Long-term Outcomes of Operatively and Non-Operatively Treated Spina Bifida Scoliosis

By

Amir Khoshbin

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Graduate Department of Institute of Medical Science

In the University of Toronto

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ABSTRACT:

Background

The purpose of this study was to evaluate outcomes in Spina Bifida Cystica adults, treated non-operatively or operatively for scoliosis during childhood.

Methods

Patients with SBC scoliosis (minimum Cobb angle ≥50°) treated at the Hospital for Sick Children or the Children’s Hospital of Eastern Ontario (1991-2007 inclusive) were recruited. In addition to clinical and radiological assessments, health related quality of life (HRQOL) outcomes included the: a) Spina Bifida Spine Questionnaire (SBSQ) and b) Medical Outcomes Study-36 Item Short Form Health Survey (SF-36).

Results

The operative and non-operative patients were statistically similar at baseline on the following variables: a) age, b) sex, c) living situation, d) ambulation, and e)
neurological motor level. At an average follow-up of 14.1±4.3 years, groups were statistically similar with respect to: a) SF-36 and b) SBSQ scores.

**Conclusion**

Spinal fusion in SBC scoliosis corrected coronal deformity and stopped progression, but had no overall effect on HRQOL.
ACKNOWLEDGMENTS:

I would like to thank the following staff and colleagues for their help and guidance throughout this thesis.

<table>
<thead>
<tr>
<th>Name</th>
<th>Affiliation</th>
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<tbody>
<tr>
<td>Lilian Wong</td>
<td>Western University: Schulich School of Medicine and Dentistry, London, Ontario, Canada</td>
</tr>
<tr>
<td>B.Sc.</td>
<td></td>
</tr>
<tr>
<td>Peggy W. Law</td>
<td>The Hospital for Sick Children, Toronto, Ontario, Canada</td>
</tr>
<tr>
<td>B.Sc. M.Sc.</td>
<td></td>
</tr>
<tr>
<td>Derek Stephens</td>
<td>The Hospital for Sick Children, Toronto, Ontario, Canada</td>
</tr>
<tr>
<td>B.Sc. M.Sc.</td>
<td></td>
</tr>
<tr>
<td>Kathryn Doughty</td>
<td>Shriners Hospitals for Children, Los Angeles, California, USA</td>
</tr>
<tr>
<td>B.A. MD MPH MSc.</td>
<td></td>
</tr>
<tr>
<td>Liora Caspi</td>
<td>The Hospital for Sick Children, Toronto, Ontario, Canada</td>
</tr>
<tr>
<td>M.Sc.</td>
<td></td>
</tr>
<tr>
<td>Aileen M. Davis</td>
<td>University Health Network: Division of Health Care and Outcomes Research, Toronto Western Research</td>
</tr>
<tr>
<td>PhD</td>
<td></td>
</tr>
<tr>
<td>Andrew Howard</td>
<td>The Hospital for Sick Children, Toronto, Ontario, Canada</td>
</tr>
<tr>
<td>MD MSc. FRCSC</td>
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</tr>
<tr>
<td>James G. Jarvis</td>
<td>The Children’s Hospital of Eastern Ontario, Ottawa, Ontario, Canada</td>
</tr>
<tr>
<td>MD FRCSC</td>
<td></td>
</tr>
<tr>
<td>James G. Wright</td>
<td>The Hospital for Sick Children, Toronto, Ontario, Canada</td>
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<td>MD MPH FRCSC</td>
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</tr>
</tbody>
</table>
# Table of Contents

LIST OF ABBREVIATIONS  

1. INTRODUCTION  
   1.1 Epidemiology  
   1.2 Aetiology  
   1.3 Scoliosis  
   1.4 Treatment Options  
      1.4.1 Operative Outcomes  
      1.4.2 Complications of Spinal Arthrodesis  
      1.4.3 Health Related Quality of Life (HRQOL)  
   1.5 Literature Limitations  
   1.6 Research Aims  

2. METHODS  
   2.1 Study Population  
   2.2 Inclusion and Exclusion Criteria  
   2.3 Study Enrolment  
   2.4 Recruitment Strategies  
   2.5 Baseline Assessment  
   2.6 Radiological Assessment  
   2.7 Clinical assessment  
   2.8 Health Related Quality of Life Outcomes  
   2.9 Data Analysis  

3. RESULTS  
   3.1 Baseline  
   3.2 Peri- & Post-Operative (Operative Participants)  
   3.3 Follow-up  

4. DISCUSSION/CONCLUSION  
   4.1 Study Limitations  
   4.2 Future Directions  

5. TABLES:  
   5.1 Table 1: Baseline Assessments  
   5.2 Table 2: Peri-operative and Post-operative (Operative Patients)  
   5.3 Table 3: Follow-up Assessments  
   5.4 Table 4: HRQOL Outcomes at Follow-up  

6. FIGURES:  
   6.1 Figure 1: Follow-up Cobb Angles and SF-36 PCS (filled circles) & MCS (unfilled squares) scores for All Patients (N=45). Best-fit lines for PCS (solid line) and MCS (dashed line) also depicted.
6.2 Figure 2: Follow-up Cobb Angles and SF-36 PCS (filled circles) & MCS (unfilled squares) scores for Operative (N=34) and Non-operative (N=11) Patients. Best-fit lines for PCS (solid line) and MCS (dashed line) also depicted.

6.3 Figure 3: a) Follow-up SF-36 PCS Scores of Ambulatory (N=10) and Non-Ambulatory Patients (N=35) and b) SF-36 MCS Scores of Ambulatory and Non-Ambulatory Patients

7. APPENDICES

7.1 Appendix 1: Research Ethics Board Decision and Amendment for Extra Site

7.2 Appendix 2: US English-language Medical Outcome Study 36-item Short Form Health Survey (SF-36v2®)

7.3 Appendix 3: Spina Bifida Spine Questionnaire

7.4 Appendix 4: Hoffer Classification

7.5 Appendix 5: Neurological Motor Level

7.6 Appendix 6: Sitting Balance Scale

7.7 Appendix 7: Patient Consent form

7.8 Appendix 8: Parent Consent Form

7.9 Appendix 9: Baseline Characteristics of Study Responders versus Non-Responders

7.10 Appendix 10: Sample Size Calculation

7.11 Appendix 11: Post-Hoc Power Analysis

7.12 Appendix 12: Non-parametric Testing for HRQOL Scores

8. REFERENCES:
# LIST OF ABBREVIATIONS

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
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<tbody>
<tr>
<td>SB</td>
<td>Spina Bifida</td>
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<tr>
<td>SBC</td>
<td>Spina Bifida Cystica</td>
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<tr>
<td>HSC</td>
<td>Hospital for Sick Children</td>
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<td>CHEO</td>
<td>Children’s Hospital of Eastern Ontario</td>
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<td>NML</td>
<td>Neurological Motor Level</td>
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<td>T-</td>
<td>Thoracic</td>
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<td>L-</td>
<td>Lumbar</td>
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<tr>
<td>AP</td>
<td>Anterior-Posterior</td>
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<td>ASA</td>
<td>American Society of Anesthesiologists Physical Status Classification</td>
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<tr>
<td>BMI</td>
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<tr>
<td>pRBC</td>
<td>Packed Red Blood Cells</td>
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<td>PFT</td>
<td>Pulmonary Function Test</td>
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<tr>
<td>%FVC</td>
<td>Percent Predicted Forced Vital Capacity</td>
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<td>%FEV₁</td>
<td>Percent Predicted Forced Expiratory Volume in 1 Second</td>
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<td>VP</td>
<td>Ventriculoperitoneal</td>
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<td>G-</td>
<td>Gastrostomy</td>
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<td>SBHAO</td>
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<td>SRS</td>
<td>Scoliosis Research Society</td>
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<td>SSI</td>
<td>Surgical site infections</td>
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<td>CRID</td>
<td>Clavicle Rib Intersection Difference</td>
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<td>Activities of Daily Living</td>
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1. INTRODUCTION

1.1 Epidemiology
Spina bifida is an embryological failure of neural tube closure\textsuperscript{1,2}. Spina bifida cystica is the most common congenital defect of the central nervous system with an estimated incidence of 0.4–0.8 neonates per 1000 pregnancies\textsuperscript{1,3,4}. This rate would be higher, but an estimated 23\% of myelodysplastic pregnancies are terminated prior to conception\textsuperscript{5}. In 1989, in the United States, it was estimated that the total health care cost associated with myelodysplasia was over $200 million annually and this cost has increased recently, as the life expectancy of individuals with SBC has increased\textsuperscript{6-8}.

1.2 Aetiology
This embryological failure may involve the meninges (meningocele) or it may involve the meninges in addition to neural elements (myelomeningocele). SBC (meningomyelocele, meningocele, lipomeningocele, or lipomeningomyelocele) most commonly occurs in the lower thoracic or lumbosacral regions, with significant neurological deficits below the lesion\textsuperscript{2,9}.

The underlying aetiology of SBC has been postulated to be multi-faceted, with both genetic and environmental factors playing a role\textsuperscript{1,10,11}. Mothers on valproic acid or carbamazepine prior to conception are at increased risk of having offspring with SBC\textsuperscript{12}. Similarly, maternal dependence on insulin for diabetes mellitus is also a known risk factor for neural tube defects\textsuperscript{13}. Population studies have reported that folic acid supplementation, especially prior to six weeks of
gestation, can decrease the incidence of SBC by 70%\textsuperscript{1,2,11,14}. In Canada, folic acid fortification of foods has further decreased the incidence by 53%\textsuperscript{1,14}.

SBC has many medical and functional implications for individuals\textsuperscript{2}. SBC is associated with both motor and sensory paralysis at or below the level of the spinal dysraphism\textsuperscript{4,15-17}. Patients typically have loss of bladder and bowel function, requiring intermittent catheterizations, with a higher propensity for recurrent bladder infections or hydroureteronephrosis\textsuperscript{18-20}. Other co-morbidities have included: skin ulcerations (pressure sores), latex hypersensitivity, seizure disorders, hip dislocations, lower extremity contractures, upper extremity dyscoordination, osteoporosis and foot anomalies\textsuperscript{9,21-31}. Furthermore, many SBC children have associated central nervous system anomalies, such as: hydrocephalus with possible need for ventriculoperitoneal (VP) shunts, Arnold-Chiari malformation, tethered cord syndrome or scoliosis\textsuperscript{9,32-40}.

1.3 Scoliosis

Scoliosis has been defined as a coronal curve of the spine, with the primary curve being quantified by the Cobb angle, the angle created between “perpendicular lines to the most-tilted vertebrae”\textsuperscript{41}.

SBC scoliosis has been defined as a fixed coronal curve of greater than ten degrees and is further classified based on the location of the spinal dysraphism\textsuperscript{42-46}. In SBC, the paralytic coronal deformity is usually a long C-shaped curve\textsuperscript{42}. Spinal dysraphism is more common in the lower thoracic or lumbosacral regions and more proximal lesions are associated with an increased
prevalence of scoliosis\textsuperscript{32,46}. Scoliosis, affecting up to 50-90\% of patients with SBC,\textsuperscript{45,47-50} can be progressive\textsuperscript{46,49,51}.

The lack of sensation in lower extremities and paralysis of abdominal and thoracolumbar extensor muscles may put these patients at an increased risk of pressure ulcers and subsequent infections\textsuperscript{52-55}. Scoliosis is often associated with other spinal deformities, such as: pelvic obliquity, shoulder tilt, truncal malalignment, lordosis and kyphosis\textsuperscript{41,56,57}. Pelvic obliquity, defined as the angle of the pelvis with the horizontal plane, can further cause unequal seating pressures for these patients, which may result in skin ulcerations\textsuperscript{41,58,59}.

The progression of neuromuscular curves can be faster than idiopathic curves. Patients with curves $>40^\circ$ have been reported to have curve progression of up to $12.5^\circ$ per year, with more than 50\% of patients progressing $>5^\circ$ per year\textsuperscript{43}. Tethered cord syndrome and syringomyelia are concurrent pathologies that can further accelerate curve progression. Other changes that may be associated with the presence of scoliosis are changes in the neurological motor level (NML), spasticity of extremities or curve progression\textsuperscript{34,36-40,60,61}. The main prognostic factor for gait and physical function for SBC patients with scoliosis is their neurological motor level, with more proximal deficits resulting in greater functional limitations\textsuperscript{9,16,49,62-64}.

\textbf{1.4 Treatment Options}

Treatment options for paediatric patients with SBC scoliosis have included: observation, orthotic bracing or operative intervention\textsuperscript{9,33,43,44,65,66}. Orthotic
treatment (bracing) for SBC scoliosis has been unsuccessful for curve correction or decreasing progression and mainly serves to delay surgical intervention until more spinal growth can be attained\textsuperscript{43,66}. Furthermore, circumferential bracing has been implicated in increasing intra-abdominal pressures and may lead to a higher occurrence of bladder incontinence, skin ulceration and failure to thrive\textsuperscript{43,66}.

As SBC scoliosis tends to be progressive, surgical stabilization of the spine is commonly undertaken to prevent further progression of deformity\textsuperscript{9,33,62}. Instrumented spinal arthrodesis is generally recommended for curves that are greater than forty to fifty degrees. However, this Cobb angle cut-off used for surgical recommendation has been mainly from small case-series (Level IV evidence) or expert opinion (Level V) studies\textsuperscript{9,33,67-69}. Although spinal arthrodesis is frequently performed for SBC patients with scoliosis, the long-term functional or quality of life benefits remain uncertain\textsuperscript{9,33,49,63,70}.

