



Economic Evaluation of Spinal Cord Injury

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1 Chapter Summary

What are economic analyses and are why are they important?

Economic analyses provide valuable information on the burden of illness or economic impact of specific health care interventions. Cost-of-illness studies estimate the total cost burden of a condition to the health care system. On the other hand, economic evaluations compare the cost and consequences of alternative health care interventions options. Depending on the unit of measure for health outcomes, the economic evaluation may be a cost effectiveness analysis (non-monetary health outcome), cost utility analysis (outcome in quality adjusted life years) or cost benefit analysis (health outcomes in monetary units). These analyses help inform health care decision-makers on the value for money of new interventions.

Are there any economic analysis studies for the SCI population?

There was a total of 31 studies that were published in peer-reviewed scientific journals between the 2004 and 2018; 19 economic evaluations and 12 cost of illness studies.

The results from several studies suggest that the following interventions may be cost effective for individuals with SCI: Hydrophilic catheters for intermittent catheterization compared to uncoated catheters.

The following interventions were also observed to be cost effective based on a single study:

Intrathecal baclofen for disabling spasticity compared to current treatment

Trans-anal irrigation compared to conservative bowel management

Sacral anterior root stimulation for neurogenic bladder

Duplex ultrasound for deep venous thrombosis surveillance

Sildenafil for erectile dysfunction

Electrical stimulation for pressure injury

Telephone support in addition to standard pressure injury management

Negative pressure wound therapy with weekly dressings compared to standard care for pressure injury

Fibrin sealant for surgical treatment of pressure injury compared to standard surgical debridement

Cough stimulator neuroprosthesis for restoration of effective cough compared to standard respiratory management

Early decompression for individuals with traumatic cervical SCI

The economic health care burden of SCI appears to be substantial. However, there is a large range of estimated costs reported in the published literature ranging from \$280 for SCI

individual out-of-pocket costs for lost income and vehicle repair and replacement in Nigeria to \$3.2 million lifetime for an individual injured at 25 years old with a C1-C4 AIS A, B or C injury in the United States. The total economic burden differs based on injury severity, jurisdiction, timeframe of the observation period and cost components included in the study.

Gaps in the Evidence

- There are numerous treatment areas and interventions where the economics has not been explored.
- Economic evidence on new technologies in development for individuals with SCI is absent.
- There is a lack of understanding on the economic impact of functional impairment.

2 Introduction

Beginning with the onset of spinal cord injury (SCI), there is a significant increase in the use of health care resources to deal with the immediate emergency and acute consequences of the injury. Later the focus shifts toward management of the individual's disability, maximizing their abilities and treating ongoing secondary complications. Clinicians, health care facility administrators and policy decision-makers must have the best possible evidence to provide individuals with SCI with optimal care in a cost-effective manner. Evidence for health care interventions comes in many forms. For clinicians, the appropriateness of an intervention is often determined by its clinical efficacy and safety. Health care administrators or policy decision makers may additionally consider ethical and economic evidence. The focus of this review is on the economics evidence for SCI rehabilitation.

2.1 Economic Evaluations

Economic evaluations (also known as cost-effectiveness studies) of health care interventions are important in decision making because of limited available health care resources. Economic analysis has been defined as “the comparative analysis of alternative courses of action in terms of both their costs and consequences.” (Drummond 2001, as described in Shemilt 2009, pg 15.2). In health care a certain condition may have direct costs, such as hospital stay, cost of a medication, or physician visits. There are also indirect costs associated with care that may need to be considered, such as lost productivity and wages due to time off from work or transportation costs associated with medical appointments. Indirect costs can be for the patient or for an informal caregiver. The purpose of the economic evaluation is to inform decision makers about the monetary value of different treatment options or to provide an estimate of the impact of a disease or treatment option to the health care system.

For economic evaluations the primary aim is to explore and combine both the incremental cost as well as the incremental effect of a treatment against a reasonable comparator. Although often used as a “catch-all” term, economic evaluations can be grouped into three categories: cost-benefit studies, cost-effectiveness studies and cost-utility studies. In cost-benefit studies, all benefits and costs are converted to a common unit (in this case monetary costs) and summed for

each intervention. Many of these benefits and costs are easily valued in terms of money (such as laboratory services consumed, or hospital bed days avoided). However, there are also many intangible items (such as patient pain or satisfaction) where assigning a monetary value may be more challenging (Morris et al. 2011). In such cases, the monetary value may be determined by patient preference, measured through their willingness to pay for the health benefits or to avoid a health cost associated with the intervention versus the comparator (Drummond 2001; Morris et al. 2011). The output of a cost-benefit study is the difference in total monetary cost between an intervention and a comparator. In cost-effectiveness studies the benefits are not converted to a monetary value. In these types of studies, the incremental effect of the intervention is usually a clinical outcome of importance to the condition of interest. One limitation to cost-effectiveness studies is the limited comparability of these studies across different disease groups, due to variation in clinical outcomes. Cost-utility studies overcome this limitation by using a common denominator of change in health (utilities) as the clinical outcome. Utilities are measured from a generic (non-condition specific) patient preference quality of life scale. This scale measures a patient's quality of life and assigns a value to it between 0 and 1 (Drummond 2001). These values measured over time are multiplied by the patient's expected life years to produce a quality-adjusted life year (QALY) value. The primary outcome of cost-utility studies reflects the incremental cost of the intervention divided by the incremental QALY gained (or lost) by the intervention. Cost-utility studies, as well as cost-effectiveness and cost-benefit analyses, provide the full spectrum of economic evaluations observed in health research publications.

2.2 Cost of Illness Studies

Another type of economic evidence that appears in the medical literature comes from cost of illness studies. Cost of illness studies, also commonly known as burden of illness studies, set out to determine the overall resource consumption associated with a specific illness. Often this is presented in monetary terms and is focused on health care resources. Originally, cost of illness studies covered all major diseases for the purposes of advocating to government for additional health care spending. Lately, studies have been narrower in scope and used for awareness of a specific disease. The purpose of disease-specific cost of illness studies is often to present the case for additional research, funding for care or raise awareness for a specific disease. Table 1 outlines the strengths and weaknesses of each type of economic study design.

Table 1. Strengths and Weaknesses of Varying Types of Economic Evaluations

Type of study	How are benefits captured?	Primary outcome	Strengths	Weaknesses
Cost Benefit Analysis	As costs (often through willingness to pay)	Incremental cost	<ul style="list-style-type: none"> • Captures all costs and benefits in one number (cost) • Includes patient preference in benefit calculation • Whether intervention is cost effective is easy to measure 	<ul style="list-style-type: none"> • Least reported type of economic analysis in published literature • Different methods for calculating benefits
Cost Effectiveness Analysis	Through clinical outcomes	Cost per clinical outcome	<ul style="list-style-type: none"> • Includes clinical outcomes that clinicians in the field are familiar with • Easy to incorporate clinical trial data 	<ul style="list-style-type: none"> • Difficult to compare across different disease groups • Does not incorporate quality of life/patient preferences • Whether intervention is cost effective requires a willingness to pay threshold
Cost Utility Analysis	In the form of quality of life utilities	Cost per quality-adjusted life year	<ul style="list-style-type: none"> • Can compare results across different studies and disease groups • Widely accepted as the preferred economic evaluation by decision making bodies 	<ul style="list-style-type: none"> • Often utility values have not been measured • Different utility measurement tools provide variable results
Cost of Illness	None	Cost	<ul style="list-style-type: none"> • Captures the economic burden of a medical condition • Easily understood by non-academics 	<ul style="list-style-type: none"> • Does not incorporate clinical outcomes or patient preferences • Often calculated as gross costs and not disease specific costs

With economic evidence playing an increasing role in health care decision making and government advocacy, there is a need for a review of the current state of economic research in the area of SCI. The purpose of this review was to describe the breadth of research, and to identify the current limitations and areas for future studies relevant to the SCI population.

Specifically, this chapter will review the economic evaluation studies (cost-effectiveness, cost-utility and cost-benefit) and cost of illness studies in SCI.

3 Methods

3.1 Economic evaluation studies

The economic search terms used for this systematic review are based on validated search algorithms published previously (Wilczynski et al. 2004). For the Medline database, the search terms “cost-benefit analysis.sh. OR costs.tw. OR cost effective.tw.” produces the best combination of sensitivity (95.7%) and specificity (97.2%) of locating methodologically sound economic publications (Wilczynski et al. 2004). The search terms “cost.tw. OR costs.tw.” used in the EMBASE database produces the optimal combination of sensitivity (96.8%) and specificity (97.6%) for economic articles (McKinlay et al. 2006).

Once all full-text articles were screened, the remaining articles were reviewed by three reviewers (AMc, BB and BC) and critically appraised using the Quality of Health Economic Studies (QHES) checklist developed by Chiou and colleagues (2003) and the Drummond checklist developed by Drummond and colleagues (Drummond et al., 1997). This information was used to quickly identify potential method limitations in the individual studies, as well as in the area of economic evaluations in SCI as a whole.

The QHES is a 16-item checklist that was developed in 2003. The checklist items were selected by consensus from a broader pool of items by a panel of 8 Health Economists. Conjoint analysis methods were used to produce utility values for each of the checklist items in relation to the questionnaire. A total of 98 researchers in the field of Health Economics participated in this analysis. The questionnaire was then validated by comparing the checklist scores of a scientific article to global scores reported by experts (Chiou et al. 2003). In a recent quality assessment of economic evaluation study critical appraisal tools, Langer (2012) observed that the QHES and the economic evaluation checklist produced by the British Medical Journal were the most comprehensive checklists. Among all the checklists reviewed, only the QHES has been validated for construct validity and pre-tested among a group of experts. Further, the QHES is also the only checklist where the items are weighted, allowing for a quality rating.

The Drummond checklist was developed in 1997. According to the Cochrane collaboration this checklist has received more scrutiny than other similar checklists (Higgins & Green, 2011). The Drummond checklist is recommended in Cochrane reviews to critically appraise the methodological quality of full economic evaluations developed in tandem with single effectiveness studies (Higgins & Green, 2011).

A brief summary of each study will be presented, describing the outcomes used, the primary results, and the methodological strengths and limitations. Due to the variability in methods, disease population, cohort country of origin and interventions, only descriptive results are reported.

3.2 Cost of Illness Studies

The search terms used to identify cost of illness studies differed from those used for cost effectiveness studies. For the Medline database search terms “exp “costs and cost analysis” OR

costs.tw. OR cost.tw.” was used. This algorithm had a sensitivity of 95% and a specificity of 95.6% (Wilczynski et al. 2004). The search algorithm “cost.mp. OR costs.tw. OR health care costs.sh.” was used for the EMBASE search and has a sensitivity of 96.8% and specificity of 97.6%.

There is currently no formal tool or checklist for the critical appraisal of the quality of cost of illness studies. Therefore, for this analysis, a modified version of a checklist presented by Larg and Moss (2011) in a critical analysis of cost of illness studies was used. This checklist focused on three major areas: 1) Analytical framework of the study, 2) Methodology and data collection and 3) Cost analysis and reporting.

Similar to the review of cost effectiveness studies, a brief summary of each study will be reported. Costs were converted to 2018 US dollars by converting currency through the Organisation for Economic Co-operation and Development (2014) reported purchasing price parity and then inflating the cost to 2018 values through United States consumer price index for medical care (United States Department of Labour 2014).

4 Results

4.1 Economic evaluation studies

A total of 19 studies met the criteria for full review. These studies were published between 2004 and 2018, each investigating a different intervention.

Review of Study Methods: A table with the full checklist results of all studies is presented in the Appendix. The study question was clearly presented in all but 2 studies. Incremental costs and effects were calculated for all studies. Statistical analyses or sensitivity analyses were conducted in 14 of 19 studies to address uncertainty. A total of 18 of the 19 studies used estimates from the best available sources. In 17 studies, cost estimation methods were clearly described. Health outcome measures used were considered reliable or otherwise justified in 17 studies. The conclusions of 17 studies were congruent to the study results. The methods for abstracting the data were explained in 17 studies. In 17 studies, authors noted the funding source of their study. The structure of the economic model, methods and analysis and numerator and denominator components were clearly presented in 16 studies. A total of 15 studies had a time horizon that included all relevant outcomes and was discounted beyond a year. The justification for the economic model used, main assumptions and limitation were also stated in 15 studies. In 14 studies, justification for the measures used for the primary outcome was reported. In 13 studies, the perspective was stated and justified. The impact of potential biases was only discussed in 10 studies.

