MEASURING THE LONG-TERM IMPACT OF CHILHOOD INJURY: A LONGITUDINAL STUDY OF HEALTH RELATED QUALITY OF LIFE

by

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Abstract

In Canada, unintentional injuries are a leading cause of hospitalization for children aged 5-19 years old. The need for longitudinal studies examining the impact of non-fatal childhood injuries across age groups and injury types has been identified internationally. Health related quality of life (HRQoL) measures assess functional limitations in multiple health domains making HRQoL an interesting and appropriate outcome to measure the impact of injury. The overarching goal of this dissertation was to advance the understanding of HRQoL among children following injury and the appropriate analysis of longitudinal HRQoL data.

A systematic review was performed to summarize the findings of research on HRQoL following pediatric injury, and to examine the methods used to measure and analyze HRQoL data in the childhood injury context. In addition, primary research was conducted with 365 children 0-16 years old and their parents who presented with an injury at a tertiary care pediatric hospital in Vancouver, British Columbia. Children aged between 5-16 years old and all parents completed questionnaire measures at the time of presentation for the injury and again at one-, four- and 12-months post-injury. How childhood injury and the process of recovery impacts children's HRQoL from both the child's and parent's perspective was investigated. Four different longitudinal models were explored to determine the model that best fit the data.

Analyses revealed that injuries among older children, children requiring hospitalization and children with lower extremity fractures had more significant impact on HRQoL at one-month post-injury. By four-months post-injury differences in HRQoL were minimal. On average, parents rated their children's HRQoL lower at one-month post-injury relative to the children's self-perceived HRQoL.

Most injured children regained HRQoL baseline status by four-months post-injury. Non-linear quantile regression provided the best fitting model as it is robust to skewness and outliers and free from any assumptions regarding the distribution of errors. Older children, those hospitalized, and children with lower extremity fractures were at higher risk of having lower HRQoL in the early part of recovery relative to younger children, those seen in the ED and children with other types of injuries.

Lay Summary

Childhood injuries are responsible for a large proportion of paediatric hospitalizations in Canada and globally. It's important to understand how injuries impact children throughout their recovery to inform healthcare services and prevention efforts. Health related quality of life (HRQoL) is a multidimensional outcome that captures how different aspects of a child's life has been impacted socially, emotionally and physically by injury. I used this outcome to understand how injuries affect children aged 0-16 years old in the year following injury. I found that most children recovered quickly from injuries, especially those only seen in the emergency department. Children who experienced greater short-term deficits in HRQoL were older children, those with lower extremity fractures and those who were hospitalized. I also found that parents tend to underrate their child's HRQoL at one-month post-injury, and that the physical dimension of health is more impacted by injury than the psychosocial dimension.

Preface

For chapter two I was the lead investigator responsible for conception of the study, and development of the protocol. Brown H assisted in refining the search strategy and addressed questions regarding study selection. Ezzat A contributed to the search strategy and we were equally involved in searching for studies, identifying eligible papers and extracting data. I was responsible for analysing and interpreting results. I am preparing the manuscript and Ezzat A will contribute to manuscript edits. Brussoni M, Bettinger J, Dipnall J, Mitton C, and Whitehurst D will provide additional interpretation and edits to the manuscript.

A combined version of Chapter 3 and Chapter 4 has been previously published applying a different analysis method (1). I am preparing new versions for publication. Brussoni M was the lead investigator on the overarching project, while I contributed to study design, data collection, and developed my research questions under the supervision of my supervisor and committee members. I conducted all of the data cleaning, statistical coding, completed the analyses and wrote the manuscript. I developed the statistical analysis plan under the supervision and with the assistance of Dipnall J, Geraci M and Bettinger J.

Ethics approval was not required for Chapter 2, given that is was a systematic review of published studies. The work presented in Chapter 3 and Chapter 4 was covered under the University of British Columbia's Children's and Women's Research Ethics Board certificate number H09 01627.

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List of Abbreviations

BC	British Columbia
BCCH	British Columbia Children’s Hospital
CHQ	Child Health Questionnaire
CHQ-CF87	Child completed version of the CHQ, 87 items
CHQ-PF28	Parent completed version of the CHQ, 28 items
CHQ-PF50	Parent completed version of the CHQ, 50 items
CI	Confidence Interval
CYBOI	Child and Youth Burden of Injury Study
ED	Emergency Department
EQ5D	European Quality of life instrument 5 dimensions
GEE	Generalized estimating equations
GLMM	Generalized linear mixed model
ICC	Interclass Correlation
ICF	International Classification of Functioning
IROS	ICF – Related outcome scale
ISS	Injury severity score
HRQoL	Health Related Quality of Life
LME	Liner mixed effects model
LRT	Likelihood ratio test
MAR	Missing at random
MCAR	Missing completely at random

MCID	Minimally clinically important difference
MNAR	Missing not at random
MVC	Motor vehicle collision
NLME	Non-linear mixed effects model
NLQMM	Non-linear quantile mixed model
OLS	Ordinary least squares
PaedsCTAS	paediatric Canadian Triage and Acuity Scale
PedsQL	Pediatric Quality of Life Inventory
QOL	Quality of life
QQ plot	Quantile quantile plot
SF-36	Medical Outcome Study Short form-36 items
TACQOL	TNO-AZL *(Netherlands Organisation for Applied Scientific Research Academic Medical Centre)* Children's Quality of Life Questionnaire
WHO	World Health Organization

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Thank you to previous mentors Dr. Will King and Dr. Stephen Hall, both of whom are brilliant researchers but more importantly wonderful people and teachers. You may not have known it, but words you have said have echoed in my mind for many years and helped me to achieve goals and continue to learn, improve and strive. Also, to Dr. Monika Naus, you set an amazing example of what an individual can do and are so generous with your time spent teaching and helping others improve themselves.

Finally, this dissertation would not have been possible without the unending support, love, and patience of my family and friends. To my epidemiology colleagues and friends providing laughs and a listening ear when needed, you are wonderful (AB, S(N)S, SP the amount I learnt from you in life and methods is unquantifiable). To my friends from another world who were willing to listen to me rant about the many ups and downs of this degree (SH, GM, ST), I would be lost without you. To Unc, you have and always will make my life better and brighter thank you for everything. Thank you to my mom, my eternal cheerleader. Your love and support have made this possible. To Geoff, there is no way to show you how much I appreciate you. Thank you so much for your patience, your willingness to listen, your encouragement and your belief in me. Finally, to Edward for always providing perspective, light and love and baby sister for lighting the fire to get this done! All my love.

Chapter 1: Introduction

1.1 Pediatric Injuries

Advances in injury prevention have reduced the mortality rates associated with childhood injury globally. However, injuries continue to play a prominent role in childhood morbidity and mortality (2). Globally, approximately 950 000 children under 18 years of age die every year as a result of an injury or violence, with almost 90% (approximately 830 000) due to unintentional injuries (3). While the highest rates of childhood mortality due to injury occur in low- and middle-income countries, injuries account for 40% of all child deaths in high-income countries representing the leading cause of child mortality and a major source of morbidity (4). The leading mechanisms of unintentional childhood injury include traffic collisions, drowning, poisoning, falls and burns (5). Mortality represents just the tip of the iceberg in terms of the impact of childhood injuries. As described by what is known as the 'injury pyramid', for every death associated with injury there are many more hospitalizations, emergency department (ED) visits and visits with primary care practitioners (6,7). The World Health Organization (WHO) estimated that in 2016, over 644 855 children under 15 years of age died as a result of an injury with between 10 million and 30 million more suffering a non-fatal injury (2).

Unintentional injuries are the leading cause of mortality in Canada among individuals 1-34 years of age (8). In 2009, 663 children aged 1-14 years of age and 2,096 youth aged 15-24 years of age died as the result of an unintentional injury (8). Unintentional injuries are also the leading cause of hospitalization in Canada among children 10-14 years of age and the second largest cause of hospitalization among children 5-9 and 15-19 years of age, amounting to almost 24,000 hospitalizations among children under 19 years of age in the 2013/14 fiscal year (9). Although indicative of the enormous public health problem that injuries comprise, mortality and hospitalization statistics are inadequate to fully understand the burden of injury. The former

Director General of the WHO and former Executive Director of the United Nations Children's Fund stated: "Once children reach the age of five years unintentional injuries are the biggest threat to their survival. Unintentional injuries are also a major cause of disabilities, which can have a long-lasting impact on all facets of children's lives: relationships, learning and play" (5).

1.2 Health Related Quality of Life

WHO's definition of 'health' includes physical, mental and social dimensions (10). While physiologic measures of injury severity are important to clinicians, measures of functional capacity and wellbeing can be of greater importance to individuals (11). Measuring health related quality of life (HRQoL) after injury facilitates quantifying the immediate impact and the recovery process on multiple dimensions of health.

With medical advances, the emphasis in pediatric healthcare has evolved in many situations from purely survival to life quality, and with this shift HRQoL is increasingly being used as an outcome across many disciplines. The number of articles identified in an Ovid MEDLINE search with the keyword "health related quality of life" or subject heading "Quality of Life" rose from 1,936 in 1995 to 9,893 in 2018 There are a number of definitions of HRQoL (eight identified by this author, see Table 1.1) and, the terms "health", "HRQoL", and "quality of life" (QoL) have been used interchangeably in the literature (12). As an example, two widely used measures (the Medical Outcome Study Short form-36 items (SF-36) and the European Quality of life instrument 5 dimensions (EQ5D)) are described as measures of 'health status', 'health-related quality of life' and 'quality of life' at different points in the literature (12). For the purpose of this dissertation, and as is generally agreed upon in the identified definitions, HRQoL is narrower than QoL, being limited to aspects of life associated with health; excluding for example, political and economic circumstances. It is multidimensional and involves the patient's own perspective.

Table 1.1 Definitions of HRQoL

1. "Health-related quality of life is the value assigned to duration of life as modified by the impairments, functional states, perceptions and social opportunities that are influenced by disease, injury, treatment, or policy." (13)

2. "How well a person functions in their life and his or her perceived wellbeing in physical, mental, and social domains of health." (14)

3. "A broad concept incorporating all factors that impact upon an individual's life. Health-related quality of life includes only those factors that are part of the individual's health." (15)

4. "The subjective assessment of the impact of a disease and treatment across the physical, psychological, social, and somatic domains of functioning and well-being." (16)

5. "A health status indicator that provides a proxy measurement of the utility or value of a particular health state. Like utility, it is usually measured on a scale from zero to one and assessed in conjunction with self-perceived or observed physical, social, and emotional function of individuals. In practice it is assessed by questionnaire or interview, using a rating scale if possible, rather than open-ended questions." (17)

6. "The specific impact of an illness or injury. medical treatment. or health care policy on an individual's QoL." (18)

7. "HRQoL is commonly conceived as dynamic, subjective, and multidimensional, and the dimensions often include physical, social, psychological, and spiritual factors. However, the specific dimensions are labeled differently by different authors." (19)

8. "Those aspects of self-perceived well-being that are related to or affected by the presence of disease or treatment." (20)

As multidimensional, patient centered outcomes, HRQoL measures capture a wide range of experiences to given health states that are grouped together into dimensions/domains based on the aspect of life being assessed (13). Most conceptualizations of HRQoL include a measure of physical functioning, social functioning, role functioning, mental health and general health perceptions. However, the specific taxonomy used to describe domains can vary across models and tools (21). Perhaps based on WHO's definition of health, it has been suggested that all measures of HRQoL should, at a minimum, include questions that address physical health, mental health, and social functioning (22). Because HRQoL goes beyond morbidity and mortality in evaluating the impact of an illness or injury, it can provide valuable information to help improve clinical management, indicate service needs, inform policy makers, identify hidden or unexpected health issues, and facilitate communication between patients and healthcare providers (23,24).

When measuring HRQoL, it is important that researchers select an appropriate tool given the condition or population under study, as well as the purpose of the data being collected. Generic HRQoL instruments include a number of dimensions that are applicable to different impairments, illnesses, patients and populations and, thus, can be used across a range of different types and severities of disease (25). While generic HRQoL tools seek to assess aspects of health that are considered to be universally important, disease-specific measures are created to assess the impact of a specific condition on specific populations. Both generic and disease-specific measurement of HRQoL are valuable; their use depends on the circumstance and purpose of data collection (26). Generic tools allow for comparisons of results between different diseases/conditions and populations (25) while disease-specific tools tend to be more responsive, allowing for more sensitive measurement of clinically important changes (26).

1.3 PedsQL

The PedsQL 4.0 Generic Core and the PedsQL Infant Scale are generic tools that were developed to assess HRQoL in children, ages two to 18 years and zero to 24 months respectively. The PedsQL 4.0 Generic Core is a 23 item scale and includes four subscales: physical functioning, emotional functioning, social functioning and school functioning (23). The PedsQL Infant Scale is an instrument composed of 45 items grouped into five subscales: physical functioning, physical symptoms, emotional functioning, social functioning and cognitive functioning (27). Both PedsQL instruments use a five-point Likert response scale where 0=”Never”, 1=”Almost Never”, 2 = “Sometimes”, 3=”Often”, and 4=”Almost Always” to assess the extent to which different items have affected the child in the previous month. For both measures, individual item scores are obtained by reverse scoring items and linearly transforming them to a scale of zero to 100 so that the original 0-4 scale is transformed into scores of 0=100, 1=75, 2=50, and 4=0, thus higher scores represent better HRQoL. Scale scores are calculated as the sum of items on that scale over the number of items answered on that scale. If more than 50% of the items on the scale are missing, the scale score should not be calculated (28). The total scale score is obtained by adding the sum of all items and dividing them by the total number of items answered. There are also two domain summary scores that can be calculated: 1) the psychosocial health summary score, which is calculated as the sum of the items divided by the number of items answered in the emotional, social and school functioning scales and 2) the physical health summary score, which is equal to the physical function scale score.

Studies that have reviewed tools for the purpose of long-term follow-up and assessing outcomes in pediatric trauma populations have identified the PedsQL as one of very few measures that is appropriate for a large age range and that also has robust psychometric properties (27,29–31). A change of 4.4 on the total scale score for self-report and 4.5 for parent-report have been established as the minimal clinically important difference for this tool (MCID) (31,32).

1.4 Children’s Health Related Quality of Life: Self Report vs Proxy Measurement

Self-report has been established as the gold standard of HRQoL measure, to the extent that the terms “Patient Reported Outcome” and HRQoL are often used interchangeably (33).

Children, like all populations, should have their own voice heard when it comes to their health and well-being. The United Nation's Convention on the Rights of the Child Article 12 states, "When adults are making decisions that affect children, children have the right to say what they think should happen and have their opinions taken into account." This clearly includes decisions regarding health and healthcare. However, when it comes to young children, or children that are too ill to respond, another individual including parents or clinicians are used as a proxy to measure some subjective outcomes including HRQoL. The age that has been established for when a child can provide a reliable and valid self-report is five years of age (34,35), although it is recommended for children of all ages that parent proxy-report be included as a secondary outcome measure (35,36). Parent-report of HRQoL is an important independent outcome as they have a unique perspective of a child's life, and it is parents' perception of their child's HRQoL that is the primary driver of health care utilization (37–39).