1.4.1 Operative Outcomes

Spinal fusion is generally successful at correcting the coronal deformity of paediatric SBC patients with scoliosis by approximately 40-60% from pre-operative levels and preventing curve progression\textsuperscript{9,56,71-75}. Spinal fusion is also believed to improve the functioning and self-perception of patients\textsuperscript{9,62}. To address the sitting balance of patients, spinal fusion typically extends from the upper thoracic spine to the pelvis or sacrum, depending on the pre-operative ambulatory status and pelvic obliquity of the patient\textsuperscript{17,52,56,59,73,76}. However, while discussed in more detail below, previous studies have reported that spinal fusion
in SBC patients have neither improved the ambulation of patients post-operatively, nor improved the ability of SBC patients to perform their activities of daily living (ADL)\textsuperscript{17,51,52,57,65,70}.

While Mazur et al. reported improved sitting balance, ambulatory capabilities in SBC patients (N=49) post-spinal fusion declined\textsuperscript{67}. Muller et al. reported that there were no change in patients’ (N=14) abilities to perform ADL post-arthrodesis, but there was a decline in ambulation, with 50% of patients losing their ability to ambulate post-operatively\textsuperscript{63}.

Schoenmakers et al. prospectively followed ten patients post-spinal arthrodesis and 75% of patients who had been ambulatory developed more limitations post-operatively\textsuperscript{17}. Furthermore, none of the ten patients had any long-term benefits (assessed at 18 months) in their abilities to perform their ADL, while an 80% complication rate was reported\textsuperscript{17}. The ability to achieve radiographical correction may be attained. However, spinal arthrodesis may decrease the ambulatory ability of patients, possibly due to rigidity of the spinal-pelvic fixation limiting lumbo-sacral mobility, which is needed for ambulation\textsuperscript{9,18,77,78}.

Eighty children with SBC were assessed by Wai et al. to examine the relationship of spinal deformity with physical function (using the Activities Scale for Kids to evaluate “locomotion, dressing, eating, personal care, standing skills, stairs, play, and miscellaneous activities”) and self-perception (using the Harter Self-Perception Profile for Children and Adolescents to evaluate “self-perception of social & athletic competence, appearance, and self-worth”)\textsuperscript{62}. Only coronal
imbalance was associated with only one aspect of functioning – seating balance\textsuperscript{62}. The authors concluded that in the short term, the potential benefits of surgery may include improvement of seating balance, but that chair modifications should be further explored as an alternative means to improve coronal balance and sitting function for these patients\textsuperscript{62}. Similarly, another study reported no relationship between spinal deformity (as defined by Cobb angles and pelvic obliquity) and self-motivation (using the Health Self-Determinism Index for Children to evaluate “intrinsic motivation”)\textsuperscript{49}.

Moreover, post-spinal arthrodesis, changes measured in the seating pressures of SBC patients has been equivocal\textsuperscript{52,54,79,80}. Ouellet \textit{et al.} reported that despite significant curve correction, only minimal improvements were seen in the seating pressures of SBC patients who used wheelchairs\textsuperscript{52}. However, many studies have failed to control for confounding factors, like hip contractures and lower extremity spasticity, that can also alter seating pressures\textsuperscript{9,21,22}.

Some studies have advocated that spinal fusion is needed to help with the respiratory function of SBC patients with significant scoliosis\textsuperscript{81-83}. Although many SBC patients have anatomical adaptive changes (barrel-chested and flared ribs) and lower aerobic demands (being non-ambulatory), limitations in pulmonary function tests (PFTs) have been reported\textsuperscript{82-84}. Carstens \textit{et al.} evaluated ten SBC patients, thirteen months post-spinal fusion and reported that 80\% of patients had an increase in vital capacity and 60\% of patients had an increase in FEV\textsubscript{1} when compared with pre-operative values\textsuperscript{85}. Similar results were reported by Banta \textit{et al.}, who reported improved PFT values post-spinal arthrodesis\textsuperscript{81}. More
recently, Patel et al. retrospectively reviewed 32 SBC patients’ (mean Cobb angle: 64°) PFTs and seated pressure maps\textsuperscript{79}. All patients had reduced FVC values; however, this reduction was not related to increasing Cobb angles\textsuperscript{79}.

1.4.2 Complications of Spinal Arthrodesis
Spinal arthrodesis has significant complications, resulting in patient morbidity and mortality\textsuperscript{9,86}. Surgical complications in patients with neuromuscular (SBC or cerebral palsy) scoliosis have included: spine or surgical site infections (1.7-33.0%)\textsuperscript{56,73,74,78,86-88} and hardware failure or pseudarthrosis (5-50%)\textsuperscript{68,77,87-93}. Less common complications have included: fractures, vascular injury, acute hydrocephalus, meningitis, sepsis and even death\textsuperscript{94-98}.

Spinal arthrodesis in patients with SBC can be more challenging when compared to patients with idiopathic scoliosis due to missing posterior bony elements and the increased prevalence of osteoporosis in SBC patients\textsuperscript{29,30}. Moreover, the incidence of surgical site infections (SSI) is also higher due to recurrent bladder or shunt infections, compromised skin and muscle integrity overlying spinal hardware\textsuperscript{24,99-105}. Risk factors for SSI in SBC patients undergoing spinal fusion have included: being a full-time wheel-chair user (non-ambulatory), baseline Cobb angles $\geq$60°, VP shunts, and previous skin ulcerations\textsuperscript{24,105,106}.

1.4.3 Health Related Quality of Life (HRQOL)
As per the World Health Organization (WHO) International Classification of Functioning, Disability and Health, the definition of health related quality of life (HRQOL) for an individual is not defined by the morbidity or limitations
associated with a medical condition\textsuperscript{107,108}. Rather, HRQOL is broadly defined by how an individual with a medical condition “perceives their condition and its impact on their physical, social or psychological functioning, in the context of their culture, value system and surroundings”\textsuperscript{7,107-109}.

Previous studies have reported that SBC patients have lower perceived HRQOL when compared to other age-matched, sex-matched or demographic-specific able-bodied individuals, or individuals with other chronic medical conditions\textsuperscript{7,64,110-112}. Both SBC specific HRQOL surveys (Health Related Quality of Life Spina Bifida Questionnaire – HRQOL-SB\textsuperscript{113-118}, Hydrocephalus Outcome Questionnaire – HOQ\textsuperscript{119,120} and the Spina Bifida Spine Questionnaire – SBSQ\textsuperscript{62}) and generic HRQOL surveys (PedsQL\textsuperscript{110,121,122}, Medical Outcome Study 36-item Short-form Health Survey – SF-36\textsuperscript{8,112,123-125}, Child Health and Illness Profile-Adolescent Edition – CHIP-AE\textsuperscript{126} and World Health Organization Quality of Life BREF Questionnaire – WHOQOL-BREF\textsuperscript{109,127}) have corroborated these results in both children and adults with SBC.

More specifically, in terms of scoliosis and its impact on HRQOL, independent ambulation and mobility have been reported to greatly influence the HRQOL of these patients\textsuperscript{8,16,112,123}. Schoenmakers \textit{et al.} reported, that of all factors, functional ambulation and mobility independence were the most influential on the quality of life (HRQOL-SB) of SBC patients (adjusted OR: 5.3 and 2.2, respectively)\textsuperscript{16}. The level of spinal dysraphism was related to independent mobility\textsuperscript{15,16}. Flanagan \textit{et al.} reported an inverse relationship between HRQOL scores (PedsQL) for SBC children and their level of neurological defects\textsuperscript{15}. 
Patients with muscle paralysis at or above the L2 level or those requiring a VP shunt had lower HRQOL scores\textsuperscript{15}. Body mass index or age had no association with HRQOL scores\textsuperscript{15}.

One of the largest population studies reporting on SBC patients has been the Adolescents with Spina Bifida in the Netherlands Study (ASPINE)\textsuperscript{8,128}. Of the 179 patients with spina bifida (mean age 20.8 years, range 16-25 years), six of the eight domains for the SF-36 survey were lower for these patients when compared to the age-matched Dutch normative population\textsuperscript{8}. Non-significant domains were: Role-emotional (RE) and Mental-health (MH)\textsuperscript{8}. Of all patients, 49 patients (of 151, 28 unknown) were reported to have scoliosis (defined as “a physical examination where there was at least one curve that deviated more than 2 cm from the perpendicular”). However, Cobb angles were not reported. A total of 39 patients underwent “scoliosis surgery”; however, operative techniques and outcomes were not reported for these patients\textsuperscript{8,128}. Overall, many studies have reported that patients with SBC have lower physical HRQOL measures but similar emotional or mental health measures, when compared to their able-bodied peers\textsuperscript{7,8,112,123,125}.

Similarly, also using the SF-36 survey, Buffart et al. reported on 51 patients with spina bifida (mean age 21.1 years, range 16-30 years) and, of all factors, being ambulatory (OR: 11.3) and having greater physical activity (defined as exercise in minutes/day; OR: 8.8), were associated with the highest perceived physical HRQOL\textsuperscript{112}. However, the proportion of patients with scoliosis or those having treatment for scoliosis were not reported\textsuperscript{112}. More recently, Sibinski et al.
reported on 19 SBC patients (mean age 21.4 years, range 13-35 years) who had not had any operative intervention for their scoliosis (mean Cobb angle: 77.5° and range: 30-120°, mean pelvic obliquity: 11.6° and range: 5-20°) and reported that no relationship existed between spinal deformity (as defined by Cobb angles and pelvic obliquity) and patients’ self-perception (Harter’s Self-Perception Profile for Adolescents – measuring “academic competence, social competence, athletic competence, physical appearance, behavioral conduct, and global self-worth”), motivation (Health Self-Determinism Index for Children – evaluating “intrinsic motivation”) or physical functioning (Activities Scale for Kids – evaluating ADL and play activities)⁴⁹.

1.5 Literature Limitations

The current literature on the outcomes of operatively or non-operatively treated SBC scoliosis has many limitations⁹,33. At present, there are no randomized clinical trials comparing operative versus non-operative treatment⁹. Furthermore, the majority of previous studies have been case series or retrospective studies, corresponding to lower levels of evidence (III-V)⁹,69. In a recent systematic review on the treatment of scoliosis in SBC, of the 39 included studies, only 9 (23.1%) studies were Level III, with no Level I or II studies⁹. Very few studies have been multi-center⁸,¹¹²,¹²⁸ and the sample size in these studies have been limited⁹. Few studies have used validated outcome measures (for radiographic, clinical, or HRQOL outcomes) to evaluate these patients⁹. Follow-up for these patients have been short and few studies have evaluated these patients as they transition into adulthood⁹. To date, there has not been a study examining the natural history or
long-term clinical course of untreated SBC scoliosis\(^9\). Finally, previous studies have grouped neuromuscular scoliosis of various etiologies together and have not specifically focused on SBC.

### 1.6 Research Aims

Despite complication rates approaching 80\%, few studies have evaluated the HRQOL of SBC patients with scoliosis\(^8,16,24,33,49,129,130\). Furthermore, no controlled study has compared operative versus non-operative treatment for SBC scoliosis\(^9\).

The purpose of this study was to evaluate validated HRQOL outcomes and radiographic parameters in SBC adults, treated non-operatively or operatively, for scoliosis during childhood (less than 18 years of age). This was accomplished by performing a multi-site study at the Hospital for Sick Children (HSC, Toronto, Ontario, Canada) and at the Children’s Hospital of Eastern Ontario (CHEO, Ottawa, Ontario, Canada). I retrospectively evaluated SBC patients who underwent spinal instrumentation for scoliosis. Scoliosis was defined \textit{a priori} as a baseline primary Cobb angle greater than or equal to fifty degrees and follow-up was after a minimum of six years post-operatively (hereinafter referred to as the “Operative Group”).

This operative cohort was compared to a control group of SBC patients, who did not have any operative treatment for their scoliosis as children (also defined as a baseline primary Cobb angle greater than or equal to fifty degrees) with the
same minimum follow-up period (hereinafter referred to as the “Non-operative Group”).

The primary outcome of this study was to assess the HRQOL experienced by SBC patients in early adulthood (minimum age ≥18 years). Several secondary outcomes were sought and compared between operative and non-operative patients and included various validated radiographical parameters and curve progression. Additionally, the ambulatory status and sitting balance of these patients, as they have transitioned into adulthood, were reviewed. Finally, I assessed the long-term sequelae of instrumented spines, the fusion status, loosening and breakage of hardware, and necessity of revision surgery. I reviewed both the peri-operative and post-operative complications, associated with instrumentation.
2. METHODS

2.1 Study Population

This study was a two center retrospective comparative review. All patients with a diagnosis of SBC (as verified by patients’ medical records) who were treated between January 1, 1991 to December 31, 2007 inclusive at the Hospital for Sick Children (HSC – Toronto, Ontario) or the Children’s Hospital of Eastern Ontario (CHEO – Ottawa, Ontario) were recruited for participation.

2.2 Inclusion and Exclusion Criteria

Inclusion criteria included any patient with SBC [either meningomyelocele, meningocele, lipomeningocele or lipomeningomyelocele, younger than 18 years of age with a primary Cobb angle of at least $\geq 50^\circ$ (fixed coronal curve on anterior-posterior – AP-radiographs)]. Other aetiologies of scoliosis (idiopathic or traumatic) and patients receiving non-instrumented arthrodesis (fusion in-situ) or having isolated kyphectomies (either apical vertebrae resections, de-cancellation techniques or vertebral osteotomies) were excluded. Congenital spine deformities have been estimated to appear in approximately 38% of SBC patients.\textsuperscript{47,48,131} SBC patients with congenital deformities (either sacral agenesis, un-segmented bars or hemi-vertebrae) were not excluded. Patients were identified through diagnosis and procedure codes from administrative databases held at each institution. Ethical approval was obtained from both institutions prior to data collection or patient enrolment (Appendix 1).
2.3 Study Enrolment

Eligible patients (N=170 patients) were contacted for study participation by the primary author. After consent for participation was obtained, patients attended for clinical and radiological assessments, as well as the administration of HRQOL questionnaires at either convenient institution. Consenting patients who were interested in participating, but were unable to attend either institution (hereinafter referred to as “remote-participants”) had HRQOL questionnaires and ambulatory status (defined below) determined via telephone by the primary author, a practice that has been commonly performed in various spinal pathologies\textsuperscript{132-135}.