4.1.1 Intrathecal Baclofen vs. Several Conventional Treatment Options

Bensmail and colleagues (2009; France) modelled a population that was poorly functioning as a result of their spasticity and required assistance for their activities of daily living. This simulated population included individuals with tetraplegia, highly dependent multiple sclerosis, traumatic brain injury (TBI), cerebral palsy and stroke. A decision analytic tree was constructed that focused on treatment success and failure over a 2-year period. The scale used to measure outcome in this

model was a combination of Goal Attainment Scale (GAS) that measures patient and caregiver satisfaction and the Ashworth Scale. A successful treatment was defined as an improvement in GAS and a minimum 1-point decrease in the Ashworth score. Rate of success was the primary outcome. Costs included hospital costs, physician visits, drug costs, surgical cost, transportation services, physical treatments, device costs, and home care nursing. In the base case analysis intrathecal baclofen (ITB) had a greater rate of success over conventional treatment. As well over a 2-year time frame the cost of ITB was less than conventional therapy. Thus, in the base case ITB had lower costs and better outcomes compared to conventional therapy (lower costs and better outcomes). A probabilistic sensitivity analysis was conducted to address the uncertainty in the data variables used in the model. This was conducted by running 5000 iterations of the model and selecting values for each data variable in the model from the distributions set where there was uncertainty. The frequency distribution of total medical costs was presented for the ITB and conventional therapy; however, the distribution of cost per effect was not presented. The authors concluded that as a first-line therapy, ITB had the lowest costs and had the highest probability of treatment success. The effectiveness measure in this analysis was patient and caregiver satisfaction combined with patient spasticity.

Key Points

According to one study, intrathecal baclofen as first-line therapy for disabling spasticity for severely impaired individuals had lower treatment costs and better outcomes (improved patient and caregiver satisfaction according to goal attainment scaling and at least 1-point reduction in Ashworth score) over a 2-year period when compared to the current treatment pattern of care in France at the time of model construction.

4.1.2 Hydrophilic Gel Reservoir vs. Non-Coated Catheters for Intermittent Self-Catheterization

A Markov model was constructed to estimate the cost-effectiveness of several types of catheters for intermittent self-catheterization in a simulated SCI population with a mean age of 40 years (Birmingham et al. 2013; United Kingdom). The model projected forward to a lifetime time horizon. The comparators included hydrophilic coated catheters, gel reservoir coated catheters, single-use sterile non-coated catheters, clean non-coated catheters changed daily and clean non-coated catheters changed weekly. The Markov model included six different health states related to an individual's movement between no symptomatic urinary tract infection, different catheter associated urinary tract infection states and death. Results were presented as cost per QALY. In the base case result, gel reservoir catheters were calculated to cost £54,350 per QALY more compared to non-coated catheters. The cost per QALY was even higher for hydrophilic catheters. Between the different options for non-coated catheters, catheters changed weekly were more effective and less expensive than catheters changed daily or single use catheters. In the scenario where non-coated catheters are not an option, the cost per QALY of gel reservoir catheters compared to hydrophilic catheters was £3,075 more per QALY gained. The sensitivity

analyses did little to change the results of the analysis suggesting that the model was robust even with uncertainty. The authors noted that there were concerns with the conclusions of this study expressed by the stakeholders of the guidelines for which this study was to inform (patient groups, manufacturers and National Health Service trusts). There were liability concerns from clinicians regarding catheter infections if single use non-coated catheters were recommended to patients. Also, there were concerns regarding the off-label recommendation by a government organization for multiple uses of a single use catheter. The level of evidence regarding this recommendation was reported as low to very low quality. Thus, the recommendation was revised to allow patient choice of gel reservoir and hydrophilic catheters.

A second cost effectiveness analysis by Clark and colleagues was conducted to compare hydrophilic versus uncoated catheters from the UK National Health Service perspective (Clark et al. 2016). A long-term Markov model was constructed to include long-term effects of catheter use. Model inputs in this study were based on published materials. The outcomes of interest were QALYs, life year (LY) and urinary tract infection (UTI) events avoided. The results presented an additional £2100 per person cost with the use of hydrophilic catheters with a gain of 0.35 QALYs, 0.64 LYs and 16% reduction in UTI events lifetime. The incremental cost effectiveness ratio was £6100 per QALY and £3300 per life year gained. According to the probabilistic sensitivity analysis, all results were below the UK willingness-to-pay threshold of £20,000 which means they were potentially fundable through the public health care system. The authors concluded that the use of hydrophilic catheters were “highly cost effective.”

In a similar study by Watanabe and colleagues, the model developed by Clark and colleagues was localized to the Japanese health care system (Watanabe et al. 2017). Most of the model inputs were based on published literature sources. Treatment for UTI and cost of UTIs, damage of the urethra, kidney and bladder stones were obtained from a survey of an expert panel, urologists and SCI specialists. The study was based on the Japanese health care payers’ perspective. The clinical outcomes of interest were QALYs, LYs and the number of pyuria events avoided. The use of hydrophilic catheters was costlier per person by 1,279,886 yen (2014 yen), but increased QALYS by 0.334 and LYs by 0.781. The ICER was 3,826,351 yen/QALY, 1,639,562 yen/LY and 152,731 yen per pyuria event avoided. In sensitivity analyses, the resulting incremental cost effectiveness ratio (ICER)s were highly sensitive to the cost of the hydrophilic catheters and the risk of UTI in hydrophilic and non-hydrophilic catheters. At a willingness-to-pay threshold of 5,000,000 to 6,700,000 yen per QALY in previous Japanese studies, hydrophilic catheters would have a 67% to 78% probability of being cost effective. Watanabe and colleagues conclude that hydrophilic catheters “can be considered highly cost-effective in Japan from a payer’s perspective.”

Another long-term model based on the study by Clark and colleagues was constructed from the Brazilian public health care payer perspective (Truzzi et al. 2018). Model inputs were obtained from published sources. The clinical outcomes of interest included QALYs, LYs and number of UTIs avoided. The use of hydrophilic catheters had a higher cost of 31,221 BRL per person compared to uncoated catheters but an additional 0.54 LYs and 0.255 QALYs. This resulted in an ICER of 122,330 BRL per QALY, 57,432 BRL per LY gained and 9,778 BRL per UTI avoided. The results remained cost effective with sensitivity analyses. According to the authors, hydrophilic

catheters can be considered cost-effective from the perspective of the Brazilian public health care system using a willingness-to-pay threshold of 147,000 BRL.

To understand the economic impact of hydrophilic catheters to the Italian Healthcare service, another long-term economic analysis using Bermingham and colleagues' model was conducted (Rognoni & Tarricone 2017). Most of the model inputs were based on published sources. The cost of UTIs was estimated through questionnaires completed by urologists and neuro-urologists. The clinical outcomes of interest were QALY, LYs and UTIs avoided. The use of hydrophilic catheters was estimated to result in an increase in LY of 1 year, and an increase in QALYs of 0.9. The cost of hydrophilic catheters was €21,500 more compared to uncoated catheters (€82,915 versus €62,457). The ICER was calculated to be €24,405 per QALY and €20,761 per LY gained. The use of hydrophilic catheters over a life time is estimated to result in a 50% reduction in UTIs. With a large range of willingness-to-pay thresholds in Italy (€25,000-€66,400), the probability that hydrophilic catheters would be cost effective range from 47% to 98%. The model inputs that resulted in the largest impact on the ICER were the relative risk of developing a symptomatic UTI, number of symptomatic UTIs per year experienced by individuals using uncoated catheters, cost of hydrophilic catheters and the number of catheters used per day.

Another long-term cost effectiveness analysis was conducted from the public health care payer and societal perspective in Ontario, Canada using the model developed by Clark and colleagues as the foundation (Welk et al. 2018). The study examined the incremental cost effectiveness of hydrophilic catheters to uncoated catheters. Publicly available sources and results from published studies were used as model inputs. The societal perspective included sick leave, early retirement and early death impact related to illness. Costs were standardized to 2016 Canadian dollars (CAD). This study observed a 0.72 QALY gain for the hydrophilic catheters compared to uncoated catheters with an additional cost of \$47,017 CAD. The resulting ICER was \$66,634 per QALY. If the utility benefit of receiving hydrophilic catheters was removed from the model, the ICER would increase to \$132,485. The model was sensitive to unit cost of hydrophilic catheters and uncoated catheters and impact on urinary tract infections. When examining the cost effectiveness from the societal perspective, hydrophilic catheters had lower costs and better QALYs compared to uncoated catheters.

Key Points

Considering the long-term outcomes associated with intermittent catheterization, hydrophilic catheters may be cost-effective when compared to uncoated catheters.

4.1.3 Transanal Irrigation vs. Conservative Bowel Management

Christensen and colleagues (2009; Europe) developed a study to determine the cost effectiveness of transanal irrigation compared to conservative bowel management. Costs were obtained from a randomized clinical trial and represented the average time between bowel management

procedures (2 days). Costs included the labour costs related to the interventions (including leakage costs), and costs related to the product, urinary tract infections and lost wages due to time spent on bowel management. The effectiveness measure for this model was the St Mark's fecal incontinence score and the Cleveland Clinic constipation scoring system. At 10 weeks all effectiveness measures had significantly lower (better) scores for all three for transanal irrigation. Overall costs were €1 less for transanal irrigation over the two days of bowel management compared to conservative bowel management. As a sensitivity analysis, the authors observed that caregiver time would have to be increased 26%, transanal irrigation time increased 12% or patient time on bowel management increased 10% before transanal irrigation becomes more expensive than conservative bowel management. The conclusion from this study was that transanal irrigation is a dominant strategy compared to conservative bowel management. This treatment was both less costly and had better outcomes. The authors also mention that their results were robust after conducting the sensitivity analyses. It was noted that presenting costs for only a 2-day period was a limiting factor in their study; consequently, it is difficult to determine whether transanal irrigation will remain less costly than conservative bowel management over the long-term.

The conclusion that transanal irrigation is the dominant strategy should be viewed with caution given that the difference in cost was €1 over a 2-day timeframe. Study limitations include a very short timeframe where costs were captured and a small cohort. Uncertainty was also not explored in this study and thus it is difficult to know how robust the results truly are.

In a separate study Emmanuel and colleagues examined the cost effectiveness of trans-anal irrigation for individuals with neurogenic bowel dysfunction and on an ineffective standard bowel program (i.e., persons who had poor outcomes with standard bowel care) (Emmanuel et al. 2016). This study was from the perspective of the National Healthcare Service (NHS) in the UK and used a Markov model to estimate costs and outcomes over a lifetime time horizon. Model inputs were mainly based on data from three UK hospital clinics and supplemented by published literature. The primary outcome was cost per QALY. Results showed an increase in QALY for the transanal irrigation cohort of 0.40 compared to continuing the standard bowel program. There was also an estimated £21,768 cost savings with the transanal irrigation program. These results were robust even when considering the uncertainty. The utility values and number of times transanal irrigation is used per week were the most sensitive model inputs. The conclusions of this study are that transanal irrigation is a cost saving and improves quality of life for individuals with neurogenic bowel dysfunction and have failed standard bowel program.

Key Points

Trans-anal irrigation was observed to be less costly than conservative bowel management for a two-day period and less costly than ineffective standard bowel management over a lifetime time horizon.

Trans-anal irrigation had better clinical outcomes (St Mark's fecal incontinence score, Cleveland Clinic constipation score and neurogenic bowel dysfunction score) over 10 weeks when compared to conservative bowel management and resulted in higher QALYs when compared to ineffective standard bowel management.

