demographics

1.3.1 Incidence and prevalence of SCI in Canada

The estimated number of people with SCI living in Canada is approximately 86,000 persons, with 4300 new cases of SCI occur each year based on national data from Rick Hansen Spinal Cord Injury Registry (RHSCIR). Of this total, an estimated 51 percent (43,974 cases) are the result of traumatic SCI and 49 percent (41,581 cases) as a consequence of diseases and non-traumatic causes. With respect to neurologic category at discharge, 44% of participants live with tetraplegia and 56% had paraplegia.[5] Neurologically incomplete tetraplegia ranked first among young and old age groups.[6] Based on the best available estimates, the results indicate trends towards increasing cases of SCI in Canada over the next few decades. The estimated incidence rate is projected to reach 6,400 new cases in 2030, and prevalence rising from 86,000 SCI patient in 2010 to 121,000 persons in 2030, with the greatest increase would be in the proportion of SCIs that resulted from non-traumatic etiology.[5] One may speculate that the aging of the Canadian population amplifies the number of SCI older age groups and hence the etiology of these injuries due to falls in the older population.

1.3.2 The global map for spinal cord injury epidemiology

Spinal cord injury is a global epidemic. Based on international epidemiological studies, SCI affects over 6 million people around the world.[7] The global estimate of SCI incidence varies from 10.4 to 83 cases per million population per year.[8,9] Over 17,000 people being injured or diagnosed with a SCI each year in the United States.[10,11] Regional data are available from North America (40 per million), Western Europe (15 per million) and Australia (16 per million). Among studies conducted in developing countries, the estimated incidence rates ranged from 18.0 to 61.6 per million inhabitants a year.[8,12] Most published reports on SCI do not include individuals who die before hospital arrival. Most of the previous studies consistently indicated trends towards increasing incidence of SCI over the last decades.

A global-prevalence rate is estimated to range from 236 to 1,298 per million population.[13,14] The National Spinal Cord Injury Database in in the United States estimated around 291,000 people living with SCI, with a range of 249,000 to 363,000 persons.[11,15] In Europe, the crude prevalence of SCI was extrapolated to be 280 per million. Australian Spinal Cord Injury Registry quantified a prevalence of 681 per million. [8,13]

These figures suggest a relatively broad variation of incidence and prevalence of SCI among different geographical areas. Those differences are partially explained by methodological discrepancies or limitations related to data collection and quality of published reports. Furthermore, diversity of healthcare systems, general level of health care, life expectancy and public health practices in a geographical region will in turn affect survival rate of SCI and hence its incidence rates and prevalence.

1.4 Etiology

On a global level, motor vehicle accidents are responsible for approximately 50% of spinal cord injuries, followed by falls (19.6%), assault (17.8%), sports (10.7%), and other reasons (6.3%). [16] In Canada, the majority of traumatic SCIs (tSCI) are caused by falls, typically 50% of all injuries. Most falls-related injury occurs in the older population. Younger victims are usually more vulnerable to sports and transportation injuries. Relevant to Canadian population statistics, the mean age of patients sustaining SCI from falls was 63 years, whereas for road traffic accidents and recreational causes the average age reported at 43 and 41 years respectively.[6]

The mechanism of injury in tSCI includes bone fractures, dislocations, ligaments tear and contusions secondary to an external physical impact affecting the vertebral column. Non-traumatic SCI (ntSCI) often associated with disease processes such as infectious conditions, tumours, vascular disorders, multiple sclerosis and congenital and developmental disorders that involve the spinal cord. [17]

1.5 Neurologic Level at Discharge

In general, the extent and level of injury determines the severity and long-term outcomes of SCI. Tetraplegia and complete injuries are frequently observed following SCI.[16] The most common neurologic sequelae following tSCI in Canada was incomplete tetraplegia. Of individuals with complete injuries the reported incidence of tetraplegia and paraplegia was comparable. [6] Overall, the prognosis is much better for patients with incomplete injuries. [18] Classification of the level and the severity of the SCI appears to be of utmost importance for the management, recovery and rehabilitation of patients surviving with SCI.

1.6 Overview on Clinical Classification

The gold standard classification of SCI is the American Spinal Injury Association (ASIA) Impairment Scale, which determines the level of impairment (complete or incomplete), assigns the severity of SCI and quantifies the extent of residual neurologic function based on a standardized sensory and motor assessment. (Figure 1.1). Since its inception, the ASIA replaced the modified Frankel classification. [19-21]

1.7 Age at Injury

The distribution of SCI varies between different age groups as well as males and females. In this vein, age-specific incidence rates for tSCI is bimodal, with a first peak described in the adolescents and young adults and a second peak involving people aged 70 years and older. Notably, ntSCI incidence rates has been steadily increasing with age. [5] This will have significant implications for both prevention and management, as the aging population have significantly worse outcomes than younger patients, and their SCIs commonly stem from falls and bone aging. [22] The mean age of an individual with SCI in Canada was 53.4 years old in 2018. More than two thirds of patients were males (77%) and 23% were females.[6]

1.8 SCI is Gender-specific

Typically, males consistently are at higher risk for both ntSCI and tSCI than females across all age groups. The gender distribution (male/female) of SCI in recent reports is 3 to 4:1, with majority of all cases falling into the early and late adulthood. Demographically, males sustain SCI mostly during young adulthood and older age (3rd and 8th decades of life), while females are at greater risk during their adolescence (15-19 years) and older age (60+). As further examples of gender differences, males are at higher risk for ntSCI during their 8th decade of their lives (85+).[9,23-25] Overall, males remain at risk for SCI and comprise the majority of all reported cases worldwide; however, a slight increasing trend has been noted among female SCI population.

1.9 Life expectancy and mortality

The life expectancy for persons with SCI in Canada has increased over the past few decades. The average life expectancy of SCI cohort has increased to 38 years post injury compared to 33 years in 1983. [26] The cumulative survival rates for SCI patients over 10-, 20-, 30-, and 40-year were

80.89%, 66.22%, 51.78%, and 37.47%, respectively. Life expectancies of persons living with SCI remain relatively below normal, compared to the overall average for general population. Several important prognostic aspects have to be considered when determining the life expectancy of these individuals, such as age, level of injury (mainly with tetraplegia), AISA grade and preserved functions, time since injury, and to a lesser extent, etiology and demographics (sex, race, level of education), access to health care and financial support.[27] Medical co-morbidities should also be taken into account if they exist.[28]

Mortality rates are significantly higher within the first year after injury and decrease steadily afterwards. Spinal cord injury patients are 2 to 5 times more likely to die early than those of their peers who do not have SCI. [5] The average annual mortality rates following the first post-injury year is 2.42% and increased over the years as the population get older. The leading cause of death for patients who survived the first year after injury were diseases of the respiratory system (65.2% of these were diagnosed with pneumonia). Infections and septicemia were the second most important cause affecting life expectancy, and included untreated urinary tract infections (UTIs), pressure ulcers or respiratory tract infections. Cancer was the third highest, followed by hypertension and heart disease.[11] The increase in proportion of tetraplegics and complete lesions, along with advanced age at injury, have negatively impacted overall survival time.[18,29] Ultimately, the level of medical care together with life expectancy in a geographic area will in turn influence the survival rate of persons with SCI, and hence its prevalence.[5]

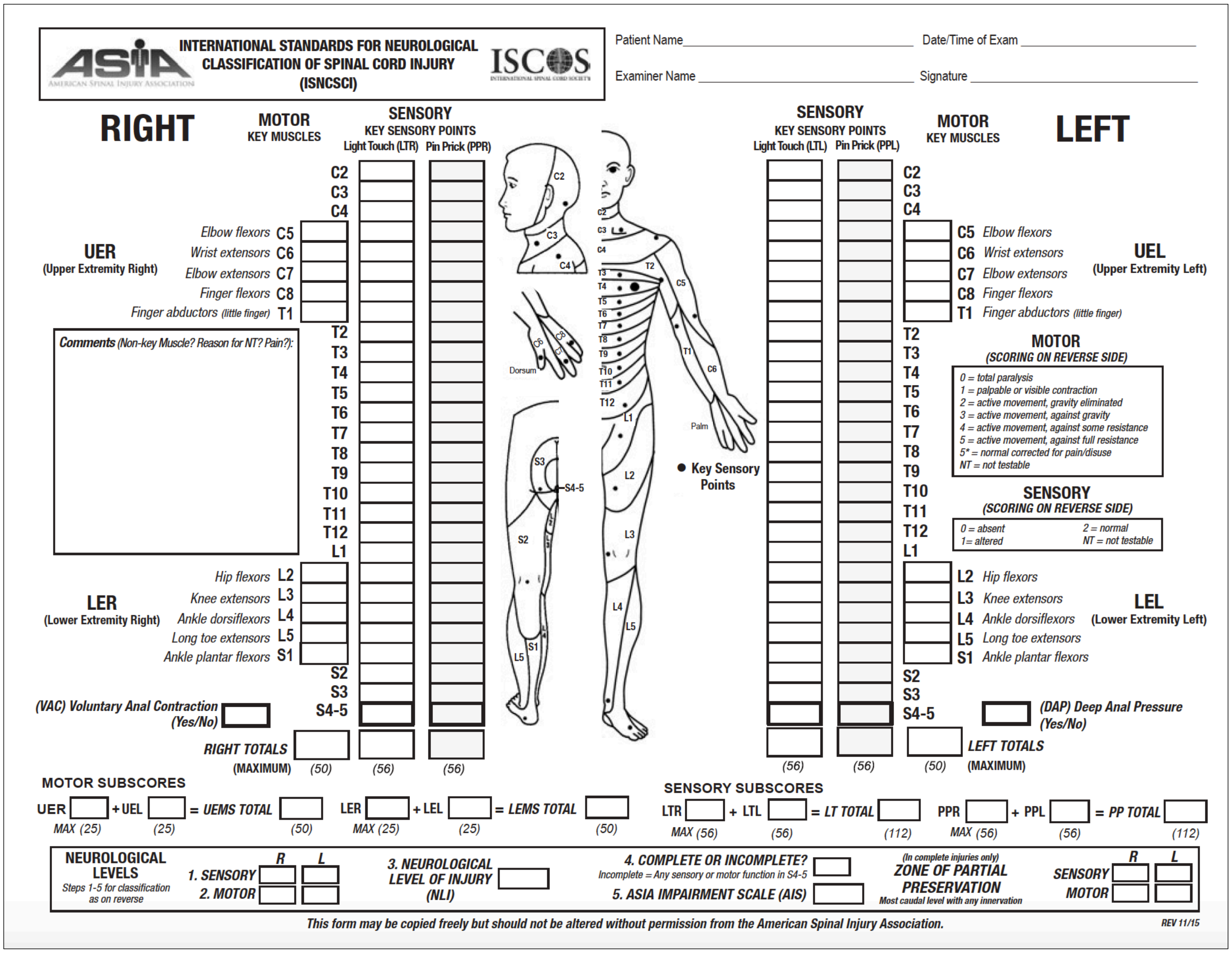

Figure1.1 International Standards for Neurological Classification of Spinal Cord Injury clinical examination form. (adopted from Kirshblum et al.[30]) International standards for neurological classification of spinal cord injury (revised 2011)

Chapter 2: Neurogenic Lower Urinary Tract Dysfunction (NLUTD)

2.1 Introduction

Spinal cord injury is detrimental on voiding and sexual function, with direct impact on health-related quality of life. NLUTD is a broad term referring to "abnormal or difficult function of the bladder, urethra (and/or prostate in men) in mature individuals in the context of clinically confirmed relevant neurologic disorder". [31] The effect of SCI on the lower urinary tract is variable and often presents with a wide range of lower urinary tract symptoms (LUTS), all of which requiring comprehensive evaluation and a multidisciplinary approach to management. People living with SCI may describe storage, voiding, and post voiding symptoms consistent with the diverse effects of SCI on urinary tract function.

NLUTD is highly prevalent among SCI individuals, with approximately 81% of SCI developing some degree of impaired detrusor function within one year of injury and less than 1% having a complete recovery.[32,33] In a recent Canadian study, the prevalence of self-reported bladder, bowel, and sexual dysfunction among traumatic spinal cord injured adults were approximately 59%.[34] SCIs are often associated with higher risk of urological complications resulting from their underlying bladder dysfunction, which commonly lead to increased morbidity and mortality in this population.

2.2 Patterns of NLUTD and classification system

Lower urinary tract dysfunctions are not the same in all patients who suffered SCI. The patterns of LUT dysfunction depends clearly on the level and the extent of the lesion in the neurological axis. Moreover, neurologic category and extent the injury is often predictive of the potential complications and allows for appropriate patient counselling with regards to expected recovery and available treatment options, which in turns improves patient care and therapeutic outcomes.

LUTD following SCI may change with time and patients in the acute stage (the spinal shock) present initially with urinary retention secondary to hypocontractile or acontractile bladder. This phase commonly resolves within 2 to 6 weeks but may last as long as one year. [35] Consequently, as spinal reflexes recover, the typical long-term pattern of voiding dysfunction will be prominent. The neuroanatomical classification of NLUTD is categorized according to the part(s) of the nervous system affected. Key categories include; (1) suprapontine lesions, (2) suprasacral spinal cord lesions, (3) sacral lesions, and (4) infrasacral (cauda equina and peripheral nerves).[35-37] Madersbacher et al. described a complementary classification system based on detrusor function and of the urethral resistance. [38] (Figure 2.1). The "suprapontine" lesions frequently associated with neurogenic detrusor overactivity (NDO) and urinary incontinence. SCI with "suprasacral" lesions often resulting in NDO and detrusor-sphincter dyssynergia (DSD) with incomplete bladder emptying. Injury at sacral, or infrasacral may lead to impaired detrusor contractility (underactive or acontractile bladder) and loss of urethral resistance, where the consequences are urinary retention and/or incontinence.[36,39,40]

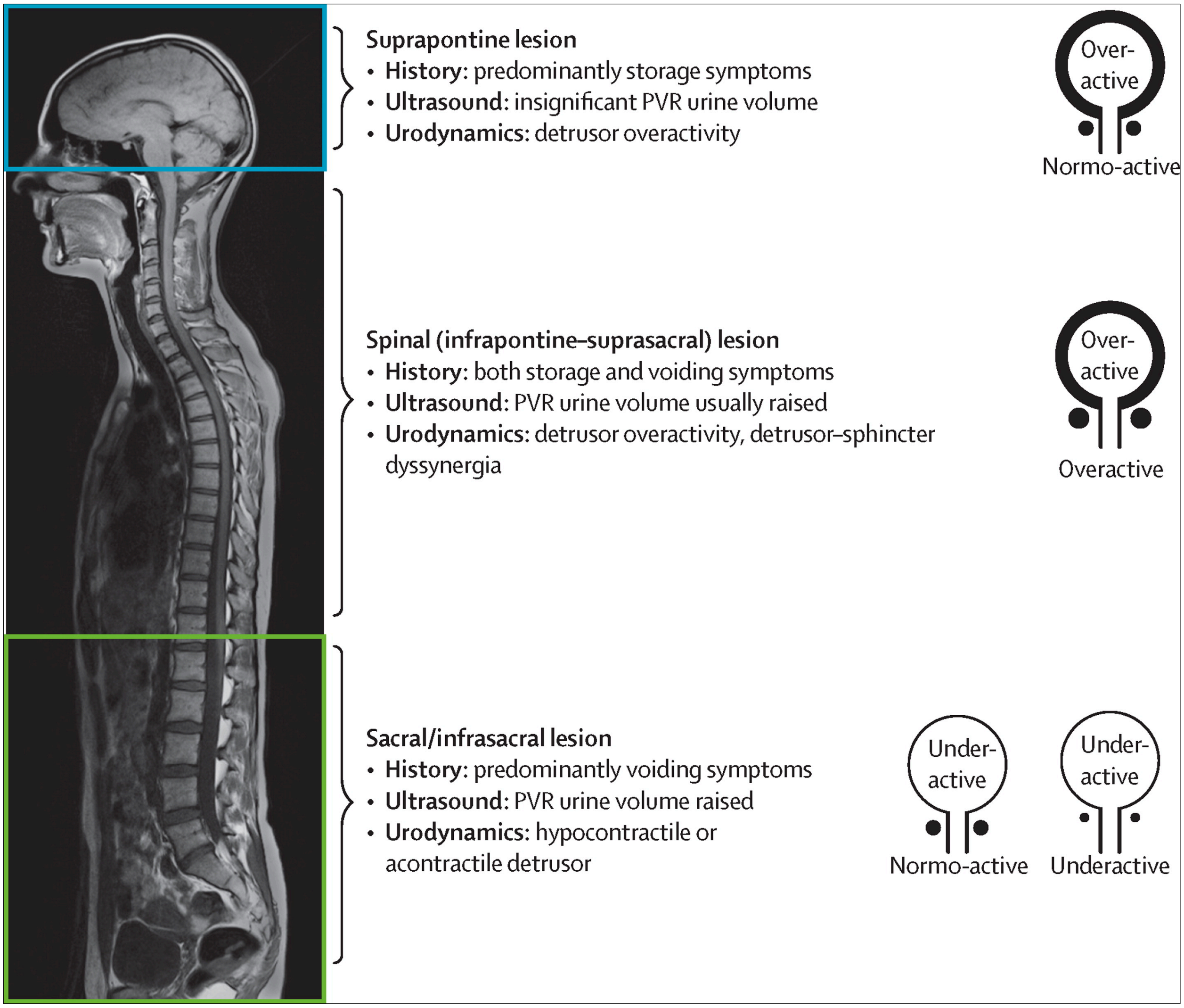

Figure 2.1 Patterns of NLUTD based on the level of neurologic insult (adopted from Panicker et al.[37]) The neuroanatomical classification of NLUTD following neurological insult is determined by the level and the extent of the lesion in the neurological axis. The blue box indicates the region above the pons and that in green denotes the sacral and infrasacral region. Figures on the right show the expected pattern of voiding dysfunction based on the detrusor–sphincter system. PVR=post-void residual.