1.5 Children's Health Related Quality of Life Following Injury

Studies have found that the impact of pediatric injuries on HRQoL can extend well into the 12 months following injury, although the literature in this area is limited. In their 2012 systematic review of HRQoL on children and adolescents following traumatic injury, Martin-Herz et al. identified 11 longitudinal studies, which used five different HRQoL instruments (40). Only four studies followed patients for at least 12 months following injury and included a minimum of three follow-up points, all of which included only children $\geq$ 12 years of age. Of the studies that looked at overall HRQoL over time, HRQoL returned to normative levels between one month and two years after injury, with longer recovery found in a study limited to older children, all of whom had been hospitalized (12-19 years) (41). The same review identified only three studies that included a baseline measure of HRQoL. The statistical methods used across the studies were not specifically reported on or critiqued in the review. A very limited number of studies include less severe injuries not requiring hospitalization. Studies that have included these types of injuries have found that a small proportion (8%) of children still reported functional limitations at nine months post-injury and that some injured children had HRQoL scores below population norms up to two years post-injury (42,43).

1.6 Longitudinal Data Analysis

When HRQoL is collected longitudinally, a number of issues must be considered in the analysis. The first is missing data, which can be for individual questions or full questionnaires. The two most important issues that arise with missing data are 1) a decrease in precision and 2) a potential for bias if missingness is associated with the outcome (for instance individuals with lower HRQoL systematically having more missing data relative to those with higher HRQoL). In addition to missing data, fitting an appropriate model to investigate factors associated with HRQoL in a multivariable fashion can be challenging. The appropriate model must account for the correlation of repeated measures, the boundedness of the outcome, the possible nonlinear temporal trajectories, all while not violating model assumptions regarding distribution of the error.

Surveys of journal editors indicate that violations of model assumptions, failing to account for clustering in data analysis and improperly addressing missing data are issues of top concern in submitted manuscripts (44). These issues highlight the need for thorough descriptive analysis of data prior to addressing specific research questions. This includes describing the extent and patterns of missingness (45), and examining the distribution of the outcome and its trajectory over time alone and in relation to other important variables.

1.7 Objectives

The overarching goal of this thesis is to advance the literature on measuring and analyzing HRQoL among children following injury. A systematic review was performed to summarize the findings of research on HRQoL following pediatric injury, and to examine the methods used to measure and analyze HRQoL data in the childhood injury context. Using data gathered over the course of the Child and Youth Burden of Injury Study (CYBOI), HRQoL was examined as an outcome, and how childhood injury and the process of recovery and rehabilitation impact children's HRQoL from both the child's and parent's perspective was investigated. The exploration of different models to analyze this bounded and skewed response variable for longitudinal analysis has contributed new knowledge on how this outcome can be approached.

The specific objectives of this thesis are as follows:

1. To describe the trajectory of, and identify factors associated with, children's HRQoL in the year following injury as reported by both the child and parent.

2. To explore longitudinal models that can be used for the analysis of HRQoL data following childhood injury by applying a selection of models to data gathered through primary research; and discussing the impact of modelling technique on results.

Chapter 2: Systematic Review

2.1 Background

Studies examining HRQoL after injuries in adult populations have found that the impacts of injury can vary in time and extent, and that injury severity is not the only predictive factor (46). Studies with pediatric samples are important as the impact of childhood injuries can differ substantially from adults (46,47). The literature on HRQoL following injury among children is growing. However, variations in study methods used to assess post-injury HRQoL vary widely with respect to age ranges, measurement instruments, timing of data collection, baseline HRQoL measurement, analyses performed, reporter of HRQoL (child or proxy), and types of injury included. In response to these issues, van Beeck et al., as part of the European Consumer Safety Association (ECOSA) injury-related disability working group, encouraged studies across age groups and recommended use of HRQoL measures that assess functional limitations in multiple health domains, with sampling at specific post-injury time points (47).

Pediatric studies using generic HRQoL measures that assess functional limitations in multiple health domains, with sampling at specific post-injury time points, are required to understand the impact injuries have on this unique population and to allow for comparisons with other disease groups (48). A 2012 systematic review on HRQoL of children and adolescents following trauma identified 16 studies, with some key studies not captured by the search strategy and absent from the review (40). Prior to that, Polinder et al. performed a systematic review of studies measuring HRQoL of general injury populations across all age ranges where six paediatric studies were identified, however, a separate presentation and critique of pediatric results was not performed.

Given it has been seven years since the previous review, and that review had gaps in terms of studies identified and the data collected and presented, there is a need for an updated review in this area. This chapter reports the results of a systematic review on HRQoL following childhood injury including summarizing methods used, the trajectory of HRQoL recovery, and variables associated with HRQoL.

2.2 Objectives

This systematic review sought to identify the relevant quantitative literature available on HRQoL among a pediatric general injury population. Specifically, the objectives of this study were to:

1) Summarize the methods used to assess HRQoL in this population including the tools used, the reporter (proxy report or child), the baseline measure of HRQoL, the timing of data collection, and statistical analyses performed

2) Provide a narrative summary of HRQoL among children following injury and report variables identified to be predictors of HRQoL

2.3 Methods

2.3.1 Search strategy

The population, indicator, comparison and outcome (PICO) elements for this review were defined as follows: Population: children (individuals ≤ 18 years of age); Indicator: unintentional injury by any mechanism; Comparison (2 groups): 1) none OR baseline injury status, and 2) children of varying injury severity or healthy children; Outcome: HRQoL. A University of British Columbia librarian with expertise in systematic reviews was consulted in the design of the search strategy for this review. A two-stage search strategy was implemented. For stage one an electronic search was developed for each of: MEDLINE (Ovid), PsycINFO, Embase, and the

Cumulative Index to Nursing and Allied Health Literature (CINAHL) (Appendix A presents the search strategy for MEDLINE). Search terms were determined by identifying the broad concepts of interest ("Health Related Quality of Life", "injury") and then identifying the subject heading(s) (Medical Subject Headings (MeSH)) that were appropriate for those terms in each database. Keywords were generated based on PICO elements and associated subject heading terms and definitions used for terms. Keywords and MeSH terms from relevant reviews (40,46) were compared to search terms identified and new terms were added as deemed appropriate. The pediatric filter from the University of Alberta for Ovid and Embase was adapted to identify articles including a pediatric population (49). In stage two, backward and forward citation chaining of all the included studies were used to identify additional relevant literature using Google Scholar and Web of Science. Google Scholar was searched as a separate database to ensure no studies were missed using the term "Health related quality of life among injured children" and the first 250 titles were screened to assess if they met the inclusion criteria. All articles identified using the above search strategies were imported to ProQuest RefWorks, Ann Arbor, Michigan, a reference manager program. Covidence, Veritas Health Innovation, Melbourne Australia was used to manage the title/abstract screening, and full review screening. Two reviewers were responsible for independent screening of title/abstracts, full text screening and data abstraction. The reviewers were blinded to each other's decisions regarding inclusion and data abstraction, discrepancies were flagged and resolved via discussion.

2.3.2 Study selection

The inclusion criteria of this study can be found in table 2.1.

Table 2.1 Systematic review inclusion criteria

- Original research
- Validated instrument measuring HRQoL*
- Study population (children ≤ 18 years of age, or if adults are included a distinct analysis of pediatric population
- Exposure unintentional injury by any mechanism, or if studies included intentional injuries it was not the primary mechanism of injury (< 50%)
- Outcome HRQoL

* This was defined as any validated instrument that reported to measure HRQoL, QOL or health status and captured the patient's perception (or proxy report) on more than one dimension of life (i.e. physical, social, emotional) in the context of the child's injury

Consistent with previous reviews on the topic, studies examining HRQoL following a specific injury type were excluded (40,46). Studies of populations who had sustained specific injuries such as traumatic brain injury, burns or spinal cord injury curate a more homogenous population with unique recovery and rehabilitation trajectories that are not representative of the general injury population that is of interest in the current review. Studies where the majority of injuries were due to self-harm and/or intentional injuries were also excluded as intentional and unintentional injuries are separate public health issues, and the possibility exists for large differences in recovery patterns and predictors of recovery across these groups.

After performing the full search on May 2nd, 2018, articles from all sources were combined and duplicates were removed. All articles identified through stage one and two of the search strategy were screened for inclusion by title and abstract (Step 1). Where studies appeared to meet the inclusion criteria, or when a definite decision could not be made based on the title and abstract, the full manuscript was obtained to assess against inclusion criteria (Step 2). Reasons for exclusions were collected at Step 2. Two reviewers (AS, AE) independently completed both Step 1 and 2. The selection process was piloted to ensure the criteria were being consistently applied by both reviewers. In the pilot phase, the inclusion criteria were applied to a sample of 50 title/abstracts and 10 full text papers and agreement between reviewers was assessed. All conflicts or uncertain decisions in the screening process were resolved through discussion and consensus in the pilot phase and at the end of each step during full screening.

Prior to data extraction, once the list of included papers was finalized, multiple papers from the same study were collated. Multiple papers were identified by juxtaposing author names and institutions and sample sizes by AS; if there was doubt as to whether data came from the same study, the authors were contacted. When multiple papers looked at different predictors of HRQoL using the same data, results were collated so HRQoL results were only reported once. However, all predictors of HRQoL were included and all relevant articles were cited. When study data were published in conferences and manuscripts, the study author was contacted to determine the most appropriate representation of the data to include.

When articles were identified that were not available in English, the authors were contacted in an attempt to ascertain their relevance to the study. When authors did not respond, these articles were excluded. When articles indicated they collected HRQoL data but did not report the results, authors were contacted. If authors did not respond or HRQoL data could not be made available, these articles were excluded.

2.3.3 Data extraction and quality assessment

Two reviewers (AS, AE) critically appraised and performed data extraction on full articles. A quality assessment form was developed for this review based the NIH National Heart, Lung and Blood Institute Quality Assessment Tool for Observational and Cohort and Cross-Sectional Studies check list (Appendix B) (50). Data were extracted using the Cochrane data extraction template adapted for this study in Microsoft Excel (Appendix C). Variables extracted beyond those included in the Cochrane data extraction template included the HRQoL tool used, reporter of HRQoL, the time points followed up and HRQoL summary scores at each time point, the distribution of the HRQoL data, variables associated with HRQoL and statistical analyses used. Where there were discrepancies in numbers between what was written in the results and what was presented in a table of a manuscript the author was contacted. If there was no response, the number in the table has been presented in the results of this review and the presence of the discrepancy has been noted. Any discrepancies between reviewers were resolved by discussion and consensus.

2.3.4 Data synthesis

HRQoL scores at each time point collected were extracted (mean/median summary score, physical and/or psychosocial health summary score and/or index value where available). Meta-analysis was not pursued due to significant heterogeneity in terms of timing of assessments and HRQoL tools applied. Where investigated, variables associated with HRQoL were also extracted. An alpha of 0.05 was used for interpretation of statistical significance across all studies.

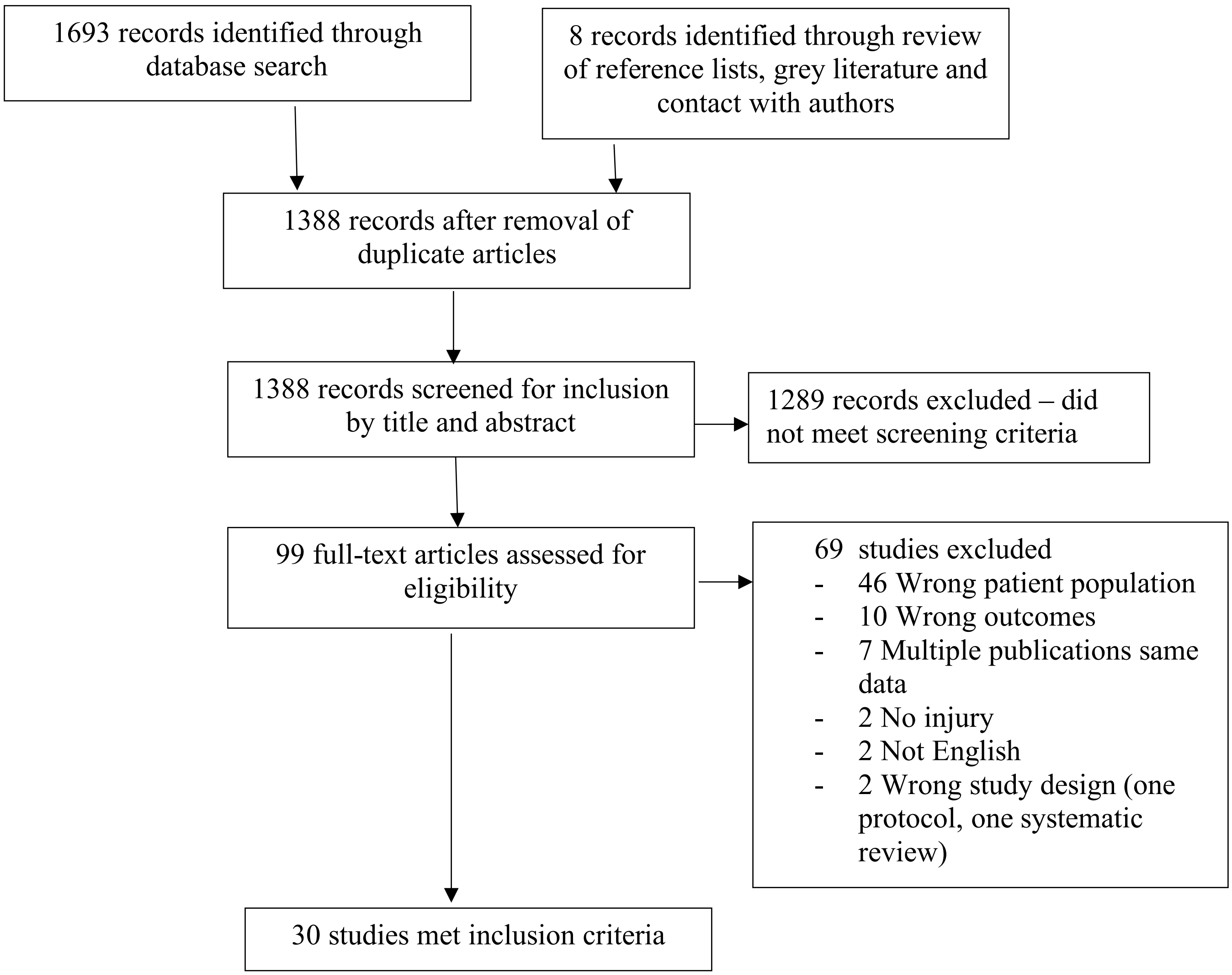
2.4 Results

2.4.1 Literature search

Searches from Medline, Embase, CINALH and PsycINFO resulted in 500, 502, 89 and 602 potentially relevant articles respectively, of which 313 were duplicate records and 1380 were unique. Eight additional articles were identified through chaining, grey literature searches and direct contact with authors. Of the 1388 studies screened, 1289 were deemed irrelevant based on title/abstract, and two studies were only available in another language: German (51) and

Portuguese (52), leaving 99 studies for full text review. Of the remaining studies, 30 met inclusion criteria and were included in the review. The main reason for exclusion at the last step was that there was not a separate analysis of pediatric results despite children being included in the study population. See Figure 2.1 for the flow chart for study inclusion.