4.1.4 Sacral anterior root stimulation for neurogenic bladder

Morliere and colleagues conducted a cost-utility analysis comparing sacral anterior root stimulation (SARS) with medical treatment (anticholinergics and urinary voiding techniques) for neurogenic bladder and complete spinal cord injury (Morliere et al. 2015; Drummond 2001). A model with a 10-year time horizon was developed using model inputs from published literature, extrapolation and assumptions. This study was conducted from the perspective of the French health system. The main clinical outcome of interest was QALYs. Costs were based on a 12-month comparative observational cost-effectiveness study and extrapolated to 10 years. This included the cost of treatment and routine care. Additional long-term costs include the cost of surgical interventions and secondary complications. Using a base case assuming that SARS was 60% effective (complete and voluntary micturition restored by 1 year), the calculated ICER was 12,710€ per QALY (EUR 2013). Assuming a willingness-to-pay threshold of 30,000€ per QALY SARS has a 60% probability of being cost-effective. At a willingness-to-pay threshold of 100,000€ per QALY this probability of being cost-effective increases to 74%. Overall, the results of the sensitivity analysis resulted in a 54% or higher probability of SARS being cost-effective.

Key Points

In a single study, sacral anterior root stimulation appears to be cost-effective for neurogenic bladder and complete spinal cord injury.

4.1.5 Duplex Ultrasound Surveillance vs. No Surveillance for Deep Venous Thrombosis

Kadyan and colleagues (2004; US) set out to determine the cost-effectiveness of duplex ultrasound screening for deep vein thrombosis in persons with SCI being admitted to rehabilitation facilities. Input parameters for their model originated from literature as well as a retrospective study conducted by the same authors of a traumatic SCI cohort admitted to a rehabilitation facility who had a duplex ultrasound at admission. Since the intervention in this study was a screening tool, parameters such as the sensitivity and specificity of the screening tool

were included in the analysis. The effect outcome in this study was life year gain measured through differences in mortality between the two treatment arms. The incremental cost of admission duplex ultrasound versus no ultrasound was calculated to be \$312.99 per person. The incremental benefit was a decrease in mortality of 0.51 %. The cost for one life saved was \$61,542. The cost per life year gained ranged between \$1,193 and \$9,050. The authors note that within this range the screening may be cost-effective, especially when compared to other cost-effectiveness studies in mass screening interventions.

Key Points

Based on one study, the implementation of duplex ultrasound for deep venous thrombosis surveillance would result in a cost per life year gained of between \$1,193 and \$9,050 depending on age and type of injury.

4.1.6 Oral vs. Non-oral Erectile Dysfunction Treatments

Mittmann and colleagues (2005; Canada) determined the cost-effectiveness of the oral erectile dysfunction treatment sildenafil citrate, compared to the following non-oral treatments: intracavernous injections of papaverine prostadil, alprostadil with papaverine and phentolamine (triple mix), transurethral suppository, surgically implanted rigid, semi-rigid, or inflatable prosthetic device and vacuum erection devices. There was a comparison of health preferences through the calculation of utilities and costs between the treatments over a one-year period. Utility inputs were collected from interviews of a cohort of individuals with SCI. Costs were estimated through clinical scenarios based on standard of care at a rehabilitation facility and confirmed through an expert panel. Total costs for one year was most expensive for the surgically implanted prosthetic device, followed by transurethral suppository, intracavernous injections of papaverine prostadil, sildenafil citrate, and then triple mix. Vacuum erectile devices were the least expensive. Utility values were highest for sildenafil citrate and lowest for surgically implanted prosthetic devices. Sildenafil citrate was less expensive and had better utilities than intracavernous injections of papaverine prostadil, transurethral suppository and surgery. When both cost and effects were incorporated, sildenafil citrate had a cost per QALY of \$9,656 compared to triple mix and \$13,399 compared to vacuum erectile device. This study was limited to a one-year timeframe and did not look at long-term outcomes due to the absence of data. The authors concluded that sildenafil citrate should be considered for inclusion in the Ontario public drug formulary and thus reimbursed for individuals in the Ontario drug beneficiary program.

Key Points

In one study, sildenafil had lower cost and better outcomes than intracavernous injections, suppositories and surgery.

Cost per QALY was \$9,656/QALY for Triple Mix intracavernous injections and \$13,399/QALY for vacuum erection device.

4.1.7 Electrical Stimulation Therapy vs. Standard Wound Care

The cost effectiveness of electrical stimulation therapy compared to standard wound care was explored in a recent study (Mittmann et al. 2011; Canada). A decision analytic model was constructed to investigate the cost per pressure ulcer healed over a one-year timeframe. Healing rates with electrical stimulation therapy and standard wound care were based on a randomized controlled trial. Recurrence of pressure injuries and complications such as infections and osteomyelitis were included in the model. Taking into consideration the cost of complications, the total cost of electrical stimulation therapy at one year was modelled to be less than standard wound care treatment. Electrical stimulation therapy also resulted in more pressure injuries healed. Thus, in the base case, electrical stimulation therapy had lower costs and better outcomes and as a result was the dominant strategy. However, the cost difference between the interventions was small and is sensitive to the percentage of pressure injuries healed. The limitation in the study includes the small sample size that the efficacy outcomes were based on. However, this is typical of studies using an SCI population where the prevalence is small. A second limitation was the short 1-year timeframe of the model.

Overall the authors concluded that electrical stimulation appears to be a cost-effective strategy over one year compared to standard wound care. However, this needs to be interpreted with caution given the model's sensitivity to the clinical trial outcomes.

Key Points

For a single study, over a one-year timeframe, electrical stimulation in addition to standard wound care had lower costs and greater number of wounds healed.

4.1.8 Telephone support for pressure ulcer management

A study of tertiary centres in Bangladesh and India examined the cost utility and cost-effectiveness of telephone-based support for pressure ulcer management in individuals with SCI (Arora et al. 2017). This study was conducted concurrently with a randomized clinical trial. The researchers adopted a societal perspective. The outcomes of interest were the decrease in pressure ulcer size and changes in quality of life (measured by the EQ-5D) at 12 weeks.

Resources such as the cost of pressure ulcer management equipment and resources and lost-productivity from work were collected through participant diaries and included purchases and time spent on pressure ulcer treatment related activities. Intervention costs (including telephone calls, health professionals, administrator and trainer time) accrued by the centres were also collected. Results were reported in 2015 Indian Rupees (INR). At time of follow-up there was a pressure ulcer size reduction of 0.53 cm² for the telephone-based support cohort compared to the control group. There was also an incremental QALY of 0.027 in favour of the intervention arm. The total cost per person was 43,781 INR for the intervention arm and 42,561 for the control group. The incremental cost effectiveness ratio was 2,306 INR per additional cm² reduction in pressure ulcer size, 44,915 INR per QALY. The probabilistic sensitivity analyses show that there is an 87% probability that the intervention is cost-effective with a willingness to pay of 3 times per capital gross domestic product (GDP) (331,650 INR). The model was observed to be sensitive to the cost of lost productivity resulting from time spent on treatment related activities. The authors conclude that the telephone-based support program provided “good value for money”.

Key Points

In one study, the addition of telephone support to standard pressure injury management appears to be cost effective.

4.1.9 Negative pressure wound therapy for pressure injuries

A cost analysis was conducted alongside a randomized controlled trial at an SCI unit in India (Dwivedi et al. 2016). This clinical trial examined the efficacy of negative pressure wound therapy on stage III and IV pressure injuries (PU) in individuals with a traumatic paraplegia. Negative pressure wound therapy (NPWT) was provided at the bed-side and changed at least weekly. Standard care consisted of a saline rinse of the ulcer followed by gauze bandages changed once or twice a day. All costs were collected from hospital records and estimates. The daily cost for the two treatment arms were calculated and then the cost of treating PU with NPWT or standard care was estimated by multiplying the daily cost by the days until wound granulation. The estimated cost of the standard care group was \$95 USD more than the negative pressure wound therapy group at nine weeks. The authors conclude that negative pressure wound therapy is cost-effective and financially viable in hospitals where there are limited resources.

Key Points

In a single study, negative pressure wound therapy with weekly dressing changes was less costly than standard care (with one to two changes a day) at nine weeks.

4.1.10 Use of a fibrin sealant for surgical treatment of pressure injuries

A cost effectiveness analysis was conducted on the use of Tissucol Duo spray during the surgical treatment of pressure injuries for individuals with SCI (Velasco et al. 2015). Costs and outcomes were based on a retrospective study of 27 individuals who received the fibrin sealant at a Spanish hospital compared to the results of an earlier retrospective study of 71 individuals treated with conventional surgical debridement at the same hospital. The clinical outcomes of interest were hematoma-seroma rates, days to drain removal, the mean volume of drainage, mean length of stay, mean days on antibiotic treatment, the percentage of surgical failure and relapse post-six months. The total hospital cost for individuals receiving the fibrin sealant was about €8,100 less than conventional surgical debridement (€23,594.7 versus €31,692.4, 2012 Euros). All outcomes of interest were improved in the sealant cohort including hematoma-seroma rates (3.7% versus 33.8%), removal of the drain (10 days versus 15 days), mean volume of drainage (155ml versus 360 ml), mean length of stay (40 days versus 55 days), percentage of surgical failure (3.7% versus 19.7%) and relapse at six-months (3.7% versus 8.5%). Overall, this study showed lower costs and better outcomes for the study cohort receiving fibrin sealant compared to an earlier cohort receiving conventional surgical debridement.

Key Points

In one study, fibrin sealant for the surgical treatment of pressure injuries resulted in less cumulative costs at six months post-discharge compared to conventional surgical debridement for individuals with SCI.

4.1.11 Implanted neuroprosthesis for restoration of effective cough

A cost analysis was conducted to determine whether a neuroprosthesis was less or more costly compared to standard respiratory management methods (DiMarco et al. 2017). Inputs for this analysis were based on a pre-post clinical trial of the Cough Stimulator at a US hospital. In this study, 14 individuals with tetraplegia received Cough Stimulator implantation. Individuals were followed up for three years. The cost of equipment, acute respiratory tract infection and caregiver support was collected through various sources over a three-year period. Caregiver support included time spent to assist the individuals with respiratory secretion clearing. The use of the Cough Stimulator decreased the number of respiratory tract infection and the need for caregiver support per year over three years. The total costs in the first year after implantation was slightly higher than it was prior to implantation, but there was a statistically significant decrease in costs (compared to cost prior to implantation) in year two and three.

Key Points

Based on a single study, the decrease in respiratory tract infection and amount of caregiver support over a three-year period resulted in lower overall cost with a Cough Stimulator neuroprosthesis compared to standard respiratory management for restoration of an effective cough.

4.1.12 Surgical management in older individuals with SCI

Furlan et al. (2016a) examined the cost effectiveness of older age on surgical intervention for individuals with acute traumatic cervical SCI. This study was conducted from the perspective of the public health care payer in Ontario, Canada. A model was developed to examine the six-month cost and outcomes. Model inputs were obtained from hospital data and publicly available sources. Costs were standardized to 2014 US dollars. Reporting on the total cost per QALY accrued over the six-month period for the older and younger cohorts, it was calculated to be \$193,990 per QALY in the older cohort and \$94,043 per QALY in the younger cohort. Subtracting the results, the ICER was \$5.7 million per QALY. The study's sensitivity analysis did not result in changes to the results. The authors concluded that surgical and rehabilitative management of older individuals with acute traumatic cervical SCI was costlier and just as effective when compared to younger individuals.

Key Points

In a single study, surgical and rehabilitative management of older individuals with traumatic cervical SCI were costlier in the first six months after injury compared to younger individuals.

4.1.13 Early decompression for individuals with traumatic cervical SCI

A cost effectiveness analysis was conducted comparing early surgical decompression of the spinal cord (<24 hours post-injury) to delayed decompression for individuals with traumatic cervical SCI (Furlan et al. 2016b). Patients from both groups had no difference in gender, age, injury severity or level (i.e ASIA). This study was from the perspective of the Ontario Ministry of Health and Long-term Care. A model with a six-month duration was constructed with inputs from hospital data and information from publicly available sources. Results were stratified by motor complete and motor incomplete SCI. For individuals with motor complete SCI, the total cost for individuals with early decompression was about \$11,000 less than delayed decompression and had an improvement in utility of 0.0002. For the motor incomplete cohort the cost of early decompression was about \$4,920 less with a utility improvement of 0.01. Both groups showed a reduction in cost and improved quality of life with early decompression. One concern is that other factors, such as comorbidities, may have influenced a delay in decompression and would also impact outcomes.