2.3 Genitourinary sequelae of NLUTD

2.3.1 UTIs

UTIs are the most common secondary complication observed among patients with SCI in hospital and community settings. Overall annual rate of UTI within SCI population is 2.5 episodes per patient and nearly one in five individuals experience recurrent UTIs.[41,42] In 2018 Rick Hansen SCI Registry, 36% of participants reported at least one UTI during acute and/or rehabilitation stays.[6] In addition to frequent hospital admissions and potentially life-threatening septicemia, UTIs have significantly impacted health related QoL and resulted in worse patient reported outcomes.[43] It has been estimated that each SCI patient experiencing one or more UTIs will add an average of $1,841 to the cost of each hospital admission.[44] In this population, patients often have atypical symptoms and are at high risk for acute, or chronic or recurrent UTIs.[45] Recurrent UTIs stem from numerous factors which include poor bladder emptying, indwelling catheters, chronic bacteriuria, vesicoureteric reflux (VUR), bladder diverticula and stones. Other potential risk factors for UTI are evidence of urethral trauma, poor hygiene and immunity associated with chronic illness.[46]

Bladder management strategy has a considerable impact on UTI and, as such, must be optimized. It has been demonstrated that clean intermittent catheterization (CIC) reduce lower urinary tract infections.[47] Indwelling urethral catheterization induce a more than 5-fold increase risk of recurrent UTIs compared with suprapubic catheterization (SPC) and CIC.[48] It is generally recommended that screening and treatment of asymptomatic bacteriuria as well as routine use of antimicrobial prophylaxis for NLUTD should be avoided unless the patient is clinically symptomatic, as it promotes the growth of multi-drug-resistant strains.[47]

2.3.2 Risk of upper urinary tract deterioration

Individuals with SCI are at increased risk for upper urinary tract (UTT) deterioration as sequelae of their LUT dysfunction. The principal goals for treatment of NLUTD after SCI are preservation of the upper tract function and improvement of the patient's quality of life (QoL). Historically, renal failure was the leading cause of death in SCI patients surviving the trauma. [49] The prevalence of chronic kidney disease (CKD) in those patients ranged from 1.3% to 5.6%, which is higher than that of the normal people.[50,51]

High-risk group include individuals with recurrent UTIs, hydronephrosis, impaired bladder compliance, bladder outlet obstruction, VUR and stone disease. Similarly, individuals with supra sacral SCI have much higher rates of UUT deterioration related to persistent high intravesical pressures.[46] Certain methods of bladder drainage (triggered reflex voiding and Credé or Valsalva maneuver) have been linked to increased risk of renal deterioration among SCI individuals.[35] Aside from being a direct risk factor for recurrent UTIs and stones, indwelling catheter users are at greater risk for impaired bladder compliance compared to normal voiding patients or those managed with CIC. [52] Recent evidence suggests that CIC is superior to chronic indwelling catheterization in terms of preserving bladder compliance.[46,53] Additionally, people living with SCI should have a regular follow-up plan tailored to the patient's individual risks in order to minimize the risk of UUT deterioration and renal disease.[47]

2.3.3 Urolithiasis

Urolithiasis is a well-known clinical problem in patients with NLUTD. Within the SCI population, it is estimated that 7% will have renal stones within 10 years after injury and around 34% chance of developing a second calculi over the next five years.[54,55] The form of bladder management, chronic bacteriuria, recurrent UTIs are main risk factors for stone development within SCI cohort. Chronic urethral or suprapubic or catheterization have an important role in determining the risk of urinary stone formation. For example, Bartel and colleagues noted that bladder stones were often observed in patients managed with SPC (11%), transurethral catheter in (6.6%) and with intermittent catheterization in (2%). However, recurrence rate was the highest in UC group (40%), followed by SPC (28%) and IC (22%). [56]

2.3.4 Urethral Complications

Urethral damage, which describes repetitive injury to urethral mucosa with or without subsequent stricture formation, has been related to a history of recurrent UTI, urinary stones and method of bladder emptying.[57] Throughout their adult life, up to 4.2% to 25% of patients will report some degree of urethral stricture formation.[58,59] Patients whose bladders are mainly managed with long-term transurethral catheterization are significantly at higher risk for urethral complications compared to intermittent catheters population.[60] In patients with extensive urethral damage, conversion to suprapubic catheterization is often recommended.[47] Despite the advances in imaging and treatment, urethral damage in this population represents a major reconstruction challenge with potential complex long-term sequelae.

2.4 Management of NLUTD

2.4.1 Assisted bladder drainage

Management of NLUTD in patients with SCI is aimed primarily at preserving renal function, achieving urinary continence, minimizing secondary urological complications and improving quality of life. In this context, two important remarks need to be emphasised: firstly, the type of bladder management is an integral part of a multidisciplinary approach, and the appropriate bladder management strategy should be tailored to individual patient needs such as anatomical factors, motor and cognitive functions, patient preference, and health-related quality of life.[52] Secondly, the changes in the preferred method of bladder drainage are frequently observed among SCI population overtime, for many different reasons.[1] Although CIC is a reliable, effective and widely advocated as a standard of care in selected SCI patients, the general use of indwelling catheters over the course of long-term urological management is still considered when feasible.

2.4.2 Indwelling catheterization (urethral or suprapubic)

Indwelling suprapubic catheterization and, to a lesser extent, transurethral provide satisfactory outcomes with regards to quality of life and long-term protection of renal function. Generally speaking, suprapubic catheters are commonly preferred over urethral catheterization (UC) in daily clinical practice.[52] While SPC requires a surgical procedure for initial insertion with potential risks of surgical complications, it poses less risk for epididymitis, avoids urethral trauma, improves functional independence and would probably facilitate involvement in sexual activities.[61] Tetraplegic patients whose bladders are primarily managed with SPC, reported greater patients' satisfaction when compared to CIC.[62] Other studies demonstrated that SPC has lower risk of bacteriuria and superior patient satisfaction as compared to urethral catheters and should therefore be adopted when possible. That being said, there are limited data to support SPC over UC in terms of prevention of catheter-associated bacteriuria and UTI over the long term.[63] Overall, indwelling catheter patients are at higher risk for long-term complications compared to IC users. According to Feifer and colleagues, suprapubic catheter management is safe and effective treatment option in select NLUTD population with the appropriate surveillance.[64] With prolonged use of indwelling catheters and resultant chronic bacteriuria, the incidence of symptomatic UTI is 1 in 100 days of catheterization.[65] The incidence of bacteriuria in patients living with indwelling catheters is 5% to 10% per catheter-day and is often the primary cause of recurrent UTIs and stones, presenting an ongoing challenge for patients and clinicians alike.[66,67]

2.4.3 Intermittent catheterization

In comparison to indwelling catheters, the use of intermittent catheterization significantly reduces the risk of UTIs, and overall rates remain acceptably low.[47] The baseline risk of catheter-associated bacteriuria in those with CIC is 1–3 % per catheterization.[68] It is estimated that between 2% and 28.5% of IC users experience urethritis and epididymo-orchitis.[69,70] Given the technique of IC, urethral trauma and subsequent stricture formation are not infrequent in those performing CIC and range from 4.2% to as high as 25%.[58,59]

According to Yavuzer and colleagues, when looking at patients with SCI, long-term use of CIC is less widely utilized in females, individuals who have quadriplegia and patients with complete SCI. The main reasons for discontinuing CIC were refractory incontinence despite anticholinergics, spasticity, urethral trauma and upper urinary tract complications.[71] In a retrospective study analyzing the database of 164 SCI patients, about 42% of patients stopped using CIC and the average time for quitting CIC was 16.09 months (range 2 -36). The latter study suggested that recurrent UTI, kidney stones, reliance on care givers and urethral stricture are the most frequent reasons for discontinuing CIC.[1] In a prospective observational study of 1479 participants with SCI, approximately 57% of patients discontinued CIC, with 63% of those were males and 38% were paraplegic. The root cause of the CIC cessation is inconvenience (36%), followed by urinary leakage (20%) and frequent UTIs (19%).[2] Similarly, Lane et al. found inconvenience, physician recommendation, and dislike of CIC more often associated with lack of long-term CIC adoption among veterans with tSCI.[72] A colinear association also exists between CIC discontinuation and upper extremity motor function, increasing age and female gender.[73]

Quality of life implications among patients performing CIC varies widely in the literature, for several reasons: inconsistent definition of patient satisfaction, comfort and convenience, as well as variability in outcome measures and evaluation tools.

Sterile and clean approaches are the main catheterization techniques described within IC context. The sterile technique is popular in hospital setting and therefore costly, whereas clean approach is commonly utilized in patients with SCI after discharge from rehabilitation.

Factors such as catheter design, coating, material and practices appear lead to variable impact on catheter associated complications and quality of life. For example, hydrophilic coated catheters are associated with reduced risk of hematuria, urethral trauma and improved bladder-related quality of life. Despite this evidence, debate continues to rage over optimal catheter design, material and/or catheterization technique.

Chapter 3: Economic burden of SCI and associated bladder management

3.1 Economic burden of SCI in Canada

To date there is no cure for SCI with many of those individuals living a relatively normal lifespan, the lifetime economic burden is significant. Individuals who sustain a spinal cord injury will incur substantial initial and ongoing expenses related to long-term care, subsequent secondary complications, hospital admissions and rehabilitation. The estimated lifetime costs attributable to SCI vary widely according to neurological disability, education and employment history. In Canada, the net lifetime cost of SCI ranges from $336,000 to $479,600 per person,[74] and the estimated lifetime costs attributable to bladder management is $72,622 per individual.[75] A Canadian population-based approach calculated the annual lifetime costs associated with 1389 new SCIs to be $2.67 billion with the uppermost cost driver was attendant care expenses, followed by hospitalization costs and physician services.[76] Dryden et al. estimated the annual direct health care costs during the first five years post-injury to be approximately $5,400 and $2,800 for patients with complete and incomplete SCIs, respectively.[77]

Besides its impact on physical, functional and psychosocial wellbeing, SCI results in significant life changes in employment status, household income and relationships. Approximately 35% of RHSCIR participants who sustain a tSCI turned to be unemployed in the subsequent five years after injury and around half (49%) of participants reported some decline in financial income.[6] It is reasonable to anticipate that SCI individuals will continue to accrue financial burden in the months and years after injury and often through the rest of life as a result of frequent contact with the health system.[78] Because of projected demographic shift to an older population, health care costs related to SCI are predicted to increase by 54% in 2032. [79]

3.2 Costs of secondary complications

Apart from their clinical impact, the economic burden of SCI related adverse events is substantial. Secondary health conditions result in frequent contact with medical community and often require health-care services and hospitalizations. Over a lifetime span, the proportion of SCI individuals ever endorsing a disease related complication reaches 95%.[80-83] In a population-based study of SCI individuals, the rate of hospitalization was estimated to be twice or three times higher than expected rate for general population of similar age group and stayed 3.3 more days in hospital. [78,84] Approximately, 50% of SCI participants experiencing at least one secondary complication and 17% endorsing multiple secondary medical conditions during hospital or rehab stays. In 2018 RHSCIR data, the leading causes of hospitalization were urinary tract infections (36%) followed by pneumonia (20%), and pressure ulcers (PU) and other skin conditions (14%) [6], whereas Noreau and associates reported a plurality of hospitalizations related to genitourinary disorders (UTI; 45%). [85]

Within direct costs estimates, the excess expenditures attributable to UTI and pressure ulcers were the central determinant of healthcare utilization from the perspective of health care facility during initial SCI admission. Within the UTI cost analysis, a mean of $7,790 (SD $6,267) added to overall direct cost of SCI admission. Whereas PU added an average of $18,758 (SD $27,574) in 2013 Canadian dollars (CAD).[86] Overall an average ~$14,333 will add to the total cost of each admission upon experiencing one or more of secondary conditions.[6] Of the most recently published Canadian cost-effectiveness studies, Welk and colleagues estimated that the cost of UTI event per patient among SCI individuals who require some form of IC range from $1,039 (UTI responsive to initial treatment) to $5,715 (complicated UTI). Kidney and bladder stones, respectively, added an average of $9,923 and $5,349 per event. Major renal impairment and renal failure will cost $2,058.93 and $7,070 per event respectively. The lowest cost per event among secondary urological complications was related to urethral injury which incur $738 per patient (2017 CAD $).[75] It is undeniable, that these reported estimates may suggest a demand for preventing and managing secondary health complications in SCI population in Canada, which in terms reduce health care utilization and most importantly improve health related quality of life.

3.3 Health technology assessment (Comparative Economic Studies)

Comparative cost-effectiveness studies of bladder care interventions are scarce in the literature and only evaluating the standard of care modality, namely CIC. Other bladder management strategies are also important in decision making and represent an existing treatment option in certain clinical settings, therefore comparative economic analysis of alternative modalities is warranted to determine the overall health care utilization and resource consumption associated with bladder care in SCI population.

The economic literature review identified a total of 8 health economic studies with varying methodological approaches evaluating the cost-effectiveness of different types of IC. These studies were published between 2013 and 2019, each investigating the cost utility of long-term intermittent catheterization with hydrophilic and uncoated urinary catheters.[75,87-93] Across the studies, results were consistent. The nature of the available evidence does support the use of hydrophilic catheters for CIC as a cost-effective treatment option over long-term period. However, these findings should be interpreted with caution, given the overall low quality of evidence and the huge difference in resource utilization.[52] Moreover, the health economic models varied in their settings, cost estimates, and complications rates, as well as six studies were designed from international contexts, therefore, the findings have limited relevance and probably deemed partially applicable to the Canadian context. Additionally, other aspects limited applicability for some models: they performed an analysis specific to the inpatient setting, or they have not examined all accessible comparators of interest (i.e., indwelling suprapubic and urethral catheters). To evaluate the cost-effectiveness of different bladder management strategies and not only available types of intermittent catheter in Canadian context, a health economic model with provincial Canadian inputs and effect estimates designed to reproduce hospital and community settings is needed to guide decision-making.

CIC and indwelling catheters (UC or SPC) are the three most commonly used bladder management modalities in SCI people in Canada. Based on Publicly funded health care system, the catheter material is usually paid by individuals or their insurance programs. Cost associated with complications or procedure required for CIC training, repeated UC insertion or initial insertion of SPC were incurred by a single payer Canadian publicly funded health care system.

Chapter 4: Research Questions and Study Rationale

4.1 Research questions

1- Within the context of the publicly funded Canadian health care system, what is the cost effectiveness of intermittent catheters (i.e., single-use noncoated and single-use hydrophilic coated) compared to indwelling suprapubic or urethral catheters, for long-term use by adult people living in the community with NLUTD owing to spinal cord injury?