2.4 Recruitment Strategies

Based on recommendations from previous systematic reviews and meta-analyses, various recruitment strategies and incentives were utilized to increase patient enrolment in this study\textsuperscript{136-140}. These strategies included: a personal letter inviting participation from the senior investigator, and providing pre-paid return envelopes with easy-to-read consent statements and HRQOL surveys already included.

Furthermore, if the recruitment package was not returned after two weeks of mailing, either the primary author or research coordinator attempted to call eligible participants and answer any questions they may have had about the study and to schedule a clinic visit should they consent to participate. For those patients who could not be located from the initial mail out, we faxed their family doctor or paediatrician (as listed in their health records) explaining our interest in doing a long-term follow-up study with the patient and requesting the contact
information that their office had on file. As well, the individual recruiting was altered based on patient preferences to aid with enrolment: primary author (male physician) versus research administrators (female).

Eligible participants also had the opportunity to participate as a “remote” participant. Some study participants were not able to attend either study site or lived too far away to make the trip. For those patients who were not able to attend a clinic visit at either location, but were interested in participating, I mailed them the consent forms, health surveys and an X-ray requisition. The informed consent discussion was performed by telephone and then the patient was asked to complete the forms and using the stamped envelope included in the package mail the forms back. The participants were able to take the X-ray requisition to their local hospital or clinic and I requested a copy of the radiographs.

All eligible patients were able to opt out of any component of the study, such as new spine radiography or the clinical examination. Furthermore, multiple follow-up sites (HSC or CHEO), dates and times were available, including evenings and weekends. Of the 45 participants included in this study 13.3% (N=6) of participants were seen after-hours (after 5 pm) or on weekends by the primary author.

Various strategies to increase awareness were also utilized. A personal recruiting message by the senior investigator and primary author was given at the Spina Bifida and Hydrocephalus Association of Ontario (SBHAO) 2012 annual meeting in Toronto, Ontario. This study was also endorsed by the
SBHAO on their website. Furthermore, incentives were provided to all study participants, and included a nominal $5 Tim Hortons™ coffee gift card (which was increased to $10 after January 2013) and travel compensation (upon presentation of valid receipts) of up to $100.

2.5 Baseline Assessment

Patient demographics (age, sex and living status), peri-operative and post-operative imaging for all operative patients were obtained from each institution’s health and imaging records. Relevant medical and surgical events or any subsequent complications were recorded as binary outcomes (yes versus no) in anonymized data collection forms and included: pressure ulcers requiring treatment (either wound care or serial irrigation and debridements), ventriculoperitoneal (VP) shunts, urinary catheterization, and gastrostomy (G-) feeding tubes. Living status was categorized as patients living at home with parents or guardians (“home”) or patients living in rehabilitation or “long-term care facilities” for the majority of a week (>4 days per week).

Peri-operative complications (defined as occurring within the anaesthetic course of the initial spinal arthrodesis procedure) or in-hospital post-operative complications were also recorded. Surgical site infections (SSI) were categorized as being early (<3 months) or late (≥3 months). SSI were also classified as superficial or deep. Superficial infections were located above the fascial layer (localized to the skin and subcutaneous tissue), while deep infections were located beneath the fascial layer. Pseudarthrosis (binary outcome – yes versus no) was defined as motion on radiography or on surgical
Operative details, extracted from nursing, operative and anaesthetic records included: weight (in kilograms, continuous variable), hematocrit (continuous variable), transfusion of packed red blood cells (pRBC – binary outcome – yes versus no), anaesthetic time (in minutes, continuous variable), the American Society of Anesthesiologists Physical Status classification (ASA – categorical variable: Class I-II or Class >III), bone graft usage (categorical variable: autograft, allograft or combination of autograft and allograft), and blood loss (continuous variable - standardized for each patient as millilitres per kilograms).

The baseline pulmonary status of each surgical patient was obtained from pulmonary function tests (PFTs), performed within six months (at either institution) preceding the spinal arthrodesis procedure, including the percent-predicted forced vital capacity (%FVC, continuous variable) and percent-predicted forced expiratory volume in 1 second (%FEV₁, continuous variable)\(^{79}\). The %FVC and %FEV₁ are commonly reported parameters in scoliosis surgery\(^{79,82,83}\). Baseline PFTs were not available for any of the non-operative patients.

Instrumented fusion constructs included: Unit-Rod/Luque Rods™, Texas Scottish Rite Hospital™ instrumentation, Miami-Moss™, Cotrel-Dubousset™, and Universal Spinal System II™. All implants were classified as either: a) pedicle screws and rods, b) sublaminar wiring and rods, or c) a combination of groups A and B. The surgical approach was categorized as follows: a) only anterior, b) combined anterior and posterior, or c) only posterior.
2.6 Radiological Assessment

All chest or full-length spine anterior-posterior (AP) and lateral radiographs (excluding traction or bending films) were reviewed by the primary author. At follow-up, participants had full length sitting AP and lateral spine radiographs. All radiographic measurements were performed by a single observer (primary author) using the same protractor to decrease variability amongst measurements, which is noted to be high in neuromuscular scoliosis.\textsuperscript{41}

Several validated radiographic parameters were recorded for all patients. From AP radiographs, Cobb angles (in degrees) and Clavicle Rib Intersection Difference (CRID, in millimetres) were measured as described by Bago \textit{et al}\textsuperscript{146-148}. Pelvic obliquity (in degrees) was measured as described by Osebold \textit{et al}\textsuperscript{68}. Coronal imbalance was measured by dropping a plumb-line from the middle of C7 and measuring the lateral displacement (in millimetres) from the central sacral vertical line as described by Li \textit{et al}\textsuperscript{147}. Lateral radiographs were assessed for thoracic kyphosis and lumbar lordosis using the techniques described by Jackson \textit{et al}\textsuperscript{58}. If radiographs were unavailable, previous radiology reports were reviewed to determine missing parameters. If radiographic parameters were not available or reported, they were not imputed\textsuperscript{149}.

For operative patients, imaging was reviewed at three time-points: a) zero to three months prior to the index spinal arthrodesis (referred to as “baseline”); b) zero to three months following the index spinal arthrodesis (referred to as the “post-operative” period), and c) at least six years following the index spinal arthrodesis (referred to as “follow-up”). For non-operative patients, imaging was
reviewed at two similar time-points: a) first clinical assessment with a primary Cobb angle of $\geq 50^\circ$ (referred to as “baseline”) and b) at least six years following the initial clinical assessment with a Cobb angle of $\geq 50^\circ$ (referred to as “follow-up”).

2.7 Clinical assessment

All clinical assessments were completed during a single visit to either institution by the primary author. Patients were transferred, either independently or assisted, onto an examination table where the most distal neurological motor level (NML), the Sitting Balance Scale (SBS), and the Hoffer Classification were determined\(^{49,62,150}\).

The Hoffer Classification has been widely utilized to assess the ambulatory status of SBC patients\(^ {17,150}\). Grade I and II (Hoffer ambulatory levels) correspond to individuals who are community ambulators or household ambulators (walk only indoors), respectively\(^ {150}\). Grade III individuals are those who are able to walk (with assistive devices only) during therapy sessions while Grade IV ambulators are individuals who are strictly wheel-chair dependent\(^ {150}\). As has commonly been done, the Hoffer Classification was categorized as either ambulatory (grades I-II) or non-ambulatory (grades III-IV) – (Appendix 4)\(^ {150}\).

The NML was recorded, as described by the International Myelodysplasia Study Protocol, and categorized as either: a) any thoracic level up to and including the L3 nerve roots, or b) L4 up to and including the most distal sacral nerve roots (Appendix 5)\(^ {49,151}\). The importance of motor-level dysfunction above the L3 level
and its effect on physical function has been previously reported on by Sibinski et al. Patients with motor deficits above the L3 level are more likely to have lower overall physical function and ambulatory ability. Examinations of neurological motor levels (NML) are reviewed in Appendix 5.

Sitting balance was evaluated using the Sitting Balance Scale (SBS) – a ten-point scale, where a score of ten is representative of a well-balanced static and dynamic sitter. The SBS was scored as described by Wai et al. and patients were categorized as those who: a) require arms to sit (score of 0-2), b) do not require arms to sit (3-4), c) able to reach while sitting (5-8), and d) able to shift weight freely while sitting (9-10) – (Appendix 6). Follow-up NML or SBS scores were not available for remote participants.

2.8 Health Related Quality of Life Outcomes

Each patient, at follow-up, was given two HRQOL questionnaires, the Spina Bifida Spine Questionnaire (SBSQ) and the US English-language Medical Outcome Study 36-item Short Form Health Survey (SF-36v2®, QualityMetric, Inc., Lincoln, RI, USA). All surveys were completed independently and without assistance by parents or caregivers. Remote patients were administered both questionnaires via telephone – a practice that has previously been performed for spine-specific conditions, including adult patients with chronic disabling spinal disorders.

The SF-36 survey, used extensively as a HRQOL measure for SBC adolescents and adults, has reported validity across ages for various aetiologies.
It has been recommended for use in transition-age and adult patients with early onset physical disability\textsuperscript{7,153}. In a recent review, the SF-36 was reported as a "well-established self-report instrument" used to measure health-related quality of life in both paediatric and adult patients with spina bifida\textsuperscript{7}. Unlike other instruments\textsuperscript{113}, the SF-36 has the advantage of providing both individual domain or overall composite measures\textsuperscript{152,154,155}. These individual domain or composite scores can be compared to the normative population, in addition to, age-matched, sex-matched, nation-specific or pathology-specific individuals\textsuperscript{7,156,157}.

Previously, when the SF-36 was compared to the WHOQOL-BREF survey, it was reported to have high internal consistency (Cronbach's alpha coefficient 0.72-0.98); and, intra-interviewer reliability (intraclass correlation coefficient 0.71-0.99)\textsuperscript{132}.

Scores for the SF-36 were calculated for eight domains including: physical functioning (PF), role-physical (RP), bodily pain (BP), general health perception (GH), energy/vitality (VT), social functioning (SF), role emotional (RE), and mental health (MH)\textsuperscript{152,154,155}. Composite Physical Component Scale (PCS) and Mental Component Scale (MCS) scores also were calculated for each patient as described by Ware et al\textsuperscript{152} with scores from 0 to 100, with 100 being the highest possible functioning level (Appendix 2)\textsuperscript{8}.

The SBSQ is a self-administered twenty-five item condition-specific HRQOL measure with high test-retest reliability (intraclass correlation coefficient 0.88)\textsuperscript{49,51,76}. The advantages of the SBSQ is that it is a spina bifida-scoliosis-specific HRQOL instrument which was created through theme analysis of
interviews of SBC patients and their primary caregivers. SBSQ includes only items of importance to this patient population as it relates to their scoliosis. Furthermore, construct validity has been evaluated through correlation with other validated scales of overall disability (e.g. The Activities Scale for Kids, $r=0.89$). Scoring was performed as described by Wai et al., with a score of 100 being representative of the highest perceived HRQOL (Appendix 3).

2.9 Data Analysis

All patients were assigned a random study identification number. Data were collected using data collection forms devoid of any patient-identifying information and then entered into an encrypted password protected electronic database held at the Hospital for Sick Children and the Children's Hospital of Eastern Ontario. Any personal patient information was kept in a separate file that was password protected. Hard copy and electronic data were stored in a locked office that was accessible only to the research team. Research ethical approval was obtained from both institutions prior to data collection or patient enrolment (REB#1000018503 – Appendix 1).

Even though the sample size for this study was determined by the number of eligible patients that were found in our retrospective review (discussed below), a study sample size calculation was performed a priori. A sample size was based upon a study power of 80% (beta value of 0.2) and an alpha value of 5%. The primary outcome in this study was the HRQOL (as measured by the SF-36 PCS score) of operatively versus non-operatively treated SBC patients. The standard deviation for PCS and MCS scores for young adults with SBC has
been previously reported to be 9.0 and 9.7, respectively. Using these parameters and the SF-36 PCS score being our primary outcome (a continuous variable ranging from 0-100), we required approximately 34 patients per group (assuming a 10% change in SF-36 PCS to be detected) – (Appendix 10).

There was a total of 125 study “non-responders” [49 males (39.2%)], of which 87 (69.6%) were from the Hospital for Sick Children. The participation rate for this study was 26.5% (45 of 170 patients). Our participation rate of 26.5% is similar to response-rates (29.8%) in another multi-center study in this patient population. Reasons for non-participation included: lack of interest (N=53, 42.4%) or inability to locate patient (N=63, 50.4%). Of the 125 patients, nine patients were deceased (7.2%). If excluding patients who had deceased at the time of study recruitment, our participation rate was 45/161 (28.0%). The mortality rate for operative patients was 5.4% (7/129) and for non-operative patients was 4.9% (2/41). Reasons for non-participation were in keeping with prior studies in this patient population. A post-hoc power analysis was also performed using the most commonly reported HRQOL outcome in this patient population (SF-36 PCS – primary outcome) and was 18.3% (Appendix 11).

The average age at follow-up for non-responders was 27.7±4.4 years. Of non-responders, 76.0% (N=95) were operative patients. Operative non-responders had baseline Cobb angles of 84.3±19.8° and follow-up Cobb angles of 45.3±28.3°. Non-operative non-responders had last known Cobb angles of 68.1±18.0°. Study participants and non-responders were similar with respect to patient demographics and radiographic parameters (Appendix 9).
In the context of this study’s research question and from previous studies reporting HRQOL in this patient population\textsuperscript{7,8,49,112}, the assumption that our sample was from a normal Gaussian distribution with homogenous variance was made\textsuperscript{149}. As the ultimate goal of this study was to show whether a relationship between HRQOL outcomes and radiographic parameters (curve magnitudes) exists, only parametric tests were performed for all analyses. Furthermore, testing for the need of non-parametric analyses was performed for all HRQOL measures (SF-36 PCS, SF-36 MCS and SBSQ) and the measures were found to be normally distributed allowing parametric statistics to be used (Appendix 12).