Figure 2.1 Flow chart for study inclusion



2.4.2 Study quality

All studies included in this review clearly stated their research question/aim and described the study population well. The aim of two of the studies was to evaluate the psychometric properties of the PedsQL (31,53) and one was to report on the performance of a predictive screening protocol (54) while all other studies indicated that at least one aim was to describe children's HRQoL following injury and for some identify variables associated with HRQoL. Participation rates (the percent of the eligible population recruited for the study) ranged from 30% - 100%. Nine studies compared the study population to the entire population of eligible individuals to assess for selection bias. Some studies did not provide the exact estimates attained from the HRQoL tool used (n=12), but rather dichotomized the outcome or presented the outcome results via figures without the corresponding values. All but two of the longitudinal studies had at least 10% lost to follow-up, with eight studies having 20% or more lost to follow-up at the final assessment. Other aspects of study quality will be addressed below.

2.4.3 Study characteristics

A total of 30 articles and 27 studies were included in this review (Table 2.2). Four articles used the same data set (41,55–57). From this point forward only Holbrook 2007 (41) will be referenced when referring to the study with multiple articles. Eight studies included in this review were conducted in the USA (31,41,54–63), five in The Netherlands (42,64–66), four in Canada (1,67–69), two in Switzerland (70,71) and one each in India (72), Croatia (61), Sweden (73), Belgium (74) and the United Kingdom (53). Dates of recruitment into the studies ranged from 1984 (69) to 2015 (72). Sample sizes (at baseline if multiple follow-ups) ranged from 50 to 527. The most common mechanism of injury was road traffic injuries with two studies (7.4%) limiting their study population to those injured in road traffic collisions. An additional eight studies (29.6%) reported road traffic collisions as the most common mechanism of injury. One study limited the study population to individuals sustaining equestrian related injuries (64), and another limited the population to those with sports injuries (63).

Table 2.2 Study characteristics*

Author, year, country, (ref #)	Age at time of injury	% Male	% hospitalized (length of stay)	Injury Severity	Mechanism of Injury (%)	Injury Type (%)
Aitken, 2002, USA (59)	3-18 years Median 9.6 years	66%	100% (Mean 9 days, Range 1-125 days)	ISS Range 4-50 < 9 (48%) 9 - 15 (37%) > 16 (15%)	Motor Vehicle Related (29%) Fall (23%) Cyclist (8%) Pedestrian (7%) Other (24%)	Head injury (44%) Extremity injury (50%) Abdominal injury (11%) Chest injury (9%)
Davey, 2005, Australia (43)	5-18 years Mean 11.3 years	65%	100% 50% admitted > 24 hr 50% 120 admitted < 24 hr	ISS Range 1-35 Mean 8.7	Fall (28%) Cyclist (14%) for those admitted >24 hrs, not reported for those admitted < 24hr	Fractures (47%) Intracranial injury (14%) - for those > 24 hrs, not reported for those admitted < 24 hr
Dekker, 2004, The Netherlands (64)	5-17 years Mean 11 years	10%	16%	ISS Range 1-13 Median 4.0	Equestrian accident (100%)	Fractures of extremity (45.5%) Soft tissue (43%) Intracranial injury (8.1%) Internal injury (3.3%)
Gabbe, 2011, Australia (30)	0-17 years 69% > 5 years	65%	100% (Median 6.3 days)	ISS Median 10 ≤ 9 48% 10-16 25% > 16 27%	Low fall (14%) Cyclist (12.7%) Struck by object or person (12.7%) Pedestrian (11.3%) Fire, flames, smoke or scald (10.7%) High fall (10.0%) Motorcyclist (9.3%) Motor vehicle (8.7%) Other (10.7%)	Extremity fractures (30%) Head injury (25.3%) Chest or abdominal injury (14.7%) Burns (9.3%) Other (20.7%)

Author, year, country	Age at time of injury	% Male	% hospitalized (length of stay)	Injury Severity	Mechanism of Injury	Injury Type (%)
Holbrook, 2007, USA (41)	12-19 years Mean 15.0	71%	100% (Mean 4.8 days, Mean days in ICU 1.4)	ISS Mean 10.8 $\leq$ 17 80%	Motor Vehicle Related (22%) - Motorcyclist (6%) - Pedestrian (10%) Intentional injuries (14%) Fall (12%) Bicycle (13%) Recreational injuries (23%)	not reported
Han, 2011, USA (57)	as above	as above	as above	as above	as above	not reported
Holbrook, 2005, USA PTSD (56)	as above	as above	not reported	not report	as above	not reported
Holbrook, 2005, USA Acute Stress (55)	as above	62%	not reported	not reported	as above	not reported
Herz, 2012, USA (60)	12-18 years Mean 15.9	66%	100% (Mean 5.33 days)	ISS Range 1-29 Mean 9.71	not reported	not reported
Hu, 1994, Canada (67)	5-16 years Mean 11.0 years	58%	100% (Mean 21.0 days)	ISS 8-15 24% 16-23 36% $\geq$ 24 32%	not reported	Head (40%) Face, chest, abdomen (29%) Extremities-external (23%)
Jagnoor, 2017, India (72)	2-16 years	72%	100% (0-1 days 30% 2-7 days 53% > 8 days 16%)	No measure (used hospital length of stay and whether or not surgery was required)	Motor Vehicle Related (35.8%) Fall (48.5%) Burn (5.7%) Poisoning (0.5%) Mechanical (6.2%)	not reported

Author, year, country	**Age at time of injury**	**% Male**	**% hospitalized (length of stay)**	**Injury Severity**	**Mechanism of Injury**	**Injury Type (%)**
Kassam-Adams, 2015, USA (54)	Mean 12.1 years	69%	100% (not reported)	not reported	Recreational activities (29%) Organized sports (27%) Falls (22%) Motor vehicle crashes (15%) Animal bites (3%) Other circumstances (4%)	not reported
Kendrick, UK, 2017 (53)***	2-5 years Mean 35.74 months	51.4%%	not reported	Measured by proxy	Fall down stairs or steps (20.9%) Fall on one level (26.4%) Fall from furniture (26.4%) Poisoning (23.0%) Scald (3.4%)	Loss consciousness (2.7%) Bang on head (37.8%) Fracture (10.1%) Cut needing stitches (8.8%) Cut or graze not needing stiches (14.2%) Other injury (20.3%)
Landolt, 2009, Switzerland (70)	6.5-14.5 years Mean 9.82 years Median 9.38 years	54.4%	100% (Mean 10.05 days Median 5.5 days)	MISS Mean 10.21, Median 9	Motor Vehicle Accident (100%) Car passenger (14.7%) Bicycle/motorcycle (30.9%) Pedestrian (44.1%) Other (10.3%)	Minor head injuries (58.8%) Lower extremity fractures (16.2%) Upper extremity fractures (14.7%) Non-extremity fractures (36.8%) Internal injuries (16.2%)
Mestrovic, 2013, Croatia (61)	1 month-18 years Mean 10 years	63%	100% in PICU	ISS Mean 20.14	Road traffic accident (68%) Falls (26%)	Head Injury (63.6%)

Author, year, country	Age at time of injury	% Male	% hospitalized (length of stay)	Injury Severity	Mechanism of Injury	Injury Type (%)
Polinder, 2005, The Netherlands (42)	5-14 years Mean age 9.6 years	57%	32.8% Hospitalized, 64.2% Not admitted, , (1-3 days 28%, % ≥ 4 days 4.8%)	not reported	Home/leisure (65%) Traffic (14.5%) Sport (19.1%) Intentional (.5%)	Head (18.5%) Face (4.9%) Upper extremity fracture (33.1%) Lower extremity fracture (12.8%) Dislocation upper and lower extremity (6.5%) Internal organ injury (2.8%) Minor external (12.5%) Other (8.9%)
Schneeberg, 2016, Canada (75)	0–17 years Mean 7.9 years Median 7.1 years	62.3	27.5% Hospitalized 72.5% ED (Median 2.7 days)	PaedsCTAS 1 (requires resuscitation; 5.4%) 2 (18.6%) 3 (21.1%) 4 (51.0%) 5 (non-urgent; 3.9%)	Leisure/entertainment activities (32%) Sports/exercise (31%)	Head injury 8.8% Lower extremity fracture 12.3% Major trauma 7.8% Minor external injury 37.7% Upper extremity fracture 24.0% Other 9%
Schweer, 2006, USA (62)	5-17 years 5-9 years (49%) 10-17 years (51%)	85%	100% hospitalized	ISS 1-9 (50%) 10-14 (28%) >15 (22%)	Bike (27%) Motorized vehicle occupant (20%) Fall (13%) Pedestrian (12%)	Head (33%) Face (19%) Chest (20%) Abdomen (38%), Extremity (40%) External (74%)
Sluys, 2015, Sweden (73)	10-16 years Median 13 years	64.7%	61% Hospitalized 39% ED only 24.4% PICU (Median 2 days)	ISS <= 8 65.5% 9-15 26% >= 16 8.5%	Traffic related (38%) Fall (40%) Other (21.5%)	Head (45.8%) Extremities (20%)

Author, year, country	Age at time of injury	% Male	% hospitalized (length of stay)	Injury Severity	Mechanism of Injury	Injury Type (%)
Stevens, 2012, USA (31)***	2-18 years Mean 8.4 years	59.3%	ED discharged home - 100%	not reported	not reported	Face/head/neck (42%) Upper extremity (32.6%) Torso/spine (3.6%) Lower extremity (21%) Facture (24.6%) Cutaneous (57%) Sprain/strain (11%) Minor head (7.2%)
Sturms, 2003, The Netherlands (76)	8-15 years Mean 12 years	57%	24% Hospitalized (Median 7 days Range 1-69 days)	ISS Mean 4.31-3 52%	Motor vehicle related 100% Cyclist (65%) Pedestrian (11%) Motor vehicle passengers (11%) Bicycle passengers (10%) Other road users (3%)	Extremity injuries (58%) Injuries affecting the face (18%) Head (15%) Thorax or abdomen (8%)
Sturms, 2005, The Netherlands (65)	8-15 years Mean 12.2 years	53%	19% (not reported)	ISS 1-3 17.64% 4-8 11.52% >= 9 17.9%	Motor vehicle related (47%) Cyclist (57%)	Intracranial head injury (29%) Fracture of the upper extremity (33%) Lower extremity fracture (8%)
Valadka, 2000, Canada (68)	≤ 18 years Mean 13 years	61%	100% (not reported)	ISS Mean 16.8	Motor vehicle related (67%) Sports (12.9%) Fall (12.1%) Other (7.8%)	Head (67%) Truncal (44%) Extremity upper (23%) Extremity Lower (26%)
Valovich McLeod, 2009, USA (63)	Injured age Mean 15.9 years Uninjured age Mean 16 years	44% of the injured 48% of the uninjured	not reported	not reported	Sports injury 100%	Lower extremity (65%) Upper extremity (29%) Overuse injuries (21%) Sprains (17.5%) Strains (15.8%) Contusions (10.5%) Fractures (7.0%) Head Injuries (3.5%) Postsurgical injuries (1.8%)

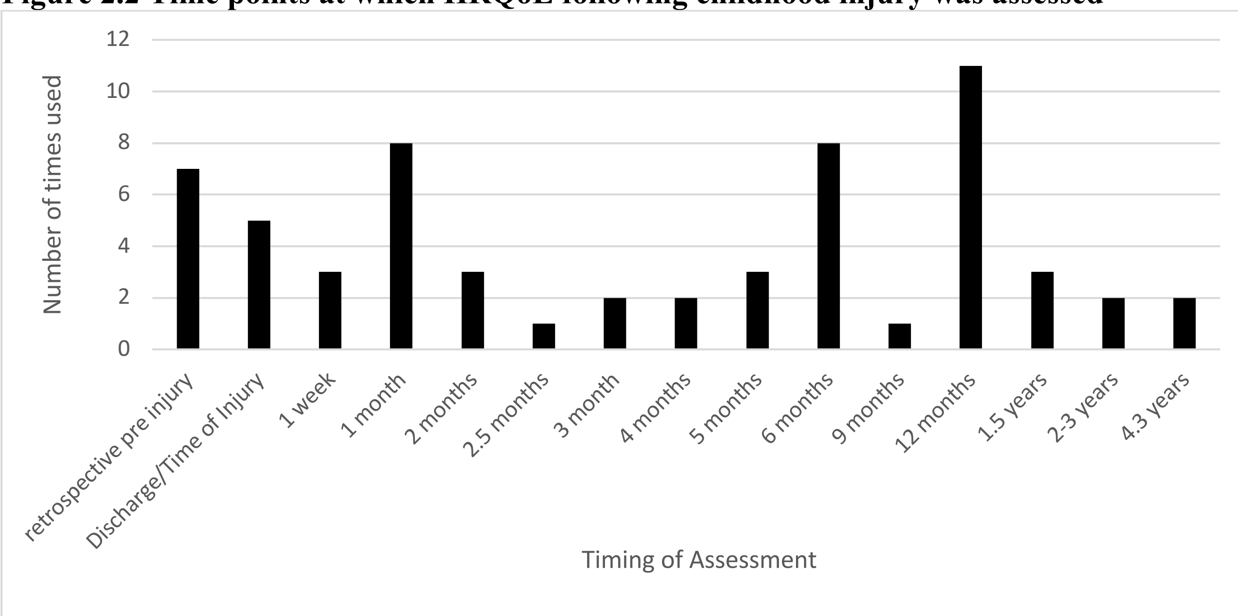
Author, year, country	Age at time of injury	% Male	% hospitalized (length of stay)	Injury Severity	Mechanism of Injury	Injury Type (%)
Van de Voorde, 2010, Belgium (74)	Control Mean 9.99 yrs Trauma Mean Mean 9.32 yrs	64% for both groups	100% all > 48 h (Median 6 days Range 2-124 days)	ISS Range 1-43 Median 9 > 15 38%	Motor vehicle related (36%) Fall (19%) Burn (13%)	Serious to critical brain injury (38.6%) Moderate injury of extremities or pelvis (17.9%)
van der Sluis, 1997, The Netherlands (66)	6-15 yrs Mean 11 yrs	50%	100% (Mean 32 days Range 5-132)	ISS mean 29 range 17-57	Motor vehicle related (85%)	Head/neck area (80%) Chest (32%) Extremities (32%)
Vollrath, 2005, Switzerland (71)	6-14.5 yrs Mean 9.8 yrs	64.5%	100% (not reported)	MISS mean 8.8 range 1-50 children incurred severe injuries >= 25	Motor vehicle related (57%) Leisure time accident (43%)	Upper extremity fracture (10%) Lower extremity fracture (17%) Non-extremity fracture (27%) Minor head injury (47%) Internal injury (14%) Burns (12%) Combined injury (36%)
Wesson, 1989, Canada (69)	0-17 yrs Mean 8.5 years	64%	100% (Mean 22 days, Median 12 days Range 0-297 days)	ISS Range 8-75 Mean 24 Median 25	Motor vehicle related (62%) Fall (23%) Child abuse (4%) Other (12%)	Head (76%) Face (18%) Chest (24%) Abdomen (32%) External (23%) Extremities (46%)
Winthrop, 2005, USA (77)	1-18 yrs Mean 9.3 years 1-4 28% 5-9 23% 10-14 31% 15-18 18%	68%	100% (Mean 6.6 days)	ISS Range 9-43 Mean 14 9-15 68% >= 16 32%	Motor vehicle related (43%) Fall (22%) Sports/recreation (20%) Burn (9%) Other (6%)	Femur fracture (45%) ** Abdomen (18%) Burns (11%) Other extremity (10%) Head (7%) Pelvic fracture (6%) Thorax (3%
Zatzick, 2008, USA (58)	12- 18 yrs Mean 15.9	67%	100% (Mean 5.3 days)	ISS Mean 9.7	not reported	not reported

* Abbreviations used: ED = emergency department, ISS = injury severity score, PaedsCTAS = Paediatric Canadian Triage and Acuity Scale
**discrepancy in written results and table, result from table is presented
*** Validation study

Seventeen studies were limited to participants who were admitted to the hospital due to their injuries (30,43,54,58–61,66–74,77,78) with six requiring hospital admission longer than 24 hours and/or an injury severity score (ISS) (79) ≥ 9 (30,61,70,72,74,77).