2- What is the potential lifelong cost impact to the Canadian funded health care system of the following bladder management approaches of NLUTD for SCI people with chronic urinary retention in the hospital and/or outpatient setting:

- Intermittent catheters (i.e., single-use noncoated and single-use hydrophilic coated)
- Suprapubic catheter (one per month)
- Urethral catheter (one per month)

Whenever possible, the present health technology assessment gathered evidence that directly evaluates bladder management modalities in a combined setting. If such consolidated evidence was not available, we considered studies conducted in either settings, i.e. outpatient or long-term care.

4.2 Study rationale

This innovative research work aims to uncover the overall lifetime cost of NLUTD associated with spinal cord injury and develop an evaluation of health outcomes and health economics related to different treatment strategies, adherence to treatments, health services utilization in this population. Up to date, there is consistent agreement on lack of evidence supporting the superiority of different bladder management strategies in neurogenic lower urinary tract dysfunction related to spinal cord injury. This was attributed to relatively few well-designed RCTs and the broad heterogeneity in study populations, designs and definitions of outcome measures, rendered the treatment decision widely variable. Furthermore, management of NLUTD represents a significant financial burden on Canadian health care system and health-related quality of life. Therefore, the current cost-effectiveness analysis will provide solid evidence to assist decision-makers and clinician leaders while evaluating the clinical and economic impacts of different treatment strategies, and, importantly, their implementation in current clinical practice. As no study evaluated bladder management modalities of interest from a Canadian healthcare perspective, we conducted a primary economic evaluation and cost-effective decision modeling over lifetime horizon.

Chapter 5: Hypothesis and Objectives

5.1 Hypothesis

The present study examined the hypothesis that CIC has a better long-term cost-effective outcome in the management of NLUTD compared to SPC or UC.

5.2 Objectives

5.1.1 Objective 1

- To establish the overall clinical efficacy, long-term sequelae and health-related quality of life of CIC compared to SPC or UC through literature review.
- **Overview:** A comprehensive literature screening was conducted on June 2018 using the clinical search approach along with relevant economic and costing studies. We developed database auto-alerts in MEDLINE, Embase, and the Cochrane Library index and observed them for the duration of the research period. Additionally, a targeted literature search of clinical trial registries, health technology assessment electronic databases, and the Cost-Effectiveness Registry was performed from their inception until August 2020.

5.1.2 Objective 2

- To estimate the lifetime costs and the lifetime outcomes (LYG, QALYs) attributable to NLUTD management strategies among Canadian SCI population.
- **Overview:** Detailed cost inputs for our model was obtained from the provincial public health system perspective (Quebec) and Canadian sources. Complications associated costs and relevant treatments were primarily derived from the RAMQ and Ministère de la Santé et des Services Sociaux (MSSS). For health conditions treated in the outpatient setting,

such as UTI responding to first-line antibiotics, we used micro costing from several sources: laboratory fees from the hospital records, physician billing fees from the RAMQ, and MSSS for hospital fees.

5.1.2 Objective 3

- To investigate the long-term cost-effectiveness/c cost-utility of CIC compared to SPC or UC from the Quebec publicly funded health care perspective.
- **Overview:** We modeled a hypothetical population of adult SCI patient with NLUTD. Our base-case scenario presumed that all patients have equal access to all bladder management approaches. The outputs of the applied model were incremental cost per quality-adjusted life years and life-year gained. we performed a cost-utility analysis comparing the costs and quality-adjusted life-years (QALYs) of CIC versus SPC or UC.

Chapter 6: A cost-effectiveness analysis of bladder management strategies in NLUTD after SCI: a publicly funded health care perspective

6.1 Abstract

Background: Intermittent catheterization remains the 'gold standard' management strategy for neurogenic lower urinary tract dysfunction (NLUTD) related to spinal cord injury (SCI). More often, indwelling urinary catheter (transurethral or suprapubic) are initiated in the long-term management for NLUTD in patients where self-catheterization is difficult or impossible.

Objective: To investigate the long-term cost-effectiveness of clean intermittent catheterization (CIC) compared with suprapubic catheters (SPC) and indwelling urethral catheters (UC) among individuals with neurogenic lower urinary tract dysfunction due to spinal cord injury from a Canadian healthcare perspective.

Design, Setting, and Participants: A Markov model with Monte Carlo simulation was developed with a cycle length of 1 year and lifetime horizon to estimate the incremental cost per quality-adjusted life years (QALYs). Patients were assigned to treatment with either CIC or SPC or UC. Transition probabilities, efficacy data, and utility values were derived from published literature and expert opinion. Costs were obtained from provincial health care system and hospital data in Canadian Dollars.

Outcome Measurements and Statistical Analysis: The primary outcome was cost per quality-adjusted life year. A standard discount rate of 1.5% was applied annually. Probabilistic and one-way deterministic sensitivity analyses were performed to evaluate the robustness of the model.

Results: CIC had a lifetime mean total cost of $ 29,161 for 20.91 QALYs. While UC had a mean total cost of $31,657 for 18.95 QALYs, SPC mean cost was $ 29,491 for 19.14 QALYs. The model predicted that a 40-year-old patient with SCI would gain an additional 1.72 QALYs if CIC were utilized instead of SPC at an incremental cost savings of $330. CIC confer 1.96 QALYs and 3 discounted life-years gained compared to UC with an incremental cost savings of $2496.

Conclusions: Intermittent catheterization appears to be a dominant and more economically attractive bladder management strategy for NLUTD compared with SPC and/or UC from the public payer perspective over a lifetime horizon.

6.2 Introduction

Spinal cord injury (SCI) is a life-changing, economically impactful condition with estimated prevalence of nearly 86,000 persons in Canada, and 4,259 new cases each year. Compared to historical trends, these figures are projected to increase exceeding 120,000 individuals, with 5800 new patients every year by 2030[94] . In the United States, 294,000 people live with SCI and around 17,810 new spinal cord injuries occur every year [11]. The most representative economical cost attributable to traumatic SCI in Canada is $2.67 billion in 2015, and the estimated lifetime costs attributable to bladder management is $72,622 per person [75,95]. The lifetime financial burden for SCI population can be significant for patients, caregivers, and health care system alike.

Neurogenic lower urinary tract dysfunction (NLUTD) is a prevalent unavoidable lifelong complication following spinal cord injury which is commonly observed in 81% of patients within the first year after injury[33,94]. Furthermore, less than 1 % of these patients will have a full bladder function recovery [96]. NLUTD appears to have a substantial impact on health related quality of life (QoL) with increased risk of recurrent urinary tract infections (UTI), stones and compromised kidney function[97]. Nearly one third of those with SCI are hospitalized more than one time per year [98]. UTIs and other urological complications are the leading cause of hospital readmissions and have the greatest impact on health care utilization in this population [99]. Management of bladder dysfunction represents a significant economic and clinical burden for our health care system, caregivers and patient's quality of life. As an example, SCI patients who experienced at least one UTI added more than $5,300 to the cost of each hospital admission.[95] One of the most essential rehabilitation strategies for SCI patients is the appropriate long-term management of chronic urinary retention related to NLUTD. The principal goals are to minimize morbidity associated with urological complications and to improve health related quality of life.

Various approaches have been described to manage impaired bladder emptying in SCI population including clean intermittent catheterization (CIC), indwelling urethral catheters (UC), suprapubic catheterization (SPC) along with pharmacotherapy. Intermittent catheterization (IC) is accepted worldwide as a standard of care for NLUTD related to SCI. Indwelling UC or SPC have been frequently used in SCI patients where self-catheterization is difficult, impossible or inconvenient [100]. Despite the complications related to chronic use of indwelling catheters, many SCI individuals switch to these catheters over time [101].

Recent study reported that only 37% of patients initially on CIC remained on this form of bladder management for long-term[1]. Reviews have shown variability in terms of urological complications, quality of life and compliance rates with the use of CIC, UC or SPC. These complications can be controlled by medications, frequent catheter change and close monitoring to the bladder condition[100,102], which adds more economical burden on the health care system. Current evidence is limited, and the clinical impact of the different bladder management strategies has been debated. Literature data available focused mainly on the clinical and user perspectives, while the cost effectiveness and economic perspective of these approaches has not been studied so far.

The cost-effectiveness of the bladder management strategies for NLUTD in SCI adds evidence to the treatment decision made by the physician in consultation with the patient, and to the policy makers especially in a publicly funded health care system. Therefore, the present study aimed to perform a cost-utility analysis with a lifetime perspective of intermittent catheterization compared to indwelling UC or SPC in an adult SCI population from a Canadian publicly funded health care system perspective.

6.3 Materials and Methods

6.3.1 Model design and population of patients

A Markov model with Monte–Carlo microsimulations (Figure 6.1) was created using TreeAge Pro Software 2020 (TreeAge, Inc, Williamstown, MA) to compare the costs and utility of IC versus SPC or UC for the treatment of NLUTD from a Canadian publicly funded healthcare perspective. We modeled a hypothetical population of adult patients with presumed neurogenic lower urinary tract dysfunction related to SCI (Table 6.1). The model was developed to estimate the long-term cost and outcomes of bladder drainage methods in patients with SCI who had already completed initial SCI treatment and inpatient rehabilitation. Each Markov cycle was set at one year, the period over which treatment benefits and genitourinary complaints would exist. We selected a lifetime horizon as this was the interval over which the SCI population would be likely to chase NLUTD treatment and current bladder management options would remain relevant.

6.3.2 Model structure

Monte Carlo Simulations of 1,000 patients were performed to estimate the incremental cost-utility ratio (ICUR) of the three comparative treatment strategies. Our base-case scenario presumed that all patients have equal access to all bladder management approaches, with the assumption that the SCI individual will continue in particular health state if treatment is effective. A hypothetical cohort of 1,000 simulated patients suffering from NLUTD following SCI was considered for a lifetime horizon. The model's target population reasonably represented the Canadian SCI data with 80% being males, and average age at injury of 40 years [86]. We conducted this analysis from the perspective of the Canadian provincial public healthcare system using Quebec's health insurance board, RAMQ (Régie de l'assurance maladie du Québec) as the reference for costs and resources.

6.3.3 Definition of health states

The Markov model consisted of different health states that a catheter dependent individual with SCI can experience. Given the chronicity of the condition and the need for lifelong bladder drainage treatment, we assumed all costs and utility values occurred within the yearly cycle. The model included four possible health states after SCI; 1) maintain intervention (defined as individuals assigned to their primary bladder management modality: CIC, SPC or UC), 2) switch intervention (defined as individuals who changed their primary treatment to a secondary treatment due to complications, inconvenience or change in underlying health condition and were diagnosed and recommended a different treatment modality by a treating physician or general practitioner), 3) adverse events (patients developed one or more urological complications related to primary bladder drainage or deterioration in health condition), and 4) death (an absorbing state for general mortality in SCI population).

At baseline, the study cohort began in the “maintain intervention” health state and would have equal access for available treatment strategies. The people could remain there or transition to the “switch” or a “adverse events” health states in the following cycle. In the “switch” health state, people also had a risk of developing complications that lead to additional costs and disutilities. Given the complexity of the model, and the availability of utility indices identified in the literature, we decided to focus on the most frequent urological complications reported in SCI, as shown in Table 6.2.

Transition between different treatment modalities within “switch” health state was permitted for a certain number of cycles/intervals based on assigned probabilities. For example, patients cannot switch between from CIC and SPC back and forth for unlimited cycles. Progression from “maintain” health state to the next was based on secondary urological complications or patient preference, and it was possible to move between the three related treatment strategies based on transition probabilities, which can be reproduced in the 'real world' setting of daily clinical practice. The transition probabilities are listed in Table 6.2.

6.3.4 Data input

In each yearly cycle, the simulated patient could remain in a particular health state or move between the health states on the basis of assigned transition probabilities. Probability estimates for maintain or switch, complications, and possible outcomes for each management strategy were adapted when possible from randomized controlled trials (RCTs). When data were unavailable in literature, an assigned probability based on expert panel was implemented.

For the CIC strategy, long-term compliance rate in the literature ranges from 20% to 79% over total follow-up period ranged from one year to 30 years [1,2,71,73,103-106]. We chose a compliance rate of 60% (at 30 years follow-up). On the other hand, stable long-term compliance rate as high as 81% has been reported with indwelling UC or SPC. In our model, compliance with SPC or UC was 71% over 30 years, parallel with those reported by other studies [1,73,103,106]. Key input parameters are listed in Table 6.2.

Patients with secondary adverse events after CIC, SPC or UC were able to maintain the same treatment or revert to another strategy. The compliance rate after a second CIC was similarly set at 60% at a mean follow-up of 30 years. Of those undergoing a second CIC, SPC or UC, the same outcome algorithm was utilized, with the exception that no further CIC would be offered for patients switched from CIC. Similarly, individuals revert from SPC were offered CIC or UC placement rather than repeat SPC. Other transitional probabilities for "switch intervention" health state between CIC, SPC or UC were obtained from previous clinical studies and assumptions determined by clinical experts. Intermittent catheters of different type, material and design from various manufacturers have equal utility and complications rate. We also assumed that individuals with a spinal cord injury have equal preference to both CIC materials (uncoated and hydrophilic coated).

With respect to the adverse events, such as urinary tract infection, bladder or kidney stones were considered as short-term adverse events and were assumed to have been resolved with appropriate treatment. Given the fact that major renal impairment (calculated using stage 3 + 4) and renal failure is irreversible conditions [107], movement to a better renal health state was not possible. There are no transitions or progression between different catheter-related complications.

Urinary tract infection

Two different settings were considered with regards to UTI event. The results from a retrospective study by Krebs et al.[48] were used to determine the baseline risks of UTIs (UTI responding vs UTI not responding to initial treatment). The study included a total of 1,107 participants with a mean NLTUD duration of 20.3±11.6 years and follow-up of more than 3 years. According to this study, the occurrence rate of a symptomatic UTI was 83.3%, 11% and 39% for UC, SPC and CIC, respectively. Nearly 70% of CIC users suffered at least one symptomatic UTI per year. The cost data for UTI not responding to initial treatment included combined hospital and community settings. The proportion of cohort that might experience UTI not responding to initial treatment was 31.2% and 17.5% for CIC and SPC, respectively. About half of UC users are at risk of developing complicated UTI.[48] Proportion of cohort with UTI not responding to initial treatment is fixed over the model duration.

Urethral damage

Three different treatment scenarios were considered with regards to catheter-associated urethral damage. Approximately, 60 to 70% of those who develop urethral damage underwent frequent urethral dilatation (60 -90%). While 20-30% would have endoscopic visual urethrotomy, only 5 to 10% will undergo urethroplasty reconstruction [58,59,108-110]. Limited evidence exists regarding the impact of hydrophilic coated and uncoated intermittent catheters on catheter-associated urethral complications. Evidence indicates that urethral complications from indwelling catheterization are clearly more frequent than for patients on CIC [111]. Complications such as strictures and urethral damage are equal between single-use (uncoated) catheters and hydrophilic coated catheters.

Urolithiasis

With respect to surgically treated kidney stones in SCI population (including kidney or ureter calculi), about (34%) treated with ureteroscopy lithotripsy, ureteral stent/percutaneous nephrostomy (30%), shockwave lithotripsy (19%) or percutaneous nephrolithotripsy (17%) [112]. Baseline mortality rate was based on spinal cord injury age-specific standardised life tables derived from United States collaborative SCI survival study database (December 2019) [11].

6.3.5 Utility values

Health outcomes were estimated as quality-adjusted life-years (QALYs). Utility indices in the model were obtained from the literature, and when not available, the expert panel with broad experience in NLUTD and the SCI population provided input. Utility values anchored between 0 to 1, with 0 representing death and 1 indicating a perfect health state. For patients treated with CIC modality and maintained, we used a baseline utility of 0.831[75,87], and for people with indwelling SPC or UC, similar baseline utility was applied. For those individuals who changed their primary bladder emptying modality or developed catheter-related complications the base-case utility score was 0.76 and 0.738, respectively. These values were derived based on previously validated assigned utilities from a NLUTD condition [87,88,93]. Each of the catheter-related adverse events involved in the model have its own definite utility value (Table 6.3).

6.3.6 Costs assignments

For the purpose of this study, we assumed that all healthcare costs were incurred by a single payer Canadian publicly funded health care system. Estimated direct costs were assigned in 2019 Canadian dollars and calculated from the provincial public health system perspective (Quebec).