Independent data were analyzed using independent samples t-tests or analysis of variance (ANOVA, for multiple group comparisons) for continuous variables or chi-square tests for categorical variables (Fisher’s Exact test when appropriate, cells containing less than five individuals), depending on the treatment method\textsuperscript{149}. Mean differences (MD) for continuous variables, with 95% confidence intervals (95% CI), were reported when appropriate\textsuperscript{149}. Levene's “Test for Equality of Variances” was performed prior to comparisons\textsuperscript{149}. Conservative Bonferroni corrections were performed in all cases of multiple comparisons (multiple testing)\textsuperscript{149}. To evaluate the relationship between HRQOL outcomes and Cobb angles at follow-up, linear regression models (Pearson) with $R^2$ and $p$-values were reported\textsuperscript{149}. Alpha values were pre-defined at 0.05 (two-sided) for all calculations\textsuperscript{149}. All data was analyzed by a biostatistician (DS) using SAS software version 9.1 (SAS Institute, Cary, NC) and concurrently by the primary
author using IBM SPSS Statistics for Windows, Version 20.0 (IBM Corporation, Armonk, NY).
3. RESULTS

3.1 Baseline

Of the possible 170 eligible patients, a total of 45 (26.5%) patients participated in the study. Of the eligible 170 patients, there were 129/170 (75.8%) operative patients and 41/170 (24.1%) non-operative patients. Of the 45 study participants, 34/45 were operative patients (75.6%) and 11/45 (24.4%) were non-operative patients.

There were a total of 17/45 (37.7%) remote study participants [with 12/45 (26.7%) being from HSC and 5/45 (11.1%) being from CHEO]. Of the 45 study participants, 46.7% were males (N=21/45), 35/45 (77.8%) were from the Hospital for Sick Children and 10/45 (22.2%) were from the Children’s Hospital of Eastern Ontario.

At baseline, 43/45 (95.6%) patients were living at home with their parents/guardians, while 2/45 (4.4%) patients were living in a rehabilitation or long-term-care facility. As expected, the majority of patients (N=30/45, 66.7%) were non-ambulatory (Hoffer Grade III-IV), and medical co-morbidities were common, including: pressure ulcers (10/45, 22.2%), VP shunts (36/45, 80.0%), incontinence (41/45, 91.1%) and feeding tubes (7/45, 15.6%). At baseline, operative and non-operative patients were similar with respect to ambulation, NML or medical co-morbidities (Table 1).

The baseline primary Cobb angle and CRID were greater in the operative group: 88.0±20.5° vs. 65.7±22.0° (p<0.01) and 12.3±8.5 mm vs. 4.1±5.9 mm (p<0.01),
respectively. The operative and non-operative patients were similar with respect to the following: kyphosis (41.2±24.8° vs. 53.3±18.6°, p=0.16) and lordosis (61.8±45.2° vs. 54.9±38.5°, p=0.67), respectively. Pelvic obliquity (18.8±12.6° vs. 10.8±8.1°, p=0.06) and coronal balance (40.1±28.0 mm vs. 22.9±17.8 mm, p=0.07) were consistent with higher Cobb angles in operative versus non-operative patients, respectively.

3.2 Peri- & Post-Operative (Operative Participants)

Eight orthopaedic surgeons, with subspecialty training in paediatric orthopaedic surgery (5 from HSC and 3 from CHEO) performed the arthrodesis procedures. The mean age and weight at the time of surgery was 12.2±2.8 years and 33.9±12.2 kilograms, respectively. Operative and anaesthetic records for one patient were unavailable. In operative patients, PFTs followed a restrictive-pattern, with reduced %FVC (53.8±18.6%) and reduced %FEV₁ (57.7±19.2%) values. Half of the operative patients (N=17/34, 50.0%) were classified as ASA three or greater. The most common surgical approach was a combined anterior-posterior approach (N=25/34, 73.5%) and five patients had concurrent kyphectomy procedures performed. Similarly, the most common instrumentation was combined constructs [sublaminar wiring, rods and pedicle screws, N=15/34 (44.1%)]. The mean arthrodesis length was 12.9±3.5 motion segments with 70.6% (N=24/34) extending distally into the pelvis or sacrum. The mean anaesthetic time was 592.0±102.4 minutes and the average blood loss was 57.4±30.0 mL/kg. Patients were discharged on average after 12.0±6.2 days.
(Table 2). Post-operatively, the mean Cobb angle was 40.4±19.2°, with an average curve correction of 52.9±25.0% (median 59.3%).

Peri-operative complications, in 5 of 34 patients (14.7%), included the following: hypotension requiring vasopressors (N=2), respiratory depression requiring endotracheal tube adjustment (N=1), lumbar vertebral body fracture (N=1), and latex anaphylaxis (N=1). There were no peri-operative deaths.

Post-operative complications, in 16 of 34 patients (47.1%), included the following: cerebrospinal fluid leaks or shunt externalizations requiring repair (N=4), respiratory or urinary tract infections (N=7), pneumothorax or pulmonary oedema (N=2), narcotic induced delirium (N=2), and sepsis (N=1). A total of 11 infections (32.4%) were reported (6 early and 5 late). Of the early infections, 5 of 6 were superficial, while 3 of 5 late infections were deep. The pseudarthrosis rate was 17.6% (N=6) and 7 patients (20.6%) underwent instrumentation removal for infection (N=4) or prominent distal instrumentation (N=3).

3.3 Follow-up

The mean age at follow-up for operative patients was 27.0±4.6 years (range of 18.8-34.7 years) and for non-operative patients was 25.6±5.1 years (range of 20.2-33.6 years). The mean time to follow-up from the date of arthrodesis was 14.9±3.9 years (range of 6.7-21.4 years). The mean time to follow-up from the date of having a Cobb angle >50° for non-operative patients was 11.6±4.7 years (range of 6.7-20.9 years). The proportion of patients to follow-up for each group
(operative *versus* non-operative) and for each institution (HSC *versus* CHEO) is represented in Appendix 9.

Operative patients had smaller Cobb angles ($47.3\pm22.4^o$ vs. $85.4\pm38.4^o$, $p<0.01$) with similar pelvic obliquity, coronal imbalance and CRID between the groups (Table 3). At follow-up, the mean Cobb angle of operative patients was higher than the immediate post-operative phase ($47.3\pm22.4^o$ vs. $40.4\pm19.2^o$), equating to an absolute loss of curve correction of approximately 8% when compared to baseline measures. The mean baseline Cobb angles of our non-operative patients were $65.7\pm22.0^o$ with a mean curve progression of $2.2\pm2.6^o$/year. As expected, mean curve progression per year was significantly lower in operative patients post-arthrodesis ($0.4\pm1.8^o$/year, $p=0.02$).

While not statistically significant, five operative patients had declined in their ambulatory status at follow-up. There were 11 (of 34) Grade I-II ambulators at baseline compared to 6 (of 34) Grade I-II ambulators at follow-up. Also, while not statistically significant, the SBS for the operative group [8 of 19 participants (42.1%) had SBS scores $\geq9$ (corresponding to being able to shift their weight freely)] was higher than the non-operative group [3 of 9 participants (33.3%) had SBS scores $\geq9$; $p=0.89$] – (Table 3).

All study participants completed both HRQOL questionnaires alone and without assistance from caregivers. The operative and non-operative groups did not differ in any of the eight SF-36 domains, the SF-36 composite PCS/MCS scores or the SBSQ scores (Table 4).
Overall all patients’ Cobb angles at follow-up (mean of $56.3 \pm 31.2^\circ$), irrespective of treatment, were not related with either SF-36 PCS ($R^2=0.24$, $p=0.33$) or SF-36 MCS ($R^2<0.01$, $p=0.99$) scores (Figure 1). When the SBSQ survey was utilized as the HRQOL measure for all patients, similar results were obtained ($R^2=0.04$, $p=0.21$). In terms of operative patients, follow-up Cobb angles (mean of $47.3\pm22.4^\circ$) were not related to PCS or MCS scores ($R^2=0.08/p=0.13$ and $R^2<0.01/p=0.73$ respectively) – (Figure 2). Similarly, for non-operative patients, follow-up Cobb angles (mean of $85.4\pm38.4^\circ$) were also not related to PCS or MCS scores ($R^2=0.30/p=0.10$ and $R^2=0.03/p=0.61$ respectively) – (Figure 2).

Subgroup analysis revealed that, irrespective of treatment, ambulatory patients [N=10/45 (22.2%): 6 (13.3%) operative and 4 (8.9%) non-operative] had significantly higher PCS scores (43.9±9.4) when compared to non-ambulatory (N=35/45 (77.8%): 28 (62.2%) operative and 7 (15.6%) non-operative) patients (35.9±8.7, $p=0.03$) – (Mean Difference: 8.0 and 95% confidence intervals of Mean Difference: 0.9-15.1 - Figure 3a). Although not significant, non-ambulatory patients had slightly higher MCS scores (59.6±10.4) when compared to ambulatory patients (50.9±11.7, $p=0.052$) – (Mean Difference: 8.8 and 95% confidence intervals of Mean Difference: 0.1-17.6 - Figure 3b). The follow-up Cobb angles of ambulatory and non-ambulatory patients were not significantly different ($49.4\pm21.4^\circ$ vs. $58.2\pm33.4^\circ$, respectively, $p=0.35$).

Five patients (of 45 which were all operative) were ambulatory at baseline and non-ambulatory at follow-up. There were no patients that were non-ambulatory at baseline that became ambulatory at follow-up. Although not significant, these five
patients who had declined in their ambulatory abilities (with a follow-up Cobb angle of 55.3±29.6°) had lower PCS scores compared to the 40 patients (with a follow-up Cobb angle of 56.5±31.8°) who had not had any decline in their ambulation over time (PCS: 31.6±12.0 versus 38.5±8.9, p=0.12). In terms of MCS scores, the five patients with a decline in ambulatory abilities had slightly higher scores when compared to patients who had not had any decline (MCS: 62.2±4.2 vs. 57.1±11.7, p=0.35).

Given we failed to achieve our a priori sample size, a post-hoc power analysis was performed. As there were 34 operative patients in our operative group and 11 patients in our non-operative group, and our primary outcome was defined to be the SF-36 PCS score, our post-hoc power (to detect a 10% difference in SF-36 PCS scores) was calculated to be 18.3% (Appendix 11).

4. DISCUSSION/CONCLUSION

This study adds to the small body of literature on SBC and scoliosis with the advantage of being the first controlled study comparing SBC patients having and not having spinal arthrodesis with the longest follow-up. As the indications for scoliosis surgery in SBC is uncertain, our findings substantiate Mazur et al. and other studies that spinal arthrodesis can better correct coronal deformity in these patients.9,33,62,78 However, the effect on HRQOL is uncertain, and there maybe a possible decline in ambulatory ability.

While health-related quality of life is an important outcome of surgery,33,62,158-160 prior studies evaluating HRQOL for patients with SBC scoliosis are limited.7,49,112
In the Adolescents with Spina Bifida in the Netherlands (ASPINE) study, 138 spina bifida adolescents (mean age of 20.6 years) were compared to Dutch population references using the SF-36 survey. Patients with hydrocephalus had lower SF-36 scores in 6 of the 8 domains (non-significant domains were Role Emotional and Mental Health). However, curve magnitudes or surgical history of participants were not included in the ASPINE study; thus, this study provided no information on the role of surgery for “significant” scoliosis in SBC.

In this study, I evaluated the relationship of not only radiographic parameters but also clinical parameters with HRQOL outcomes in SBC adults treated operatively or non-operatively for scoliosis. No significant differences existed between patients treated operatively or non-operatively for all SF-36 domains and composite scores. Furthermore, follow-up Cobb angles in both groups had no correlation with HRQOL outcomes. These findings are in keeping with: a) Wai et al., who reported no relationship between spinal deformity (as defined by Cobb angles) and self-perception (as defined by the Harter Self-Perception Profile for Children and Adolescents survey) or physical function (as defined by the ASK questionnaire) and b) Sibinski et al., who reported that the curve magnitudes (as defined by Cobb angles or pelvic obliquity) were not related to the physical function abilities (as defined by the ASK questionnaire) of SBC patients treated non-operatively (N=19, mean Cobb angle of 77.5 ± 28.6°).

In terms of surgical outcomes, the mean immediate post-operative curve correction was approximately 54%, consistent with prior studies. At a follow-up of approximately 14.9 years, the mean curve correction (as compared to
baseline measures) was 46%, representing an absolute loss of only 8% (progression of approximately 0.4±1.8°/year). Of interest, over the span of approximately fifteen years non-operative patients had progressed to a point that at least in terms of primary Cobb angles (85.4±38.4° at follow-up) was similar to operative patients at baseline (88.0±20.5°). Overall, spinal arthrodesis was successful not only in correcting coronal deformity, but also in slowing curve progression.

Spinal arthrodesis has been advocated to prevent the loss of physical function and ambulatory abilities⁹,33. However, Kahanovitz et al. reported that ambulatory status of patients declined over 20 years following spinal arthrodesis⁵⁷. Similarly, Mazur et al. reported that those with spinal fusion had reduced ambulatory status, with minimal improvements in ADL performance⁶⁷. Muller et al. evaluated 14 patients with different levels of dysraphism and reported no difference in patients’ abilities to manage ADL post-operatively and half of the patients had lost their ability to ambulate independently⁶³. However, all of these studies were case series and none evaluated patients who had not had surgery. In our study, 11 (32.4%) of our operative patients were ambulatory (Hoffer Grade I-II) prior to arthrodesis, but only 6 (17.6%) were ambulatory at follow-up. In contrast, the same proportion of non-operative patients (N=4, 36.4%) both at baseline and follow-up were ambulatory. The importance of maintaining independent ambulation in this patient population has been previously identified ¹⁶,¹¹². Schoemakers et al. reported that independent mobility was the most important determinant of HRQOL in SBC patients¹⁶. Similarly, Buffart et al. found that
independent ambulation was the main determinant of SF-36 composite physical scores amongst Dutch SBC patients\textsuperscript{112}. While surgery may attain curve correction, the increased stiffness imparted from arthrodesis may reduce ambulatory ability.