Thirteen different HRQoL instruments were used across all of the studies with the PedsQL being applied most frequently (n=7, 25.9%) (Table 2.3) (30,31,54,72,73,75). Eighteen studies (66.7%) collected HRQoL at more than one time point with the most common timing of data collection being 12 months post-injury which was collected in 11 of the 27 studies (40.7%) (Figure 2.2, Table 2.3) (30,41,58,60,61,63,67,70–72,75).

Figure 2.2 Time points at which HRQoL following childhood injury was assessed



Of the studies that collected data at 12 months post-injury, follow-up rates ranged from 63% to 100% at that time point. Seven papers collected a retrospective measure of pre-injury HRQoL at the time of injury (31,53,58,60,65,72,75), while 13 papers compared injured children's HRQoL to population norm scores (30,41,43,58,59,62,64,66,70–72,76,77). Ten of 27 studies had only a child self-reported measure of HRQoL (41,54,58,60,63–66,70,71), three had both parent/guardian report and child self-report HRQoL scores (31,73,76) while the remaining 14 studies had only parent/guardian report HRQoL.

Table 2.3 Health related quality of life measurement across studies

Author, Year	n (at baseline)	HRQoL Instrument	Reporter	Timing of HRQoL Measurement (% follow-up if reported)	Bivariable Predictors of HRQoL
Aitken, 2002 (59)	195	CHQ-PF50	Parent or Guardian	Discharge (100%) 1 month (88%) 6 months (73%)	ISS > 16 associated with lower HRQoL at discharge and 1 month
Davey, 2005 (43)	241	CHQ-PF50	Parent or Guardian	1-2 years following injury, average time since admission 1.5 years	None reported
Dekker, 2004 (64)	100	CHQ-CF87	Child self-report	Range 2-7 years Mean 4.3 years following injury	Age, older age associated with lower HRQoL Level of riding proficiency (advanced vs beginners) - advanced rider associated with lower HRQoL Type of injury (all other injures, vs fractures of the extremities) - other injuries associated with lower HRQoL Whether the patient sustained new injury follow their horse-riding accident - additional injury associated with lower HRQoL
Gabbe, 2011 (30)	150 (96% complete data at all time points)	CHQ-PF28 and PedsQL	Parent or Guardian	1 month 6 months 12 months	Head injured patients and those in the "other" injury category demonstrated the lowest physical and psychosocial health scores at 12 months
Han, 2011 (57)	For this analysis 399	Quality of well-being scale (ranges from 0 for death and 1 for asymptomatic full functioning)	Child self-report	discharge (100%) 3 months (96%) 6 months (89%) 12 months (89%) 18 months (88%) 24 months (88%)	Adolescents with clinically significant depression post-injury had significantly lower QoL at all follow-up points 3-24 months

Author, Year	n (at baseline)	HRQoL Instrument	Reporter	Timing of HRQoL Measurement (% follow-up if reported)	Bivariable Predictors of HRQoL
Holbrook, 2007 (41)	For this analysis 356	Quality of well-being scale (ranges from 0 for death and 1 for asymptomatic full functioning)	Child self-report	discharge (100%) 3 months (96%) 6 months (89%) 12 months (89%) 18 months (88%) 24 months (88%)	HRQoL scores at 18 months follow-up were lower in adolescent girls than in boys, and older adolescents (aged 16 to 19 years) compared with younger adolescents. Other factors significantly associated with long-term QoL deficits were perceived threat to life, pedestrian struck mechanism, an ISS of greater than 16, and three or more body regions injured.
Holbrook, 2005 PTSD (56)	For this analysis 381	as above	as above	as above	QoL outcomes based on the QWB score at follow-up were significantly lower in injured adolescents with long-term PTSD compared with subjects without PTSD.
Holbrook, 2005, Acute Stress (55)	Not reported	as above	as above	as above	QoL outcomes were significantly lower in injured adolescents with ASD compared with study subjects without ASD before discharge. This effect was significant beginning at 3-month follow-up and continued through the last long- term follow-up time point, 24 months.
Herz, 2012 (40)	108	Youth Quality of Life Instrument (Items are on a 10-point scale ranging from 0 not at all to 10 completely)	Child self-report	retrospective baseline (97%) 2 months (87%) 5 months (83%) 12 months 89%	The following were associated with lower HRQoL scores: - being female relative to male - being of non-white race relative to white race - having lower household income relative to higher household income - baseline post-traumatic stress syndrome - subsequent post-traumatic stress syndrome - depressive symptoms - pre- and post-injury traumatic or stressful life events
Hu, 1994 (67)	92	RAND health insurance study (Physical health scales)	Parent or Guardian	Discharge 6 months 1 year	head injuries experienced the slowest recovery, those with extremity injuries recovered more quickly
Jagnoor, 2017 (72)	373	PedsQL (0-100 with higher scores reflecting better HRQoL)	Parent or Guardian	retrospective baseline (100%) 1 month (75.3%) 2 months (75.6%) 4 months (74%) 12 months (80%)	None investigated

Author, Year	n (at baseline)	HRQoL Instrument	Reporter	Timing of HRQoL Measurement (% follow-up if reported)	Bivariable Predictors of HRQoL
Kassam-Adams, 2015 (80)	177	PedsQL (0-100 with higher scores reflecting better HRQoL)	Child self-report	6 months (80%)	On average, children screening as ‘‘at risk’’ on the three-component study screening protocol were approximately two-thirds of a standard deviation lower in PedsQL score at 6 months than those who screened as low risk
Kendrick, 2017 (53)	148	Toddler version of the PedsQL (0-100 with higher scores reflecting better HRQoL)	Parent or guardian	2 weeks post-injury & retrospective baseline (n = 148) 1-month (n=16) 3 months (n = 4) 12 months (n=2) months post-injury -- individuals were not lost to follow-up per se, they recovered and did not return subsequent surveys as a result	Analyses limited to responses from 2 weeks post injury due to sample size. Being treated for an injury, undergoing radiography, and receiving medication following their injury were all associated with statistically significantly lower HRQoL
Landolt, 2009 (70)	68	TACQOL German version of a short form of the Toegepast Natuurwetenschappelijk Onderzoek-Academisch Ziekenhuis Leiden (TNO-AZL) Children’s Quality of Life (TACQOL) questionnaire, Child Form. Higher scores represent better HRQoL.	Child self-report	1 month 1 year	Girls reported poorer HRQoL at 1 month compared to boys, life events preceding accident were significantly related to HRQoL at 1 year, the child’s functional status at 1 month was associated with the overall HRQoL at the first assessment, TACQOL total score at 1 month was significantly correlated with the TACQOL total score at 1 year; child’s PTSS at 1 month was significantly correlated with HRQoL at both assessments
Mestrovic, 2013 (61)	118	Royal Alexandra hospital for children measure of function. Scored 1-100, patients divided into 2 groups score of 81-100 for minimal ongoing problems, and score below 80 points to obvious health problems and impaired quality of life	Parent or Guardian	At time of injury 12 months (100%, no loss to follow-up)	Having a head injury: a greater proportion of children with head injuries fell into the lower HRQoL group relative to other injuries. Circumstance of injury being road traffic accident: a greater proportion of children that had been in a road traffic accident fell into the lower HRQoL group relative to children who had other circumstances of injury

Author, Year	n (at baseline)	HRQoL Instrument	Reporter	Timing of HRQoL Measurement (% follow-up if reported)	Bivariable Predictors of HRQoL
Polinder, 2005 (81)	527	EuroQol 5D classification of health. Health is defined along 5 dimensions of 3 levels. The EQ5D summary score ranges from 1 for full health to 0 for death.	Parent or Guardian	2.5 months (100%) 5 months (73%) 9 months (69%)	At 9 months post-injury, girls had higher odds of suboptimal functioning than boys and hospitalized children had higher odds of suboptimal functioning than those not hospitalized
Schneeberg, 2016 (1)	256	PedsQL (0-100 with higher scores reflecting better HRQoL)	Parent or Guardian	Retrospective baseline (100%) 1 month (90.6%) 4 months (82.8%) 12 months (62.9%)	One-month post-injury older children had lower HRQoL than younger; those hospitalized had lower HRQoL than those not hospitalized, those with lower PaedsCTAS score had lower HRQoL than those with higher PaedsCTAS score, those with major trauma and lower extremity fractures reported lower HRQoL relative to other injury types. Four months post-injury, children 6-10 years had lower HRQoL relative to other children
Schweer, 2006 (62)	161	CHQ-PF50	Parent (for this study)	1 month (100%) 6 months (79.5%)	At 1 month post-injury: higher ISS, Face injury and Extremity injuries were associated with lower HRQoL. At 6 months post-injury: older age, higher ISS relative to lower ISS, lower Glasgow Coma Score relative to higher Glasgow Coma Score, having an extremity injury relative to all other injuries were associated with lower HRQoL
Sluys, 2015 (73)	177	PedsQL (0-100 with higher scores reflecting better HRQoL)	Parent & Child self-report	6 years after injury	None reported
Stevens, 2012 (31)	404	PedsQL 0-100, higher scores indicate better quality of life	Parent & Child self-report	retrospective baseline at time of injury 100% 1-2 weeks after injury 82.7%	Increased number of days of pain, and Increased number of days with missed or disrupted activities were both associated with decreased HRQoL
Sturms, 2003 (76)	157	TACQOL	Parent and child self-report	mean follow-up time was 2.4 years (range 1.5-3.4 years) after the accident	ISS was significantly associated with scores in the motor scale, with children with severe injuries (ISS $\geq$ 9) reporting more problems in this scale compared with children with lower ISS scores

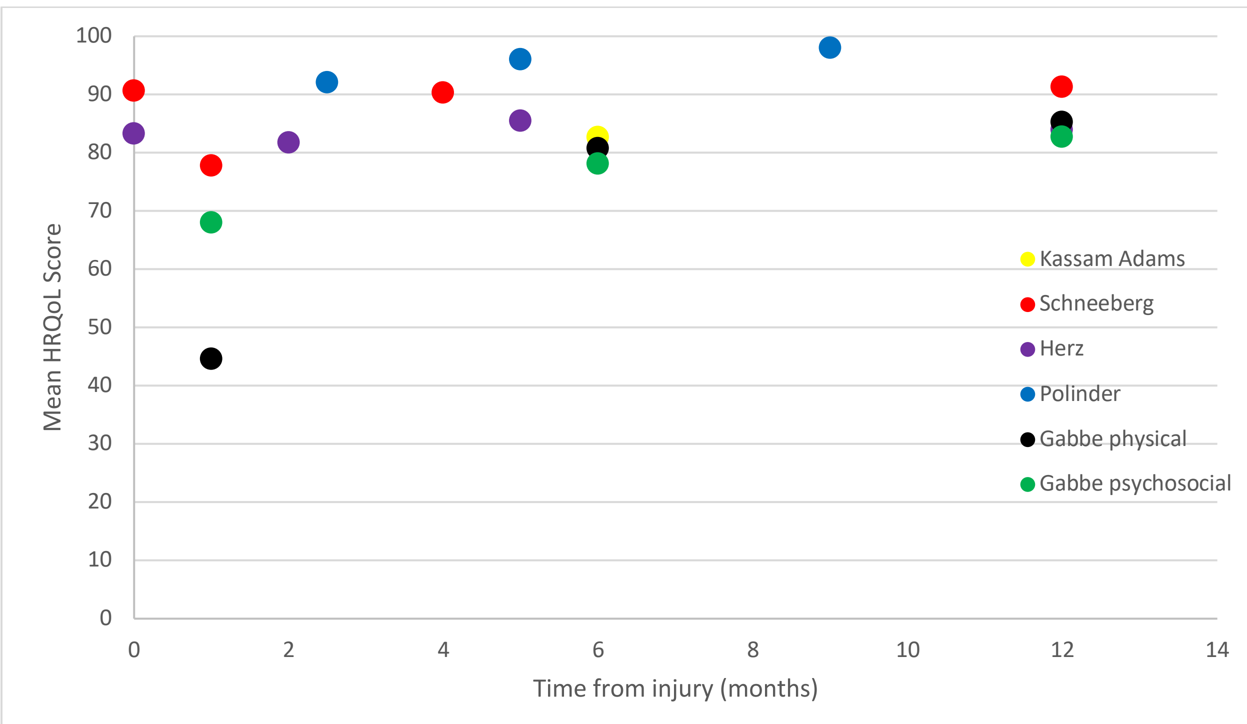
Author, Year	n (at baseline)	HRQoL Instrument	Reporter	Timing of HRQoL Measurement (% follow-up if reported)	Bivariable Predictors of HRQoL
Sturms, 2005 (65)	79	TACQOL	Child self-report	retrospective baseline measurement shortly after accident 100% 3 months (81%) 6 months (64.6%)	None reported
Valadka, 2000 (68)	116	Modified Rand Health Insurance Study	Parent or guardian	Mean 4.4 years	ISS, post-traumatic stress, number of injuries, truncal injury, leg injury and mechanism of injury had significant correlations with presence of disability
Valovich McLeod, 2009, (63)	169 uninjured, 45 injured	SF36 (0-100 with higher scores reflecting better HRQoL)	Child self-report	Injury within one week	None reported
Van de Voorde, 2010 (74)	133 propensity score matched pairs of injured & control	ICF IROS - 54 questions, 4 sum scores physical, mental, social and total measure the overall burden of health problems on an 11 point scale between 0 no burden to 10 maximum burden	Parent or guardian	12 months after injury	State at discharge (normal, mild, moderate, severe) was significantly associated with the latent trait 'health status' with more severe state at discharge being associated with worse health status
van der Sluis, 1997 (66)	50	RAND-36 - measures health from 8 multi item perspectives each subscale score ranges from 0-100 with higher score indicating better quality of life. Identical to the SF36	Child self-report	average of 9 years (7-11 years) after injury	None reported
Vollrath, 2005 (71)	138	German version of TACQOL	Child self-report	1 month 138 1 year 107 - complete case analysis	Girls reported lower HRQoL scores than boys at both time points, MISS correlated with HRQoL at 1 month but not at one year, Concurrent physician rate functional status correlated with HRQoL at both time points
Wesson, 1989 (69)	250	Questions developed for the RAND Health Insurance Study, dichotomized to those with disability and those without	Parent or guardian	discharge (100%) 6 months after injury (62.4%)	None
Winthrop, 2005 (77)	162	CHQ-PF28	Parent or guardian	1 month 80% 6 months 50%	ISS - significant negative correlation between ISS and the CHQ-IT physical ability and behaviour overall sub scores

Author, Year	n (at baseline)	HRQoL Instrument	Reporter	Timing of HRQoL Measurement (% follow-up if reported)	Bivariable Predictors of HRQoL
Zatzick, 2008 (58)	108	CHQ-87	Child self-report	Retrospective Baseline (100%) 2 Months (87%) 5 Months (83%) 12 months (82%)	None reported

2.4.4 HRQoL over time

Given the heterogeneity of the studies included in this review with regard to timing of assessment, instruments used and study population, a metanalysis of these data was not attempted. Data from studies that collected HRQoL with an instrument that rated HRQoL from 0-100 with 0 representing worst possible health state and 100 being the best possible health are summarized in Figure 2.3 (27,54,60,75,81). The instruments included were the PedsQL (30,75,82), the Youth Quality of Life Instrument (60) and the EQ5D (42).