Hospital and medical expenses were estimated based on the RAMQ and Ministère de la Santé et des Services Sociaux (MSSS) lists [113,114]. Calculated intermittent and urethral catheterization initial costs included: material fees, nursing fees and hospital fees (Table 6.2). Suprapubic catheter insertion costs include: urologist fees, anaesthesia physician fees, procedure cost and hospitalization fees; day surgery (medications cost, nursing care, and therapeutic services). Catheter, lubrication and acquisition costs were obtained from sales reports at the Jewish General Hospital in Montreal, Quebec, Canada and commercial online sales websites specialized in continence products [115-118]. The cost of annual follow-up as well as cost related to adverse events treatment were extracted from RAMQ, MSSS and hospital records. Treatment-related adverse event expenditures were calculated in accordance with a clinically validated treatment pathway, based on those reported in CUA guidelines [111]. Costs related to renal health states (major renal impairment and renal failure) were calculated based on healthcare expenditures associated with nephrology care of pre-dialysis chronic kidney disease [107]. Annualized healthcare costs from a managed care perspective include outpatient and inpatient services and medications costs (Table 6.4).

A conventional uncoated catheter was found to cost an average of $0.65 per catheter compared with a hydrophilic coated material, which costs an average of $4.89 per catheter. Additionally, all uncoated catheter users have to pay a monthly dispensing fee and lubricant daily acquisition cost. The debate regarding the single-use catheters over repeated multiple use for CIC users remains unresolved. Guidelines advocate single-use catheters with average 4 to 6 daily catheterizations in patients with NLUTD [111,119]. In the scenario analysis, we assumed that patients only practice single-use disposable catheters (uncoated) similar to hydrophilic (coated) catheters. Table 6.2

provides data on base-case costs as well as further information regarding assumptions and calculations. Because of limited data, indirect, societal costs or out-of-pocket expenses related to sick leaves, early retirement, and early death are difficult to calculate in monetary terms and were not included in the scenario analysis.

6.3.7 Model output

The Markov model outputs were incremental costs, quality-adjusted life years (QALYs), and life years gained (LYG). The model estimates the cost-per-QALY associated with using three different assisted bladder drainage strategies based on catheter-associated adverse events rates in community and hospital setting. Following Canadian recommendations, an annual discount rate of 1.5% was applied to costs, quality-adjusted life years and life years gained [120]. Results are expressed as incremental cost-utility ratios (ICURs) for a lifetime perspective (+60 years).

6.3.8 Sensitivity analysis

To investigate the overall uncertainty in the model, a probabilistic sensitivity analysis was conducted using a Monte Carlo simulations of 1,000 iterations and presented through a scatterplot. The UC and SPC modality were compared, individually, to the CIC strategy One-way deterministic sensitivity analyses were also performed using the mean 25% of the values in order to determine key model parameters and the impact of variations and assumptions on the ICUR. The cost of catheterization, adverse events, the transition probabilities between health states and the utilities were included to evaluate their independent effects on the ICUR. We examined different discount rates of 0%, and 3% in the sensitivity analyses. Finally, a shorter 15- and 25-year time horizon were also explored.

6.4 Results

Intermittent catheterization had a lifetime mean total cost of $ 29,161 for 20.91 QALYs. While UC had a mean total cost of $31,657 for 18.95 QALYs, SPC mean cost was $ 29,491 for 19.14 QALYs (Table 6.5). At an incremental cost of $2,496 per SCI patient, CIC confer 1.96 QALYs and 3 discounted life-years gained compared to UC, resulting in an ICUR of $1,273 per QALY gained and $832 per life years gained per individual. Similarly, CIC-dependent SCI patient would gain an additional 1.77 QALYs and 1.72 discounted life-years compared to SPC at an incremental cost of $330, contributing to an ICUR of $186 per QALY gained and $191 per life years gained per patient. Consequently, the CIC is the dominant strategy over the indwelling UC or SPC over lifetime horizon.

Over a Canadian provincial public healthcare system perspective, our model estimated that a spinal cord injury patient with NLUTD would live for an average of 23.43 additional life years when using SPC, which increases to 25.15 years when using intermittent catheters. Indwelling urethral catheter-dependent patients are expected to live for 22.15 extra years.

The one-way deterministic sensitivity analysis showed that study results are robust. (Table 6.6) The analyses were performed for key parameters that could impact the base case results. Mainly, the probability of catheter-associated complications resulted in the great uncertainty (Figure 6.2a, 6.2b). From a cost perspective, hydrophilic coated intermittent catheters were shown to greatly influence the results; when the cost per hydrophilic coated catheter varied between $3.99 to $5.99, the ICUR range was $1,295 to $4,812 and CIC became cost-effective versus SPC or UC. If the cost for uncoated IC was assumed to be $2.00, the ICURs became $82 and showed that the CIC strategy is cost-effective. The relative utility benefit (+0.05) of using hydrophilic catheters instead of conventional (uncoated) was also tested for the value of 0.881, which gave an ICUR range of $1,440 to $1,068. The difference between the sensitivity analysis and base-case in regard to the ICUR was up to $4,812/QALY. For the model parameters, the 15- and 25-year time horizon showed that the CIC strategy remains the dominant technology and resulted in an ICUR ranged between $211 to $317/QAL against SPC or UC. The key message here is that when utilizing HC catheters, the total cost will increase, however due to improved efficacy, utility and reduced complications the net result of the cost-effectiveness analysis showed that CIC using HC catheters is cost-effective against SPC or UC. CIC using uncoated catheters is the dominant treatment strategy (provides better effectiveness and a higher cost), while CIC with HC catheter is cost-effective (better efficacy with lower cost).

The incremental cost of various sensitivity analysis comparing both CIC and SPC modalities stretched between $160 (five IC daily) to $4,523 (hydrophilic catheters; unit cost $5.99). Similarly, incremental cost of CIC vs UC for different sensitivity scenarios ranged from $832 (uncoated catheters; unit cost $2.00) to $5,500 (hydrophilic catheters). When the CIC adverse events rate in the long-term setting have increased, SPC is considered a cost-effective treatment at an incremental cost of $1,632, resulting in an ICUR of $8,388/QALY gained.

Probabilistic sensitivity analyses with 1,000 simulations, indicated almost 100% probability of CIC being cost-effective versus SPC or UC for cost-utility threshold of $50,000 per QALY gained. The majority of the data points lied below and to the right of the diagonal dashed line which corresponds to the commonly accepted cost-effectiveness societal willingness-to-pay threshold of

$50,000 per QALY. Taking that on board, the scatterplot expresses the low uncertainty related to the base case results. (Figure 6.3a, 6.3b).

6.5 Discussion

Spinal cord injuries lead to life-long complications and disease related deaths that represent a heavy burden on the patient's quality of life and the health care system. The cost-effectiveness of the bladder management strategies for NLUTD in SCI adds evidence to the treatment decision made by physician in consultation with the patient, and to the policy makers especially in a publicly funded health care system.

Optimal bladder management modalities remain of paramount importance for catheter-related adverse events as well as health-related quality of life (HRQoL). Despite that CIC is a standard of care for SCI patients with incomplete bladder emptying, it isn't without limitations, such as impaired dexterity, poor functional bladder capacity and anatomic restrictions (obese or bedridden) [111]. While every effort should channel patients with NLUTD to use the gold standard of CIC, many patients change to indwelling catheters (UC or SPC) over time [1]. These approaches vary in their benefits and risks, as well as cost related to long-term catheterization. In our publicly funded health care system, the cost of each strategy of treatment option should be validated, and the choice made by the treating physician should be based on both the best treatment outcome and health care cost. In addition, the managing physician should discuss any of these approaches with the patient based on solid knowledge about the benefits and the costs. The aim of the present study was to compare the long-term cost effectiveness of the different approaches to manage the NLUTD in spinal cord injury patients and to identify the best option among the current approaches with respect to health care system requirements.

To the best of our knowledge, this is the first study evaluating the cost-utility of different bladder management techniques in a publicly funded health care system context. Our results demonstrated that CIC is dominant strategy in comparison to indwelling UC or SPC. CIC (single-use uncoated catheters) offers more QALYs at lower costs than treatment with SPC or UC in this cohort. The base-case analysis demonstrated an ICUR of $2,496 /QALY when comparing CIC versus UC, and $186/QALY when implementing CIC instead of SPC technique. These low ICURs were driven by marginal differences in costs but significant relative increases in QALYs across bladder drainage modalities. From a lifetime perspective, CIC were deemed to be a dominant management strategy as compared with SPC or UC, which is within the Canadian threshold of $50,000 per QALY. The results of this economic analysis are valid for our Canadian health care system, however; we believe it may easily translate to other publicly funded health care systems and can be used to guide rationale decision-making about the urological management in SCI patient populations. All these are very important at the planning and policy level.

Even though there are marginal incremental cost differences based on the base-case analysis, the lowest-cost intervention, CIC (single-use, noncoated), likely offers the best value for money. This inference was reinforced by the probabilistic sensitivity scatterplot of the 1000 ICUR, as 99% of model iterations indicated CIC was cost-effective against UC at a willingness-to-pay amount of $50,000 per QALY, and UC was not cost-effective at any willingness-to-pay amount vs CIC. At the same willingness-to-pay amount, there was an 86.8% chance that CIC is cost-effective versus

SPC. These results remain robust even in different one-way deterministic sensitivity analyses, for instance variations in catheterization frequency, catheter design, complications and compliance rate relative to each treatment strategy. This borderline increase could be explained by the relatively high transitioning rate to other bladder drainage methods in patients utilizing CIC.

Fortunately, the majority of patients with NLUTD after SCI demonstrate successful long-term outcomes with CIC particularly for the preservation of kidney function and reduced risks of urinary tract complications such as UTIs and stones, which compensates for urethral complications and quality of life implications, such as comfort, convenience, and compliance [52]. We considered for our model the most frequent urological complications that patient with NLUTD would encounter over the short- and long-term periods, which need medical and/or surgical treatment. The quoted incidence of overall urological complications for CIC bladder drainage over 18 years was 27%, compared to 44% and 53% for SPC and UC, respectively [61]. However, the reported frequencies of complications following bladder evacuation are heterogeneous. Other studies have reported lower (17–20%)[121,122] or higher (29–45%)[105,123-125] CIC complication rates. The discrepancies are related to variation in the study populations and design, utilized intermittent catheter type, reported complications, outcome measures and follow-up duration between the studies. Total costs repartition in the current model showed that the weight of cost associated with complications were similar for CIC (11%) and SPC (10%), whereas it accounted around 21% for UC, this might justify that UC is the least likely cost-effective strategy over lifetime.

In the present model, we assumed that 60% of SCI individuals would maintain CIC over lifetime, which is in accordance with other reports [1,104,106]. Other authors documented lower compliance rate with CIC over the long-term. These studies reported about 20% compliance rate at 30 and 45 years follow-up [103,126]. On the contrary, approximately two-third of SCI patients would maintain indwelling SPC or UC over the long run [1,73,103,127]. In spite of established efficacy of CIC, the greater rate of reverting to other assisted bladder drainage methods has a strong impact on their overall elevated cost. Our cost-utility analysis showed that nearly fifty percent of lifetime cost were allocated to lack of CIC adoption. This might also explain why the overall cost of CIC were almost comparable to other bladder management options.

Several studies have investigated the economics of the CIC treatment for NLUTD. Welk et al analyzed the cost-effectiveness of two different types of IC (hydrophilic coated vs uncoated) from a Canadian societal perspective including direct and indirect costs; their base-case result identified a lifetime expenditure of $72,622 for 5.37 QALYs by using uncoated catheters compared to $120,639 for 6.09 QALYs with hydrophilic catheters. Additionally, they predicted that a 50-year-old SCI patient would gain an average of 12.36 to 13.14 years when implementing CIC [75]. In another study, the average lifetime treatment cost for CIC was £59,000 for 6.58 QALYs for the SCI patients utilizing two different single-use intermittent catheter designs from a UK perspective. The model further predicted an additional 22.5 years when using CIC (uncoated catheters), which increases to 23.9 years with HC catheters [88].

The present study revealed a rather high average additional life expectancy of 25.15 years and 20.91 gained LYG when using CIC in SCI cohort with a starting age of 40 years. This relatively high average life expectancy might be explained by the absence of disease specific mortality in this model, which is a potential limitation of this study. Given that the data used for the estimations are built upon combined hospital and community settings, the findings are similar to the actual life expectancy found for SCI population [11].

Similar to the results presented in previous cost-effectiveness studies [75,87,88], it is likely that CIC using hydrophilic catheters would become even cost-effective strategy (CIC is more effective and less costly) for the management of NLUTD using a lifetime perspective. Despite the weak correlation between long-term compliance and catheter type/design [1], it is often recommended that SCI patients should be offered HC catheters where possible given a lower risk of UTIs and urethral complications [128], good efficacy, and improved bladder related QoL [52].

Multiple-use uncoated PVC-catheters are still widely used, which may be due to the fact that initial cost and reimbursement is in favor of PVC catheters rather than the HC design, or possibly ~~patient preference~~. The evidence for endorsing the use of uncoated PVC-catheters (multiple-use) remains inconclusive. If the multiple-use IC scenario was applied in our analysis, the results would have been even more favorable for CIC approach. This highlights the need for more RCTs comparing different IC techniques/materials. Additional studies are also required to describe utility indices for health states experienced by SCI patients with NLUTD.

Additionally, it is important to emphasize that the impact cost-effectiveness is affected by the financial source: Although we assumed that all healthcare costs were incurred by a single payer Canadian publicly funded health care system, in reality, catheter material is usually paid by individuals or their insurance programs. Therefore, the total cost analysed in our cost-effectiveness strategies includes costs from the healthcare, but also cost incurred by the patient directly, or possible insurance programs. The cost-effectiveness CIC in particularly affected by the fact that a large amount of the cost over lifetime may need to be paid by the individual. This may also be a reason to abandon CIC.

As with any cost-effectiveness model, the limited availability of data and inherent hypothetical design are the most obvious limiting factors, therefore results are entirely dependent on the quality of available evidence. A potential weakness of the current study was the lack of RCTs evaluating different bladder management techniques from clinical and user perspective. Furthermore, the reported data concerning the rate of associated complications and long-term compliance are even more diverse. Therefore, we have limited our findings to the accuracy of our assumptions. While various types and designs of catheters are available, the model only examined the most frequently used catheters in Canada. Finally, additional analysis of SCI subpopulations was not feasible due to limited availability of data on female SCI population, coping and level of neurological impairment and bladder management directed by caregivers.

6.6 Conclusions

This economic analysis demonstrates that CIC is a dominant treatment strategy (offering increased benefits at lower cost) to manage SCI patients with NLUTD compared to indwelling UC or SPC over lifetime horizon, from a Canadian publicly funded health care system perspective. Given the marginal differences in overall costs across bladder management approaches, the uppermost-QALYs intervention—CIC uncoated catheters (single-use)—had the highest likelihood of being cost-effective when compared with SPC or UC. Despite high ongoing cost of using hydrophilic coated intermittent catheters; it was perceived as a cost-effective technology. Although suprapubic or transurethral catheters represent a minimally invasive and cost competitive management option with acceptable long-term efficacy, they do not appear as an effective and cost-effective alternative for long-term treatment of NLUTD. That being said, SCI patients with chronic retention often switch to these catheters over time for various reasons. This remains an ongoing debate for health care providers and patients alike. Future research should strive to address the implications of various bladder care practices among different SCI subpopulation.

6.7 Tables and Figures

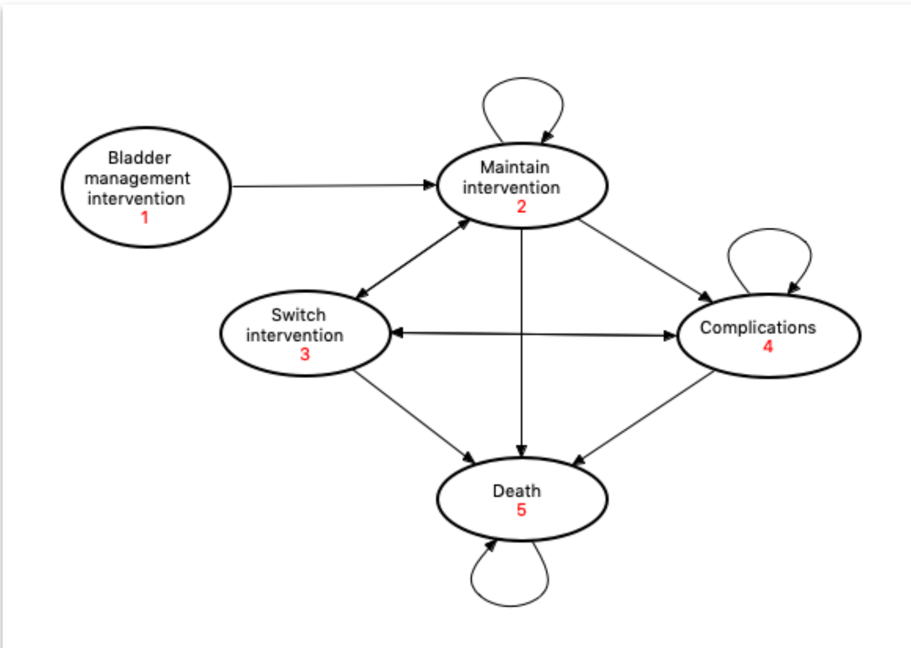

FIGURE 6.1 Schematic representation of the Markov model with four different health states. The patient can progress to different states: maintain, switch, complications, and death. The arrows either represent "remain in health state" or the "progression to next health state".