Key Points

In one study, early decompression for individuals with traumatic cervical SCI resulted in lower costs in the first six months after injury for both motor complete and motor incomplete individuals.

4.1.14 Supported employment for US veterans with SCI

A study was conducted to examine the cost-effectiveness of a supported employment intervention for US veterans (Sinnott et al. 2014). This intervention included the services of vocational rehabilitation counselors to the interdisciplinary health care teams. Cost inputs were identified through questionnaires administered to the vocational rehabilitation counselors, participants and from Veterans Affairs databases. The clinical outcome of interest was QALYs extrapolated from a modified SF-36 survey completed at quarterly visits by veterans. Total and incremental costs and effects were estimated using bivariate and multivariate regression models. In the bivariate analysis, the cost for the supported employment cohort was about \$5,800 USD less than those not receiving this intervention. There was a QALY gain of 0.01 in the conventional care cohort. Neither the cost nor QALY gain was statistically significant. In the multivariate analysis, the cost was \$6,400 USD less and the authors reported a decrease in QALYs. Neither were found to be statistically significant. The authors concluded that the supported employment intervention was not cost-effective when compared to usual care.

Key Points

In a single study, additional services for supported employment for US veterans did not result in a statistically significant reduction in cost or gain in QALYs.

4.2 Cost of Illness Studies

A total of 37 studies were extracted for full review. After reviewing the text of all the articles, 6 were excluded because the studies were not cost of illness (Hedrick 1971, Hollingworth et al. 2007, Relyea-Chew et al. 2009, Macciocchi et al. 2004, Smith et al. 2012, Young-Hughes and Simbartl 2011) and 17 analyzed a specific patient population within SCI (French et al. 2007, Gore et al. 2013, Hung et al. 2012, Jawa et al. 2011, Jones et al. 2003, Kitchener et al. 2005, Mac-Thiong et al. 2012, Liu et al. 1994, Morgan et al. 2008, Palsbo et al. 2006, Smith et al. 2003, Stroupe et al. 2011, St. Andre et al. 2011, Sundance et al. 2004, Webster et al. 2004; Yu 2003, 2008) one study was for spine trauma (Chu et al. 2009) and one study only focused on monetizing informal care (Sapountzi-Krepia et al. 2006). The remaining 12 studies of the general SCI population were critically appraised.

In general, the SCI cost of illness studies spanned six different countries, presented results from costs as early as 1999, were mostly based on an observational cohort and calculated gross costs in

an incidence cohort without a non-SCI comparator. Only two studies included indirect costs (Garcia-Altes et al. 2012, Kawu et al. 2011) or sensitivity analyses (Garcia-Altes et al. 2012, Cao et al. 2011). Cost perspective and health care settings included in the studies varied.

For each study a summary of the results including the costs adjusted to 2018 US dollars (\$1 US dollar= \$1.29 CA dollar 2018) is presented below. The results presented focus on the cost per patient. Due to the differences in health care systems, studies were stratified by country.

4.2.1 Australia

New and Jackson (2010) evaluated the 2004 cost of hospitalizations after SCI in Victoria, Australia using administrative data. Gross costs were measured as mean and median per episode costs and were stratified by initial hospitalizations and subsequent hospitalizations. The data was also stratified for traumatic and non-traumatic SCI. Results are presented in Table 2 and 3.

Table 2. Mean SCI hospital costs reported by New et al. (2010).

	Mean hospital cost per episode	
	Initial hospitalization	Subsequent hospitalizations
Traumatic SCI	\$52,287	\$10,720
Non-traumatic SCI	\$17,868	\$17,352

Table 3. Median SCI hospital costs reported by New et al. (2010).

	Median hospital cost (25%-75% interquartile range)	
	Initial hospitalization	Subsequent hospitalizations
Traumatic SCI	\$23,176 (\$5,188-\$80,343)	\$7,106 (\$2,340-\$11,558)
Non-traumatic SCI	\$9,620 (\$4,476-\$17,379)	\$6,702(\$3,214-\$16,151)

Gabbe and colleagues also calculated the cost of initial hospitalization as a result of SCI in Victoria, Australia. The cost of acute hospitalization per admission in the first 2 years post SCI are presented stratified by the secondary condition reported during the hospitalization. The mean cost of initial hospitalization for the study cohort is \$33,716 (\$33,169 standard deviation), median of \$22,483 (\$11,531-\$43,149 interquartile range). Acute hospitalization and ED costs per admission or visit were also reported stratified by location and severity of SCI. Results are presented in Table 4 and Table 5.

Table 4. Cost per hospital visit (admission and readmissions within 2 years post SCI) stratified by secondary condition (Gabbe & Nunn, 2016).

Secondary condition	Cost per admission	
	Mean (standard deviation)	Median (interquartile range)
All conditions	\$10,731 (\$14,821)	\$6,003 (\$3,456-\$11,330)
Any urological condition	\$10,854 (\$15,488)	\$6,134 (\$2,261-\$11,330)
Pressure injury	\$22,052 (\$24,433)	\$22,801 (\$9,446-\$22,801)
Respiratory	\$19,352 (\$25,773)	\$10,134 (\$5,092-\$22,801)
Bowel	\$15,211 (\$22,033)	\$7,772 (\$5,092-\$22,801)
Fracture	\$11,121 (\$9,859)	\$6,267 (\$4,161-\$17,507)
Other	\$13,454 (\$22,637)	\$5,755 (\$4,258-\$12,430)

Table 5. Cost per hospital visit (admission and readmissions within 2 years post SCI) stratified by location and severity of injury (Gabbe & Nunn, 2016).

Secondary condition	Cost per admission	
	Mean (standard deviation)	Median (interquartile range)
Cervical spine/complete injury	\$13,033 (\$11,631)	\$10,134 (\$5,092-\$22,801)
Cervical spine/incomplete injury	\$9,842 (\$14,594)	\$5,250 (\$2,190-\$10,225)
Thoracic spine/complete injury	\$13,103 (\$19,112)	\$6,214 (\$5,092-\$22,801)
Thoracic spine /incomplete injury	\$7,704 (\$5,815)	\$5,755 (\$5,092-\$10,134)
Lumbar	\$10,307 (\$17,911)	\$5,872 (\$3,227-\$10,365)

Table 6. Cost per emergency department visit (within 2 years post SCI) stratified by location and severity of injury (Gabbe & Nunn, 2016).

Secondary condition	Cost per admission	
	Mean (standard deviation)	Median (interquartile range)
Cervical spine/complete injury	\$485 (\$136)	\$487 (\$350-\$591)
Cervical spine/incomplete injury	\$454 (\$152)	\$487 (\$351-\$591)
Thoracic spine/complete injury	\$584 (\$49)	\$591 (\$577-\$591)
Thoracic spine /incomplete injury	\$454 (\$149)	\$487 (\$298-\$577)
Lumbar	\$404 (\$110)	\$378 (\$325-\$487)

The cost of initial hospitalization for SCI for individuals above and below the age of 65 was also examined by Mitchell and colleagues in a New South Wales cohort (Mitchell et al. 2018).

Key Points

The mean hospital cost for traumatic SCI in Australia is approximately \$52,000 for initial hospitalization and \$10,700 for subsequent hospitalizations; for non-traumatic SCI it is approximately \$17,900 for initial hospitalization and \$17,350 for subsequent hospitalizations.

The mean cost of a secondary condition results in a hospital visit costing \$10,900 for any urological condition to \$22,100 for pressure injuries.

The mean cost per hospital visit can range between \$7,700 for an individual with incomplete thoracic SCI and \$13,100 for a complete thoracic SCI.

The mean cost per emergency department visit is between \$404 for lumbar SCI and \$584 for complete thoracic SCI.

4.2.2 Belgium

Kiekens and colleagues (2011) examined the 2006 cost of SCI inpatient and outpatient rehabilitation in Belgium using data from literature, administrative data as well as clinical opinion. The authors focused on the direct costs borne by the rehabilitation providers and payments made by the public funder. The total incident costs including staff and overhead costs stratified by type of injury and inpatient or outpatient rehabilitation is presented below.

Table 7. Mean costs of inpatient and outpatient rehabilitation by level of injury as reported in Kiekens et al. (2011).

	Mean costs	
	Inpatient rehabilitation	Outpatient rehabilitation
Paraplegia	\$45,770	\$7,908
Tetraplegia	\$70,965	\$10,675

Key Points

In Belgium, mean cost for inpatient and outpatient rehabilitation is approximately \$46,000 and \$7,900 for paraplegia and approximately \$71,000 and \$10,700 for tetraplegia, respectively.

4.2.3 Canada

A total of 6 studies investigated SCI cost of illness from a Canadian health care system perspective (Dryden et al. 2005, Bradbury et al. 2008, Munce et al. 2013, Radhakrishna et al.

2014, White et al. 2017, Chan et al. 2018). Dryden and colleagues (2005) examined a cohort of individuals from Alberta. Costs were stratified by level of injury (tetraplegia versus thoracic versus lumbar) and whether it was complete or incomplete. Results were further stratified for first year after injury and years 2-6. Inpatient hospital, physician, home-care and long-term care costs were included in their analysis. Since this study had a non-SCI comparator both incidence and attributable costs were calculated. Administrative data was used to identify cohort and extract costing information; thus the study is limited by the quality of the administrative data. Results were calculated from 2009 costs and are shown in tables 8-10.

Table 8. SCI costs for initial hospitalization as reported by Dryden et al. (2005).

Population	Mean cost		
	Total	Hospital	Physician
Tetra complete	\$163,517	\$152,887	\$10,630
Tetra incomplete	\$48,286	\$45,233	\$3,053
Thoracic complete	\$112,743	\$105,845	\$6,898
Thoracic incomplete	\$37,317	\$34,603	\$2,940
Lumbar/Cauda Equina	\$50,548	\$46,703	\$3,845
Unspecified	\$17,415	\$15,040	\$2,375

Table 9. SCI costs for first year as reported by Dryden et al. (2005).

Population	Mean Cost				
	Total	Hospital	Physician	Home care	Long-term care
Tetra complete	\$170,641	\$5,654	\$905	\$565	\$0
Tetra incomplete	\$51,679	\$1,922	\$565	\$339	\$565
Thoracic complete	\$118,284	\$3,166	\$678	\$1,018	\$678
Thoracic incomplete	\$39,579	\$679	\$565	\$0	\$792
Lumbar/Cauda Equina	\$53,375	\$1,809	\$792	\$226	\$0
Unspecified	\$25,104	\$7,124	\$565	\$0	\$0

Table 10. SCI costs for years 2 to 6 as reported by Dryden et al. (2005).

Population	Mean cost				
	Total	Hospital	Physician	Home care	Long-term care
Tetra complete	\$60,612	\$17,867	\$4,863	\$37,204	\$679
Tetra incomplete	\$17,867	\$6,220	\$2,488	\$3,732	\$5,428
Thoracic complete	\$27,931	\$10,630	\$2,488	\$7,237	\$7,577
Thoracic incomplete	\$18,093	\$5,993	\$3,279	\$792	\$792
Lumbar/Cauda Equina	\$7,690	\$3,958	\$2,375	\$1,357	\$0
Unspecified	\$14,927	\$5,541	\$1,696	\$7,690	\$0

Radhakrishna and colleagues also examined the health care costs for the first- and second-year post-SCI resulting from motor vehicle accidents in Quebec, Canada. The cohort was stratified by level and severity of injury. The total costs for the first year are presented in Table 11. Second year costs are presented in Table 12.

Table 11. First-year mean acute hospital care and total care costs stratified by level and severity of injury (Radhakrishna et al. 2014).

Population	Mean cost (standard error)	
	Acute hospital care	Total
C1-C7/complete injury	\$126,555 (\$23,805)	\$153,045 (\$24,290)
C8-T6/complete injury	\$61,459 (\$8,218)	\$93,609 (\$12,120)
T7-L1/complete injury	\$40,405 (\$3,913)	\$68,860 (\$8,186)
C1-C7/incomplete injury	\$42,648 (\$3,643)	\$54,830 (\$4,108)
C8-T6/incomplete injury	\$45,195 (\$8,817)	\$55,995 (\$12,568)
T7-L1/incomplete injury	\$36,702 (\$2,690)	\$43,208 (\$3,282)
L2-S5/incomplete injury	\$50,750 (\$7,728)	\$66,872 (\$10,462)

Table 12. Second-year mean total care costs stratified by level and severity of injury (Radhakrishna et al. 2014).