Arthrodesis has also been reported to aid with sitting balance and to correct pelvic obliquity \textsuperscript{78,79}. Patel \textit{et al.} reported that smaller curve magnitudes were associated with lower sitting pressures\textsuperscript{79}. However, the association of sitting pressure with the development of subsequent pressure ulcers has been inconsistent\textsuperscript{52,79}. Ouellet \textit{et al.} reported that arthrodesis did not decrease the risk of skin ulcerations in patients, despite significant curve corrections\textsuperscript{52}. In this study, I did not include any pressure mappings of the patients. However, using the Sitting Balance Scale to examine static and dynamic sitting capabilities, the sitting balances between operative and non-operative patients did not differ\textsuperscript{62}.

Overall, the life expectancy of SBC patients has increased and the importance of iatrogenic morbidity has become more important as more patients transition into adulthood\textsuperscript{8}. Population registry studies have reported a complication rate of approximately 17.9\% for paediatric patients undergoing neuromuscular scoliosis surgery\textsuperscript{86,161}. The Scoliosis Research Society (SRS) registry reported that approximately 1.7\% and 3.8\% of paediatric neuromuscular patients develop early and late infections, respectively\textsuperscript{86,161}. VP shunts and the use of bone allograft have been reported to be independent risk factors for subsequent spinal infections\textsuperscript{24,105}. In our study, of the 34 operative patients, 11 (32.4\%) had infections, with 5 being late and 6 being deep infections. Of the 11 patients with
infections, 8 (72.7%) had VP shunts and 9 (81.8%) patients had allograft bone use during their arthrodesis procedure – risk factors known for paediatric spine SSI\(^{24,106,162}\). Thus, even after the arthrodesis surgery, many patients require subsequent procedures. Furthermore, the implications of a definitive arthrodesis procedure on a societal or health-care level have not been evaluated in this or other studies for this patient population. The operative and post-operative financial implications of surgery, and revision surgery if needed, should be evaluated in the decision making of treatment for scoliosis in children with spina bifida cystica. The health-care or financial burdens these procedures pose on the patient and society may favour non-operative over operative management.

### 4.1 Study Limitations

This study has several limitations. First, this was a retrospective review and we lacked any HRQOL measurements at baseline or immediately post-operatively, and were unable to comment on any interval changes that may have occurred. Second, the HRQOL for operative patients may have initially been lower than non-operative patients resulting in a selection bias. However, we assessed our patients at mid-adulthood, an age most representative of their current HRQOL. Third, we had a small sample size, especially for our non-operative cohort, resulting in lower statistical power\(^{149}\). We incorporated two study centres to minimize bias with respect to patient characteristics, surgical techniques, surgeon preferences and post-operative care. All patients, irrespective of treatment, were compared in a consistent fashion using the same validated outcome measures with a minimum follow-up of six years.
Fourth, no late outcomes such as PFTs were reported, and thus, we are unable to evaluate whether surgery had any long-term influence on the pulmonary abilities of these patients. Fifth, our recruitment rate was relatively low. However, responders and non-responders were similar at baseline. Our response rate and reasons for non-participation (lack of interest, time commitment or inability to locate patients) is consistent with other large studies evaluating the HRQOL of SBC patients in the same age range8,112,128.

The primary outcome of this study was HRQOL. While the mean difference between the operative and non-operative patients’ HRQOL scores (SF-36 PCS, SF-36 MCS and SBSQ) were strikingly small (ranging from 0-3.9), the 95% confidence intervals were large and crossing zero. When the differences between groups in a study are not statistically different the following question must be asked, “is the study powered to provide a definitive answer?” One potential method to address this question is to consider the observed difference or change in the HRQOL or patient reported outcomes (PRO) against the “minimal important difference” (MID) for an intervention163-168. The “minimally important difference” (MID) has been defined as “the smallest difference in score in the domain of interest that patients perceive as important, either beneficial or harmful, and which would lead the clinician to consider a change in the patient’s management”166,167. However, the use of MID for HRQOL or PRO is not without its limitations165,167.

The 2009 Food and Drug Administration (FDA) Guidance for Industry Patient-Reported Outcomes (PRO) Measures guideline reported on the use of MID for
within-individual or within-group changes for HRQOL or PRO measures. As per the FDA recommendations, the MID was recommended to be a measure for intra-individual changes and not translatable to groups. This is in keeping with other studies that have advocated reporting the proportion of individuals who reach MID thresholds, rather than reporting a group’s change over time, as group changes can be swayed by individual outliers. On the other hand, several studies continue to utilize MID thresholds within and across groups.

Whether group-level differences or intra-individual differences are reported, time-interval assessments are often used to show benefit (or harm) for patients undergoing an intervention. The change in HRQOL is also dependent on patient’s baseline measure or “starting point” of HRQOL. In our study, operative patients may have had greater disability and limitations pre-operatively (compared to non-operative patients); thus, translating to greater improvements over time or vice-versa. The lack of baseline HRQOL measurements for our patients and the comparability of our groups at baseline are two known limitations of this study.

Any type of treatment has potential harms and complications. The fine balance of benefit and harm and the severity of each can be difficult to capture by MID thresholds. Patients may show improvement in HRQOL, but at what harm, cost or inconvenience? While the summary of harm is difficult and outside the scope of this study, the spectrum of harm can range from potential life-threatening complications (as in spinal surgery) to more benign side-effects,
such as nausea caused by medications. Individuals might show benefit in HRQOL, but the ratio of benefits gained relative to the potential harm is rather difficult to quantify\textsuperscript{163-167}.

The derivation of MID thresholds has also been controversial\textsuperscript{165,167}. Anchor-based methods can be prone to bias and dependent on the arbitrarily selected clinical criteria by field experts\textsuperscript{165,167}. Distribution-based methods (based on standard error of measurements or effect sizes) incorporate more statistical rigor at the expense of clinical significance\textsuperscript{167,175}. Many studies have advocated that a ten-point change be used as the rule for MID thresholds irrespective of HRQOL, PRO or clinical context\textsuperscript{172,176}. Nonetheless, no universal MID exists\textsuperscript{167}. Furthermore some authors have argued that the MCID is dependent on the magnitude of the intervention and/or risk, where the MCID for an intervention of low risk is presumably much smaller than for major interventions such as spinal surgery. Finally, a meaningful improvement in HRQOL for some patients may not be related to the difference in an outcome, but achieving a threshold. In summary, the MCID has been used to judge the power of a study, but any interpretation must consider the limitations noted above.

Based on the methods used for its construction, the MID for the SF-36 PCS measure (for various spinal procedures in adults) has ranged from 1.26-5.95\textsuperscript{158}. In our study, the absolute mean difference between the operative and non-operative groups’ PCS scores was 3.9. The mean difference between our groups was lower than the upper threshold of the MID and the 10\% MID rule\textsuperscript{172,176}, but given that the large confidence interval for the mean difference of PCS scores
encompasses the MID threshold, larger studies are still needed to conclude that HRQOL is not different between operative and non-operative patients\textsuperscript{167}.

In conclusion, spinal fusion in SBC scoliosis corrected coronal deformity and stopped progression, but had no overall effect on HRQOL in this study. In view of the significant complications, the benefits of surgery for spina bifida scoliosis are uncertain.

4.2 Future Directions

Having interacted and examined all study participants in this study, I had the unique opportunity to interact with patients and their primary caregiver(s) over extended periods of time. As an orthopaedic surgery resident, I was able to form an overall gestalt of patient’s physical functioning, mental health, and perceived quality of life, which might not have been captured by standardized health surveys.

The life expectancy of patients with SBC has increased and the importance of iatrogenic morbidity – at times, many years removed from treatment – is paramount for these patients and their caregiver(s). Reviewing study participants almost fifteen years post-operatively, as young adults, I developed a great appreciation of the unique considerations and implications that operative management may have for these patients, which may only come to light in young adulthood.

Given the two main limitations of this study being the comparability of patients at baseline and the sample size of non-operative patients, moving forward as a
surgeon-to-be, this study has changed my practice by how I obtain informed consent (for this procedure in this specific patient population) and the information disseminated during this process, including the many potential morbidities associated with spinal arthrodesis. Based on this study, these include the possibility of having a decline in their ambulatory abilities post-operatively (~14.7%), having a surgical site infection (~32.4%), having a post-operative complication (~47.1%) or having their instrumentation removed (~20.6). In addition, the effect spinal arthrodesis may have on their health-related quality of life is uncertain in the long-term.

In summary, decision-making in the treatment of spina bifida cystica scoliosis needs to be evaluated, not only in terms of technical outcomes, but also with respect to the quality of life to be expected.
5. TABLES:

5.1 Table 1: Baseline Assessments

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<td></td>
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</tr>
<tr>
<td>Male</td>
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<td>Female</td>
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<td>8 (72.7%)</td>
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<tr>
<td>Home</td>
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<td><strong>Neurological Motor Level</strong></td>
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<td></td>
<td></td>
<td></td>
</tr>
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<td>L4-Sacral</td>
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<td><strong>Hoffer Classification</strong></td>
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<td><strong>Urinary Incontinence</strong></td>
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<td>10 (90.9%)</td>
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<td><strong>G-Tube</strong></td>
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<td><strong>VP Shunt</strong></td>
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**Baseline Radiographic**

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<th>P value</th>
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<td>N=11</td>
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<tr>
<td><strong>Lordosis (°)</strong></td>
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<td>59.6±42.7</td>
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<tr>
<td><strong>Pelvic Obliquity (°)</strong></td>
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<td><strong>CRID (mm)</strong></td>
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<td></td>
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<td>N=38</td>
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5.2 Table 2: Peri-operative and Post-operative (Operative Patients)

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<td>Age at surgery (years)</td>
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<tr>
<td>Hematocrit</td>
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<tr>
<td>Surgical Duration (minutes)</td>
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<td>Blood Loss (mL/kg)</td>
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<td>Peri-operative Blood Transfusion</td>
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<tr>
<td>Approach</td>
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<tr>
<td>Anterior</td>
<td>4 (11.8%)</td>
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<td>Anterior + Posterior</td>
<td>25 (73.5%)</td>
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<td>Posterior</td>
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<tr>
<td>Instrumentation</td>
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<td>Pedicle Screws and Rod</td>
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<td>Sublaminar Wiring and Rod</td>
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<td>Bone Graft</td>
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## 5.3 Table 3: Follow-up Assessments

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<th>Age at Follow-up (years)</th>
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<th>P value</th>
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<tr>
<td></td>
<td>27.0±4.6</td>
<td>25.6±5.1</td>
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<td>Neurological Motor Level</td>
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<td>Thoracic-L3</td>
<td>14(73.6%)</td>
<td>7(77.8%)</td>
<td>21(75.0%)</td>
<td>0.30</td>
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<td>L4-Sacral</td>
<td>5(26.3%)</td>
<td>2(22.2%)</td>
<td>7(25.0%)</td>
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<tr>
<td>Hoffer Classification</td>
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<td></td>
</tr>
<tr>
<td>Ambulatory (I-II)</td>
<td>6(17.6%)</td>
<td>4(36.4%)</td>
<td>10(22.2%)</td>
<td>0.23</td>
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<tr>
<td>Non-ambulatory (III-IV)</td>
<td>28(82.4%)</td>
<td>7(63.6%)</td>
<td>35(77.8%)</td>
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<tr>
<td>Sitting Balance Scale</td>
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<tr>
<td>Requiring arms</td>
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<td>3(33.3%)</td>
<td>8(28.5%)</td>
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<tr>
<td>Not requiring arms</td>
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<tr>
<td>Able to reach</td>
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<td>3(33.3%)</td>
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<td>Able to shift weight</td>
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<td>3(33.3%)</td>
<td>11(39.3%)</td>
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<tr>
<td>Follow-up Radiographic</td>
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<tr>
<td>Cobb Angle (°)</td>
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<td>85.4±38.4</td>
<td>56.3±31.2</td>
<td>&lt;0.01</td>
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<td>Kyphosis (°)</td>
<td>39.2±25.3</td>
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<td>Lordosis (°)</td>
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<td>Pelvic Obliquity (°)</td>
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<td>Coronal Balance (mm)</td>
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<td>CRID (mm)</td>
<td>7.3±8.9</td>
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<td>8.1±9.1</td>
<td>0.31</td>
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<tr>
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### 5.4 Table 4: HRQOL Outcomes at Follow-up