Table 6.1 Characteristic of the Hypothetical Patient Population & Assumptions	
Characteristic	Details
General	• Adult patients Age ≥18years • Traumatic SCI with NLUTD who received long-term urologic care
History	• With or Without urologic complications • With or without previous Rx for NLUTD • With or without bowel dysfunction • With or without history of other neurological conditions • ASIA score
Physical Examination	• Level of injury (Paraplegia or Tetraplegia) • Hand function (Intact or impaired hand function)
Study Setting	• Combined scenario (hospital and community settings)

Table 6.2 Key input parameters to the model				
Parameters	**CIC**	**SPC**	**UC**	**Source**
Annual transition probabilities to health state				
Probability of maintain intervention	0.0074	0.0404	0.0404	[103]
Need to switch intervention	0.0522	0.0114	0.0114	[103]
Complications related to bladder management	0.0175	0.0321	0.0414	[61]
Death	0.0129	0.0129	0.0129	[76,78]
Annual transition probabilities to complications				
UTI responding to initial treatment	0.7050	0.5830	0.8330	[48]
UTI not responding to initial treatment	0.3120	0.1750	0.5000	[48]
Bladder stones	0.0165	0.0362	0.0202	[124,127]
Kidney stones	0.0045	0.0208	0.0163	[127,129]
Urethral damage	0.0476	0.0159	0.0233	[59]
Major renal impairment	0.0159	0.0102	0.0247	[129]
Renal failure	0.004	0.004	0.004	[51,130]
Cost Components and Unit Costs (2019 Canadian dollars)				
Hydrophilic coated catheter (single-use)	$4.89	-	-	[115-118]
Uncoated intermittent catheter (single-use)	$0.65	-	-	[115-118]
Daily acquisition cost (lubricant)	$0.15	-	-	[115-118]
Monthly dispensing fee	$8.15	-	-	[115-118]
Urethral indwelling catheter (UC)	-	-	$0.5	[115-118] hospital record
Suprapubic indwelling catheter (SPC)	-	$1.32	-	[115-118] hospital record
Initial cost of insertion	$67.35 [a]	$622.58 [b]	$95.52 [a]	[113,131] hospital record
Cost of monthly change (1catheter/month) [a]	-	$95.52	$95.52	[113,131] hospital record
Follow-up (yearly thereafter) [c]	$109.3	$109.3	$109.3	[113,131]
Average cost (first year)	$1099.3	$1768.82	$1255.54	
Average cost (yearly thereafter)	$1099.3	$1255.54	$1255.54	
Other parameters				
Catheterization frequency	4.0 per day	1.0 per month	1.0 per month	[119]
Proportion of cohort with UTI not responding to initial treatment (complicated)	31.2% (CI 26.8–35.8)	17.5% (CI 11.2- 25.5)	50.0% (CI 26.0–74.0)	48
Length of hospitalization (UTI unresponsive to initial treatment)	3.9 days	3.9 days	3.9 days	[75]
Cohort starting age	40	40	40	Assumption, [6]

Abbreviation: RAMQ, Régie de l'assurance maladie du Québec; MSSS, Ministère de la Santé et des Services Sociaux; CIC, Clean intermittent catheterization; SPC, Suprapubic catheter; UC, Urethral indwelling catheter

[a] This amount includes material fees, nursing fees and hospital fees.

[b] This amount includes urologist fees, anaesthesia physician fees, procedure cost and hospitalization fees; day surgery (medications cost, nursing care, and therapeutic services).

[c] This amount includes physician fees and hospital fees.

Table 6.3 Health utility associated with key health states		
Health state	**Mean value (95% CI)**	**Source**
Baseline utility of catheterization	0.831 (0.809 to 0.852)	[75]
UTI responsive to initial treatment	0.782 (0.764 to 0.799)	[132,133]
UTI not responding to initial treatment	0.760 (0.685 to 0.834)	[87]
Bladder stones	0.80 (0.76–1.00)	Assumed same as kidney stones
Kidney stones	0.80 (0.76–1.00)	[134]
Urethral damage	0.738 (0.688 to 0.787)	[87]
Major renal impairment	0.67 ± 0.31	[135]
Renal failure	0.54 ± 0.33 (0.49 to 0.64)	[135,136]

Abbreviations: RAMQ, Régie de l'assurance maladie du Québec; MSSS, Ministère de la Santé et des Services Sociaux; UTI, Urinary tract infection.

Table 6.4 Main cost inputs

Healthcare costs	Mean	Source
UTI responding to initial treatment (per event) [a]	$164.3	Calculated following [87,137]; RAMQ list [113], Quebec MSSS [131]
UTI not responding to initial treatment (per event) [b]	$5704.14	Calculated following [137-139]; RAMQ list [113],Quebec MSSS [131]
Bladder stones (per event) [c]	$1411.95	RAMQ list [113], Quebec MSSS [131],hospital record
Kidney stones (per event) [c]	$2086.96	Calculated following [112,140,141];RAMQ list [113], Quebec MSSS [131], hospital record
Urethral damage (per event) [d]	$975.68	Calculated following [58,59,108-110,142] Expert opinion; RAMQ list [113], Quebec MSSS[131], hospital record
Major renal impairment (per year) *	$21714	Calculated using stages 3 and 4 following [107,143]
Renal failure (per year) *	$43915	Calculated using stages 3 and 4 following [107,143]

Abbreviation: RAMQ, Régie de l'assurance maladie du Québec; MSSS, Ministère de la Santé et des Services Sociaux; UTI, Urinary tract infection.
[a] This amount includes medications cost, urine test, physician fees, and hospital fees.
[b] This amount includes physician fees, and hospital admission fees (medications cost, nursing care, and therapeutic services).
[c] This amount includes (hospitalization fees, urologist fees, anaesthesia physician fees, technician fees and procedure cost for stones removal)
[d] This amount includes (hospitalization fees, urologist fees, anaesthesia physician fees, technician fees, dynamic studies of urinary tract and procedure cost; urethral dilatation, visual urethrotomy, urethroplasty)
*This amount includes (Outpatient and Inpatient services and medications costs)

Table 6.5 Base-case scenario (lifetime horizon)

	Cost	Δ Cost*	QALY	Δ QALY*	LGY	Δ LGY	ICUR*
CIC	$ 29161		20.91		25.15		
SPC	$ 29491	-$330	19.14	1.77	23.43	1.72	Dominated
UC	$ 31657	-$2496	18.95	1.96	22.15	3	Dominated

Abbreviation: CIC, Clean intermittent catheterization; SPC, Suprapubic catheter; UC, Urethral indwelling catheter; QALYs: Quality-Adjusted Life Years; LGY: Life year gained. * Compared to CIC

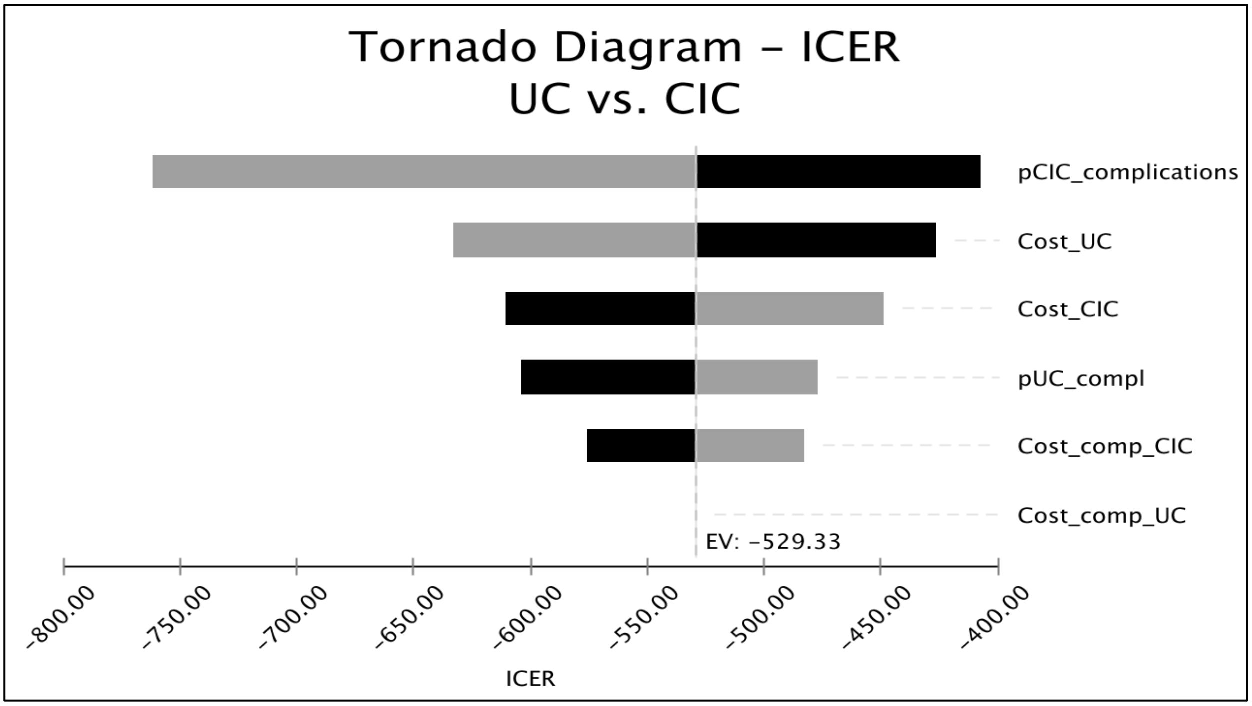

FIGURE 6.2a Schematic Tornado diagram, One-Way sensitivity analyses: Intermittent Catheters Versus Indwelling Urethral Catheters. The ICUR calculations were based on a willingness to pay corresponding to the Base-Case ICUR, that is, $50 K/QALY. Abbreviations: CIC, clean intermittent catheter; Compl, complications; UC, urethral catheterization.

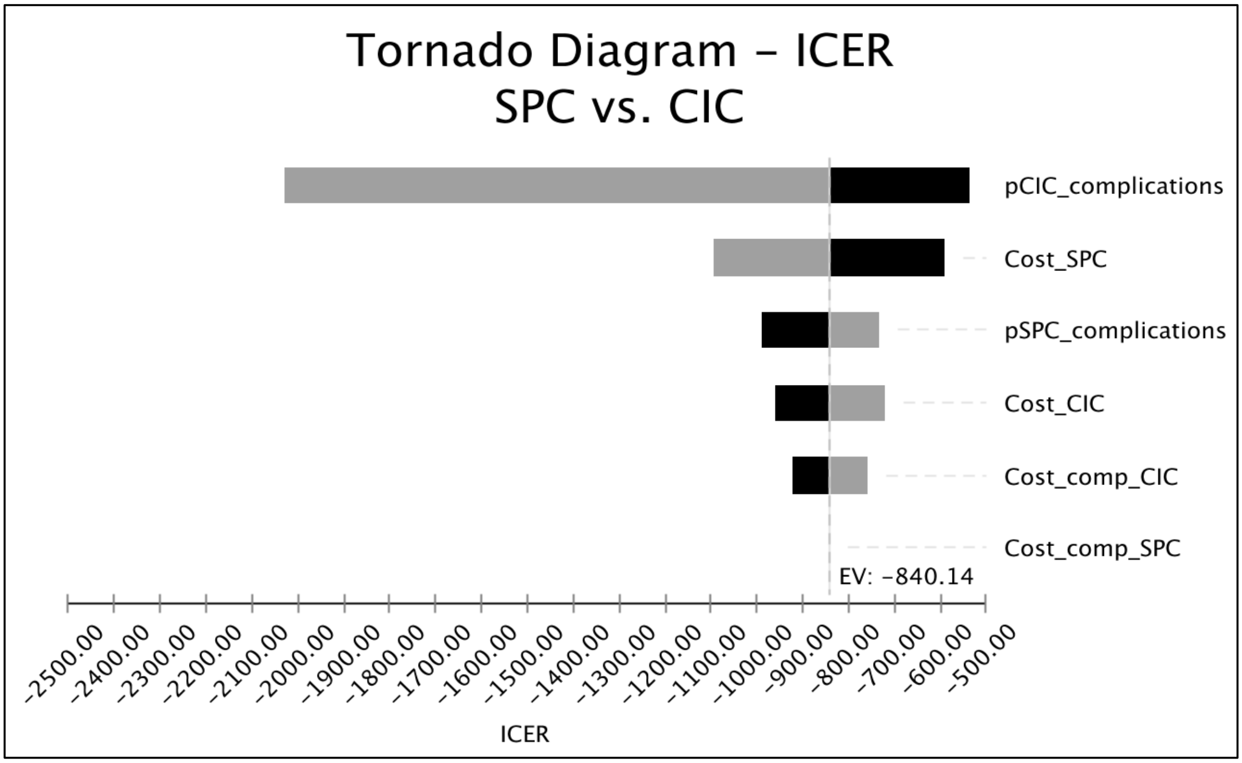

FIGURE 6.2b Schematic Tornado diagram, One-Way sensitivity analyses: Intermittent Catheters Versus Indwelling Suprapubic Catheters. The ICUR calculations were based on a willingness to pay corresponding to the Base-Case ICUR, that is, \$50 K/QALY. Abbreviations: CIC, clean intermittent catheter; Compl, complications; SPC, Suprapubic catheterization.