Figure 2.3 Summary of HRQoL* scores (0-100) at each time point



* HRQoL instruments used: Kassam Adams (PedsQL), Schneeberg (PedsQL), Herz (Youth Quality of Life Instrument), Polinder (EQ5D), Gabbe (PedsQL)

Twelve studies (44.4%) reported that the injured population's HRQoL remained statistically significantly lower relative to a retrospective baseline measurement, or population norm values at the final follow-up between one week and 4.3 years after injury (27,41,43,58,59,62–64,74,76,77,83) (Table 2.5). Of these twelve studies, seven (58.3%) had the final assessment of HRQoL at or beyond one year post-injury (27,41,43,58,64,74,76). Eight of the 27 studies (29.6%) reported their injured population HRQoL values returned to baseline/population norm values within the study period and seven studies did not make a comparison between the injury population at follow-up and a baseline measure or population norm value (Table 2.4).

Among the studies reporting decreased HRQoL at one year or more post-injury, four studies reported decreased scores on all or most of the measured health domains (41,43,64,74). Zatzick et al.(58) reported decreased scores on the physical domain and Sturms et al. reported the injured population had more problems in motor and autonomy scales, but they had fewer physical complaints relative to uninjured peers (76). Gabbe et al measured HRQoL with two instruments, with CHQ-87 results demonstrating decreased physical domain scores but not psychosocial at 12 months and conversely psychosocial scores were decreased at all follow points including 12 months on the PedsQL and the physical health summary score had returned to baseline by the final assessment (30). These studies covered all pediatric age groups, circumstances of injury and types of injuries. In five of the seven studies with decreased HRQoL at one year or more post-injury, 100% of the injured population had been hospitalized for their injury (27,41,43,58,74). The remaining two studies with decreased HRQoL had only 16% (64) and 24% (76) of the injured populations being admitted to hospital at the time of injury.

2.4.5 Predictors of HRQoL

Of the 30 manuscripts included in this review, approximately half (n=14, 46.7%) performed a multivariable analysis examining predictors of HRQoL (1,41–43,58,60,62,64,65,68,70,71,73,83). Tables 2.3 and 2.5 summarize the predictors that were evaluated in bivariable and multivariable analyses.

The following variables were found to be statistically significantly associated with decreased HRQoL in at least one of the adjusted models: female gender, older age, more severe injury (as measured by ISS, or injuries requiring hospitalization vs those not requiring hospitalization), lower extremity fractures (vs upper extremity fractures) and symptoms of PTSD post-injury. Details of variables investigated as predictors of HRQoL in multivariable models can be found in Table 2.5 (details in Appendix D).

Table 2.4 HRQoL recovery across studies

Instrument	Author, Year	Last follow-up	HRQoL Deficits at last follow-up	Comparison Group
CHQ-PF50				
	Aitken, 2002 (59)	6 months	Yes Mean physical and psychosocial summary scores statistically significantly lower than the normative population	Normative sample of 391 healthy children from large national surveys, benchmark mean scores of chronically ill children
	Davey, 2005 (43)	1-2 years post-injury	Yes on the majority of subscales of CHQ study participants recorded scores statistically significantly lower	Australian normative population
	Schweer, 2006 (62)	6 months	Yes mean statistically significantly lower than norm population	US population norms
CHQ-CF87				
	Dekker, 2004 (64)	Mean 4.3 years	Yes In relation to the reference population patients had significantly lower outcome regarding physical functioning, role functioning, physical, bodily pain, general behaviour, mental health, self-esteem and family cohesion. In comparison with matched controls, patients had more complaints about physical functioning.	Reference data on Dutch school children and healthy friend
	Zatzick, 2008 (58)	12 months	Yes injured adolescents had significantly lower scores on the physical function, role/social physical, bodily pain, general health perceptions and family cohesion subscales.	Population norms
CHQ-PF28				
	Winthrop, 2005 (77)	6 months	Yes Physical CHQPF28 scores remained statistically significantly lower than normative comparison group at 6 months There was no statistically significant difference in psychosocial score from normative population at 6 months.	Population norms

Instrument		Last follow-up	HRQoL Deficits at last follow-up	Comparison Group
	Gabbe, 2011 (30)	12 months	Yes Physical health scores were significantly below population norms at all time points. Psychosocial summary score was no longer different from population norms at 6 months.	Population norms
PedsQL				
	Gabbe, 2011 (30)	12 months	Yes Psychosocial summary scores were statistically significantly lower than population norm values across all time points. Physical summary score returned to baseline at 12 months.	Population norms
	Jagnoor, 2017 (72)	12 months	No No significant differences from baseline to 12 months post-injury across all age groups. By 4 months post-injury both physical and psychosocial summary scores had returned to baseline values across all age groups.	Retrospective baseline measurement at time of injury
	Kassam-Adams, 2015 (80)	6 months	No comparison made with baseline/reference population (compares injured children screening at high risk for post-traumatic stress to those at low risk of post-traumatic stress)	
	Kendrick, 2017 (53)	12 months post-injury	No Over 95% of children recovered within 2 weeks of injury and almost 99% recovered within 1 month	Age and sex matched community controls
	Schneeberg, 2016 (1)	12 months	No Summary scores returned to baseline by 4 months post-injury	Retrospective baseline measurement at time of injury
	Sluys, 2015 (73)	6 years	No comparison made with baseline/reference population	
	Stevens, 2012 (31)	1-2 weeks post-injury	Yes Effect sizes for the full sample of all injuries were small for total score, moderate to large for the physical summary score, and minimal or insignificant in the psychosocial summary score.	Retrospective baseline measurement at time of injury

Instrument		Last follow-up	HRQoL Deficits at last follow-up	Comparison Group
Quality of Well Being Scale				
	Holbrook, 2007 (41)	24 months	Yes QoL outcomes throughout the long-term follow-up period of 24 months were significantly and markedly lower in injured study participant relative to population norms.	Uninjured National Health Institute Survey adolescents
	Han, 2011 (57)			
	Holbrook, 2005 PTSD (56)			
	Holbrook, 2005, Acute Stress (55)			
Youth Quality of Life Instrument				
	Herz, 2012 (40)	12 months	No There was no significant difference in total QOL between study group and comparison group at either baseline or 2 months post-injury, the study group showed normative levels of overall QOL at both times, at 5 months and 12 months post-injury the study sample reported significantly better overall QOL than the comparison group.	age matched cohort of non-injured typically developing adolescents
Rand				
physical health scales	Hu, 1994 (67)	12 months	No statistical tests done however a greater proportion of trauma patients relative to controls had ongoing limitations at 1 year follow-up (55.4% relative to 8.5%)	59 children with uncomplicated appendicitis requiring appendectomy
	Valadka, 2000 (68)	4.4 years	No comparisons made with baseline/population norms. Forty seven percent of the sample reported disability at time of follow-up.	No comparison
Rand 36	van der Sluis, 1997 (66)	Mean 9 years	No There were no statistically significant differences between the pediatric patients and the reference populations regarding any concept measured by the Rand.	Healthy Dutch reference population n 18-24 years of age

Instrument		Last follow-up	HRQoL Deficits at last follow-up	Comparison Group
	Wesson, 1989 (69)	6 months	No comparisons made with baseline/population norms. Fifty four percent of the sample reported disability at time of follow-up.	
TACQOL				
	Landolt, 2009 (70)	12 months	No HRQoL was significantly lower at 1 month, however not significantly lower at 1 year.	1048 healthy Dutch children
	Sturms, 2003 (76)	Mean 2.4 years	Yes Traffic victims differed from reference group at follow-up in the physical scale of the TACQOL, traffic victims reported FEWER physical complaints compared with the reference group but reported more problems in the motor and autonomy scales.	Reference data gathered from 2 random sample groups of children from the general Dutch population
	Sturms, 2005 (65)	6 months	No Summary score returned to baseline by 6 months post-injury	baseline retrospective score
	Vollrath, 2005 (71)	1 year	No There was a statistically significant difference at 1 month but not one year between injured population and healthy population norms.	861 healthy children 8-11 years
Royal Alexandra hospital for children measure of function				
	Mestrovic, 2013 (61)	12 months	No comparisons made with baseline/population norms. Fifty four percent of the sample reported disability at time of follow-up.	
EQ5D				
	Polinder, 2005 (81)	9 months	No comparison made with baseline/population norm. Of all the injured children, 8% still reported functional limitations after 9 months.	None

Instrument		Last follow-up	HRQoL Deficits at last follow-up	Comparison Group
SF36				
	Valovich McLeod, 2009, (63)	1 week	Yes Adolescent athletes with self-reported injuries demonstrated lower HRQoL than their uninjured peers. Domains that were decreased included physical functioning, pain, social functioning and global HRQoL.	Uninjured adolescent athletes
ICF IROS				
	Van de Voorde, 2010 (74)	12 months	Yes There were statistically significant differences for emotional problems, mobility, societal life, burden on family and for all burden sum scores between trauma and no trauma group.	children without recent severe trauma or severe chronic disease, recruited from different groups: children of hospital personnel, a nursery and a secondary school
PODCI				
	Valovich McLeod, 2009, (63)	1 week	Yes Adolescent athletes with self-reported injuries demonstrated lower HRQoL than their uninjured peers. Domains that were decreased included physical functioning, pain, social functioning and global HRQoL.	Uninjured adolescent athletes

Table 2.5 Predictors of HRQoL following childhood injury from multivariable models across studies

	Higher ISS/MISS*** scores	Female Sex	Age Group	PTS/ PTSD post-injury	Hospitalized	Cause of injury	Baseline HRQoL	Type of injury	Multiple injuries	Race other than Caucasian
Number of studies with listed variable in a multivariate model	9	10	8	2	3	2	5	5	2	2
Number of studies with listed variable having a significant association ($p < 0.05$) with HRQoL	4 ISS - 1 ISS +	3 Female - 1 Female +	5 older - 1 older +	2 -	3 -	1 -	3 +	4^	1 -	1 -

* For details of significant associations see Appendix D
** "-" indicates variable is associated with lower HRQoL, "+" indicates variable is associated with higher HRQoL
*** ISS = injury severity score, MISS = modified injury severity score
^ 1: truncal and leg injury had higher odds of disability relative to other injuries, 2: lower HRQoL for injuries not concerning an extremity fracture relative to individuals with a fracture of the extremities, 3: injury to an extremity was significantly associated with lower physical health summary score whereas injury to head/neck was significantly associated with lower psychosocial summary score,4: lower extremity fractures associated with lower HRQoL compared with children with upper extremity fractures or without an extremity fracture

2.4.6 HRQoL variable distribution and analyses used

Of the 27 studies included, three (11.1%) directly stated the distribution of the HRQoL variable. One study indicated the TACQOL composite score was normally distributed at both time points collected (70), one study found the TACQOL composite score was normally distributed at one year and skewed at one month (71), and the third indicated the SF36 was skewed at the single time point it was collected (within one week of injury) (63). Two additional studies did not mention testing for normality but one implied the ICF IROS variable had a skewed distribution in the discussion (74). The other did not report on normality, but presented both the mean and median CHQ-PF50 scores and given the difference in the two measures there is evidence of skewness (43). Finally, one study indicated in the analysis section that they tested for normality of the PedsQL summary scores, but did not report the results (31). The remaining 21 studies did not report on the distribution of the HRQoL variable. In terms of adjusting the analysis to account for a skewed distribution, of the 27 studies, only two (7.4%) indicated they used non parametric tests due to lack of normality of the HRQoL variable when examining the relationship between it and demographic and injury related variables (63,71).

Three studies reported on the possibility of a ceiling effect with the HRQoL instrument used: Gabbe et al. found that only the physical summary score of the PedsQL demonstrated a substantial ceiling effect (27), Kendrick et al. found ceiling effects for the four domains of the toddler version of the PedsQL and stated they were less marked for the psychosocial summary and total PedsQL scores relative to the physical summary score (53), and Stevens et al. found that at one week post-injury there was minimal evidence of ceiling effect with parent report PedsQL and none with child report (31). The remaining studies did not report on the number or proportion of participates receiving the upper bound score on the HRQoL instrument used.

Eighteen studies collected HRQoL data at more than one time point, with ten collecting HRQoL data at more than two times points. Of those that collected data at more than two time points, four performed longitudinal analyses, with one study using repeated measures analysis (59), two built multilevel mixed effects models (58,60) and one using multivariable generalized estimating equations (1) (Table 2.6).