Population	Mean total cost (standard error)
C1-C7/complete injury	\$79,171 (\$12,321)
C8-T6/complete injury	\$49,230 (\$9,487)
T7-L1/complete injury	\$32,391 (\$6,878)
C1-C7/incomplete injury	\$15,990 (\$3,009)
C8-T6/incomplete injury	\$9,368 (\$4,493)
T7-L1/incomplete injury	\$6,575 (\$1,754)
L2-S5/incomplete injury	\$13,568 (\$3,894)

An Ontario SCI cohort was investigated by Munce and colleagues (2013) using administrative data. Prevalent cost per year for SCI was calculated for inpatient hospital, emergency department visits, physician, home care, long-term care and drugs. Results were presented for fiscal years 2003 to 2005 and were presented in 2005 dollars. The general SCI cohort was explored with no further SCI subgrouping. Regression analyses were conducted to look at factors that may influence increased costs (Table 13).

Table 13. SCI costs as reported by Munce et al. (2013).

Total	Mean cost (standard deviation)						
	Index hospital	Hospital re-admission	Inpatient rehab	Complex continuing care	Emergency department	Physician	Home-care
\$114,993	\$34,016 (\$43,899)	\$19,045 (\$33,175)	\$116,138 (\$76,202)	\$159,802 (\$105,124)	\$433 (\$379)	\$4,945 (\$7,845)	\$2,915 (\$7,845)

Bradbury and colleagues (2008) investigated the cost of rehabilitation in 2006 dollars for individuals with SCI from the perspective of the rehabilitation facility. The primary focus of this study was to investigate the clinical and economic impact of TBI in patients with SCI in a rehabilitation setting. Mean costs for an incidence population were presented and stratified for individuals with and without TBI. Costs per change in functional independence motor score were also computed. In total, 10 patients with TBI and SCI were compared with 10 patients without TBI (Table 14).

Table 14. SCI costs as reported by Bradbury et al. (2008).

	Mean hospital cost (standard deviation)
SCI with TBI	\$174,544 (\$86,373)
SCI without TBI	\$134,555 (\$93,251)

The estimated 5 year and lifetime cost of SCI from the perspective of the Ontario Ministry of Health and Long-term Care was calculated by Chan and colleagues (Chan et al. 2018). The primary data source for this study was health care administrative data. The estimated lifetime additional health care cost of SCI for the entire SCI cohort and stratified by location of injury is presented in Table 15. The calculated five-year additional cost of SCI is \$150,810 (\$146,973-\$154,131 95% confidence interval)

Table 15. Mean estimated lifetime additional cost of SCI stratified by location of injury.

Location of injury	Mean cost (95% confidence interval)
Total cohort	\$284,163 (\$275,877-\$291,603)
Cervical	\$278,668 (\$270,805-\$285,939)
Thoracic	\$308,513 (\$300,650-\$315,784)
Lumbar	\$189,132 (\$183,298-\$194,712)

The additional acute hospital cost of hospital-acquired UTI and PU was examined in a cohort of individuals enrolled in the Rick Hansen SCI registry (White et al. 2017). Individuals with SCI identified by hospital-acquired UTI or PU were matched with those without the complication. The difference in acute hospital costs was considered the additional cost of the complication. Mean hospital costs are presented in Table 16.

Table 16. Additional acute hospital costs of hospital-acquired secondary complications estimated by White and colleagues (2017).

	Mean hospital cost (standard deviation)
Hospital-acquired UTI	\$6,832 (\$5,497)
Hospital-acquired PU	\$16,452 (\$24,185)

Key Points

In Canada, mean costs range between \$17,500 and \$164,000 for initial hospitalization, \$25,000 to \$170,500 in the first-year and \$7,500 to \$60,500 for following years depending on type of injury. Second-year mean costs were between \$6,600 and \$79,200 depending on level and severity of SCI. Total mean cost of inpatient rehabilitation is approximately \$134,500 for SCI and is increased to approximately \$174,500 if the patient also has a TBI.

Total mean annual cost per individual with SCI in Ontario is approximately \$115,000. Individuals with SCI who develop a UTI during an acute hospital stay have \$6,800 higher hospital cost. Hospital-acquired PU for individuals with SCI is associated with an increase of \$16,500 in acute hospital cost.

4.2.4 Nigeria

The 2009 cost of conservative management of SCI in Nigeria was analyzed by Kawu and colleagues (2011) over a one-year timeframe. The total direct hospital costs were paid out-of-pocket by the patient or family. Indirect costs included lost income and vehicle repair or replacement (Table 17).

Table 17. Mean direct and indirect costs as reported by Kawu et al. 2011.

	Mean cost	
	Direct	Indirect
Total cohort	\$278	\$1,863

Key Points

The direct out-of-pocket cost for conservative SCI management in Nigeria is approximately \$280 and \$1,900 for lost income and vehicle repair/replacement.

4.2.5 Spain

The economic 2007 cost of SCI and TBI in Spain was examined by Garcia-Altes and colleagues (2012). Costs were calculated by combining prevalence data with estimates of resource utilization. From this, total direct and indirect costs for SCI resulting from a motor vehicle crash, or other causes, as well as TBI from a motor vehicle crash or other causes was calculated. The results presented here will focus on SCI (Table 18).

Table 18. Mean total direct and indirect costs as reported in Garcia-Altes et al. (2012).

	Total direct and indirect cost
SCI resulting from motor vehicle accident	\$279,533
SCI resulting from other causes	\$296,532

Key Points

Total mean lifetime cost for an individual with a SCI that is a result of a motor crash is approximately \$279,500 and \$296,500 from other causes in Spain.

4.2.6 United States

There were a total of 6 cost-of-illness studies from the US that examined an SCI cohort.

In a review of the 2009 Health Care Utilization Project Nationwide Inpatient Sample database, hospitalizations where the primary diagnosis was SCI had a mean charge of \$165,958 (\$8,662 standard deviation) (Mahabaleshwarkar et al. 2014). This was higher than the mean charge of \$40,813 (\$1,223 standard deviation) for a matched non-SCI group (Mahabaleshwarkar et al. 2014).

DeVivo and Farris (2011) calculated the incident cost of SCI in a US population. Costs were presented in 2009 dollars. Results were separated to first year costs and annual costs for subsequent years. Results were presented for the entire cohort as well as stratified by level of injury and severity (C1-C4 and AIS A, B or C, C5-C8 AIS A, B or C and AIS D). Total mean costs were presented. This study provides updated data from the National SCI Statistical Center including new variables that were not available in past reports.

Table 19. First year SCI costs as reported by DeVivo and Farris (2011).

Population	Mean cost
Total group	\$258,890
C1-C4 AIS A, B or C	\$493,275
C5-C8 AIS A, B or C	\$342,171
T1-S5 AIS A, B or C	\$223,154
AIS D	\$143,095

Table 20. SCI costs after the first year as reported by DeVivo and Farris (2011).

Population	Mean cost
Total group	\$80,219
C1-C4 AIS A, B or C	\$175,449
C5-C8 AIS A, B or C	\$104,045
T1-S5 AIS A, B or C	\$57,291
AIS D	\$39,092

In another US study, Cao et al. (2011) calculated the mean cost of the same SCI cohort as DeVivo and Farris (2011) but modelled the lifetime costs for SCI. Results were divided in a similar manner to DeVivo and Farris (2011) and were based on the 2009 dollar.

Table 21. Estimated lifetime SCI costs for a hypothetical 25 year-old, using 4% discount rate as reported by Cao et al. (2011).

Population	Mean cost
C1-C4 AIS A, B or C	\$3,161,079
C5-C8 AIS A, B or C	\$2,153,811
T1-S5 AIS A, B or C	\$1,292,696
AIS D	\$930,696

Table 22. Estimated lifetime SCI costs for a hypothetical 50 year old, using 4% discount rate as reported by Cao et al. (2011).

Population	Mean cost
------------	-----------

C1-C4 AIS A, B or C	\$1,777,250
C5-C8 AIS A, B or C	\$1,390,013
T1-S5 AIS A, B or C	\$904,193
AIS D	\$702,364

Lifetime all-cause hospitalization cost for individuals with thoracic SCI was estimated by Dukes and colleagues using data from the National Spinal Cord Injury Statistical Center. Estimates were based on an individual injured at the age of 35 years. Results were stratified by AIS grade. Results are presented in Table 24.

Table 23. Estimated life-time all-cause hospital costs for a hypothetical individual with SCI injured at 35-year old stratified by severity (Dukes et al. 2018).

SCI severity	Estimated lifetime cost
AIS A	\$339,267
AIS B	\$263,275
AIS C	\$199,412
AIS D	\$71,877

For individuals with a work-related SCI and eligible for workers' compensation, health care claims made to a compensation insurer were analyzed. Total costs for claims per person for the first five years is presented in Table 25.

Table 24. Estimated total costs of health care claims submitted to insurer for individuals with SCI on workers' compensation.

Year	Mean cost in thousands (median costs in thousands)					
	C2-4 AIS A-C	C5 AIS A-C	C6 AIS A-C	C7-8 AIS A-C	Central cord	AIS D
1	\$853 (\$850)	\$635 (\$613)	\$670 (\$659)	\$373 (\$373)	\$237 (\$211)	\$276 (\$264)
2	\$238 (\$205)	\$232 (\$218)	\$292 (\$228)	\$160 (\$155)	\$54 (\$55)	\$42 (\$31)
3	\$169 (\$169)	\$113 (\$116)	\$213 (\$225)	\$129 (\$110)	\$47 (\$47)	\$36 (\$16)
4	\$230 (\$227)	\$145 (\$113)	\$158 (\$110)	\$128 (\$123)	\$55 (\$39)	\$7 (\$7)
5	\$164 (\$142)	\$176 (\$150)	\$205 (\$134)	\$135 (\$134)	\$48 (\$38)	\$64 (\$7)

The cost of acute hospitalization for PU along with readmissions up to one year after the initial hospitalization was calculated for individuals with SCI resulting from gun-shot by Chopra and colleagues (Chopra et al. 2016). The mean total cost of hospitalizations (initial admission with readmissions) for the total cohort and stratified by infected and uninfected PU is presented in Table 25.

Table 25. Mean cost of hospitalizations (up to one year from initial hospitalization) for individuals with PU and gun-shot related SCI reported in Chopra et al. (2016).

	Mean cost (standard deviation)
Total cohort	\$21,070 (\$7,005)
Individuals with infected PU	\$17,658 (\$8,768)
Individuals with non-infected PU	\$13,038 (\$7,393)

A separate study examining the additional health care cost of neuropathic pain (NeP) for individuals with SCI in the first year post-injury (Margolis et al. 2014b). In this study, the total first year cost for individuals with NeP and SCI was compared to a matched cohort without NeP. The presence of NeP resulted in an increase in mean cost of \$18,920 (\$10,624-\$27,836 95% confidence interval) in the first year. The cost components in this analysis included acute hospital admissions, emergency department visits, physician visits, procedures and outpatient drug claims. In a similar analysis of a larger data set with the same cost components with the addition of physical therapy, the additional health care cost for individuals with NeP was \$24,558 (\$20,707-\$28,504 95% confidence interval) in the first year (Margolis et al. 2014a).

Key Points

In the US, mean costs are approximately \$260,000 for first year, and \$80,000 for following years. Mean costs range from approximately \$143,000 to \$493,000 in first year and \$39,000 to \$175,500 in following years depending on location and severity of injury. Estimated lifetime costs for an individual injured at 25 years old is approximately between \$931,000 and \$3.2 million and for an individual injured at 50 years old, approximately between \$702,000 to \$1.8 million depending on location and severity of injury. The estimated lifetime hospital costs for an individual injured at 35 years old is between \$72,000 and \$339,000 depending on level of SCI severity. First year cost for health care claims through workers' compensation for individuals with work-related SCI ranged from \$276,000 to \$853,000 depending on level of injury. By the fifth year the cost was between \$64,000 and \$205,000.