Table 6.6 Deterministic sensitivity analysis

	Strategy	Δ Incremental cost ($)	Δ QALYs	ICUR	ICUR interpretation	Δ ICUR from base case ($)
Base-case (vs CIC)	SPC	-330	1.77	-186	Dominant	-
	UC	-2,496	1.96	-1,273	Dominant	-
Daily catheterization frequency (CIC)						
3	SPC	-510	2.47	-207	Dominant	-21
	UC	-2,223	2.97	-749	Dominant	524
5	SPC	-160	2.47	-65	Dominant	121
	UC	-1,802	2.97	-607	Dominant	666
Cost per catheter (CIC: uncoated catheters)						
$0.50	SPC	-1468	2.20	-667	Dominant	-481
	UC	-2,763	2.70	-1,025	Dominant	248
$2.00	SPC	180	2.20	82	Cost-effective	104
	UC	-832	2.70	-309	Dominant	964
Cost per catheter (CIC: hydrophilic coated catheter)						
$3.99	SPC	2,306	0.94	2,453	Cost-effective	-2,267
	UC	2,902	2.24	1,295	Cost-effective	-22
$5.99	SPC	4,523	0.94	4,812	Cost-effective	-4,626
	UC	5,500	2.24	2,455	Cost-effective	-1,182
Probability for maintain intervention (CIC)						
0.0074	SPC	-1,734	2.48	-699	Dominant	-513
	UC	-2,831	3.74	-756	Dominant	517
0.174	SPC	-212	2.25	-94	Dominant	92
	UC	-2,325	2.69	-864	Dominant	409
Utility benefit from using hydrophilic coated versus uncoated (CIC)						
0.881	SPC	-1,944	1.35	-1,440	Dominant	-1,254
	UC	-3,163	2.96	-1,068	Dominant	205
Probability of complications (CIC)						
-25%	SPC	-319	3.85	-83	Dominant	103
	UC	-1,454	4.54	-320	Dominant	953
25%	SPC	-1,632	-0.19	-8,388	Dominant	-8,202
	UC	-1,642	1.1	-1,492	Dominant	-219
Probability of complications (SPC)						
-25%	SPC	-654	1.27	-516	Dominant	-430
	UC	-1,486	2.07	-717	Dominant	556
25%	SPC	-909	1.12	-812	Dominant	-626
	UC	-1,486	2.07	-717	Dominant	556
Probability of complications (UC)						
-25%	SPC	-3,809	0.16	-24,335	Dominant	-24,149
	UC	-2,233	2.38	-939	Dominant	334
25%	SPC	-3,809	0.16	-24,335	Dominant	-24,149
	UC	-2,328	2.76	-844	Dominant	429

Cost of CIC						
-25%	SPC	-1,288	1.21	-1,062	Dominant	-876
	UC	-1,687	2.23	-755	Dominant	518
25%	SPC	-858	1.21	-707	Dominant	-521
	UC	-1200	2.23	-537	Dominant	736
Cost of SPC						
-25%	SPC	-376	1.64	-230	Dominant	-44
	UC	-1,196	2.51	-476	Dominant	797
25%	SPC	-1,261	1.64	-770	Dominant	-584
	UC	-1,558	2.51	-620	Dominant	653
Cost of UC						
-25%	SPC	-1,390	2.08	-668	Dominant	-482
	UC	-1,071	3.61	-296	Dominant	977
25%	SPC	-1,535	2.08	-738	Dominant	-552
	UC	-1,698	3.61	-470	Dominant	803
Cost of complications (CIC)						
-25%	SPC	-2,046	2.01	-1,016	Dominant	-830
	UC	-2,879	3.32	-866	Dominant	407
25%	SPC	-1,755	2.01	-871	Dominant	-685
	UC	-2,589	3.32	-779	Dominant	494
Cost of complications (SPC)						
-25%	SPC	-2,245	0.85	-2629	Dominant	-2,443
	UC	-3,670	2.11	-1,741	Dominant	-468
25%	SPC	-2,522	0.85	-2952	Dominant	-2,766
	UC	-3,670	2.11	-1,741	Dominant	-468
Cost of complications (UC)						
-25%	SPC	-1,937	1.75	-1109	Dominant	-923
	UC	-2,554	3.07	-832	Dominant	441
25%	SPC	-1,937	1.75	-1109	Dominant	-923
	UC	-3,350	3.07	-1,092	Dominant	181
Time horizon						
15 years	SPC	-1,726	5.44	-317	Dominant	-131
	UC	-1,250	5.91	-211	Dominant	1,062
25 years	SPC	-1,277	5.96	-214	Dominant	-28
	UC	-1,341	6.33	-212	Dominant	1,061
Discount rate (costs and benefits)						
0%	SPC	-1,414	2.49	-567	Dominant	-381
	UC	-2,197	3.5	-627	Dominant	646
3%	SPC	-367	2.35	-156	Dominant	30
	UC	-2,500	2.52	-992	Dominant	281
Abbreviation: * Dominant is CIC; Comparator is SPC or UC						

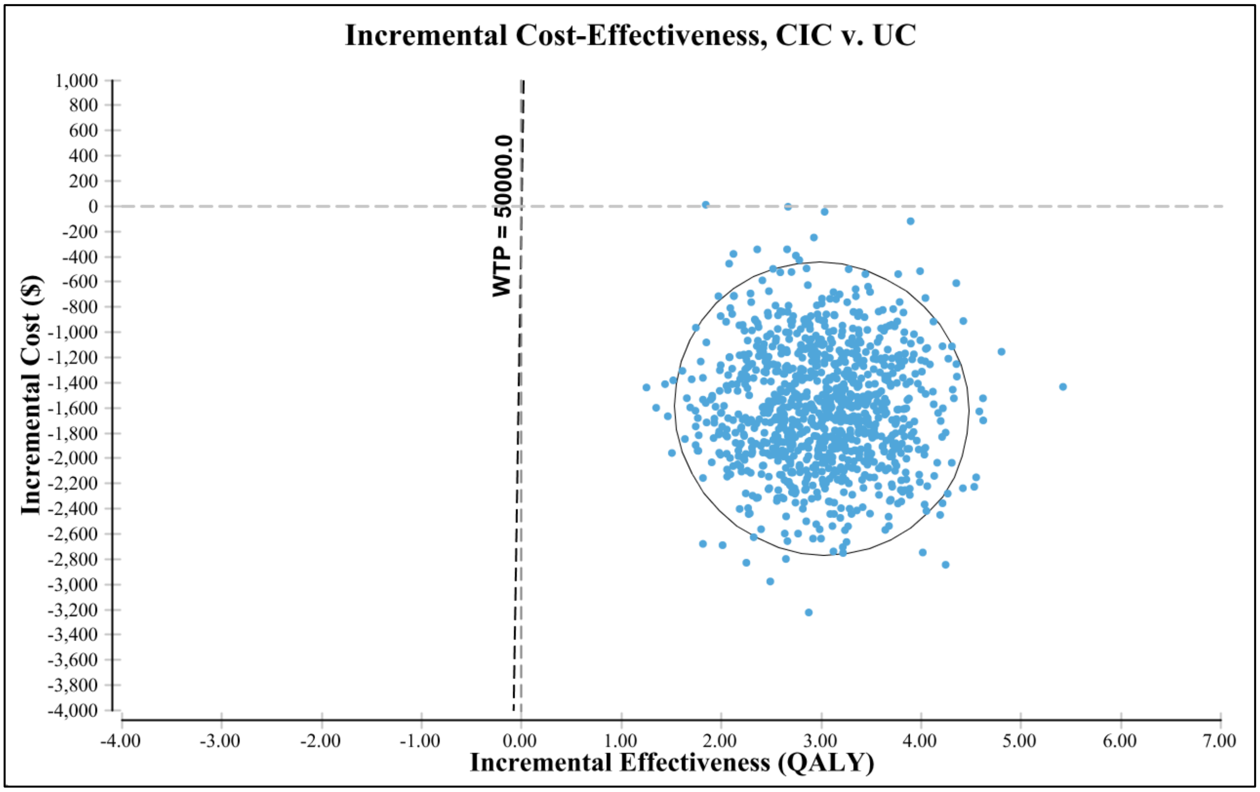

FIGURE 6.3a Probabilistic analysis. Scatterplot of the 1000 incremental cost-utility ratio (ICUR) simulations. Each data point represents the incremental costs and benefits (QALYs) of two bladder management technologies, including uncertainty parameters simultaneously sampled during each run. The probabilistic analysis results show that the probability that the incremental cost-utility ratio be under $50,000/QALY for CIC versus UC is 99%.

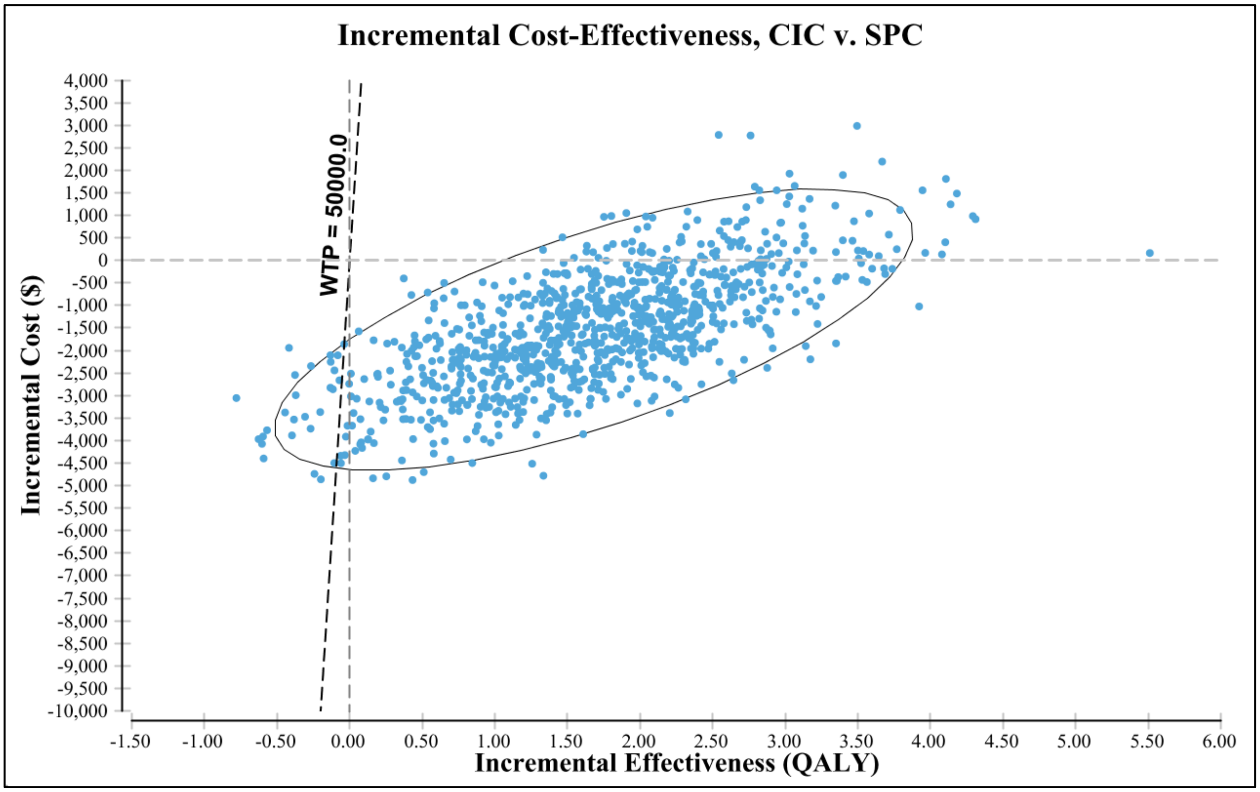

FIGURE 6.3b Probabilistic analysis. Scatterplot of the 1000 incremental cost-utility ratio (ICUR) simulations. Each data point represents the incremental costs and benefits (QALYs) of two bladder management technologies, including uncertainty parameters simultaneously sampled during each run. The probabilistic analysis results show that the probability that the incremental cost-utility ratio be under $50,000/QALY for CIC versus SPC is 86.8%

Chapter 7: Overall Discussion

7.1 Contribution to the literature

Quantifying disease burden and associated health care costs at a population level is a core domain in health economics and outcome research. Cost-utility studies measuring health outcomes using a common denominator highlight the impact of healthcare management strategies as well as advocate health care spending by government. In this context, it is important to highlight that many publicly funded health care systems don't fund enough catheters per month for single use CIC but do fund indwelling catheters fully. Consequently, it is essential to justify funding for care for a specific disease entity and increase awareness of a definite health condition expenditures.

Although evidence is still limited, current data indicate that not all SCI individuals with chronic urinary retention have to be treated using CIC to achieve maximum benefit. Indeed, many can be treated using other available strategies such as SPC or UC. Furthermore, a "one size fits all" approach to the management of NLUTD related to SCI has been debated, as patients select their preferred bladder emptying modality to suit the complex local anatomy, motor function and quality of life regardless of their individual risk of a catheter-related events.

In Canada, NLUTD is managed using either CIC, indwelling UC, or SPC, depending on factors such as clinical practice, patient convenience, anatomic limitations, bladder characteristics, catheter reimbursement/out-of-pocket costs, and conventions among the patients and treating physicians. In Quebec, there is no reimbursement of catheter material/s associated with CIC by the provincial healthcare system for SCI individuals requiring frequent catheterization. In this cost-effectiveness analysis the total cost analysed incorporates costs from the healthcare and also cost incurred by the patient directly, or possible health insurance programs. CIC cost-effectiveness is greatly affected by the fact that a large amount of the cost over lifetime may need to be paid by the individual. This may also be a reason to abandon CIC. Because of this, further evidence is essential, and broader evaluation of economic burden over the public health care system is currently being advocated.

Only few studies have explored this subject; however, none were implemented in a Canadian publicly funded health care system perspective. Thus, the current study sought to investigate the cost-effectiveness of CIC compared with indwelling suprapubic or urethral catherization in Canadian community-dwelling persons with NLUTD due to SCI. To the best of our knowledge, this is the first cost-effectiveness analysis of bladder management strategies to incorporate a clinical perspective with the catheter related impact on HRQoL by using QALYs, thus presenting a more elaborate representation of the benefits and cost associated with each treatment approach for spinal cord injury population.

7.2 Summary of the major findings

This dissertation provides clues to the health economic benefits of CIC in the management of NLUTD among spinal cord injured adults. Several techniques of assisted bladder emptying are available in Canada and current evidence suggests that there is no superior or robust bladder management approach for managing NLUTD from the user perspective. SCI individuals may change their assisted bladder emptying methods over time. We therefore developed a sequential analysis to compare the most widely used bladder care interventions: CIC, SPC, UC. In accordance with our analysis results, extended dominance (i.e., better effectiveness and a higher ICUR) was identified with single use noncoated and hydrophilic coated ICs.

In our comparison of the three catheter-based management modalities; uncoated IC (single use) had an incremental cost greater than $2,400 per 1.96 QALYs and 3 discounted life-years gained compared to UC. A 40-year-old SCI individual would gain an additional 1.77 QALYs and 1.72 LYGs if CIC was utilized instead of SPC at an incremental cost savings of $330. The cost differences were more pronounced between conventional and hydrophilic coated ICs. In the Canadian setting, the average cost for hydrophilic and noncoated ICs were $4.99 and $1.05 per unit, respectively. Alternatively, when indwelling catheters compared to single-use hydrophilic coated IC; CIC was perceived as cost-effective strategy (ICUR range from $1,295 to $4,812 per QALY in a probabilistic sensitivity analysis). These results were reinforced by the probabilistic sensitivity scatterplot, as 99% and 86.8% of model iterations indicated that noncoated ICs were cost-effective at a willingness-to-pay aggregate of $50,000 per QALY against UC and SPC, respectively. This model also incorporated additional utility gains when using hydrophilic ICs; however, based on overall low quality of evidence, it remains unclear whether a particular material or design of IC greatly enhance patient satisfaction or reduces catheter related complications compared with another type.

We performed a scenario analysis to evaluate people for whom greater or lesser daily catheterization frequency would be recommended. Conventional noncoated ICs would obviously deliver the best value for money for this cohort. This is because single use noncoated catheter had an ICUR of up to $749 per QALY gained in this direct comparison. This was also true for patients with varying degree of complications, compliance rate and cost acquisition. Given raised concerns in the literature with regard to efficacy and safety of catheter cleansing techniques, we did not examine multiple-use catheters in our scenario analysis. Additionally, the liability with off-label reuse has often ended up being questioned.[144]

7.3 Overall limitations and strength

While other economic evaluations only examined CIC, a key strength of this study is that it represents a comprehensive health economic examination of the most common bladder management strategies utilized in daily clinical practice in a population with NLUTD due to SCI. From a clinical perspective, assuming that a SCI individual will adhere to the same treatment modality over lifetime would be practically challenging. This cost-effectiveness study was modeled to reproduce the actual bladder management scenarios including potential catheter related events, genitourinary sequelae and quality of life indicators over life-time horizon. These treatment scenarios are guided by the values, utilities and Qol context inferred from RCTs when possible. Another important practical implication is that our model incorporated two important health states: switch and maintain intervention. These states reflect an individual's overall satisfaction with proposed management approach and indicate the extent to which patient's own priorities coincide with a particular bladder emptying method. Patients will maintain or change their treatment strategy according to their goals and healthcare professionals advice. An additional strength of the present model is the use of data from a mixed setting (i.e., inpatient/outpatient), different time horizons (i.e., 15 years and lifetime), and varied discount rates (i.e., 0%, 1.5%, and 3.0%,). These figures will reasonably reflect current clinical setting in Canada, where SCI individuals who use different bladder management techniques do so as either outpatients or during hospital or rehab stay. Our results seem to be rather robust, because the alternative scenario analysis confirmed that the majority of ICURs data points located in the northeast-quadrant of the cost-effectiveness plane, thus postulating a more comprehensive understanding of the merits associated with intermittent catheters for the health care system and users.