Table 2.6 Statistical analyses across studies

Author, Year	Study Type	Type of bivariable statistics	Multivariable Modelling	How were missing data addressed
Aitken, 2002 (59)	Prospective Cohort	Differences between mean CHQ domain scores for the injury population and other populations for normal and chronically ill children were compared using t tests	To compare subgroups of different severity within each of the CHQ subscales, a repeated measures analysis was used with the subgroup as a fixed effect. Differences among subgroups were then examined at each time point using least square means.	Not reported
Davey, 2005 (43)	Historical Cohort	CHQ-PF50 scores for study respondents were compared with Australian norms using z-statistics.	"Multiple regression analyses" conducted to investigate variables predicted CHQ summary scores	Cross sectional, no missing data
Dekker, 2004 (64)	Cross Sectional	Chi square and t tests used to compare means of continuous variables	To determine if variables were risk factors of disability, chi square tests and ANOVA were performed. The outcome was the physical functioning scale of CHQ-CF87. To determine long term problems, variables were then entered in a logistic regression with CHQ-CF87 dichotomised into favourable scores and unfavourable.	Cross sectional, no missing data
Gabbe, 2011 (30)	Prospective Cohort	Mean HRQL summary scores were compared with population norms for the CHQ-PF28, and healthy children for the PedsQL, using independent t tests. Change in instrument scores over time was assessed using multilevel mixed effects models with a random effect for participant	None	Complete case analysis, 96% complete data at all time points
Holbrook, 2007 (41)	Prospective Cohort	Student's t test and ANOVA to compare participant HRQoL to NHIS scores. The association of HRQoL outcomes scores with demographic injury event related factors, mechanism and injury severity variables was analyzed with student's t test and ANOVA	"Multivariately adjusted" model predicting QWB scores at 24 months	Complete case analysis
Han, 2011 (57)	as above	Pearson's chi square test	None including HRQoL	Complete case analysis
Holbrook, 2005 PTSD (56)	as above	For the QoL outcome analysis, the Student's *t* test was used to examine the difference in QWB score by PTSD status at each follow-up time point.	None including HRQoL	Complete case analysis

Author, Year	**Study Type**	**Type of bivariable statistics**	**Multivariable Modelling**	**How was missing data addressed**
Holbrook, 2005, Acute Stress (55)	as above	QoL as measured by the QWB scale was considered as the primary outcome variable. For the functional outcome analysis, the Student's t test was used to examine the difference in QWB score by ASD status at each follow-up time point. Comparisons by ASD status were made using 2 analysis and the association of ASD with injury-event related factors and mechanism were quantified using the odds ratio.	None including HRQoL	Not reported
Herz, 2012 (40)	Prospective cohort	unpaired 2 sided t tests were conducted to evaluate differences between study participant QoL and that of the comparison sample at each of the 4 time points.	Mixed model regression	a variety of imputation methods
Hu, 1994 (67)	Prospective Cohort	Chi square tests were used to examine whether the frequency distribution of one variable was significantly different at various levels of another variables, fisher's exact test was applied if 25% of more cells had an expected value less than 5	None	Complete case analysis
Jagnoor, 2017 (72)	Prospective Cohort	None	None including HRQoL	Complete case analysis
Kassam-Adams, 2015 (80)	Prospective Cohort	t-tests to examine mean differences in 6-month total PedsQL score among those who were screened as at-risk of psychosocial distress versus low-risk based on the study screening protocol and calculated the effect size (Cohen's d) as the standard mean difference the between-group mean difference in PedsQL score standardized by the pooled standard deviation of the two groups.	None	Complete case analysis
Kendrick, 2017 (53)	Prospective cohort	Independent sample t-tests and ANOVA were used to compare HRQoL of different categories of injury related variables.	None	Complete case analysis for those providing data at baseline and 2 weeks post injury
Landolt, 2009 (70)	Prospective Cohort	Comparisons of TACQOL scales with published reference data were determined using one-sample t-tests. Spearman Brown rank correlations were calculated to measure associations between the TACQOL total score and various predictors. Wilcoxon matched-pairs signed-ranks tests were used to compare HRQoL scores at 1 month and at 1 year.	A linear regression model was set up using the normally distributed TACQOL total score as the dependent variable. Predictors were chosen on the basis of significant bivariate correlations with the dependent variable.	Complete case analysis

Author, Year	Study Type	Type of bivariable statistics	Multivariable Modelling	How was missing data addressed
Mestrovic, 2013 (61)	Prospective Cohort	t test for independent samples and chi-square test were used to compare 2 samples of children (head injury and other body region), Pearson correlation was used to evaluate association between RAHC and clinical scoring systems	None	Complete case analysis
Polinder, 2005 (81)	Prospective Cohort	Unadjusted logistic regression model at 9 months after injury	Adjusted logistic regression model at 9 months after injury for key indicators of functioning	nonresponse analysis performed using multivariate logistic regression at each time point all variables used to adjust for response bias. Inverse probability of response weighting used. Hot deck imputations, using the reported values of people with similar scores in the health domains.
Schneeberg, 2016 (1)	Prospective Cohort	The relationship between PedsQL score at each time point and demographic and injury related variables was explored using bivariable linear regression.	A multivariable GEE model was built including all variables identified to be statistically or conceptually important. The model was run with all observations in the analytic sample.	GEE uses all available data
Schweer, 2006 (62)	Prospective Cohort	t test was used to compare scores with US normative data and between 1- and 6-month data paired t test (parametric)	regression models at 1 and 6 months (type of regression not specified)	not reported
Sluys, 2015 (73)	Historical Cohort	Wilcoxon signed rank test were performed to test the differences in PedsQL scale and summary scores between child self-report and parent proxy	stepwise multiple regression analysis to find out how parents mental health status correlated with ratings of child HRQoL	cross sectional no missing data
Stevens, 2012 (31)	Prospective Cohort	group comparisons were made using adjusted marginal means derived from univariate generalized linear models with age and sex as covariates	Group comparisons were made using adjusted marginal means derived from univariate generalized linear models, with age and sex as covariates.	Complete case analysis

Author, Year	Study Type	Type of bivariable statistics	Multivariable Modelling	How was missing data addressed
Sturms, 2003 (76)	Historical Cohort	TACQOL scores of the traffic victims and their parents were compared with use of paired t test	TACQOL scores of the traffic victims and the reference group were analyzed with ANOVA and corrected for age, gender and the presence of chronic illnesses.	NA, only one data point
Sturms, 2005 (65)	Prospective Cohort	Univariate analyses of covariance (ANCOVAs) were applied to compare the study sample's preinjury HRQoL with the HRQoL of the reference group, taking children's age and gender into account.	Group differences over time in postinjury HRQoL were examined using three- and six-months follow-up HRQoL scores as dependent variables and the children's preinjury HRQoL scores as a covariate (repeated-measures MANCOVAs). The between-subject factors, concerned age, gender, SES, ISS, head injury, extremity fracture, need for hospitalization and accident characteristics	complete case analysis
Valadka, 2000 (68)	Historical Cohort	6 variables were tested for significance by ANCOVA against presence of any disability	logistic regression with presence of any disability as outcome	only one data point
Valovich McLeod, 2009, (63)	Cross Sectional	non-parametric Mann Whitney U test to determine group differences with results reported as median and interquartile range	None	cross sectional no missing data
Van de Voorde, 2010 (74)	Prospective Cohort	GEE approach for ordinal data to test for significant differences between trauma and control group, linear regression to investigate the effect of covariates on patient health status	None	one follow-up
van der Sluis, 1997 (66)	Prospective Cohort	A one-sample Student's t test was used to compare the study group's RAND-36 scores with the scores of a healthy reference population of 18 to 24 years of age.	The relation between short-term and long-term outcome measures was assessed by single linear regression analysis.	one follow-up, no missing data
Vollrath, 2005 (71)	Prospective Cohort	Because the TACQOL scales showed nonnormal distributions, nonparametric statistical techniques were used where possible (Wilcoxon tests for pair wise comparisons over time, spearman brown rank correlations to calculate associations)	Hierarchical regression analyses of TACQOL composite scores at 1 month and 1 year (clusters by hospital).	complete case analysis
Wesson, 1989 (69)	Prospective Cohort	The patients who were still disabled at 6 months were compared with those who had recovered via unpaired t test	None	descriptive of all available

Author, Year	**Study Type**	**Type of bivariable statistics**	**Multivariable Modelling**	**How was missing data addressed**
Winthrop, 2005 (77)	Prospective Cohort	Analysis was by paired t test for change in outcome scores over time and by unpaired t test for comparison of subgroups of study patients.	None	not reported
Zatzick, 2008 (58)	Prospective Cohort	Compared adolescent baseline and 12-month CHQ-87 subscale scores to previously published population norms using unpaired, 2-tailed t tests.	Mixed-model regression analyses were used to examine the longitudinal association between dichotomized PTSD-RI and CES-D scores and each of the 10 CHQ-87 subscales.	Mix Models uses all available data

Of the longitudinal studies that collected HRQoL at more than one time point, missing data were addressed primarily through complete case analysis (n=10), two studies performed multiple imputation (60,84), and one study used a mixed model which is appropriate for data that are missing at random (MAR) (58) (Table 2.6). None of the studies reported on missing data mechanism.

2.5 Discussion

The objectives of this review were to provide insight into the methodology used among studies examining HRQoL following childhood injury, to provide a summary of HRQoL among children following injury and to report variables identified to be predictors of HRQoL following childhood injury. Consistent with previous systematic reviews of HRQoL following injury (40,46), I found substantial heterogeneity in methodology across studies including timing of assessment, severity and circumstances of injury, and tools used to measure HRQoL. In addition, significant variation was observed in the statistical analyses applied to the HRQoL data collected, with not all of the studies using appropriate analysis for the data. Although the literature in this field is growing, with almost double the number of studies included relative to the 2012 review, the heterogeneity among study populations, HRQoL measures, outcomes and statistical analysis limits the ability to draw summary level conclusions regarding the trajectory and variables association with HRQoL.

Perhaps the most important methodological difference across studies is that in the 27 studies included 13 different HRQoL instruments. The 2007 ECOSA group guidelines for the conduct of follow-up studies measuring injury-related disability made specific recommendations of HRQoL instruments to use among adult populations; however, to date, no such recommendations have been made for children (48). Polinder et al. suggest the ideal measure should include all relevant health dimensions, produce a 0-1 range, a utility or summary score, be responsive to changes over time and be generic in nature (46). It is promising that the PedsQL was observed to be the most commonly applied instrument of the 13 tools used. This instrument meets Polinder et al.'s recommendations and there is evidence that it has good psychometric properties for the injured pediatric population including being feasible, reliable, demonstrating good construct and discriminant validity and responsiveness (31,85). The PedsQL is also appropriate for a wide pediatric age range, allows for both parent and child-response and is robust to method of application (pen and paper, telephone and internet) and as such has been recommended by studies that have reviewed tools for the purpose of long-term follow-up and assessing outcomes in pediatric trauma populations (86,87). A ceiling effect was observed in the physical summary score of the PedsQL among 150 injured children at six and 12 months post-injury by Gabbe et al, but not with the psychosocial score (30). This study only included children who were admitted to hospital with a length of stay of greater than three days, so some of the observed ceiling effect may be due to the narrowly defined population that was sampled. Stevens et al observed a ceiling effect of the total scale score and both the physical health and psychosocial health domains of the PedsQL among children 2-18 years with minor injuries at baseline and at one to two weeks post-injury (31). This study included a more heterogeneous population and suggests the ceiling effect may be real.

The 2007 ECOSA group guidelines (48) recommended the application of two instruments to measure HRQoL, as different HRQoL instruments assess different dimensions of health. In spite of this, in this review only two studies reported the use of two HRQoL instruments. The importance of the use of two instruments is highlighted by Gabbe et al.'s 2011 study in which the CHQ-PF50 and the PedsQL provided conflicting results throughout follow-up

(30). The EOCSA guidelines also recommended that the timing of HRQoL assessments take place at 1, 2, 4, and 12 months post-injury. There was no meaningful change before or after the publication of these guidelines in terms of the proportion of studies meeting this recommendation with four of 14 studies published before or during 2007 and four of 12 published after 2007 collecting data at three or more time points, with only one study collecting data at all four of the recommended time points (72). This raises the issue of why the guidelines are not being followed. It is possible that researchers are unaware of their existence or it might be possible that individuals interested in childhood injury are hesitant to apply guidelines that were written for adult populations. It also points to a clear need for guidelines created for pediatric studies.

In the majority of studies reviewed, analyses were inadequate for the type of data collected and the data distribution, casting doubt on the results. Of the 18 studies that collected HRQoL at more than one time point, only four used a form of longitudinal analysis (58,59,65,75). Thirteen studies examined longitudinally collected data independently at each time point. Addressing data collected longitudinally with an independent analysis at each time point can lead to underestimation of variability and increased likelihood of type I error. In addition, less than 60% of the studies examining possible predictors of HRQoL used a form of multivariable analysis with adjusted models. Multivariable models are important as potential confounders are controlled for in order to better understand the true relationships between demographic and injury related variables and HRQoL. The lack of multivariable models makes the results of these studies difficult to adequately infer on the wider population. It is important to note that the type of analysis used is not only dependent on the data collected, but on the aims of the study. Three studies included in this review included longitudinal HRQoL data, however the aim was to validate an instrument or test a screening protocol which required a different approach to the data (31,53,54).

As in all longitudinal research, missing data were a factor in most studies, with follow-up rates ranging from 50% to 100%. The majority of studies applied complete case analyses, one used all available data in mixed models (58) and only two used more advanced methods of dealing with missing data (42,60). Complete case analysis only provides unbiased estimates when data are missing completely at random (MCAR), otherwise selection bias is introduced. Even if data are MCAR a lot of data are disregarded resulting in statistical inefficiency and ethical issues given study participants used their time to provide research data that is now being disregarded (45).

Seven studies collected a retrospective baseline measure of HRQoL (31,53,58,60,65,72,75). It has been suggested that baseline measures collected at recruitment are more appropriate than healthy population norms for the purpose of determining the impact of injury on HRQoL in an adult population (88). A recent systematic review of assessment of pre-injury HRQoL found that retrospective measures may systematically overestimate pre injury HRQoL, with pre-injury HRQoL scores collected in this manner being consistently higher than population norms (89). With this in mind, it may be of interest in future work to include both retrospective measures of baseline HRQoL and population norms, with the gold standard, of course, being a prospective cohort starting before an injury event occurs.

The timing of recovery of HRQoL to baseline or population norm levels varied across studies from within weeks to one year and beyond. There was no clear difference in studies that reported recovery within one year, and those reporting recovery beyond one year. Both groups were comprised of studies including a breadth of injuries, injury severities and mechanism of injury, a wide range of ages and in both groups several different tools were used across the studies. There is no clear factor explaining why some studies report long term HRQoL deficits while others report children recovery quickly from injuries in terms of their HRQoL.

Given the variability of HRQoL tools used, timing of measurements, study populations and analyses applied, the fact that three factors stood out as being associated with decreased HRQoL in several multivariable analyses may be even more significant than if all studies had used the same methodology because these factors were robust (remained significant under various conditions) to different HRQoL tools, populations, and timing of assessments. The results of the available multivariable analyses performed suggest that 1) children suffering more severe injuries (41,62,68,71), 2) older children (41,60,62,73,75), and 3) females (41,42,71) are at higher risk of long term HRQoL deficits relative to their counterparts. Only one study reported on modifiers of HRQoL following injury (1) and it suggested that children with larger HRQoL deficits at one month (older children and those hospitalized) had caught up to their peers in returning to baseline HRQoL by one year. More research and longitudinal analyses are required to understand how demographic and injury related variables can modify HRQoL recovery, and if referrals to rehabilitation specialists including physiotherapists for physical recovery and psychologists for psychosocial recovery can act to prevent long term HRQoL deficits.