The cost of hospitalization and readmissions for individuals with PU and gun-shot related SCI is approximately \$21,100. The presence of neuropathic pain increased first-year health care costs by \$18,900 to \$24,600.

5 Discussion

A systematic search of economic evaluation studies for interventions in an SCI population yielded 19 studies. From the results of the base case analyses it would appear that ITB for management of spasticity, transanal irrigation for bowel care and electrical stimulation therapy, negative pressure wound therapy for treatment of pressure injuries, fibrin sealant for surgical treatment of pressure injuries all had better clinical outcomes and lower costs versus conventional treatment. Similar results were observed for sildenafil citrate in treating erectile dysfunction when compared to intracavernous injections of papaverine prostadil, transurethral suppository or surgical implantation of prosthetic and also for duplex ultrasound at admission for screening deep vein thrombosis. Sildenafil citrate had results that would be considered cost effective compared to triple mix and vacuum erectile device. Gel reservoir catheters versus non-coated catheter for bladder management, sacral anterior root stimulation for neurogenic bladder

and telephone support with standard pressure injury management were considered cost-effective. However, supported employment did not result in a reduction in cost or gain in outcomes for US veterans compared to standard care. Early decompression for individuals with traumatic cervical SCI and neuroprosthesis implant for cough restoration was associated with lower costs. Older individuals requiring surgical and rehabilitation management had higher costs for individuals with traumatic cervical SCI.

Unfortunately, there are numerous concerns that limit the comparability of economic evaluations. First, the studies were from different jurisdictions that have different health care systems. Each country has a different mix of public/private payment for health care services. Some countries such as Canada and many European nations rely more heavily on the public funding while other countries such as the US rely more on private/third party payment. As well, each health care system has different emphases when providing health care to their citizens. Some countries may focus more on treatment modalities while others may focus more on prevention. Second, all studies have different perspectives in costing. Many of the studies focused on the government payer perspective. Even in the studies that took a government payer perspective, each study took a different bundle of health care costs, ranging from 5-6 different costs to only 1 cost item (clinician time in providing care).

The cost of illness study methods for the included studies varied widely making comparison of results difficult. This is compounded by the difficulty of comparing cost of illness between jurisdictions where different health care systems have different patient care modalities, behaviours, habits and resource limitations. Many of the limitations of interpreting economic evaluation studies apply for cost of illness studies. The results of the cost of illness studies in most cases only represent the health care resource utilization and associated gross costs experienced by an individual with SCI. The absence of a matched non-SCI population in many of the studies does not allow us to understand the additional health care costs attributable to SCI and the additional economic burden that is associated with this injury. The lack of studies exploring net costs in other disease areas in general also does not facilitate a comparison of SCI attributable cost to other diseases.

Despite the limitations in methods in the studies reviewed, limitations in applicability to other jurisdictions and the lack of comparability, this review provides an interesting summary of the state of economic research in SCI. Currently, comparative cost analyses for interventions in the SCI population are sparse with only a few studies identified in the last 15 years. There appear to be a strong interest in understanding the cost-effectiveness of hydrophilic catheters as well as interventions for treating pressure injuries. For cost of illness studies there are over a dozen analyses conducted in the general SCI population in the last 10 years representing 8 different jurisdictions. Both Canada and the US have the highest number of studies. The studies from Canada were based on various data sources. In the US, studies were driven by data from the Model Systems Centre through the National SCI statistical centre. With the limited number of cost of illness studies, many countries are not represented and the cost impact of SCI remains unknown. Despite the relative lack of data, it remains that there are substantial costs associated with SCI even though it is a relatively low prevalence condition.

There is a need for additional economic studies in the area of SCI given the sizable impact of this condition to the health care system and the large number of interventions that an individual with SCI would require throughout their lifetime. Given the substantial health care costs associated with SCI, identifying and implementing cost-effective health care strategies would benefit all parties including the health care recipient, provider and funder. The authors hope that this review will shed light on the state of economic studies in SCI and spark increased interest in researchers to pursue studies in this field.

6 Summary

According to one study, intrathecal baclofen as first-line therapy for disabling spasticity for severely impaired individuals had lower treatment costs and better outcomes (improved patient and caregiver satisfaction according to goal attainment scaling and at least 1-point reduction in Ashworth score) over a 2-year period when compared to the current treatment pattern of care in France at the time of model construction.

Considering the long-term outcomes associated with intermittent catheterization, hydrophilic catheters may be cost-effective when compared to uncoated catheters.

Trans-anal irrigation was observed to be less costly than conservative bowel management for a two-day period and less costly than ineffective standard bowel management over a lifetime time horizon. Trans-anal irrigation had better clinical outcomes (St Mark's fecal incontinence score, Cleveland Clinic constipation score and neurogenic bowel dysfunction score) over 10 weeks when compared to conservative bowel management and resulted in higher QALYs when compared to ineffective standard bowel management.

In a single study, sacral anterior root stimulation appears to be cost-effective for neurogenic bladder.

Based on one study, the implementation of duplex ultrasound for deep venous thrombosis surveillance would result in a cost per life year gained of between \$1,193 and \$9,050 depending on age and type of injury.

In one study, sildenafil had lower cost and better outcomes than intracavernous injections, suppositories and surgery. Cost per QALY was \$9,656/QALY for Triple Mix intercavernous injections and \$13,399/QALY for vacuum erection device.

For a single study, over a one-year timeframe, electrical stimulation in addition to standard wound care had lower costs and greater number of wounds healed.

In one study, the addition of telephone support to standard pressure injury management appears to be cost effective.

In a single study, negative pressure wound therapy with weekly dressing changes was less costly than standard care (with one to two changes a day) at nine weeks.

In one study, fibrin sealant for the surgical treatment of pressure injuries resulted in less cumulative costs at six months post-discharge compared to conventional surgical debridement for individuals with SCI.

Based on a single study, the decrease in respiratory tract infection and amount of caregiver support over a three-year period resulted in lower overall cost with a Cough Stimulator neuroprosthesis compared to standard respiratory management for restoration of an effective cough.

In a single study, surgical and rehabilitative management of older individuals with traumatic cervical SCI were costlier in the first six months after injury compared to younger individuals.

In one study, early decompression for individuals with traumatic cervical SCI resulted in lower costs in the first six months after injury both motor complete and motor incomplete individuals.

In a single study, additional services for supported employment for US veterans did not result in a statistically significant reduction in cost or gain in QALYs.

The mean hospital cost for traumatic SCI in Australia is approximately \$52,000 for initial hospitalization and \$10,700 for subsequent hospitalizations; for non-traumatic SCI it is approximately \$17,900 for initial hospitalization and \$17,350 for subsequent hospitalizations. The mean cost of a secondary condition results in a hospital visit costing \$10,900 for any urological condition to \$22,100 for pressure injuries. The mean cost per hospital visit can range between \$7,700 for an individual with incomplete thoracic SCI and \$13,100 for a complete thoracic SCI. The mean cost per emergency department visit is between \$404 for lumbar SCI and \$584 for complete thoracic SCI.

In Belgium, mean cost for inpatient and outpatient rehabilitation is approximately \$46,000 and \$7,900 for paraplegia and approximately \$71,000 and \$10,700 for tetraplegia, respectively.

In Canada, mean costs range between \$17,500 and \$164,000 for initial hospitalization, \$25,000 to \$170,500 in the first-year and \$7,500 to \$60,500 for following years depending on type of injury. Second-year mean costs were between \$6,600 and \$79,200 depending on level and severity of SCI. Total mean cost of inpatient rehabilitation is approximately \$134,500 for SCI and is increased to approximately \$174,500 if the patient also has a TBI. Total mean annual cost per individual with SCI in Ontario is approximately \$115,000. Individuals with SCI who develop a UTI during an acute hospital stay have \$6,800 higher hospital cost. Hospital-acquired PU for individuals with SCI is associated with an increase of \$16,500 in acute hospital cost.

The direct out-of-pocket cost for conservative SCI management in Nigeria is approximately \$280 and \$1,900 for lost income and vehicle repair/replacement.

Total mean lifetime cost for an individual with a SCI that is a result of a motor crash is approximately \$279,500 and \$296,500 from other causes in Spain.

In the US, mean costs are approximately \$260,000 for first year, and \$80,000 for following years. Mean costs range from approximately \$143,000 to \$493,000 in first year and \$39,000 to \$175,500 in following years depending on location and severity of injury. Estimated lifetime costs for an individual injured at 25 years old is approximately between \$931,000 and \$3.2 million and for an individual injured at 50 years old, approximately between \$702,000 to \$1.8 million depending on

location and severity of injury. The estimated lifetime hospital costs for an individual injured at 35 years old is between \$72,000 and \$339,000 depending on level of SCI severity. First year cost for health care claims through workers' compensation for individuals with work-related SCI ranged from \$276,000 to \$853,000 depending on level of injury. By the fifth year the cost was between \$64,000 and \$205,000.

The cost of hospitalization and readmissions for individuals with PU and gun-shot related SCI is approximately \$21,100. The presence of neuropathic pain increased first-year health care costs by \$18,900 to \$24,600.

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Abbreviations

GAS	Goal Attainment Scale
GDP	Gross Domestic Product
GAS	Goal Attainment Scale
ICER	Incremental Cost-Effectiveness Ratio
INR	Indian Rupees
ITB	Intrathecal Baclofen
LY	Life Year
NeP	Neuropathic Pain
NHS	National Healthcare Services
NPWT	Negative Pressure Wound Therapy
PU	Pressure Ulcer
QALY	Quality-Adjusted Life Year
QHES	Quality of Health Economic Studies
SARS	Sacral Anterior Root Stimulation
SCI	spinal cord injury
TBI	traumatic brain injury
UTI	urinary tract infection

Appendix

Table A1. Critical Appraisal of Economic Studies using the Quality of Health Economic Studies Checklist

Criterion	Arora et al.	Bensamil et al.	Berningham et al.	Christensen et al.	Clark et al.	Dwivedi et al.	Emmanuel et al.	Furlan et al. (A)
Was the study objective presented in a clear, specific, and measureable manner?	Y	Y	Y	Y	Y	N	Y	Y
Were the perspective of the analysis (societal, third-party payer, etc.) and reasons for its selection stated?	Y	N	N	Y	Y	N	Y	Y
Were variable estimates used in the analysis from the best available source (i.e., randomized control trial = best, expert opinion = worst)?	Y	N	Y	Y	Y	Y	Y	Y
If estimates came from a subgroup analysis, were the groups prespecified at the beginning of the study?	N/A	Y	Y	Y	N/A	N/A	N/A	N/A
Was uncertainty handled by (1) statistical analysis to address random events, (2) sensitivity analysis to cover a range of assumptions?	Y	Y	Y	Y	N	N	Y	Y
Was incremental analysis performed between alternatives for resources and costs?	Y	Y	Y	Y	Y	Y	Y	Y
Was the methodology for data abstraction (including the value of health states and other benefits) stated?	Y	N	Y	Y	Y	Y	Y	Y
Did the analytic horizon allow time for all relevant and important outcomes? Were benefits and costs that went beyond one year discounted (3% to 5%) and justification given for the discount rate?	Y	N	Y	N	Y	Y	Y	Y
Was the measurement of costs appropriate and the methodology for the estimation of quantities and unit costs clearly described?	Y	Y	Y	Y	Y	Y	Y	Y
Were the primary outcome measure(s) for the economic evaluation clearly stated and did they include the major short-term justification given for the measures/scales used?	Y	Y	N	N	Y	Y	Y	Y
Were the health outcomes measures/scales valid and reliable? If previously tested valid and reliable measures were not available, was justification given for the measures/scales used?	Y	Y	Y	Y	Y	Y	Y	Y
Were the economic model (including structure), study methods and analysis, and the components of the numerator and denominator displayed in a clear, transparent manner?	Y	Y	Y	N	Y	Y	Y	Y
Were the choice of economic model, main assumptions, and limitation of the study stated and justified?	Y	Y	Y	N	Y	N	Y	Y
Did the author(s) explicitly discuss direction and magnitude of potential biases?	Y	N	Y	N	Y	N	N	Y
Were the conclusions/recommendations of the study justified and based on the study results?	Y	Y	Y	Y	Y	Y	Y	Y
Was there a statement disclosing the source of the funding for the study?	Y	N	Y	Y	Y	Y	Y	Y