<table>
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<tr>
<th>SF-36</th>
<th>Operative N=34 (Mean ± SD)</th>
<th>Non-Operative N=11 (Mean ± SD)</th>
<th>Mean Difference (Operative - Non-Operative)</th>
<th>95% CI of Mean Difference</th>
<th>P-value</th>
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<tbody>
<tr>
<td></td>
<td>Lower</td>
<td>Upper</td>
<td>Lower</td>
<td>Upper</td>
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<tr>
<td>Physical Functioning</td>
<td>26.1+24.6</td>
<td>37.3+32.7</td>
<td>-11.2</td>
<td>-34.2 11.9</td>
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<tr>
<td>Role-Physical</td>
<td>73.5+34.8</td>
<td>90.9+23.1</td>
<td>-17.4</td>
<td>-36.2 1.5</td>
<td>0.13</td>
</tr>
<tr>
<td>Bodily Pain</td>
<td>79.7+27.4</td>
<td>78.6+26.1</td>
<td>1.1</td>
<td>-18.2 20.4</td>
<td>0.91</td>
</tr>
<tr>
<td>General Health Perception</td>
<td>74.8+19.0</td>
<td>69.0+22.1</td>
<td>5.8</td>
<td>-10.0 21.6</td>
<td>0.40</td>
</tr>
<tr>
<td>Energy/Vitality</td>
<td>67.7+19.8</td>
<td>73.2+20.8</td>
<td>-5.5</td>
<td>-20.6 9.6</td>
<td>0.43</td>
</tr>
<tr>
<td>Social Functioning</td>
<td>83.5+20.3</td>
<td>86.4+19.7</td>
<td>-2.9</td>
<td>-17.4 11.6</td>
<td>0.68</td>
</tr>
<tr>
<td>Role-Emotional</td>
<td>89.2+24.2</td>
<td>85.8+32.1</td>
<td>3.5</td>
<td>-19.2 26.1</td>
<td>0.71</td>
</tr>
<tr>
<td>Mental Health</td>
<td>78.8+16.7</td>
<td>79.9+14.8</td>
<td>-1.1</td>
<td>-12.2 10.0</td>
<td>0.84</td>
</tr>
<tr>
<td>Physical Component Scale (PCS)</td>
<td>36.7+9.1</td>
<td>40.6+10.3</td>
<td>-3.9</td>
<td>-11.2 3.5</td>
<td>0.24</td>
</tr>
<tr>
<td>Mental Component Scale (MCS)</td>
<td>57.8+10.7</td>
<td>57.3+13.3</td>
<td>0.5</td>
<td>-9.0 10.0</td>
<td>0.90</td>
</tr>
<tr>
<td>Spina Bifida Scoliosis SBSQ</td>
<td>65.2+20.7</td>
<td>65.2+28.5</td>
<td>0.0</td>
<td>-20.0 20.0</td>
<td>0.99</td>
</tr>
</tbody>
</table>
6. FIGURES:

6.1 Figure 1: Follow-up Cobb Angles and SF-36 PCS (filled circles) & MCS (unfilled squares) scores for All Patients (N=45). Best-fit lines for PCS (solid line) and MCS (dashed line) also depicted.
6.2 Figure 2: Follow-up Cobb Angles and SF-36 PCS (filled circles) & MCS (unfilled squares) scores for Operative (N=34) and Non-operative (N=11) Patients. Best-fit lines for PCS (solid line) and MCS (dashed line) also depicted.
6.3 Figure 3: a) Follow-up SF-36 PCS Scores of Ambulatory (N=10) and Non-Ambulatory Patients (N=35) and b) SF-36 MCS Scores of Ambulatory and Non-Ambulatory Patients
7. APPENDICES

7.1 Appendix 1: Research Ethics Board Decision and Amendment for Extra Site

RESEARCH ETHICS BOARD

August 10, 2012

Dr. James Wright
Orthopaedic Surgery
The Hospital for Sick Children

Dear Dr. Wright:

Your study “Long-term follow-up of unit rod instrumentation in Spina Bifida Scoliosis”
REB File No.: 1000118503

On behalf of the REB, I am writing to confirm that the above noted study was re-approved by the REB for one year ending in August 2013. The REB approved continuing review at level 2C. As necessary, the Clinical Research Office will be contacting you to arrange follow-up.

Please note that, in accordance with the Personal Health Information Protection Act of Ontario, you are responsible for adhering to all conditions and restrictions imposed by the REB governing the use, security, disclosure, return and disposal of the research subjects’ personal health information. You are also responsible for reporting immediately any privacy breaches to the REB Chair and to Janice Campbell, the Sick Kids privacy officer.

Yours truly,

[Signature]

Richard Sugarman
Chair, Research Ethics Board

555 University Ave
Toronto, Ontario
Canada M5G 1X8

www.sickkids.ca
Amendment Request Form

1- REB File Number: 1000018503 (James Wright/Rosanna Yankanah)
2- Study Title: Long Term Follow-up of Unit Rod Instrumentation in Spina Bifida Scoliosis
3- Describe the proposed study amendment or modification with rationale. For each item, please specify whether it is Minor eg, administrative changes such as deleting the name of a co-investigator, or Major eg, change in sponsorship that causes the investigator to have a conflict of interest, adding an intervention such as additional blood tests, or any substantive change that will be made to the consent form.

Please note; commercial sponsors will be charged a $500 REB review fee for amendments that require full Board review.

Minor Change #1: We would like to add the Children’s Hospital of Eastern Ontario (CHEO) as a sub-site to this research study. There will be three sites involved in this study: Hospital for Sick Children (lead site), Holland Bloorview Kids Rehabilitation Hospital (sub-site) and CHEO (sub-site).


Minor Change #2: The names of the hospitals were replaced with the phrase ‘study sites’.

Minor Change #3: The title research coordinator was replaced with ‘research team member’.

4- Science Review: Science review may be needed for major amendments. If in doubt, please take advice with the REB Office. Please attach a copy of the completed science review form.

5- Will this amendment alter the study monitoring requirements?

☐ Yes ☑ No

☐ Yes (please describe)

6- What follow up action do you recommend for HSC study subjects who are already enrolled in the study?

☐ Inform study subjects ASAP

☐ Revise the consent/assent forms (Please attach a copy with the changes highlighted)

☐ Other (please describe)

☐ ☑ No action Required

7- Does this amendment alter the level of monitoring required for this study? If uncertain, please discuss with the Clinical Research Office staff; Julie Gibson or Velma Marzinotto.

☐ Yes ☑ No ☐ Perhaps

8- If Health Canada approved the original protocol (effective September 2001), their approval may also be required for this proposed amendment.

9- If the study sponsor requires a formal letter of approval, please attach a draft letter and forward an electronic copy as well.

HSC Research Ethics Board Amendment Request Form (Appendix P) June 2013
10- Signature of Primary Investigator

11- Signature(s) of Co-Investigator(s)*
   *for Major amendments only

12- Signature of Clinical Chief or Supervisor

13- Approved & Signature of REB Chair

Date 03/9/12

Date

Date 03/5/2012

Date 1/7/2013

This REB approval is only for those amendments described on this amendment request form.
7.2 Appendix 2: US English-language Medical Outcome Study 36-item

Short Form Health Survey (SF-36v2®)

![SF36 Health Survey](image)

INSTRUCTIONS: This set of questions asks for your views about your health. This information will help keep track of how you feel and how well you are able to do your usual activities. Answer every question by marking the answer as indicated. If you are unsure about how to answer a question please give the best answer you can.

1. In general, would you say your health is: (Please tick one box.)
   - Excellent
   - Very Good
   - Good
   - Fair
   - Poor

2. Compared to one year ago, how would you rate your health in general now? (Please tick one box.)
   - Much better than one year ago
   - Somewhat better than one year ago
   - About the same as one year ago
   - Somewhat worse than one year ago
   - Much worse than one year ago

3. The following questions are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much? (Please circle one number on each line.)

<table>
<thead>
<tr>
<th>Activities</th>
<th>Yes, Limited A Lot</th>
<th>Yes, Limited A Little</th>
<th>Not Limited At All</th>
</tr>
</thead>
<tbody>
<tr>
<td>3(a) Vigorous activities, such as running, lifting</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>heavy objects, participating in strenuous sports</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3(b) Moderate activities, such as moving a table,</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>pushing a vacuum cleaner, bowling, or playing</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>golf</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3(c) Lifting or carrying groceries</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>3(d) Climbing several flights of stairs</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>3(e) Climbing one flight of stairs</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>3(f) Bending, kneeling, or stooping</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>3(g) Walking more than a mile</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>3(h) Walking several blocks</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>3(i) Walking one block</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>3(j) Bathing or dressing yourself</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

4. During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of your physical health? (Please circle one number on each line.)

<table>
<thead>
<tr>
<th>Problems</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>4(a) Cut down on the amount of time you spent on work or other activities</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>4(b) Accomplished less than you would like</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>4(c) Limited in the kind of work or other activities</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>4(d) Had difficulty performing the work or other activities (for example,</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>it took extra effort)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

5. During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (e.g. feeling depressed or anxious)? (Please circle one number on each line.)

<table>
<thead>
<tr>
<th>Problems</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>5(a) Cut down on the amount of time you spent on work or other activities</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>5(b) Accomplished less than you would like</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>5(c) Didn’t do work or other activities as carefully as usual</td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>
6. During the past 4 weeks, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbours, or groups? (Please tick one box.)

<table>
<thead>
<tr>
<th></th>
<th>None</th>
<th>Slightly</th>
<th>Moderately</th>
<th>Quite a bit</th>
<th>Extremely</th>
</tr>
</thead>
</table>

7. How much physical pain have you had during the past 4 weeks? (Please tick one box.)

<table>
<thead>
<tr>
<th></th>
<th>None</th>
<th>Very Mild</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
<th>Very Severe</th>
</tr>
</thead>
</table>

8. During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)? (Please tick one box.)

<table>
<thead>
<tr>
<th></th>
<th>None</th>
<th>A little bit</th>
<th>Moderately</th>
<th>Quite a bit</th>
<th>Extremely</th>
</tr>
</thead>
</table>

9. These questions are about how you feel and how things have been with you during the past 4 weeks. Please give the one answer that is closest to the way you have been feeling for each item. (Please circle one number on each line.)

<table>
<thead>
<tr>
<th>Question</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
</tr>
</thead>
<tbody>
<tr>
<td>9(a). Did you feel full of life?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9(b). Have you been a very nervous person?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9(c). Have you felt so down in the dumps that nothing could cheer you up?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9(d). Have you felt calm and peaceful?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9(e). Did you have a lot of energy?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9(f). Have you felt downhearted and blue?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9(g). Did you feel worn out?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9(h). Have you been a happy person?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9(i). Did you feel tired?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

10. During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting with friends, relatives etc.)? (Please tick one box.)

<table>
<thead>
<tr>
<th></th>
<th>None</th>
<th>A Little of the Time</th>
<th>Some of the Time</th>
<th>Most of the Time</th>
<th>All of the Time</th>
</tr>
</thead>
</table>

11. How TRUE or FALSE is each of the following statements for you? (Please circle one number on each line.)

<table>
<thead>
<tr>
<th>Statement</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
</tr>
</thead>
<tbody>
<tr>
<td>11(a). I seem to get sick a little easier than other people</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11(b). I am as healthy as anybody I know</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11(c). I expect my health to get worse</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11(d). My health is excellent</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Thank You!
7.3 Appendix 3: Spina Bifida Spine Questionnaire

The Spina Bifida Spine Questionnaire

Last week how hard was it for me to ... 

1. Walk
   - not hard at all
   - a little hard
   - moderately hard

2. Walk without a body brace
   - not hard at all
   - a little hard
   - moderately hard
   - I did not wear a brace

3. Keep up with my friends when walking
   - not hard at all
   - a little hard
   - I can't do it

4. Wheel my wheelchair
   - not hard at all
   - a little hard
   - I can't do it
   - I did not use a wheelchair

5. Keep up with my friends in my wheelchair
   - not hard at all
   - a little hard
   - I can't do it
   - I did not use a wheelchair

6. Move into and out of the tub (or shower) from my wheelchair
   - not hard at all
   - a little hard
   - I can't do it
   - I did not use a wheelchair

7. Move on and off the toilet from my wheelchair
   - not hard at all
   - a little hard
   - I can't do it
   - I did not use a wheelchair

8. Move into and out of the car from my wheelchair
   - not hard at all
   - a little hard
   - I can't do it
   - I did not use a wheelchair

9. Put on braces myself
   - not hard at all
   - a little hard
   - I can't do it
   - I did not wear braces

10. Put on my shoes and socks myself
    - not hard at all
    - a little hard
    - I can't do it

11. Put on my pants myself
    - not hard at all
    - a little hard
    - I can't do it
    - I did not wear a brace

12. Get clothes to fit me
    - not hard at all
    - a little hard
    - I can't do it
    - I did not wear a brace

13. Look good in my wheelchair
    - not hard at all
    - a little hard
    - I can't do it

14. Do my own dressing
    - not hard at all
    - a little hard
    - I can't do it
    - I do not use a brace

15. Insert the catheter myself
    - not hard at all
    - a little hard
    - I can't do it
    - I did not use a catheter

16. Take a bath (or shower) by myself
    - not hard at all
    - a little hard
    - I can't do it
    - I did not take a bath

17. Balance so I don't feel like I'm falling when sitting
    - not hard at all
    - a little hard
    - I can't do it

18. Sit straight in my wheelchair
    - not hard at all
    - a little hard
    - I can't do it

19. Bend over to pick something up from the floor
    - not hard at all
    - a little hard
    - I can't do it
    - I did not pick anything up

20. Turn to reach while sitting
    - not hard at all
    - a little hard
    - I can't do it
    - I did not reach

21. Go from sitting to standing
    - not hard at all
    - a little hard
    - I can't do it

22. Go up and down stairs
    - not hard at all
    - a little hard
    - I can't do it
    - I did not climb stairs

23. Play wheelchair sports
    - not hard at all
    - a little hard
    - I can't do it
    - I did not play sports

Last week how bad was ... 