The limitations of this review should be kept in mind when interpreting the results. Specifically, the *a priori* planned meta-analysis could not be performed due to the heterogeneity of the methods used across included studies. While combining information from independent studies addressing similar questions can provide more reliable estimates, combining data that were collected with different tools, on different scales at different timepoints was determined to not be a valuable addition to the literature. Secondly, the decision was made to exclude qualitative literature based on the objectives of this review to abstract and critique statistical methods and to summarize HRQoL quantitively. However, the exclusion of qualitative literature limits the perspective of this review and may have resulted in missing relevant and interesting findings regarding the narrative summary of HRQoL following childhood injury.

Based on the limitations observed in the studies included in this review and the lack of consensus on analyses to use when performing longitudinal research of HRQoL following childhood injury, I propose that future research, in addition to referring to and meeting the ECOSA guidelines, should also aim to:

1) Use a HRQoL tool that provides a summary estimate that ranges from 0-1 or 0-100, has good psychometric properties, is generic, and can be applied to both parents and children;

2) Report on the amount and nature of missing data, including missing data mechanism, and how this has been addressed; if data are not MCAR, avoid the use of complete case analysis;

3) Report the distribution of the HRQoL variable and the mean or median of the summary variable (as appropriate if normal or skewed) at all time points collected;

4) Compare follow-up assessments of HRQoL to baseline measured prospectively where possible or retrospectively within 1 week using the same method of data collection as follow-up assessment (89); and,

5) If predictors of HRQoL are investigated, provide longitudinal multivariable analyses appropriate for the distribution of the outcome variable and the nature of missing data.

2.6 Conclusion

More research in this field is required that follows the ECOSA guidelines, performs appropriate multivariable longitudinal analyses, and addresses missing data issues transparently and validly. Official guidelines regarding the reporting and analysis of HRQoL data in observational longitudinal pediatric research could aid in reducing the heterogeneity in analytic approaches observed in this field and across all HRQoL pediatric research, allowing for greater comparisons across studies. Further research is required to understand the best model to use with an HRQoL outcome, as it has some unique statistical attributions that should be considered.

In the chapters to follow, HRQoL data collected among a cohort of injured children and their parents throughout the year following childhood injury will be described in detail, including an analysis of the missing data. Exploratory data analysis including data visualization will be presented to examine bivariable relationships of demographic and injury related variables and HRQoL. Longitudinal analyses of predictors of HRQoL will be compared to determine the model that best fits the nature of the data.

Chapter 3: Descriptive Analysis

3.1 Background

The preceding literature review observed that critical pieces of information about the analysis were often missing, including the distribution of the HRQoL variable, the mechanism of missingness in the data and how missing data were addressed. It is important that studies include a thorough description of the analysis that addresses these issues. The importance of performing and reporting on descriptive analysis prior to hypothesis testing is emphasized by Bottomley *et al* in *The Lancet,* "The multi-dimensional nature of HRQoL, combined with repeated measurements and the prevalence of missing data, invites errors in the use of multiple statistical tests and also inflates type 1 errors" (90). Further, HRQoL data are bounded and often skewed which also impacts analyses and should influence interpretation of data (91,92).

There are three patterns of missing data as defined by Rubin et al., 1) data missing completely at random (MCAR) in which the probability of missing data is unrelated to the patient's outcome with no systematic differences between missing and observed data; 2) data missing at random (MAR) where the probability of missing data is dependent on variables that have been collected, for instance if someone in an injury study was missing a value for injury severity as assigned in hospital charts, the missing value wouldn't be associated with injury severity itself, but it would be associated with other collected variables such as hospitalization status and; 3) data not missing at random (MNAR) where the probability of missingness depends on the value of the missing data itself, for example if individuals with missing HRQoL had systematically lower HRQoL than those who completed the study unrelated to any of the variables that were collected in the study (93). Many of the problems observed with the handling of missing data in the literature arise from the incorrect assumption that data are MCAR, which is unlikely in most studies with long term follow-up (45). Analyses that assume data are MCAR include complete case analysis, repeated univariate analyses, and unweighted generalized estimating equations. Maximum likelihood methods are unbiased if data are MAR with a correctly specified model. However, more sophisticated statistical methods exist to account for MNAR and these should be used with greater frequency in HRQoL analyses.

Examining patterns of missing data is an important step in all research. The consequences of missing data are twofold: 1) a decrease in precision and power, increasing the risk of a type II error (i.e., failing to reject a false null hypothesis) and 2) the potential for bias (94). A type II error results in concluding there is no significant relationship between a predictor and outcome, when in fact a relationship is present. The bias that can be introduced through missing data (selection bias) can mean that the individuals in the study are not representative of the target population and results would not be generalizable outside of the study population. For example, if individuals with systematically worse HRQoL were lost to follow-up, the population retained in the study would represent only those with better HRQoL and any findings would be less applicable to individuals whose HRQoL remained low. There are many examples of the mishandling of missing data specifically with regard to patient reported outcomes, such as HRQoL, across all disciplines, including in medicine and epidemiology (45). As observed in the preceding literature review, missing data have been an issue in previous longitudinal studies of HRQoL following childhood injury, with follow-up rates at 12 months ranging from 63% - 100% (i.e. missing data ranging from 0%-37%). The analyses that have been used to address missing data range from analyzing only complete cases, multiple imputation methods and using analyses that make use of all available data. However, which of these options represents the best approach, and their individual strengths and weaknesses, remains in dispute and often relies on assumptions within the underlying data itself. The first step in working with a dataset with missing values is to explore the extent and patterns of missingness (45).

The distribution of the response variable and its temporal trajectory are also important issues to consider prior to hypothesis testing. A ceiling effect is considered present when a large proportion of subjects (e.g., $\geq$ 15% as suggested by Terwee et al.) attain the highest possible value on the scale (95). A large proportion of subjects reporting the upper bound of a tool does not necessarily mean a tool is flawed, rather it could represent a large proportion of the population perceiving full health. Regardless of the reason for an apparent ceiling effect, it impacts analyses. When present in a response variable in longitudinal data, a ceiling effect can lead to incorrect model selection and biased parameter estimation with the magnitude of bias being positively related to the proportion of participants with the highest possible score (96). Thus, it is important to calculate the proportion of individuals reporting the highest possible score and to adjust analyses accordingly (96).

Given the issues surrounding the analyses of HRQoL data, this chapter has been dedicated to an intensive descriptive analysis of longitudinal HRQoL data collected during the Child and Youth Burden of Injury (CYBOI) study, a longitudinal study of children and their parents' perceptions of health following injury over the course of 2011-2013 in Vancouver, Canada. As well as a discussion of the analyses that can be used to address missing data, bounded outcomes and violated normality assumptions.

3.2 Objectives

The overall aim of this chapter is to describe the data collected through the CYBOI study in an attempt to identify appropriate analysis techniques to test study hypotheses.

The specific objectives of this chapter are to:

1) Describe the CYBOI study population of children with parent proxy report (children 0-16 years of age) and children with self-report HRQoL (children 5-16 years of age),); examine how representative the study population is of the target population; explore patterns of data

missingness; and investigate demographic and injury related variables associated with loss to follow-up.

2) Describe the distribution and trajectory of parent-reported children's PedsQL scores (total scale, physical health summary, and psychosocial summary) in the year following injury.
3) Describe the distribution and trajectory of child self-reported HRQoL scores in the year following injury, as measured by the PedsQL for a population of children 5-16 years of age.

3.3 Methods

3.3.1 Study population

The CYBOI study collected data longitudinally from a sample of children aged 0 to 16 years and their parents who presented with a primary injury diagnosis at the British Columbia Children's Hospital (BCCH) emergency department (ED) or were admitted to the hospital wards between February 2011 and December 2013. Only parents completed surveys for children 0 to 5 years of age. For all other ages, both children and parents completed surveys, with children aged 5-8 years of age receiving assistance from their parents in completing the survey.

3.3.2 Data collection

This study was reviewed and approved by the University of British Columbia / Children's and Women's Health Centre of British Columbia Research Ethics Board (certificate number H09 01627). A research assistant recruited participants directly from the ED and hospital wards on different days of the week and times of day to help ensure a mix of patients with different injury types and severities. In addition, real time hospital admissions data were reviewed twice daily during regular office hours to identify children presenting with injury for study recruitment. Because most medically attended visits for injuries do not result in hospitalization, injuries requiring hospitalization were purposively over-sampled to ensure a mix of patients with injuries of varying severity. Approximately thirty percent of the study population was hospitalized relative to only ten percent of the population of all children presenting to the hospital with an injury.

After identifying eligible participates via the hospital admissions data, researchers gained permission from the nurse or physician responsible for the child's care to approach parents in hospital wards regarding study recruitment. In the ED waiting rooms, eligible parents were approached regarding study recruitment after triage confirmed that the primary reason for the visit was injury. The research team member explained the study to parents and children in simple language including what was involved in participation, ensuring potential participants understood that the decision to participate or not would not affect quality of care, and provided the parent with consent forms. Participants aged 7 to 13 years provided assent to participate if they were deemed competent to do so. Participants aged 14 years and over signed an assent statement on the parents' consent form. In addition to explaining that participation in the study was completely voluntary, the risks and benefits of the study and the study objectives, the consent form explained that part of participation in the study was for parents, and children over five years of age, to fill out four questionnaires over the course of the study with two options for completing the questionnaire (either on paper or online). The consent form also asked for permission to access the child's hospital medical chart and health records relating to injury. Only individuals for whom parent/guardian consent as well as child assent was provided (if applicable) were eligible to participate in the study. Individuals excluded from the study included: parents who did not speak English or did not have an address in British Columbia (BC) and children with pre-existing medical conditions that were deemed to impact risk of injury and hospitalization.

A study-specific survey tool (baseline survey in appendix E) was created by Dr. Mariana Brussoni for the purpose of the CYBOI project. The tool includes pre-existing measures including the PedsQL, standard questions regarding background and demographics, questions used in previous studies of childhood injury, as well as specific questions to fit the sample. The questionnaire was piloted among a sample of 10 parents and three children to check for clarity and comprehension with responses being discarded from the full analysis. The PedsQL component of the questionnaire had previously been validated (97,98). It was administered to parents/guardians at baseline and one, four and 12 months post-injury, as per guidelines outlined by van Beeck et al (48). At baseline, the PedsQL was assessed as a retrospective measure of pre-injury health reflecting HRQoL in the month prior to injury. The only time varying variables included in this thesis are the results of the PedsQL tools, all other variables were collected at baseline or from hospital records.

All CYBOI baseline survey data were collected via self-administered questionnaires that were completed on paper, and follow-up surveys could be completed on paper and mailed back to the research office in a stamped self-addressed envelope provided by the research team or completed on-line. Electronic study data were collected, and paper data were entered and managed using REDCap electronic data capture tools hosted at the BC Children's Hospital Research Institute (99). REDCap (Research Electronic Data Capture) is a secure web application for building and managing online surveys and databases. Data on the date and time of injury, diagnosis and treatment, including length of stay, type of injury, and anatomical location of injury, were collected from hospital charts. The specific variables collected via the survey tool and hospital records relevant to this thesis are in listed in Table 3.1.

Table 3.1 Variables collected via survey and hospital records*

Survey	Hospital Records
Postal code	Canadian Triage and Acuity Scale paediatric (PaedsCTAS)
Child's date of birth	Date of injury
Child's sex (male/female)	Nature of injury
What type of activity the child was doing when injured (education, sports or exercise, general leisure, paid work, unpaid work, housework, other)	Anatomic location of injury
Where did the injury happen? (at school, in own home, in some other person's home, in a group home, at work, on a public road or on a pavement, in an entertainment area, countryside, sports grounds, public buildings, some other area)	Length of hospital stay
Was a motor vehicle involved in the child's accident?	
In the 4 weeks before your child was injured, on how many days did ill health restrict their normal activities?	
Are you the injured child's mother, father or other caregiver?	
The status of the relationship between the child's parents (living together, no longer living together, living apart and have never lived together, never had a relationship as a couple, other parent is deceased)	
Living situation of the child: (with both parents, mostly with mother, mostly with father, equally with each parent)	
Do you rent or own your home?	
What is the highest level of education of each parent (some high school, graduated high school, some trade school, college or university, diploma from trade school or college, university degree, post graduate degree)	
Has the injured child had any other injuries in the last 12 months that required medical attention by a doctor, nurse or dentist (yes/no)? How many?	

* The PedsQL question list is not included in this list, but was collected via the questionnaire, variables limited to those used in this thesis

Research on the PedsQL indicates the mode of administration (pen and paper, online or telephone) does not influence scores (85). At the time of recruitment and with each subsequent survey, parents received a $2 gift card accompanying the survey in the mail, irrespective of whether they completed the survey. Follow-up surveys were sent at each time point regardless of completion of the previous survey and whether or not full recovery had been indicated previously. Paper copies of the study questionnaire, sent to all participants, included a personalized, hand written note thanking study participants for their participation. Active follow-up of participants was performed through calls and email. To reduce non-response bias, parents who had not returned their survey were sent an email reminder one week later, and if there was no response to this email within 24 hours, a telephone call. Up to five emails and three phone messages were left for all missing surveys.

3.3.3 Descriptive variables

At baseline, the survey instrument included questions about the circumstances around the injury and demographic information including the child's age, and sex (Table 3.1). Hospital records were used to determine each child's length of hospitalization and the paediatric Canadian Triage and Acuity Scale (PaedsCTAS) score. The PaedsCTAS scale is used in all Canadian EDs to triage patients based on urgency. This scale has five ordinal categories ranging from one (requires resuscitation) to five (non-urgent) (100), injury specific reasons to assign a given level are provided in Appendix F. This score can be used to predict the nature and scope of care that is likely to be required. The scoring is highly standardized, as nurses assigning the score receive continuous training. Both PaedsCTAS score and hospitalization status were used as independent proxies of injury severity. Research indicates the utility of the PaedsCTAS as an alternate proxy of injury severity that is not as sensitive to extraneous factors that can influence hospitalization status (101). Participants' postal codes were used to derive a measure of socioeconomic status (neighborhood income quintiles) using Statistics Canada's Postal Code Conversion File Plus (PCCF+) (102).

3.3.4 Health related quality of life

The PedsQL 4.0 Generic Core or the PedsQL Infant Scale was included in each survey as appropriate by age.

3.3.5 Statistical analysis

All tables present both raw and weighted data. Descriptive analyses have been performed on the weighted data to account for the over sampling of hospitalized children, with weights calculated at each time point to account for attrition. Sampling weights were calculated as the inverse of the likelihood of being sampled for children who were hospitalized and those seen in the ED.

$$\mathit{Weight\ for\ hospitalized\ children} = \frac{\mathit{Total\ number\ of\ injured\ children\ hospitalized\ during\ study\ period}}{\mathit{Number\ of\ injured\ children\ hospitalized\ in\ study\ sample}}$$

This weighting was based on the actual number of injured children who were seen in the ED (n=12,617) and admitted (1,624) to BCCH during the study period.