Note: N=no, did not satisfy the criterion; N/A= not applicable, does not apply to study; U=unknown, did not specify in study; Y=yes, satisfied the criterion

Criterion	Furlan et al. (B)	Kadyan et al.	Mittmann et al. (A)	Mittmann et al. (B)	Morliere et al.	Rognoni et al.	Sinnott et al.	Truzzi et al.
Was the study objective presented in a clear, specific, and measureable manner?	Y	Y	Y	Y	Y	Y	Y	Y
Were the perspective of the analysis (societal, third-party payer, etc.) and reasons for its selection stated?	Y	N	N	Y	Y	Y	Y	Y
Were variable estimates used in the analysis from the best available source (i.e., randomized control trial = best, expert opinion =worst)?	Y	Y	Y	Y	Y	Y	Y	Y
If estimates came from a subgroup analysis, were the groups prespecified at the beginning of the study?	N/A	Y	Y	Y	N/A	N/A	N/A	N/A
Was uncertainty handled by (1) statistical analysis to address random events, (2) sensitivity analysis to cover a range of assumptions?	Y	Y	Y	Y	Y	Y	N	N
Was incremental analysis performed between alternatives for resources and costs?	Y	Y	Y	Y	Y	Y	Y	Y
Was the methodology for data abstraction (including the value of health states and other benefits) stated?	Y	N	Y	Y	Y	Y	Y	Y
Did the analytic horizon allow time for all relevant and important outcomes? Were benefits and costs that went beyond one year discounted (3% to 5%) and justification given for the discount rate?	Y	Y	Y	Y	Y	Y	Y	N
Was the measurement of costs appropriate and the methodology for the estimation of quantities and unit costs clearly described?	Y	N	Y	Y	Y	Y	Y	Y
Were the primary outcome measure(s) for the economic evaluation clearly stated and did they include the major short-term justification given for the measures/scales used?	Y	N	N	N	Y	Y	Y	Y
Were the health outcomes measures/scales valid and reliable? If previously tested valid and reliable measures were not available, was justification given for the measures/scales used?	Y	Y	Y	N	Y	Y	Y	Y
Were the economic model (including structure), study methods and analysis, and the components of the numerator and denominator displayed in a clear, transparent manner?	Y	N	N	Y	Y	Y	Y	Y
Were the choice of economic model, main assumptions, and limitation of the study stated and justified?	Y	N	Y	Y	Y	Y	Y	Y
Did the author(s) explicitly discuss direction and magnitude of potential biases?	Y	N	N	N	Y	Y	N	N
Were the conclusions/recommendations of the study justified and based on the study results?	Y	N	Y	Y	U	Y	Y	Y
Was there a statement disclosing the source of the funding for the study?	Y	N	Y	Y	Y	Y	Y	Y

Note: N=no, did not satisfy the criterion; N/A= not applicable, does not apply to study; U=unknown, did not specify in study; Y=yes, satisfied the criterion

Criterion	Velaasco et al.	Watanabe et al.	Welk et al.
Was the study objective presented in a clear, specific, and measureable manner?	N	Y	Y
Were the perspective of the analysis (societal, third-party payer, etc.) and reasons for its selection stated?	N	Y	Y
Were variable estimates used in the analysis from the best available source (i.e., randomized control trial = best, expert opinion = worst)?	Y	Y	Y
If estimates came from a subgroup analysis, were the groups prespecified at the beginning of the study?	N/A	N/A	N/A
Was uncertainty handled by (1) statistical analysis to address random events, (2) sensitivity analysis to cover a range of assumptions?	N	Y	Y
Was incremental analysis performed between alternatives for resources and costs?	Y	Y	Y
Was the methodology for data abstraction (including the value of health states and other benefits) stated?	Y	Y	Y
Did the analytic horizon allow time for all relevant and important outcomes? Were benefits and costs that went beyond one year discounted (3% to 5%) and justification given for the discount rate?	N	Y	Y
Was the measurement of costs appropriate and the methodology for the estimation of quantities and unit costs clearly described?	Y	Y	Y
Were the primary outcome measure(s) for the economic evaluation clearly stated and did they include the major short-term justification given for the measures/scales used?	Y	Y	Y
Were the health outcomes measures/scales valid and reliable? If previously tested valid and reliable measures were not available, was justification given for the measures/scales used?	N	Y	Y
Were the economic model (including structure), study methods and analysis, and the components of the numerator and denominator displayed in a clear, transparent manner?	Y	Y	Y
Were the choice of economic model, main assumptions, and limitation of the study stated and justified?	N	Y	Y
Did the author(s) explicitly discuss direction and magnitude of potential biases?	Y	Y	Y
Were the conclusions/recommendations of the study justified and based on the study results?	Y	Y	Y
Was there a statement disclosing the source of the funding for the study?	Y	Y	Y

Note: N=no, did not satisfy the criterion; N/A= not applicable, does not apply to study; U=unknown, did not specify in study; Y=yes, satisfied the criterion

Table A2. Critical Appraisal of Economic Studies using the Drummond Checklist

Criterion		Arora et al.	Bensamil et al.	Bermingham et al.	Christensen et al.	Clark et al.	Dwivedi et al.	Emmanuel et al.
Was a well-defined question posed in answerable form?	Did the study examine both costs and effects of the service(s) or programme(s)?	Y	Y	Y	Y	Y	Y	Y
	Did the study involve a comparison of alternatives?	Y	Y	Y	Y	Y	Y	Y
	Was a viewpoint for the analysis stated and was the study placed in any particular decision-making context?	Y	N	Y	Y	Y	N	Y
Was a comprehensive description of the competing alternatives given?	Were there any important alternatives omitted?	N	N	N	N	N	N	N
	Was (should) a do-nothing alternative be considered?	Y	Y	Y	Y	Y	Y	Y
Was the effectiveness of the programme or services established?	Was this done through a randomised, controlled clinical trial? If so, did the trial protocol reflect what would happen in regular practice?	Y	N	N	Y	N	Y	N
	Was effectiveness established through an overview of clinical studies?	N	N	Y	N	N	N	N
	Were observational data or assumptions used to establish effectiveness? If so, what are the potential biases in results?	N	N	N	N	Y	N	Y
Were all the important and relevant costs and consequences for each alternative identified?	Was the range wide enough for the research question at hand?	Y	Y	Y	Y	Y	Y	Y
	Did it cover all relevant viewpoints? (Possible viewpoints include the community or social viewpoint, and those of patients and third-party payers. Other viewpoints may also be relevant depending upon the particular analysis.)	Y	U	Y	Y	Y	U	Y
	Were the capital costs, as well as operating costs, included?	Y	Y	Y	Y	Y	N	Y
Were costs and consequences measured accurately in appropriate physical units (e.g. hours of nursing time, number of physician visits, lost work-days, gained life years)?	Were any of the identified items omitted from measurement? If so, does this mean that they carried no weight in the subsequent analysis?	N	N	N	N	N	N	N
	Were there any special circumstances (e.g., joint use of resources) that made measurement difficult? Were these circumstances handled appropriately?	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Were the cost and consequences valued credibly?	Were the sources of all values clearly identified? (Possible sources include market values, patient or client preferences and views, policy-makers' views and health professionals' judgements)	Y	Y	Y	Y	Y	N	Y
	Were market values employed for changes involving resources gained or depleted?	Y	Y	Y	Y	Y	N	Y

	Where market values were absent (e.g. volunteer labour), or market values did not reflect actual values (such as clinic space donated at a reduced rate), were adjustments made to approximate market values?	N/A	N/A	N/A	Y	Y	N/A	Y
	Was the valuation of consequences appropriate for the question posed (i.e. has the appropriate type or types of analysis – cost-effectiveness, cost-benefit, cost-utility – been selected)?	Y	Y	Y	Y	Y	Y	Y
Were costs and consequences adjusted for differential timing?	Were costs and consequences that occur in the future 'discounted' to their present values?	N	N	Y	N/A	Y	N	Y
	Was there any justification given for the discount rate used?	Y	N/A	Y	N/A	Y	N	Y
Was an incremental analysis of costs and consequences of alternatives performed?	Were the additional (incremental) costs generated by one alternative over another compared to the additional effects, benefits, or utilities generated?	Y	Y	Y	Y	Y	N	Y
Was allowance made for uncertainty in the estimates of costs and consequences?	If data on costs and consequences were stochastic (randomly determined sequence of observations), were appropriate statistical analyses performed?	Y	Y	Y	N/A	Y	N	Y
	If a sensitivity analysis was employed, was justification provided for the range of values (or for key study parameters)?	Y	N	Y	N	Y	N	Y
	Were the study results sensitive to changes in the values (within the assumed range for sensitivity analysis, or within the confidence interval around the ratio of costs to consequences)?	N	N	N	N	N	N/A	N
Did the presentation and discussion of study results include all issues of concern to users?	Were the conclusions of the analysis based on some overall index or ratio of costs to consequences (e.g. cost-effectiveness ratio)? If so, was the index interpreted intelligently or in a mechanistic fashion?	Y	Y	Y	Y	Y	N	Y
	Were the results compared with those of others who have investigated the same question? If so, were allowances made for potential differences in study methodology?	N	Y	N	N	Y	Y	Y
	Did the study discuss the generalisability of the results to other settings and patient/client groups?	N	Y	Y	N	Y	N	Y
	Did the study allude to, or take account of, other important factors in the choice or decision under consideration (e.g. distribution of costs and consequences, or relevant ethical issues)?	Y	Y	Y	N	Y	N	Y
	Did the study discuss issues of implementation, such as the feasibility of adopting the 'preferred' programme given existing financial or other constraints, and whether any freed resources could be redeployed to other worthwhile programmes?	N	Y	Y	N	Y	N	Y

Note: N=no, did not satisfy the criterion; N/A= not applicable, does not apply to study; U=unknown, did not specify in study; Y=yes, satisfied the criterion

Criterion		Furlan et al. (A)	Furlan et al. (B)	Kadyan et al.	Mittmann et al. (A)	Mittmann et al. (B)	Morliere et al.	Rognoni et al.
Was a well-defined question posed in answerable form?	Did the study examine both costs and effects of the service(s) or programme(s)?	Y	Y	Y	Y	Y	Y	Y
	Did the study involve a comparison of alternatives?	Y	Y	Y	Y	Y	Y	Y
	Was a viewpoint for the analysis stated and was the study placed in any particular decision-making context?	Y	Y	Y	Y	Y	Y	Y
Was a comprehensive description of the competing alternatives given?	Were there any important alternatives omitted?	N	N	N	N	N	N	N
	Was (should) a do-nothing alternative be considered?	N/A	Y	Y	N	Y	Y	Y
Was the effectiveness of the programme or services established?	Was this done through a randomised, controlled clinical trial? If so, did the trial protocol reflect what would happen in regular practice?	N	N	N	N	N	N	N
	Was effectiveness established through an overview of clinical studies?	N	N	N	N	Y	Y	Y
	Were observational data or assumptions used to establish effectiveness? If so, what are the potential biases in results?	Y	Y	Y	Y	N	N	N
Were all the important and relevant costs and consequences for each alternative identified?	Was the range wide enough for the research question at hand?	Y	Y	Y	Y	Y	Y	Y
	Did it cover all relevant viewpoints? (Possible viewpoints include the community or social viewpoint, and those of patients and third-party payers. Other viewpoints may also be relevant depending upon the particular analysis.)	U	U	Y	U	U	Y	Y
	Were the capital costs, as well as operating costs, included?	N	N	Y	Y	Y	Y	Y
Were costs and consequences measured accurately in appropriate physical units (e.g. hours of nursing time, number of physician visits, lost work-days, gained life years)?	Were any of the identified items omitted from measurement? If so, does this mean that they carried no weight in the subsequent analysis?	N	N	N	N	N	N	N
	Were there any special circumstances (e.g., joint use of resources) that made measurement difficult? Were these circumstances handled appropriately?	N/A	N/A	U	N/A	Y	N/A	N/A
Were the cost and consequences valued credibly?	Were the sources of all values clearly identified? (Possible sources include market values, patient or client preferences and views, policy-makers' views and health professionals' judgements)	Y	Y	N	Y	Y	Y	Y
	Were market values employed for changes involving resources gained or depleted?	Y	Y	U	Y	Y	Y	Y