The present study was subject to a number of potential weaknesses. The quality of the available evidence with regards to frequency of catheter associated complications and transition rate between catheter modalities over time was limited. In general, data from cohort studies have consistently shown greater diversity in patient satisfaction and Qol, particularly when comparing SPC and CIC, and most often dependent on the nature of the diagnosis, patient factors, and the indication of catheterization. Another limitation of this study is that head-to-head trial data are inadequate to provide clear answers to all relevant comparisons between catheter modalities in all relevant clinical scenarios. Additionally, large scale trials using database registry lack the clinical granularity and consequently, cannot be generalized to all patients with SCI. To overcome this limitation, it was necessary to have some assumptions, and thus limit our results to the accuracy of our assumptions. We used mixed (inpatient and outpatient) data which might impact the estimates when it comes to certain scenarios such as UTI, as prevalence and incidence of UTI might differ across settings. For example, Cardenas and associates [145] reported lower rate of UTI in a community setting compared to inpatient data; this could be explained by improved health status of outpatients or likely because hospitalized patients are more closely monitored and thus more UTIs will be diagnosed. Results were not stratified for different SCI subpopulations; male and female populations, neurologic category and extent the injury due to insufficient data available to determine complication rates, effectiveness and Qol among SCI subgroups. Finally, indirect or societal costs related to change in employment status or household income, sick leaves and premature death are difficult to estimate in the monetary standpoint and were not examined in this study.

7.4 Future research

This research provides a grand total health care spending related to bladder management that would be expected for each newly diagnosed SCI case in Canada from the perspective of the public health care payer. In the future, it will be important to explore the broader societal impact of various bladder management practices, this should also include intangible components such as out-of-pocket costs, social welfare, and low income due to change in employment status and reduced productivity. Furthermore, many patients would switch from CIC to SPC or UC because they don't have good, clean access to bathroom at work. Considering the pandemic could play out for months, physicians and other healthcare providers need to implement new strategies which would enable more CIC in the future. Though the reported overall lifetime health costs related to bladder care in SCI individuals is not enormous compared to other chronic health conditions, interestingly, it is forecasted that the proportion of SCI individuals will continue to rise as the population ages in Canada. Therefore, the total net cost per individual experiencing a SCI and requiring a long-term assisted bladder care suggests that this condition warrants greater attention. Further work is needed to fully understand the impact of different bladder management strategies and devices on patient satisfaction and quality of life. Owing to a lack of trials within different SCI subpopulation with diverse settings, more research using controlled trials or "real world evidence" is needed to explore how different bladder management practices in these subgroups might impact the overall cost-effectiveness over the long-term. Furthermore, a larger population database registry is required to accurately analyze costs in SCI subgroups. Future research should strive to address the liability and efficacy concerns associated with reuse of ICs since multiple-use of ICs have an inherently greater risk of recurrent UTIs.[146] Our society needs to support protocols and policies to minimize catheter associated complications in SCI individuals and invest in educational and awareness programs of neurogenic bladder dysfunction and benefits and burdens of different bladder management options.

7.5 Conclusions

Our health economic modelling study demonstrates that intermittent catheterization utilized by an adult population with SCI is the dominant and more economically attractive treatment strategy compared with SPC or UC over lifetime horizon, from a Canadian public payer perspective. Single-use noncoated IC have higher effectiveness and a higher ICUR, while single-use hydrophilic IC offer increased benefits at lower cost. While it may be cost attractive for some patients to use noncoated ICs, single-use hydrophilic coated catheters have the greatest opportunity of being cost-effective. This highlights the fact that coverage for HC catheters is nonexistent in most government plans. Therefore, new strategies about noncoated ICs as well as HC catheters should be implemented.

Taking into account the marginal differences in overall costs across the three bladder management approaches, indwelling catheterization (SPC or UC) may appear as cost competitive modality with acceptable long-term efficacy. However, these results should be treated with caution in the context of long-term treatment of NLUTD within SCI cohort. It is also important to consider the markedly higher costs of complications-associated and device transition costs in the Canadian setting, which is a key driver of the overall bladder management associated costs throughout the lifetime simulation. The insights gained from this thesis may be of assistance to health care decision making and government advocacy groups to highlight the current limitations and areas of important health care expenditures relevant to the SCI population.

References

1. Afsar S, Yemisci O, Cosar S, Cetin N. Compliance with clean intermittent catheterization in spinal cord injury patients: a long-term follow-up study. *Spinal Cord.* 2013;51(8):645.
2. Patel DP, Herrick JS, Stoffel JT, et al. Reasons for cessation of clean intermittent catheterization after spinal cord injury: Results from the Neurogenic Bladder Research Group spinal cord injury registry. *Neurourology and Urodynamics.* 2020;39(1):211-219.
3. Cadotte DW, Fehlings MG. Spinal cord injury. *Principles of Neurological Surgery*: Elsevier; 2012:445-454.
4. Vercelli A, Boido M. Spinal Cord Injury. *Neurobiology of Brain Disorders*: Elsevier; 2015:207-218.
5. Farry A, Baxter D. *The incidence and prevalence of spinal cord injury in Canada: overview and estimates based on current evidence.* Rick Hansen Institute; 2011.
6. Praxis Spinal Cord Institute, Rick Hansen SCI Registry. Community Report. [Community Report]. 2019; http://praxisinstitute.org/wp-content/uploads/2019/10/RHSCIR_CommunityReport_2017.pdf.
7. DeVivo MJ. Epidemiology of traumatic spinal cord injury: trends and future implications. *Spinal cord.* 2012;50(5):365-372.
8. Sekhon LH, Fehlings MG. Epidemiology, demographics, and pathophysiology of acute spinal cord injury. *Spine.* 2001;26(24S):S2-S12.
9. Wyndaele M, Wyndaele J-J. Incidence, prevalence and epidemiology of spinal cord injury: what learns a worldwide literature survey? *Spinal cord.* 2006;44(9):523-529.
10. Jain NB, Ayers GD, Peterson EN, et al. Traumatic spinal cord injury in the United States, 1993-2012. *Jama.* 2015;313(22):2236-2243.
11. Center NSCIS. National Spinal Cord Injury Statistical Center Annual Statistical Report. *Birmingham, AL, University of Alabama at Birmingham.* 2019.
12. Furlan JC, Krassioukov A, Miller WC, von Elm E. Epidemiology of traumatic SCI. *Spinal cord injury rehabilitation evidence.* 2010;3:1-15.
13. Singh A, Tetreault L, Kalsi-Ryan S, Nouri A, Fehlings MG. Global prevalence and incidence of traumatic spinal cord injury. *Clinical epidemiology.* 2014;6:309.
14. Furlan JC, Sakakibara BM, Miller WC, Krassioukov AV. Global incidence and prevalence of traumatic spinal cord injury. *Canadian journal of neurological sciences.* 2013;40(4):456-464.
15. Lasfargues J, Custis D, Morrone F, Nguyen T. A model for estimating spinal cord injury prevalence in the United States. *Spinal Cord.* 1995;33(2):62-68.
16. Jackson AB, Dijkers M, DeVivo MJ, Poczatek RB. A demographic profile of new traumatic spinal cord injuries: change and stability over 30 years. *Archives of physical medicine and rehabilitation.* 2004;85(11):1740-1748.
17. Campagnolo DI, Kirshblum S, Nash MS, Heary RF, Gorman PH. *Spinal cord medicine.* Lippincott Williams & Wilkins; 2011.
18. Branco F, Cardenas DD, Svircev JN. Spinal cord injury: a comprehensive review. *Physical medicine and rehabilitation clinics of North America.* 2007;18(4):651-679.
19. Ditunno J, Young W, Donovan W, Creasey G. The international standards booklet for neurological and functional classification of spinal cord injury. *Spinal Cord.* 1994;32(2):70-80.
20. Ditunno Jr J. Functional assessment measures in CNS trauma. *Journal of neurotrauma.* 1992;9:S301-305.

21. Frankel H, Hancock D, Hyslop G, et al. The value of postural reduction in the initial management of closed injuries of the spine with paraplegia and tetraplegia. *Spinal Cord.* 1969;7(3):179-192.
22. Hachem LD, Ahuja CS, Fehlings MG. Assessment and management of acute spinal cord injury: From point of injury to rehabilitation. *The journal of spinal cord medicine.* 2017;40(6):665-675.
23. Dryden DM, Saunders LD, Rowe BH, et al. The epidemiology of traumatic spinal cord injury in Alberta, Canada. *Canadian journal of neurological sciences.* 2003;30(2):113-121.
24. Couris C, Guilcher S, Munce SE, et al. Characteristics of adults with incident traumatic spinal cord injury in Ontario, Canada. *Spinal Cord.* 2010;48(1):39-44.
25. New P, Simmonds F, Stevermuer T. A population-based study comparing traumatic spinal cord injury and non-traumatic spinal cord injury using a national rehabilitation database. *Spinal cord.* 2011;49(3):397-403.
26. McColl MA, Walker J, Stirling P, Wilkins R, Corey P. Expectations of life and health among spinal cord injured adults. *Spinal cord.* 1997;35(12):818-828.
27. DeViro MJ, Stover SL, Black KJ. Prognostic factors for 12-year survival after spinal cord injury. *Archives of physical medicine and rehabilitation.* 1992;73(2):156-162.
28. DeVivo M. Estimating life expectancy for use in determining lifetime costs of care. *Topics in Spinal Cord Injury Rehabilitation.* 2002;7(4):49-58.
29. Shavelle RM, Paculdo DR, Tran LM, Strauss DJ, Brooks JC, DeVivo MJ. Mobility, continence, and life expectancy in persons with ASIA impairment scale grade D spinal cord injuries. *American journal of physical medicine & rehabilitation.* 2015;94(3):180-191.
30. Kirshblum SC, Burns SP, Biering-Sorensen F, et al. International standards for neurological classification of spinal cord injury (revised 2011). *The journal of spinal cord medicine.* 2011;34(6):535-546.
31. Gajewski JB, Drake MJ. Neurological lower urinary tract dysfunction essential terminology. *Neurourology and Urodynamics.* 2018;37(S6):S25-S31.
32. Stover SL, Michael J, Go BK. History, implementation, and current status of the National Spinal Cord Injury Database. *Archives of physical medicine and rehabilitation.* 1999;80(11):1365-1371.
33. Ku JH. The management of neurogenic bladder and quality of life in spinal cord injury. *BJU international.* 2006;98(4):739-745.
34. Park SE, Elliott S, Noonan VK, et al. Impact of bladder, bowel and sexual dysfunction on health status of people with thoracolumbar spinal cord injuries living in the community. *The journal of spinal cord medicine.* 2017;40(5):548-559.
35. Corcos J. Practical guide to diagnosis and follow-up of patients with neurogenic bladder dysfunction. *Textbook of the Neurogenic Bladder*: CRC Press; 2015:443-448.
36. Wyndaele J-J. The management of neurogenic lower urinary tract dysfunction after spinal cord injury. *Nature Reviews Urology.* 2016;13(12):705-714.
37. Panicker JN, Fowler CJ, Kessler TM. Lower urinary tract dysfunction in the neurological patient: clinical assessment and management. *The Lancet Neurology.* 2015;14(7):720-732.
38. Madersbacher H. The various types of neurogenic bladder dysfunction: an update of current therapeutic concepts. *Spinal Cord.* 1990;28(4):217-229.

39. Drake M, Apostolidis A, Cocci A, et al. Neurogenic lower urinary tract dysfunction; management recommendations of the Neurologic Incontinence committee of the fifth International Consultation on Incontinence 2013.
40. Health UDo, Services H. Consortium for Spinal Cord Medicine. Bladder management for adults with spinal cord injury: a clinical practice guideline for health-care providers. *J Spinal Cord Med.* 2006;29(5):527-573.
41. Siroky MB. Pathogenesis of bacteriuria and infection in the spinal cord injured patient. *The American journal of medicine.* 2002;113(1):67-79.
42. Biering-Sørensen F, Nielans H-M, Dørflinger T, Sørensen B. Urological situation five years after spinal cord injury. *Scandinavian journal of urology and nephrology.* 1999;33(3):157-161.
43. Theisen KM, Mann R, Roth JD, et al. Frequency of patient-reported UTIs is associated with poor quality of life after spinal cord injury: a prospective observational study. *Spinal Cord.* 2020:1-8.
44. Chan B, Ieraci L, Mitsakakis N, Pham B, Krahn M. Net costs of hospital-acquired and pre-admission PUs among older people hospitalised in Ontario. *journal of wound care.* 2013;22(7):341-346.
45. Buczynski AZ. Complications related to neurogenic bladder dysfunction–I: infection, lithiasis and neoplasia. *Evaluation and Treatment of the Neurogenic Bladder*: CRC Press; 2004:329-336.
46. Nseyo U, Santiago-Lastra Y. Long-term complications of the neurogenic bladder. *Urologic Clinics.* 2017;44(3):355-366.
47. Kavanagh A, Baverstock R, Campeau L, et al. Canadian urological association guideline: diagnosis, management, and surveillance of neurogenic lower urinary tract dysfunction–full text. *Canadian Urological Association Journal.* 2019;13(6):E157.
48. Krebs J, Wöllner J, Pannek J. Risk factors for symptomatic urinary tract infections in individuals with chronic neurogenic lower urinary tract dysfunction. *Spinal Cord.* 2016;54(9):682-686.
49. Donnelly J, Hackler RH, Bunts RC. Present urologic status of the World War II paraplegic: 25-year followup. Comparison with status of the 20-year Korean War paraplegic and 5-year Vietnam paraplegic. *The Journal of urology.* 1972;108(4):558-562.
50. Sung BM, Oh DJ, Choi MH, Choi HM. Chronic kidney disease in neurogenic bladder. *Nephrology.* 2018;23(3):231-236.
51. Lawrenson R, Wyndaele J-J, Vlachonikolis I, Farmer C, Glickman S. Renal failure in patients with neurogenic lower urinary tract dysfunction. *Neuroepidemiology.* 2001;20(2):138-143.
52. Campeau L, Shamout S, Baverstock RJ, et al. Canadian Urological Association Best Practice Report: Catheter use. *Canadian Urological Association Journal.* 2020;14(7).
53. Weld KJ, GRANEY MJ, DMOCHOWSKI RR. Differences in bladder compliance with time and associations of bladder management with compliance in spinal cord injured patients. *The Journal of urology.* 2000;163(4):1228-1233.
54. Chen Y, DeVivo MJ, Stover SL, Lloyd LK. Recurrent kidney stone: a 25-year follow-up study in persons with spinal cord injury. *Urology.* 2002;60(2):228-232.
55. Chen Y, DeVivo M, Roseman J. Current trend and risk factors for kidney stones in persons with spinal cord injury: a longitudinal study. *Spinal Cord.* 2000;38(6):346-353.

56. Bartel P, Krebs J, Wöllner J, Göcking K, Pannek J. Bladder stones in patients with spinal cord injury: a long-term study. *Spinal Cord.* 2014;52(4):295-297.
57. Gormley EA. Urologic complications of the neurogenic bladder. *Urologic Clinics.* 2010;37(4):601-607.
58. Cornejo-Dávila V, Durán-Ortiz S, Pacheco-Gahbler C. Incidence of urethral stricture in patients with spinal cord injury treated with clean intermittent self-catheterization. *Urology.* 2017;99:260-264.
59. Krebs J, Wollner J, Pannek J. Urethral strictures in men with neurogenic lower urinary tract dysfunction using intermittent catheterization for bladder evacuation. *Spinal Cord.* 2015;53(4):310-313.
60. Ruffion A, Chartier-Kastler E. Specific features of urethral diseases in spinal cord injury patients. *Progres en urologie: journal de l'Association francaise d'urologie et de la Societe francaise d'urologie.* 2007;17(3):436-439.
61. Weld KJ, DMOCHOWSKI RR. Effect of bladder management on urological complications in spinal cord injured patients. *The Journal of urology.* 2000;163(3):768-772.
62. Mitsui T, Minami K, Furuno T, Morita H, Koyanagi T. Is suprapubic cystostomy an optimal urinary management in high quadriplegics? *European urology.* 2000;38(4):434-438.
63. Hooton TM, Bradley SF, Cardenas DD, et al. Diagnosis, prevention, and treatment of catheter-associated urinary tract infection in adults: 2009 International Clinical Practice Guidelines from the Infectious Diseases Society of America. *Clinical infectious diseases.* 2010;50(5):625-663.
64. Feifer A, Corcos J. Contemporary role of suprapubic cystostomy in treatment of neuropathic bladder dysfunction in spinal cord injured patients. *Neurourology and Urodynamics: Official Journal of the International Continence Society.* 2008;27(6):475-479.
65. Warren JW. The catheter and urinary tract infection. *Medical Clinics of North America.* 1991;75(2):481-493.
66. Warren JW. Catheter-associated urinary tract infections. *International journal of antimicrobial agents.* 2001;17(4):299-303.
67. Garibaldi RA, Burke JP, Dickman ML, Smith CB. Factors predisposing to bacteriuria during indwelling urethral catheterization. *New England Journal of Medicine.* 1974;291(5):215-219.
68. Warren JW. Catheter-associated urinary tract infections. *Infectious disease clinics of North America.* 1997;11(3):609-622.
69. Ku JH, Jung T, Lee J, Park W, Shim H. Influence of bladder management on epididymo-orchitis in patients with spinal cord injury: clean intermittent catheterization is a risk factor for epididymo-orchitis. *Spinal Cord.* 2006;44(3):165.
70. Vaidyanathan S, Soni B, Dundas S, Krishnan K. Urethral cytology in spinal cord injury patients performing intermittent catheterisation. *Spinal Cord.* 1994;32(7):493.
71. Yavuzer G, Gök H, Tuncer S, Soygür T, Arikan N, Arasil T. Compliance with bladder management in spinal cord injury patients. *Spinal cord.* 2000;38(12):762-765.
72. Lane GI, Driscoll A, Tawfik K, Chrouser K. A cross-sectional study of the catheter management of neurogenic bladder after traumatic spinal cord injury. *Neurourology and urodynamics.* 2018;37(1):360-367.