24. Feeling uncomfortable when sitting in my wheelchair
    - not bad at all
    - a little bad
    - extremely bad
    - I didn't sit in a wheelchair

25. The pain when wearing a body brace
    - not bad at all
    - a little bad
    - extremely bad
    - I did not wear a brace
<table>
<thead>
<tr>
<th>Item: Last week how hard was it for me to ...</th>
<th>Not hard at all</th>
<th>A little hard</th>
<th>Moderately hard</th>
<th>Very hard</th>
<th>I can’t do it at all</th>
<th>NA</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Walk</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>Delete</td>
</tr>
<tr>
<td>2. Walk without a body brace</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>Delete</td>
</tr>
<tr>
<td>3. Keep up with my friends when walking</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>Delete</td>
</tr>
<tr>
<td>4. Wheel my wheelchair</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>5. Keep up with my friends in my wheelchair</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>6. Move to and from the tub (or shower) from my wheelchair</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>7. Move to and from the toilet from my wheelchair</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>8. Move to and from the car from my wheelchair</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>9. Put on my braces myself</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>Delete</td>
</tr>
<tr>
<td>10. Put on my shoes and socks myself</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>Delete</td>
</tr>
<tr>
<td>11. Put on my pants myself</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>Delete</td>
</tr>
<tr>
<td>12. Get clothes to fit me</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>Delete</td>
</tr>
<tr>
<td>13. Look good in my wheelchair</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>Delete</td>
</tr>
<tr>
<td>14. Do my enema myself</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>Delete</td>
</tr>
<tr>
<td>15. Insert the catheter myself</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>Delete</td>
</tr>
<tr>
<td>16. Take a bath or shower by myself</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>Delete</td>
</tr>
<tr>
<td>17. Balance so I don’t feel like I’m falling when sitting</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>Delete</td>
</tr>
<tr>
<td>18. Sit straight in my wheelchair</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>Delete</td>
</tr>
<tr>
<td>19. Bend over to pick something up from the floor</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>Delete</td>
</tr>
<tr>
<td>20. Turn to reach while sitting</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>Delete</td>
</tr>
<tr>
<td>21. Go from sitting to standing (with or without braces)</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>Delete</td>
</tr>
<tr>
<td>22. Go up and down stairs</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>Delete</td>
</tr>
<tr>
<td>23. Play wheelchair sports</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>Delete</td>
</tr>
<tr>
<td>Last week, how bad was ...</td>
<td>Not bad at all</td>
<td>A little bit bad</td>
<td>Bad</td>
<td>Very bad</td>
<td>Extremely bad</td>
<td>NA</td>
</tr>
<tr>
<td>24. Feeling uncomfortable when sitting in my wheelchair</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>Delete</td>
</tr>
<tr>
<td>25. The pain when wearing a body brace</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>Delete</td>
</tr>
</tbody>
</table>

Raw score = sum of item’s score =
Number of items answered = 25 - number of deleted items =
Total score = (raw score/number of items answered) × 25 =

NA, not applicable.
7.4 Appendix 4: Hoffer Classification

<table>
<thead>
<tr>
<th>Type of Ambulation</th>
<th>Description</th>
<th>Pre-operative [from chart]</th>
<th>At Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Community</td>
<td>Walk indoors and outdoors for most activities (may need crutches, braces or both or wheelchair for long trips)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Household</td>
<td>Walk only indoors and with apparatus (may use a wheelchair for some indoor activities at home/school and all community activities)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-functional</td>
<td>Walking in a therapy session at home/school/hospital, use wheelchair as transportation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-Ambulator</td>
<td>Full time wheelchair users</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
7.5 Appendix 5: Neurological Motor Level

<table>
<thead>
<tr>
<th>Level</th>
<th>Description</th>
<th>Pre-op*</th>
<th>Post-op*</th>
<th>At Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>T12 or</td>
<td>No muscle power in lower extremities</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>higher‡</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>L1‡</td>
<td>Weak ilopsoas</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>L2‡</td>
<td>Iliopsoas, Sartorius, Adduction All grade 3 power</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>L3‡</td>
<td>All of L2 AND Quadriceps grade 3 power</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>L4‡</td>
<td>All of L3 and either:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Medial Hamstrings OR</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Tibialis Anterior grade 3 power</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>L5‡</td>
<td>All of L4 and Lateral Hamstrings grade 3 and ONE of:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Gluteus Medius grade 2 OR</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Peroneal Tertius grade 4 OR</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Post Tibialis grade 3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>S1‡</td>
<td>All of L5 AND TWO of:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Gastrocnemius/Soleus grade 3 AND/OR</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Gluteus Medius grade 3 AND/OR</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Gluteus Medius grade 4 and Pudendal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>S2‡</td>
<td>All of S1 AND</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Gastrocnemius/Soleus grade 3 AND</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Gluteus Medius grade 4 AND **</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>S2-3‡</td>
<td>All muscles normal except 1 or 2 muscle groups may be grade 4</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### 7.6 Appendix 6: Sitting Balance Scale

The **Sitting Balance Scale**

Test should be done on a flat surface without lateral or posterior supports. The hips and knees should be bent ninety degrees (if contractures allow) and feet should be rested on the floor. Stable sitting balance is achieved if subject can maintain position for at least three seconds and return to neutral position without using the hands for support or balance. Subjects are allowed three attempts to achieve each level, give one point after successful completion of each item at any attempt.

<table>
<thead>
<tr>
<th>Explicit Item</th>
<th>Attempt #1</th>
<th>Attempt #2</th>
<th>Attempt #3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unable to sit without external supports <em>(0 points given if unable)</em></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sit balanced using two hands for support</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sit balanced using one hand for support</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sit balanced with both hands rested in lap <em>(but not pushing in thighs for support)</em></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Turns head fully in both directions</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Raise both hands above head</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reach in one direction</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reach in two directions</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reach in three directions</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shifts weight in one direction <em>(transfer all weight onto one ischial tuberosity)</em></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shifts weight in two directions</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| Total                                                                 |            |            |            |
7.7 Appendix 7: Patient Consent form

Research Consent Form

(Patients with the capacity to consent for themselves)

Title of Research Project:

Long Term Follow-up of Unit Rod Instrumentation in Spina Bifida Scoliosis

Investigator(s):

Dr James G. Wright  Principal Investigator
Department of Surgery, The Hospital for Sick Children

416-813-6433

Research Team:

Peggy Law  Clinical Research Coordinator
Division of Orthopaedic Surgery, The Hospital for Sick Children

416-813-7654 ext 28731

Dr. Amir Khoshbin  Clinical Resident
Purpose of the Research:

This is a research study. We are inviting you to participate in this research study because you have Spina Bifida Scoliosis. Spina Bifida involves the incomplete formation of the spine and spinal cord that develops prior to birth and it affects about one child per one thousand births. Nearly fifty percent of children with Spina Bifida will also develop a curvature of the spine called scoliosis. This curvature can result in deformities of the trunk and sometimes surgery is done to correct these deformities. However, surgery is a major undertaking and may have a high rate of complications and some studies have shown that there is limited improvement in things such as sitting balance, ambulation and activities of daily living following spinal fusion surgery.

The purpose of this study is to find out if spinal surgery is an effective way of correcting the scoliosis and trunk deformities or preventing the scoliosis and trunk deformities from
getting worse. Also, we want to find out whether having surgery affects your quality of life.

**Description of the Research:**

**Study Overview:**

The main goal of this study is to follow-up on approximately 40 patients who had surgery on their backs for Spina Bifida Scoliosis at The Hospital for Sick Children (SickKids) and approximately 15 patients who did not have surgery on their backs for Spina Bifida Scoliosis between the years of 1989 and 2007.

**Recruitment/Initial Contact:**

Because this is a comparative research study we are looking for people who had spinal fusion surgery for Spina Bifida Scoliosis at SickKids as well as those who did not have spinal fusion for Spina Bifida Scoliosis, as such, you have received a package in the mail from our research team that includes an introductory letter from the principal investigator and study details. In two weeks a research team member will telephone you to see if you would like to participate in this study.

If you would like to be involved in this study, you will come to the SickKids outpatient Orthopaedic Clinic for one follow-up visit.
At this appointment, you will meet with one of the research team member to sign a consent form(s) and fill out two 10-minute questionnaires about your daily functional abilities and your health and wellness. You will be seen by an orthopaedic surgeon who will take a medical history and do a physical exam. If you agree, you will have two x-rays taken of your back. At most, the radiation dose from the procedures is equal to the risk that an average person experiences from 6 months of natural background radiation. If you agree, we will also take a photograph of you from the back while you are seated. (This will require you to complete a separate consent form regarding the use of photographs for research purposes). The appointment requires approximately 2 hours.

If you would like to be involved in this study but cannot come to SickKids or Bloorview for one follow-up visit, you may still complete the questionnaires about your daily functional abilities and your health and wellness as well as have the x-rays taken at your local hospital or clinic and return the completed forms, including this consent form, to us by mail.

The research team (Orthopedic surgeon and research coordinator) may review your medical records from SickKids for information and details about any surgical procedures and/or complications you may have had in the past.

Pregnant or nursing women are not eligible to participate in the x-ray portion of this study due to the risk associated with x-ray exposure. If you are female we will ask you about your sexual activity and if you use any methods of birth control and whether you
are pregnant or think you may be pregnant. If you are pregnant, you will not be eligible to have x-rays taken. However, you may still participate in the clinical portion (the medical history, physical examination, and questionnaires) of the study if you wish.

Details of the Study Assessment:

*Physical Exam*

The orthopaedic surgeon will take a medical history and do a physical exam, do some clinical assessments and measurements of your sitting balance and shoulder balance.

If you agree, we will take a photograph of your back while you are sitting and you will have two x-rays taken of your back.

*Questionnaires*

You will complete two short 10-minute questionnaires about your daily functional abilities and your health and wellness.

*Potential Harms:*

We know of no harm that taking part in this study could cause to the patient. The only discomforts associated with the participation in this study are the inconvenience of traveling to the hospital and/or the time commitment required in the research project.
**Potential Inconvenience:**

If you decide to participate in this study there is also the inconvenience of traveling to the hospital and/or the time commitment required to participate in the research project. The study coordinator will schedule and facilitate the clinic visit in a manner that minimizes wait-time for the patients.

**Potential Benefits to Participants:**

There are no direct individual benefits to you other than the opportunity to share your post-operative experience and to contribute to research. This is an opportunity to have a follow-up visit with an orthopaedic surgeon. Any incidental findings from x-ray images or questionnaires can be shared with you, and if necessary, you will be referred to the appropriate physician/health care provider. A letter thanking you for your participation and your reimbursement will be provided to you shortly after your appointment, and the study results will be available to you upon study completion.

**Potential Benefits to Society:**

Future patients suffering from Spina Bifida Scoliosis may benefit from the results of this study. The results of this research study may provide information about how well patients function after surgery and their long-term quality of life.
**Alternative Treatments or Procedures:**

There is no treatment being offered in this study. Our work seeks to follow-up on patients who were surgically treated for Spina Bifida Scoliosis at SickKids. As an alternative, you may choose not to participate.

**Confidentiality:**

We will respect your privacy. No information about who you are will be given to anyone or be published without your permission, unless the law makes us do this.

For example, the law could make us give information about you

- If a child has been abused
- If you have an illness that could spread to others
- If you or someone else talks about suicide (killing themselves), or
- If the court orders us to give them the study papers

SickKids Clinical Research Monitors, and the research team may see your health record to check on the study. By signing this consent form, you agree to let these people look at your records. We will put a copy of this research consent form in your patient health record and give you a copy as well.
The data produced from this study will be stored in a secure, locked location. Only members of the research team (and maybe those individuals described above) will have access to the data. This could include external research team members. Following completion of the research study the data will be kept as long as required then destroyed as required by Sick Kids policy. Published study results will not reveal your identity.

**Reimbursement:**

We will reimburse you for all your reasonable out of pocket expenses for being in this study (e.g., meals, babysitters, parking and getting you to and from Sick Kids). If you stop taking part in the study, we will pay you for your expenses for taking part in the study up until that point. We will also provide you with some compensation for this study visit ($5 Tim Horton’s gift card) in recognition of your time and effort.

**Participation:**

It is your choice to take part in this study. You can stop at any time. The care you get at SickKids will not be affected in any way by whether you take part in this study.

New information that we get while we are doing this study may affect your decision to take part in this study. If this happens, we will tell you about this new information. And we will ask you again if you still want to be in the study. In some situations, the researchers may decide to stop the study. If this happens, a research coordinator will talk to you about what will happen next.
During this study we may create new tests, new medicines, or other things that may be worth some money. Although we may make money from these findings, we cannot give you any of this money now or in the future because you took part in this study.

If you become ill or are harmed because of study participation, we will treat you for free. Your signing this consent form does not interfere with your legal rights in any way. The staff of the study, any people who gave money for the study, or the hospital are still responsible, legally and professionally, for what they do.

**Sponsorship:**

This study is sponsored by Dr. James Wright and the Hospital for Sick Children.

**Conflict of Interest:**

Dr. James Wright and the other research team members have no conflict of interest to declare.
Consent:

I have read and understood pages 1-6 of this consent form.

By signing this form, I agree that:

1) You have explained this study to me. You have answered all my questions.

2) You have explained the possible harms and benefits (if any) of this study.

3) I know what I could do instead of taking part in this study. I understand that I have the right not to take part in the study and the right to stop at any time. My decision about taking part in the study will not affect my health care at Sick Kids.

4) I am free now, and in the future, to ask questions about the study.

5) I have been told that my medical records will be kept private except as described to me.

6) I understand that no information about who I am will be given to anyone or be published without first asking my permission.

7) I agree, or consent, to take part in this study.

Please check off one of the following:

☐ I would like to participate in the medical history, physical examination, questionnaires and x-ray portions of the research study

☐ I would like to participate only in the medical history, physical examination, and questionnaires portion of the research study
☐ I would like to participate only in the questionnaires portion of the research study

☐ I would like to participate in the questionnaires and the x-ray portions of the study

____________________________________  ________________
Printed name of subject & age  Subject’s signature & date

____________________________________  __________________
Printed name of person who explained consent  Signature of person who explained consent & date

____________________________________  __________________
Printed Witness’ name (if the subject does not read English).  Witness’ signature & date

If you have any questions about this study, please call Peggy Law at 416-813-7654 ext 28731 or Magdalena Lysenko at 416-813-7654 ext 2959.