	Where market values were absent (e.g. volunteer labour), or market values did not reflect actual values (such as clinic space donated at a reduced rate), were adjustments made to approximate market values?	Y	Y	N/A	N/A	N/A	Y	Y
	Was the valuation of consequences appropriate for the question posed (i.e. has the appropriate type or types of analysis – cost-effectiveness, cost-benefit, cost-utility – been selected)?	Y	Y	Y	Y	Y	Y	Y
Were costs and consequences adjusted for differential timing?	Were costs and consequences that occur in the future 'discounted' to their present values?	N	N	N/A	N/A	N/A	Y	Y
	Was there any justification given for the discount rate used?	Y	Y	N/A	N/A	N/A	Y	Y
Was an incremental analysis of costs and consequences of alternatives performed?	Were the additional (incremental) costs generated by one alternative over another compared to the additional effects, benefits, or utilities generated?	Y	Y	Y	Y	Y	Y	Y
Was allowance made for uncertainty in the estimates of costs and consequences?	If data on costs and consequences were stochastic (randomly determined sequence of observations), were appropriate statistical analyses performed?	Y	Y	N/A	N/A	Y	Y	Y
	If a sensitivity analysis was employed, was justification provided for the range of values (or for key study parameters)?	Y	Y	Y	Y	Y	Y	Y
	Were the study results sensitive to changes in the values (within the assumed range for sensitivity analysis, or within the confidence interval around the ratio of costs to consequences)?	N	N	Y	N	Y	N	N
Did the presentation and discussion of study results include all issues of concern to users?	Were the conclusions of the analysis based on some overall index or ratio of costs to consequences (e.g. cost-effectiveness ratio)? If so, was the index interpreted intelligently or in a mechanistic fashion?	Y	Y	Y	Y	Y	Y	Y
	Were the results compared with those of others who have investigated the same question? If so, were allowances made for potential differences in study methodology?	Y	Y	N	Y	N	Y	Y
	Did the study discuss the generalisability of the results to other settings and patient/client groups?	Y	N	Y	Y	N	Y	Y
	Did the study allude to, or take account of, other important factors in the choice or decision under consideration (e.g. distribution of costs and consequences, or relevant ethical issues)?	N	N	N	Y	Y	N	N
	Did the study discuss issues of implementation, such as the feasibility of adopting the 'preferred' programme given existing financial or other constraints, and whether any freed resources could be redeployed to other worthwhile programmes?	N	N	N	Y	Y	N	N

Note: N=no, did not satisfy the criterion; N/A= not applicable, does not apply to study; U=unknown, did not specify in study; Y=yes, satisfied the criterion

Criterion		Sinnott et al.	Truzzi et al.	Velaasco et al.	Watanabe et al.	Welk et al.
Was a well-defined question posed in answerable form?	Did the study examine both costs and effects of the service(s) or programme(s)?	Y	Y	Y	Y	Y
	Did the study involve a comparison of alternatives?	Y	Y	Y	Y	Y
	Was a viewpoint for the analysis stated and was the study placed in any particular decision-making context?	Y	Y	N	N	Y
Was a comprehensive description of the competing alternatives given?	Were there any important alternatives omitted?	N	N	N	N	N
	Was (should) a do-nothing alternative be considered?	Y	Y	Y	Y	Y
Was the effectiveness of the programme or services established?	Was this done through a randomised, controlled clinical trial? If so, did the trial protocol reflect what would happen in regular practice?	Y	N	N	N	N
	Was effectiveness established through an overview of clinical studies?	N	Y	N	N	Y
	Were observational data or assumptions used to establish effectiveness? If so, what are the potential biases in results?	N	N	Y	Y	N
Were all the important and relevant costs and consequences for each alternative identified?	Was the range wide enough for the research question at hand?	Y	Y	Y	Y	Y
	Did it cover all relevant viewpoints? (Possible viewpoints include the community or social viewpoint, and those of patients and third-party payers. Other viewpoints may also be relevant depending upon the particular analysis.)	Y	Y	U	U	Y
	Were the capital costs, as well as operating costs, included?	Y	Y	Y	Y	Y
Were costs and consequences measured accurately in appropriate physical units (e.g. hours of nursing time, number of physician visits, lost work-days, gained life years)?	Were any of the identified items omitted from measurement? If so, does this mean that they carried no weight in the subsequent analysis?	N	N	N	N	N
	Were there any special circumstances (e.g., joint use of resources) that made measurement difficult? Were these circumstances handled appropriately?	N/A	N/A	N/A	N/A	N/A
Were the cost and consequences valued credibly?	Were the sources of all values clearly identified? (Possible sources include market values, patient or client preferences and views, policy-makers' views and health professionals' judgements)	Y	Y	Y	Y	Y
	Were market values employed for changes involving resources gained or depleted?	Y	Y	Y	Y	Y
	Where market values were absent (e.g. volunteer labour), or market values did not reflect actual values (such as clinic space donated at a reduced rate), were adjustments made to approximate market values?	Y	N/A	N/A	N/A	Y

	Was the valuation of consequences appropriate for the question posed (i.e. has the appropriate type or types of analysis – cost-effectiveness, cost-benefit, cost-utility – been selected)?	Y	Y	Y	Y	Y
Were costs and consequences adjusted for differential timing?	Were costs and consequences that occur in the future 'discounted' to their present values?	N/A	Y	N/A	Y	Y
	Was there any justification given for the discount rate used?	N/A	N	N/A	N	Y
Was an incremental analysis of costs and consequences of alternatives performed?	Were the additional (incremental) costs generated by one alternative over another compared to the additional effects, benefits, or utilities generated?	Y	Y	Y	Y	Y
Was allowance made for uncertainty in the estimates of costs and consequences?	If data on costs and consequences were stochastic (randomly determined sequence of observations), were appropriate statistical analyses performed?	Y	Y	N/A	Y	Y
	If a sensitivity analysis was employed, was justification provided for the range of values (or for key study parameters)?	Y	Y	N/A	N	Y
	Were the study results sensitive to changes in the values (within the assumed range for sensitivity analysis, or within the confidence interval around the ratio of costs to consequences)?	N	N	N/A	Y	N
Did the presentation and discussion of study results include all issues of concern to users?	Were the conclusions of the analysis based on some overall index or ratio of costs to consequences (e.g. cost-effectiveness ratio)? If so, was the index interpreted intelligently or in a mechanistic fashion?	N	Y	Y	Y	Y
	Were the results compared with those of others who have investigated the same question? If so, were allowances made for potential differences in study methodology?	N	Y	N	Y	Y
	Did the study discuss the generalisability of the results to other settings and patient/client groups?	Y	Y	Y	Y	N
	Did the study allude to, or take account of, other important factors in the choice or decision under consideration (e.g. distribution of costs and consequences, or relevant ethical issues)?	Y	Y	N	N	N
	Did the study discuss issues of implementation, such as the feasibility of adopting the 'preferred' programme given existing financial or other constraints, and whether any freed resources could be redeployed to other worthwhile programmes?	Y	Y	N	N	N

Note: N=no, did not satisfy the criterion; N/A= not applicable, does not apply to study; U=unknown, did not specify in study; Y=yes, satisfied the criterion

Table A3. Summary of SCI cost of illness studies using a checklist modified from Lang and Moss.

Criterion	Bradbury et al.	Cao et al.	Chan et al.	Chopra et al.	DeVivo et al.	Dryden et al.	Dukes et al.	Gabbe & Nunn	Garcia-Ates et al.	Holland et al.
Country	Canada	US	Canada	US	US	Canada	US	Australia	Spain	US
Was the perspective of the study stated?	N	N	Y	N	N	N	Y	N	Y	N
What was the perspective	Rehab	N/A	Healthcare Provider	Hospital	N/A	Govern	Healthcare, Hospital	Hospital	Society	Hospital
Year of costs	2006	2009	N/A	2004-2008/2015	2009	2002	2011	2012	2007	N/S
Currency	Canadian Dollar	US Dollar	Canadian Dollar	US Dollar	US Dollar	Canadian Dollar	US Dollar	Australian Dollar	Euro	Charges
What health care settings were included in the analysis?	Inpatient rehab	ER, inpatient hospital, LTC, outpatient	N/A	Hospital	ER, inpatient hospital, LTC, outpatient	Hospital, physician home care, LTC	Hospital	Hospital	Hospital, home care	Hospital
Was the incidence-based or prevalence-based approach used?	Incidence	Prevalence	Incidence	Incidence	Incidence/Prevalence	Incidence	Incidence	Incidence	Incidence	Incidence
Are the study results based on a model or observational cohort, or both?	OC	Model	OC and Model	OC	OC	OC	Model	OC	Model	OC
If based on an observational cohort, how large is the sample size?	10	N/A	1716	201	735	233	1572	356	N/A	159,875
Is there a non-SCI comparator?	N	N	Y	Y	N	N	N	N	Y	Y
Are the results presented as gross or net	Gross	Gross	Net	Gross	Gross	Gross Net	Gross	Gross	Gross	Gross
Were indirect costs included?	N	N	N	N	N	N	N	N	Y	N
Were sensitivity analyses included?	N	Y	N	N	N	N	N	N	Y	N
Were uncertainties described?	N	Y	Y	N/A	Y	Y	N/A	N/A	Y	N/A

Note: LTC=long-term care; N=no; N/A=not available; OC=observational cohort study; Rehab=rehabilitation; US=United States; Y=yes

Table A3. Summary of SCI cost of illness studies using a checklist modified from Lang and Moss.

Criterion	Kawu et al.	Kiekens et al.	Mahabaleshwarkar & Khanna	Margolis et al. (A)	Margolis et al. (B)	Mitchell et al.	Munce et al.	New et al.	Radharishna et al.	Wang et al.	White et al.
Country	Nigeria	Belgium	US	US	US	Australia	Canada	Australia	Canada	China	Canada
Was the perspective of the study stated?	N	Y	Y	Y	Y	N	Y	N	Y	N	Y
What was the perspective	Patient	Rehab/ Govern	Hospital	Health insurance provider	Health insurance provider	Hospital	Govern	Govern	Public health care provider	Hospital	Hospital
Year of costs	2009	2006	N/S	2012	2012	2013-2014	2005	2004	2009	2010	2013
Currency	US Dollar	Euro	US Dollar Charges	US Dollar	US Dollar	Australian Dollar	Canadian Dollar	Australia Dollar	Canadian Dollar	Chinese Yuan	Canadian Dollar
What health care settings were included in the analysis?	Hospital	Rehab	hospital	Inpatient, outpatient, physician, procedure, physical therapy, drugs	Inpatient, ED visits, physician, procedure, drugs	hospital	ER, inpatient hospital, CCC, home care	Hospital, inpatient rehab	N/A	Hospital	Hospital
Was the incidence-based or prevalence-based approach used?	Incidence	Incidence	Prevalence	Incidence/ Prevalence	Incidence/ Prevalence	Incidence	Prevalence	Prevalence	Incidence	Incidence	Incidence
Are the study results based on a model or observational cohort, or both?	OC	Model	cohort	OC	OC	OC	OC	OC	OC	OC	cohort
If based on an observational cohort, how large is the sample size?	34	N/A	11,848	3524 with NeP/3524 without	546 with NeP/546 without	6392 under 65 years, 7037 over 65 years	936	1,320	439	3,142	10 UTI, 15 PU
Is there a non-SCI comparator?	N	N	Y	Y	Y	Y	N	N	N	N	Y
Are the results presented as gross or net	Gross	Gross	Net	Gross	Net	Gross	Gross	Gross	Gross	Gross	Net
Were indirect costs included?	Y	N	N	N	N	N	N	N	N	N	N
Were sensitivity analyses included?	N	N	N	N	N	N	N	N	N	N	N
Were uncertainties described?	N	N	N/A	N/A	N/A	N/A	Y	Y	N/A	N	N/A

Note: LTC=long-term care; N=no; N/A=not available; OC=observational cohort study; Rehab=rehabilitation; US=United States; Y=yes