73. Zlatev DV, Shem K, Elliott CS. Predictors of long-term bladder management in spinal cord injury patients—Upper extremity function may matter most. *Neurourology and urodynamics.* 2018;37(3):1106-1112.
74. Chan BC-F, Cadarette SM, Wodchis WP, Krahn MD, Mittmann N. The lifetime cost of spinal cord injury in Ontario, Canada: A population-based study from the perspective of the public health care payer. *The Journal of Spinal Cord Medicine.* 2019;42(2):184-193.
75. Welk B, Isaranuwatchai W, Krassioukov A, Husted Torp L, Elterman D. Cost-effectiveness of hydrophilic-coated intermittent catheters compared with uncoated catheters in Canada: a public payer perspective. *Journal of medical economics.* 2018;21(7):639-648.
76. Krueger H, Noonan V, Trenaman L, Joshi P, Rivers CS. The economic burden of traumatic spinal cord injury in Canada. *Chronic diseases and injuries in Canada.* 2013;33(3).
77. Dryden DM, Saunders LD, Jacobs P, et al. Direct health care costs after traumatic spinal cord injury. *Journal of Trauma and Acute Care Surgery.* 2005;59(2):441-447.
78. Dryden D, Saunders L, Rowe B, et al. Utilization of health services following spinal cord injury: a 6-year follow-up study. *Spinal cord.* 2004;42(9):513-525.
79. Ahn H, Lewis R, Santos A, et al. Forecasting financial resources for future traumatic spinal cord injury care using simulation modeling. *Journal of neurotrauma.* 2017;34(20):2917-2923.
80. Chen Y, DeVivo MJ, Jackson AB. Pressure ulcer prevalence in people with spinal cord injury: age-period-duration effects. *Archives of physical medicine and rehabilitation.* 2005;86(6):1208-1213.
81. Henzel MK, Ho CH. Pressure ulcer management and research priorities for patients with spinal cord injury: consensus opinion from SCI QUERI Expert Panel on Pressure Ulcer Research Implementation. *Journal of rehabilitation research and development.* 2011;48(3):XI.
82. Houghton PE, Campbell K. *Canadian best practice guidelines for the prevention and management of pressure ulcers in people with Spinal Cord Injury: a resource handbook for clinicians.* Ontario Neurotrauma Foundation; 2013.
83. Kruger EA, Pires M, Ngann Y, Sterling M, Rubayi S. Comprehensive management of pressure ulcers in spinal cord injury: current concepts and future trends. *The journal of spinal cord medicine.* 2013;36(6):572-585.
84. Johnson RL, Gerhart KA, McCray J, Menconi JC, Whiteneck GG. Secondary conditions following spinal cord injury in a population-based sample. *Spinal cord.* 1998;36(1):45-50.
85. Noreau L, Proulx P, Gagnon L, Drolet M, Laramée M-T. Secondary impairments after spinal cord injury: a population-based study. *American journal of physical medicine & rehabilitation.* 2000;79(6):526-535.
86. White BAB, Dea N, Street JT, et al. The Economic Burden of Urinary Tract Infection and Pressure Ulceration in Acute Traumatic Spinal Cord Injury Admissions: Evidence for Comparative Economics and Decision Analytics from a Matched Case-Control Study. *J Neurotrauma.* 2017;34(20):2892-2900.
87. Bermingham SL, Hodgkinson S, Wright S, Hayter E, Spinks J, Pellowe C. Intermittent self catheterisation with hydrophilic, gel reservoir, and non-coated catheters: a systematic review and cost effectiveness analysis. *Bmj.* 2013;346:e8639.

88. Clark JF, Mealing SJ, Scott DA, et al. A cost-effectiveness analysis of long-term intermittent catheterisation with hydrophilic and uncoated catheters. *Spinal Cord.* 2015.
89. Watanabe T, Yamamoto S, Gotoh M, et al. Cost-Effectiveness Analysis of Long-Term Intermittent Self-Catheterization with Hydrophilic-Coated and Uncoated Catheters in Patients with Spinal Cord Injury in Japan. *LUTS: Lower Urinary Tract Symptoms.* 2017;9(3):142-150.
90. Håkansson MÅ, Neovius K, Lundqvist T. Healthcare Costs Associated With Hydrophilic-Coated and Non-Coated Urinary Catheters For Intermittent Use in the United States. *Urologic Nursing.* 2016;36(5).
91. Rognoni C, Tarricone R. Healthcare resource consumption for intermittent urinary catheterisation: cost-effectiveness of hydrophilic catheters and budget impact analyses. *BMJ open.* 2017;7(1):e012360.
92. Truzzi JC, Teich V, Pepe C. Can hydrophilic coated catheters be beneficial for the public healthcare system in Brazil?-A cost-effectiveness analysis in patients with spinal cord injuries. *International braz j urol.* 2018;44(1):121-131.
93. Ontario HQ. Intermittent Catheters for Chronic Urinary Retention: A Health Technology Assessment. *Ontario health technology assessment series.* 2019;19(1):1.
94. Noonan VK, Fingas M, Farry A, et al. Incidence and prevalence of spinal cord injury in Canada: a national perspective. *Neuroepidemiology.* 2012;38(4):219-226.
95. Institute RH. *Rick Hansen Spinal Cord Injury Registry - A look at traumatic spinal cord injury in Canada in 2017.* Vancouver, BC: RHI;2018.
96. Birmingham A. br/> National spinal cord injury statistical center, facts and figures at a glance.[Prevalence of SCI (2013)]. March; 2013.
97. Frankel H, Coll J, Charlifue S, et al. Long-term survival in spinal cord injury: a fifty year investigation. *Spinal cord.* 1998;36(4):266-274.
98. Injury SC. Facts and Figures at a Glance. *J Spinal Cord Med.* 2016;39(4):493-494.
99. Skelton F, Hoffman JM, Reyes M, Burns SP. Examining health-care utilization in the first year following spinal cord injury. *The journal of spinal cord medicine.* 2015;38(6):690-695.
100. Feifer A, Corcos J. Contemporary role of suprapubic cystostomy in treatment of neuropathic bladder dysfunction in spinal cord injured patients. *Neurourology and urodynamics.* 2008;27(6):475-479.
101. Peatfield R, Burt A, Smith P. Suprapubic catheterisation after spinal cord injury: a follow-up report. *Paraplegia.* 1983;21(4):220-226.
102. Hunter KF, Bharmal A, Moore KN. Long-term bladder drainage: Suprapubic catheter versus other methods: A scoping review. *Neurourology and urodynamics.* 2013;32(7):944-951.
103. Cameron AP, Wallner LP, Tate DG, Sarma AV, Rodriguez GM, Clemens JQ. Bladder management after spinal cord injury in the United States 1972 to 2005. *The Journal of urology.* 2010;184(1):213-217.
104. Hansen R, Biering-Sørensen F, Kristensen J. Bladder emptying over a period of 10–45 years after a traumatic spinal cord injury. *Spinal Cord.* 2004;42(11):631.
105. Perkash I, Giroux J. Clean intermittent catheterization in spinal cord injury patients: a followup study. *The Journal of urology.* 1993;149(5 Part 1):1068-1071.

106. Savic G, Frankel HL, Jamous MA, Soni BM, Charlifue S. Long-term bladder and bowel management after spinal cord injury: a 20-year longitudinal study. *Spinal Cord.* 2018;56(6):575-581.
107. Vekeman F, Yameogo N-D, Lefebvre P, Bailey RA, McKenzie RS, Piech CT. Healthcare costs associated with nephrology care in pre-dialysis chronic kidney disease patients. *Journal of medical economics.* 2010;13(4):673-680.
108. Casey JT, Erickson BA, Navai N, Zhao LC, Meeks JJ, Gonzalez CM. Urethral reconstruction in patients with neurogenic bladder dysfunction. *J Urol.* 2008;180(1):197-200.
109. Secrest CL, Madjar S, Sharma AK, Covington-Nichols C. Urethral reconstruction in spinal cord injury patients. *J Urol.* 2003;170(4 Pt 1):1217-1221; discussion 1221.
110. Hillary CJ, Osman NI, Chapple CR. Current trends in urethral stricture management. *Asian journal of Urology.* 2014;1(1):46-54.
111. Kavanagh A, Baverstock R, Campeau L, et al. Canadian Urological Association guideline for the diagnosis, management, and surveillance of neurogenic lower urinary tract dysfunction. 2019;13(6).
112. Welk B, Shariff S, Ordon M, Craven BC, Herschorn S, Garg A. The surgical management of upper tract stone disease among spinal cord-injured patients. *Spinal cord.* 2013;51(6):457.
113. Régie de l'assurance maladie du Québec. Manuel des médecins spécialistes. 2019; Québec: RAMQ. Available at: http://www.ramq.gouv.qc.ca/fr/professionnels/medecins-specialistes/manuels/Pages/remuneration-acte.aspx. Accessed June, 2019.
114. Régie de l'assurance maladie du Québec. Manuel des médecins spécialistes. 2015; Québec: RAMQ. Available at: www.ramq.gouv.qc.ca/fr/professionnels/medecinsspecialistes/manuels/Pages/facturation.asp. Accessed June, 2015.
115. SCI supply inc. 2019; Intermittent Catheters. Available at: https://www.scisupply.ca/intermittent-catheters. Accessed May, 2019.
116. Canmeddirect. 2019; CONTINENCE PRODUCTS. Available at: https://www.canmeddirect.ca/. Accessed May, 2019.
117. CathetersPLUS™. 2019; Continence products. Available at: https://www.cathetersplus.com/. Accessed May, 2019.
118. Alba Medical. 2019; Continence products. Available at: http://www.albamedical.ca/shop/catalogue/index.php?idctg_ctg=187. Accessed May 2019.
119. Groen J, Pannek J, Diaz DC, et al. Summary of European Association of Urology (EAU) guidelines on neuro-urology. *European urology.* 2016;69(2):324-333.
120. Lee KM, McCarron CE, Bryan S, Coyle D, Krahn M, McCabe C. Guidelines for the Economic Evaluation of Health Technologies: Canada—4th Edition.
121. Bennett CJ, Young MN, Adkins RH, Diaz F. Comparison of bladder management complication outcomes in female spinal cord injury patients. *The Journal of urology.* 1995;153(5):1458-1460.
122. Wyndaele J-J, Maes D. Clean intermittent self-catheterization: a 12-year followup. *The Journal of urology.* 1990;143(5):906-908.
123. Gao Y, Danforth T, Ginsberg DA. Urologic management and complications in spinal cord injury patients: a 40-to 50-year follow-up study. *Urology.* 2017;104:52-58.

124. Chai T, Chung A, Belville W, Faerber G. Compliance and complications of clean intermittent catheterization in the spinal cord injured patient. *Spinal Cord.* 1995;33(3):161-163.
125. Maynard FM, Diokno AC. Clean intermittent catheterization for spinal cord injury patients. *The Journal of Urology.* 1982;128(3):477-480.
126. Krebs J, Wöllner J, Pannek J. Bladder management in individuals with chronic neurogenic lower urinary tract dysfunction. *Spinal cord.* 2016;54(8):609-613.
127. Katsumi H, Kalisvaart J, Ronningen L, Hovey R. Urethral versus suprapubic catheter: choosing the best bladder management for male spinal cord injury patients with indwelling catheters. *Spinal cord.* 2010;48(4):325.
128. Shamout S, Biardeau X, Corcos J, Campeau L. Outcome comparison of different approaches to self-intermittent catheterization in neurogenic patients: a systematic review. *Spinal Cord.* 2017.
129. Ku JH, Choi WJ, Lee KY, et al. Complications of the upper urinary tract in patients with spinal cord injury: a long-term follow-up study. *Urological research.* 2005;33(6):435-439.
130. Clark J, Mealing S, Scott D, et al. A cost-effectiveness analysis of long-term intermittent catheterisation with hydrophilic and uncoated catheters. *Spinal Cord.* 2016;54(1):73-77.
131. Gouvernement du Québec. Ministère de la Santé et des Services sociaux. 2015; Performance hospitalière. Available at: www.informa.msss.gouv.qc.ca. Accessed June, 2016.
132. Vogel LC, Krajci KA, Anderson CJ. Adults with pediatric-onset spinal cord injuries: part 3: impact of medical complications. *The journal of spinal cord medicine.* 2002;25(4):297-305.
133. Zebracki K, Anderson C, Chlan K, Vogel L. Outcomes of adults with pediatric-onset spinal cord injury: Longitudinal findings and implications on transition to adulthood. *Topics in spinal cord injury rehabilitation.* 2010;16(1):17-25.
134. Joshi H, Stainthorpe A, MacDonagh R, Keeley F, Timoney A. Indwelling ureteral stents: evaluation of symptoms, quality of life and utility. *The Journal of urology.* 2003;169(3):1065-1069.
135. Gorodetskaya I, Zenios S, Mcculloch CE, et al. Health-related quality of life and estimates of utility in chronic kidney disease. *Kidney international.* 2005;68(6):2801-2808.
136. Laupacis A, Keown P, Pus N, et al. A study of the quality of life and cost-utility of renal transplantation. *Kidney international.* 1996;50(1):235-242.
137. Lee YR, Tashjian CA, Brouse SD, et al. Antibiotic Therapy and Bacterial Resistance in Patients With Spinal Cord Injury. *FEDERAL PRACTITIONER.* 2014.
138. Karlowsky JA, Lagacé-Wiens PR, Simner PJ, et al. Antimicrobial resistance in urinary tract pathogens in Canada from 2007 to 2009: CANWARD surveillance study. *Antimicrobial agents and chemotherapy.* 2011;55(7):3169-3175.
139. Waites KB, Chen Y-y, DeVivo MJ, Canupp KC, Moser SA. Antimicrobial resistance in gram-negative bacteria isolated from the urinary tract in community-residing persons with spinal cord injury. *Archives of physical medicine and rehabilitation.* 2000;81(6):764-769.

140. Baldea KG, Blackwell RH, Vedachalam S, et al. Outcomes of percutaneous nephrolithotomy in spinal cord injury patients as compared to a matched cohort. *Urolithiasis.* 2017;45(5):501-506.
141. Morhardt DR, Hadj-Moussa M, Chang H, et al. Outcomes of Ureteroscopic Stone Treatment in Patients With Spinal Cord Injury. *Urology.* 2018;116:41-46.
142. Ferguson GG, Bullock TL, Anderson RE, Blalock RE, Brandes SB. Minimally invasive methods for bulbar urethral strictures: a survey of members of the American Urological Association. *Urology.* 2011;78(3):701-706.
143. Manns B, Hemmelgarn B, Tonelli M, et al. The Cost of Care for People With Chronic Kidney Disease. *Canadian journal of kidney health and disease.* 2019;6:2054358119835521.
144. Håkansson MÅ. Reuse versus single-use catheters for intermittent catheterization: what is safe and preferred? Review of current status. *Spinal Cord.* 2014;52(7):511.
145. Cardenas DD, Moore KN, Dannels-McClure A, et al. Intermittent catheterization with a hydrophilic-coated catheter delays urinary tract infections in acute spinal cord injury: a prospective, randomized, multicenter trial. *PM R.* 2011;3(5):408-417.
146. Christison K, Walter M, Wyndaele J-JJ, et al. Intermittent catheterization: The devil is in the details. *Journal of neurotrauma.* 2018;35(7):985-989.