If you have questions about your rights as a subject in a study or injuries during a study please call the Research Ethics Manager at (416) 813-5718.
7.8 Appendix 8: Parent Consent Form

Research Consent Form

(Parent/Legal Guardian of patients without the capacity to consent for themselves)

Title of Research Project:

Long Term Follow-up of Unit Rod Instrumentation in Spina Bifida Scoliosis

Investigator(s):

Dr James G. Wright  Principal Investigator
Department of Surgery, The Hospital for Sick Children
416-813-6433

Research Team:

Liora Caspi  Clinical Research Coordinator
Division of Orthopaedic Surgery, The Hospital for Sick Children
416-813-7654 ext 28731

Dr. Amir Khoshbin  Clinical Resident
Division of Orthopaedic Surgery, The Hospital for Sick Children

Magdalena Lysenko  Clinical Research Coordinator
Division of Orthopaedic Surgery, The Hospital for Sick Children
**Purpose of the Research:**

This is a research study. We are inviting your child to participate in this research study because your child has Spina Bifida Scoliosis. Spina Bifida involves the incomplete formation of the spine and spinal cord that develops prior to birth and it affects about one child per one thousand births. Nearly fifty percent of children with Spina Bifida will also develop a curvature of the spine called scoliosis. This curvature can result in deformities of the trunk and sometimes surgery is done to correct these deformities. However, surgery is a major undertaking and may have a high rate of complications and some studies have shown that there is limited improvement in things such as sitting balance, ambulation and activities of daily living following spinal fusion surgery.

The purpose of this study is to find out if spinal surgery is an effective way of correcting the scoliosis and trunk deformities or preventing the scoliosis and trunk deformities from getting worse. Also, we want to find out whether having surgery affects your child’s quality of life.

**Description of the Research:**

**Study Overview:**
The main goal of this study is to follow-up on approximately 40 patients who had surgery on their backs for Spina Bifida Scoliosis at The Hospital for Sick Children (SickKids) and approximately 15 patients who did not have surgery on their backs for Spina Bifida Scoliosis between the years of 1989 and 2007.

**Recruitment/Initial Contact:**

Because this is a comparative research study we are looking for people who had spinal fusion surgery for Spina Bifida Scoliosis at SickKids as well as those who did not have spinal fusion for Spina Bifida Scoliosis, as such, you have received a package in the mail from our research team that includes an introductory letter from the principal investigator and study details. In two weeks a research coordinator, Liora Caspi, will telephone you to see if your child would like to participate in this study.

If your child would like to be involved in this study, your child will come to the SickKids outpatient Orthopaedic Clinic for one follow-up visit.

At this appointment, your child will meet with one of the research coordinators to sign a consent form(s) and fill out two 10-minute questionnaires about your child’s daily functional abilities and your child’s health and wellness. Your child will be seen by an orthopaedic surgeon who will take a medical history and do a physical exam. If you agree, your child will have two x-rays taken of their back. At most, the radiation dose from the procedures is equal to the risk that an average person experiences from 6 months of natural background radiation. If you agree, we will also take a photograph of your child from the
back while they are seated. (This will require you to complete a separate consent form regarding the use of photographs for research purposes). The appointment requires approximately 2 hours.

If your child would like to be involved in this study but cannot come to SickKids or Bloorview for one follow-up visit, your child may still complete the questionnaires about their daily functional abilities and their health and wellness as well as have the x-rays taken at their local hospital or clinic and return the completed forms, including this consent form, to us by mail.

The research team (Orthopedic surgeon and research coordinator) may review your child’s medical records from SickKids for information and details about any surgical procedures and/or complications your child may have had in the past.

Pregnant or nursing women are not eligible to participate in the x-ray portion of this study due to the risk associated with x-ray exposure. If your child is female we will ask her if she is sexually active and if she uses any methods of birth control and whether she is pregnant. If she is pregnant or unsure whether she may be pregnant, she will not be eligible to have x-rays taken. However, your child may still participate in the clinical portion (the medical history, physical examination, and questionnaires) of the study if they wish.

Details of the Study Assessment:
Physical Exam

The orthopaedic surgeon will take a medical history and do a physical exam, do some clinical assessments and measurements of your child’s sitting balance and shoulder balance.

If you agree, we will take a photograph of your child’s back while your child is sitting and your child will have two x-rays taken of their back.

Questionnaires

Your child will complete two short 10-minute questionnaires about your child’s daily functional abilities and their health and wellness.

Potential Harms:

We know of no harm that taking part in this study could cause to the patient. The only discomforts associated with the participation in this study are the inconvenience of traveling to the hospital and/or the time commitment required in the research project.

Potential Inconvenience:

If you choose to let your child participate in this study there is also the inconvenience of traveling to the hospital and/or the time commitment required to participate in the research
project. The study coordinator will schedule and facilitate the clinic visit in a manner that minimizes wait-time for the patients.

**Potential Benefits to Participants:**

There are no direct individual benefits to your child other than the opportunity to share your child’s post-operative experience and to contribute to research. This is an opportunity to have a follow-up visit with an orthopaedic surgeon. Any incidental findings from x-ray images or questionnaires can be shared with you and your child. If necessary, your child will be referred to the appropriate paediatric or adult physician/health care provider. A letter thanking your child for their participation will be provided to them shortly after the appointment, and the results of the study will be available to you and your child after the study’s completion.

**Potential Benefits to Society:**

Future patients suffering from Spina Bifida Scoliosis may benefit from the results of this study. The results of this research study may provide information about how well patients function after surgery and their long-term quality of life.

**Alternative Treatments or Procedures:**
There is no treatment being offered in this study. Our work seeks to follow-up on patients who were surgically treated for Spina Bifida Scoliosis at SickKids. As an alternative, you and your child may choose not to participate.

**Confidentiality:**

We will respect your child’s privacy. No information about who your child is will be given to anyone or be published without your permission, unless the law makes us do this. For example, the law could make us give information about you:

- If a child has been abused
- If you have an illness that could spread to others
- If you or someone else talks about suicide (killing themselves), or
- If the court orders us to give them the study papers

SickKids Clinical Research Monitors, and the research team may see your child’s health record to check on the study. By signing this consent form, you agree to let these people look at your child’s records. We will put a copy of this research consent form in your child’s patient health record and give you a copy as well.

The data produced from this study will be stored in a secure, locked location. Only members of the research team (and maybe those individuals described above) will have access to the data. This could include external research team members. Following
completion of the research study the data will be kept as long as required then destroyed as required by Sick Kids policy. Published study results will not reveal your child’s identity.

**Reimbursement:**

We will reimburse you for all your reasonable out of pocket expenses for being in this study (e.g., meals, babysitters, parking and getting you to and from Sick Kids). If you stop taking part in the study, we will pay you for your expenses for taking part in the study up until that point. We will also provide you with some compensation for this study visit ($5 Tim Horton’s gift card) in recognition of your time and effort.

**Participation:**

If you choose to let your child take part in this study you can take your child out of the study at any time. The care your child gets at Sick Kids will not be affected in any way by whether your child takes part in this study.”

New information that we get while we are doing this study may affect your decision to take part in this study. If this happens, we will tell you and your child about this new information. And we will ask you again if you and your child still want to be in the study. In some situations, the researchers may decide to stop the study. If this happens, a research coordinator will talk to you and your child about what will happen next.
During this study we may create new tests, new medicines, or other things that may be worth some money. Although we may make money from these findings, we cannot give you or your child any of this money now or in the future because your child took part in this study.

If your child becomes ill or are harmed because of study participation, we will treat your child for free. Your signing this consent form does not interfere with you or your child’s legal rights in any way. The staff of the study, any people who gave money for the study, or the hospital are still responsible, legally and professionally, for what they do.

**Sponsorship:**

This study is sponsored by Dr. James Wright and the Hospital for Sick Children.

**Conflict of Interest:**

Dr. James Wright, and the other research team members, have no conflict of interest to declare.
Consent:

I have read and understood pages 1-6 of this consent form.

By signing this form, I agree that:

1) You have explained this study to me. You have answered all my questions.

2) You have explained the possible harms and benefits (if any) of this study.

3) I know what I could do instead of having my child take part in this study. I understand that I have the right to refuse to let my child take part in the study. I also have the right to take my child out of the study at any time. My decision about my child taking part in the study will not affect my child’s health care at Sick Kids.

4) I am free now, and in the future, to ask questions about the study.

5) I have been told that my child’s medical records will be kept private except as described to me.

6) I understand that no information about my child will be given to anyone or be published without first asking my permission.

7) I agree, or consent, that my child___________________ may take part in this study

Please check off one of the following:

☐ I would like my child to participate in the medical history, physical examination, questionnaires and x-ray portions of the research study

☐ I would like my child to participate only in the medical history, physical examination, and questionnaires portion of the research study
☐ I would like to participate only in the questionnaires portion of the research study

☐ I would like to participate in the questionnaires and the x-ray portions of the study

______________________________________  _______________________
Printed Name of Parent/Legal Guardian                  Parent/Legal Guardian’s signature & date

______________________________________  _______________________
Printed Name of person who explained consent          Signature of Person who explained consent & date

______________________________________  _______________________
Printed Witness’ name (if the Parent/Legal Guardian does not read English).  Witness’ signature & date

If you have any questions about this study, please call Liora Caspi at 416-813-7654 ext 28731 or Magdalena Lysenko at 416-813-7654 ext 2959.

If you have questions about your rights as a subject in a study or injuries during a study please call the Research Ethics Manager at (416) 813-5718.
### 7.9 Appendix 9: Baseline Characteristics of Study Responders versus Non-Responders

<table>
<thead>
<tr>
<th></th>
<th>Responders (N=45)</th>
<th>Non-Responders (N=125)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>21 (46.7%)</td>
<td>49 (39.2%)</td>
<td>0.39</td>
</tr>
<tr>
<td>Female</td>
<td>24 (53.3%)</td>
<td>76 (60.8%)</td>
<td></td>
</tr>
<tr>
<td><strong>Institution</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HSC</td>
<td>35 (77.8%)</td>
<td>87 (69.6%)</td>
<td>0.34</td>
</tr>
<tr>
<td>CHEO</td>
<td>10 (22.2%)</td>
<td>38 (30.4%)</td>
<td></td>
</tr>
<tr>
<td><strong>Treatment</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Operative</td>
<td>34 (75.6%)</td>
<td>95 (76.0%)</td>
<td>0.99</td>
</tr>
<tr>
<td>Non-operative</td>
<td>11 (24.4%)</td>
<td>30 (24.0%)</td>
<td></td>
</tr>
<tr>
<td><strong>Age at Follow-up (years)</strong></td>
<td>26.7±4.7</td>
<td>27.7±4.4</td>
<td>0.20</td>
</tr>
<tr>
<td><strong>Last known Cobb Angle (°)</strong></td>
<td>56.3±31.2</td>
<td>65.7±22.0</td>
<td>0.03</td>
</tr>
</tbody>
</table>
7.10 Appendix 10: Sample Size Calculation

\[ N = \frac{\sigma^2 (z_{1-\beta} + z_{1-\alpha/2})^2}{(\mu_0 - \mu_1)^2} \]

\[ N = \frac{(9^2(0.84 + 1.96))^2}{(43.1 - 38.79)^2} \]

\[ N = 34 \]

Where \( \mu_0 \) = estimated population mean\(^{112} \), \( \mu_1 \) = mean of entire study population, \( N \) = sample size of study population, \( \sigma \) = estimated variance of study population\(^{112} \), \( \alpha \) = probability of type I error (0.05), \( \beta \) = probability of type II error (0.2) and \( z \) = critical Z value\(^{149} \).
### 7.11 Appendix 11: Post-Hoc Power Analysis

Tests of Between-Subjects Effects

Dependent Variable: Physical Component Scale (PCS) and Independent Variable: Cobb Angle at Follow-up

<table>
<thead>
<tr>
<th>Source</th>
<th>Type III Sum of Squares</th>
<th>df</th>
<th>Mean Square</th>
<th>F</th>
<th>Sig.</th>
<th>Partial Eta Squared</th>
<th>Noncent. Parameter</th>
<th>Observed Power^b</th>
</tr>
</thead>
<tbody>
<tr>
<td>Corrected Model</td>
<td>3220.881^a</td>
<td>36</td>
<td>89.469</td>
<td>.977</td>
<td>.581</td>
<td>.876</td>
<td>35.189</td>
<td>.183</td>
</tr>
<tr>
<td>Intercept</td>
<td>54976.227</td>
<td>1</td>
<td>54976.227</td>
<td>600.636</td>
<td>.000</td>
<td>.992</td>
<td>600.636</td>
<td>1.000</td>
</tr>
<tr>
<td>Cobb Angle at</td>
<td>3220.881</td>
<td>36</td>
<td>89.469</td>
<td>.977</td>
<td>.581</td>
<td>.876</td>
<td>35.189</td>
<td>.183</td>
</tr>
<tr>
<td>Follow-up</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Error</td>
<td>457.650</td>
<td>5</td>
<td>91.530</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>63621.790</td>
<td>42</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Corrected Total</td>
<td>3678.531</td>
<td>41</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

a. R Squared = .876 (Adjusted R Squared = -.020)

b. Computed using alpha =0.05

Power: 18.3
### 7.12 Appendix 12: Non-parametric Testing for HRQOL Scores

<table>
<thead>
<tr>
<th>Null Hypothesis</th>
<th>Test</th>
<th>Sig.</th>
<th>Decision</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. The distribution of Physical Component Scale (PCS) is the same across categories of Treatment.</td>
<td>Independent-Samples Mann-Whitney U Test</td>
<td>.396$^1$</td>
<td>Retain the null hypothesis.</td>
</tr>
<tr>
<td>2. The distribution of Mental Component Scale (MCS) is the same across categories of Treatment.</td>
<td>Independent-Samples Mann-Whitney U Test</td>
<td>.630$^1$</td>
<td>Retain the null hypothesis.</td>
</tr>
<tr>
<td>3. The distribution of Spina Bifida Scoliosis Questionnaire (SBSQ) is the same across categories of Treatment.</td>
<td>Independent-Samples Mann-Whitney U Test</td>
<td>.805$^1$</td>
<td>Retain the null hypothesis.</td>
</tr>
</tbody>
</table>

Asymptotic significances are displayed. The significance level is .05.

$^1$Exact significance is displayed for this test.
8. REFERENCES:


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