3.3.5.1 Study population description and missing data analysis

The study population has been described by demographic and injury related variables using mean and standard deviation and median and interquartile range or frequencies and percentages, as appropriate. To explore the patterns of missingness, a graph of mean PedsQL total scale score by time, stratified by dropout time has been created. To investigate the effect of attrition on the distribution of the study population over time, demographic and injury related variables have been described at each time point for the full population of parent report (children 0-16) and for the population of children with self-report (children five to 16 years). Demographic and injury related variables associated with loss to follow-up were explored using bivariable logistic regression to compare the population lost to follow-up (those who provided a single survey) to those who completed at least two surveys. Bivariable logistic regression was also used to compare the study population, to the entire sample of children presenting with injury to BCCH wards or ED during the study period using administrative data obtained from BCCH. BCCH administrative data included postal code, sex, age, and hospitalization status.

3.3.5.2 HRQoL trajectory

The crude and weighted parent-report and child self-reported PedsQL total scale score, along with the physical health and psychosocial health scores were described at each time point by mean, median, standard deviation, interquartile range. The relationships between the weighted mean total scale score, and the weighted physical and psychosocial health summary mean scores at each time point within and between reporter groups were investigated via paired t-tests to better understand the relationships that existed.

3.3.5.3 HRQoL distribution

The distribution of the PedsQL total scale score and physical health and psychosocial health scores for both parents and children has been explored using histograms and box plots to establish the distribution and identify any out of range data. Out of range values are those < 0 and > 100; if an out of range value was found the original paper survey was looked at again (online surveys did not allow for out of range values), and all coding was reviewed to determine the cause. To explore the possibility of a ceiling effect, the number and percent of reporters with a score of 100 on the PedsQL total scale score (100), as well those with the highest possible physical or psychosocial health score (also 100) were examined. A ceiling effect was considered present if >15% of reporters had a score of 100 as suggested by Terwee et al (95). To better understand the meaning of a score of 100 on the PedsQL total scale score, the number of parents who had both a perfect PedsQL total scale score for their child and answered “Yes” to the question “Now (today) do you feel your child’s injury is still affecting them in anyway?” was described. A total scale score of 100 is congruent with parents who indicate their child is completely recovered and no longer affected by their injury. If, on the other hand, parents felt their child was not completely recovered and was still affected by their injury, a PedsQL total scale score of 100 would be indicative of a true ceiling effect or lack of construct validity for injured children.

3.4 Results

3.4.1 Study population – parent-response

While the study did not deliberately exclude intentional injuries (e.g., acts of deliberate violence), it is recognized that there would be different impacts on HRQoL. Three participants with intentional injuries who had agreed to participate were excluded from the analysis due to small base size for meaningful analysis. See Figures 3.1 and 3.2 for flowcharts outlining participant disposition.

A total of 365 parents reported their child's HRQoL for at least one time point. At baseline, there were 354 parent-responses of HRQoL, with 266 (75.1%), 240 (67.8%), and 225 (63.6%) responses at one, four and 12 months, respectively. Of the 365 parent reports, 76 (20.8%) provided HRQoL at only a single time point (71 baseline only, and five only a single follow-up survey). The primary variable of interest that was collected longitudinally was the PedsQL total scale score. As shown in Figure 3.1, a total of 178 parents were missing the total scale score for at least one time point. Missing data in the parent total scale score variable were primarily observed to be monotone meaning that most parents who dropped out of the study at any time point did not return (n =121, 68% of the 178 parents with missing total scale score). There were 187 (50.8%) parents with complete total scale scores at all time points, an additional 24 parent-reporters had completed this variable to four-months post-injury but did not return the 12-month survey, while an additional 26 parent-reporters had just baseline and one-month follow-up total scale scores. As surveys were sent regardless of response on the previous survey there is some intermittent missingness of PedsQL total scale score (n=57): 11 parent-reporters were only missing the parent reported total scale score at one-month, and 21 were missing four-month data. For a full description of participant follow-up see Figure 3.1 and Table 3.1 for a description of the pattern of missingness of this variable. Figure 3.2 displays weighted, unadjusted mean PedsQL total scale scores by time, stratified by drop out time for parent reporters with monotone data missingness, illustrating no statistically significant difference in weighted mean total scale score across different drop out times.

There were also missing data to consider in two time-invariant covariates. The PaedsCTAS, which was collected as a proxy for injury severity, was missing for 85 participants (23%). This missingness was due to changes that were made in how hospital electronic records were kept at the beginning of the study, so PaedsCTAS score were only available after July 2011. In addition, 21 individuals (5.7%) were missing the income quintile variable, this was due to postal codes being missing in the Statistics Canada's Postal Code Conversion File Plus (PCCF+).

Table 3.2 Pattern of missing parent-reported PedsQL total scale score

	Baseline	One-month	Four-months	Twelve-months	n
	✓	✓	✓	✓	187
	✓	✓	✓		24
	✓	✓			26
	✓				71
	✓		✓	✓	11
	✓	✓		✓	21
		✓	✓	✓	1
			✓	✓	1
		✓	✓		4
	✓		✓		10
	✓			✓	4
		✓			3
				✓	2
Total	354	266	240	225	365

* ✓ indicates parent reported PedsQL total scale score are present, shading indicates missing data, n is the number of reporters with the given pattern of missing data

Figure 3.1 Parent proxy report, study population disposition

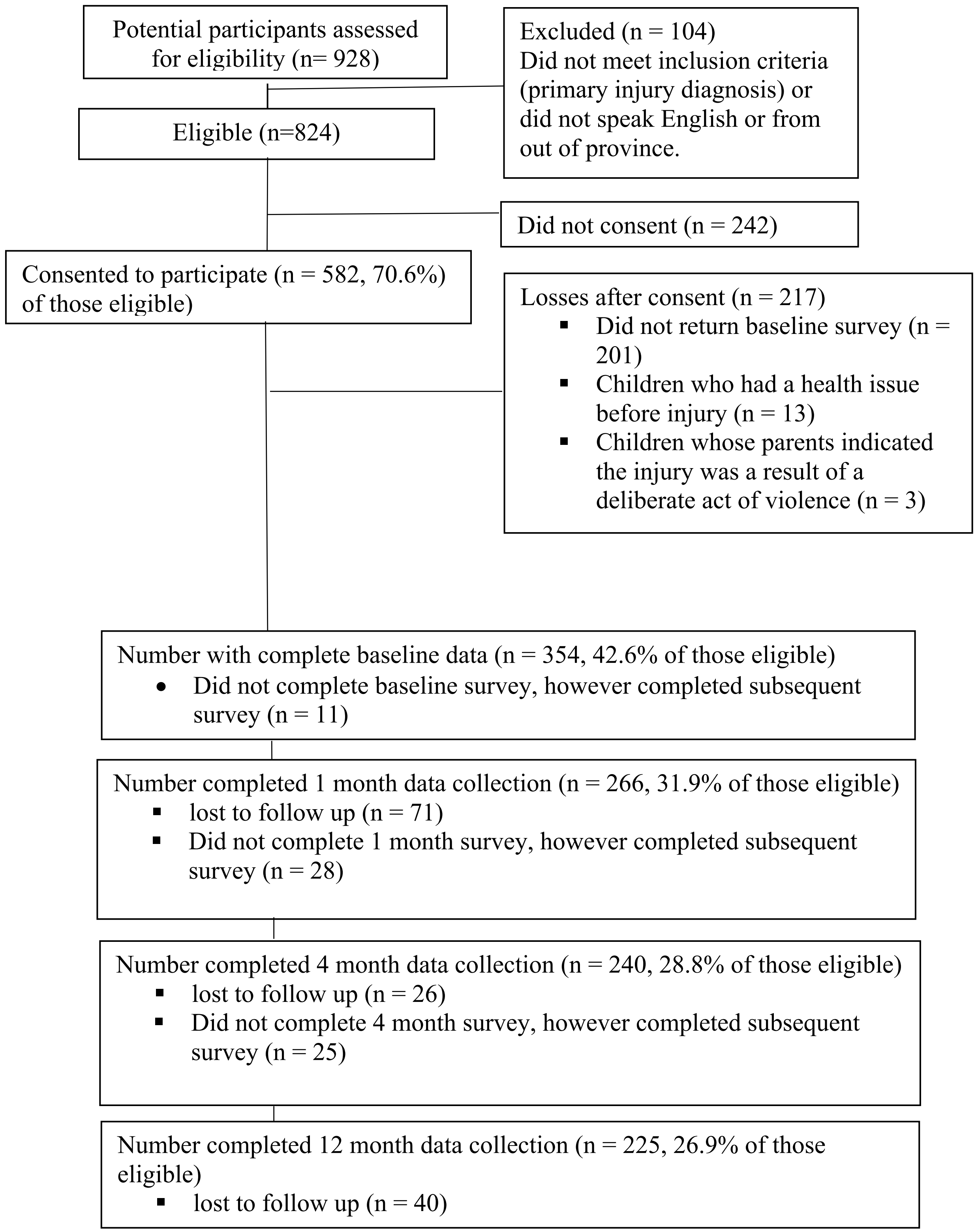
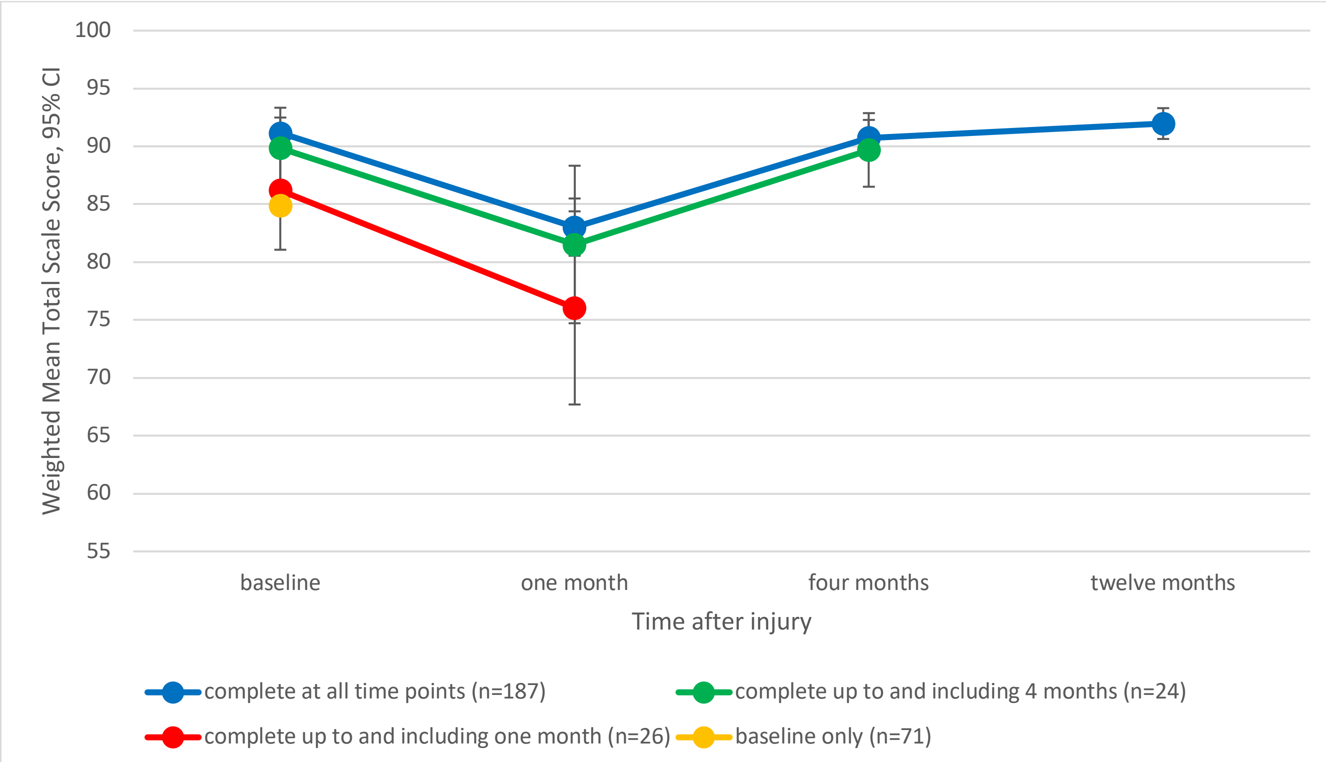


Figure 3.2 Parent proxy report, unadjusted, weighted mean total scale score by dropout time, 95% CI



* Within time points there are no statistically significant differences

In the majority of cases (73%, n= 256), the parent- reporter at baseline was the child's mother. Almost 70% of parents owned their own homes (n= 242) and most children (83%) lived together with two parents who were either legally married or in a common-law relationship. Eighty percent of households had at least one parent with a post-secondary education (a diploma from a trades school or college, a university degree or post-graduate degree) and 60% of households reported incomes of $80,000 or greater. Most children were healthy, having missed no days of school/did not have usual activities restricted due to ill health in the four weeks prior to injury (86%). The most common place of injury occurrence was at school (23.7%), followed by home (21.6%). Twenty one percent of the children with baseline surveys (n= 75) experienced a medically attended injury in the past 12 months, with most (75%) reporting a single event.

Parents who were lost to follow-up had significantly higher odds of having older children (for continuous age OR=1.11, 95% CI (1.04, 1.17), $p < 0.001$) and significantly higher odds of having reported lower baseline total scale score for their children (OR = 0.97, 95% CI (0.95, 0.99), $p = 0.001$) (Table 3.3).

Table 3.3 Parent-report, unweighted and weighted demographic and injury related characteristics by follow-up*

	Followed up	Followed Up - Weighted	Lost to Follow-up	Lost to Follow-up Weighted	OR (95% CI)**	OR (95% CI) - Weighted***	p Value	p Value - weighted
n	289		76					
Baseline PedsQL total scale score (median [IQR])	92.39 [84.77, 97.83]	92.39 [84.78, 97.83]	90.91 [78.26, 98.32]	90.33 [77.60, 97.83]	**0.97 (0.94, 0.99)**	**0.97 (0.95, 0.99)**	**0.001**	**<0.001**
Sex (%)								
Male	179 (62.2)	174.3 (60.6)	50 (65.8)	46.4 (67.0)	ref****			
Female	110 (37.8)	113.1 (39.4)	26 (34.2)	22.8 (33.0)	0.86 (0.50, 1.46)	0.75 (0.43, 1.30)	0.570	0.304
Hospitalization Status (%)								
Emergency Department	211 (73.4)	256.1 (89.1)	47 (61.8)	57.3 (82.8)	ref	ref		
Hospitalized	78 (26.6)	31.3 (10.9)	29 (38.2)	11.9 (17.2)	1.70 (1.00, 2.90)	1.67 (0.81, 3.44)	0.049	0.150
Length of Stay days (mean (sd))	5.61 (7.67)		6.95 (8.95)		1.02 (0.94, 1.10)		0.432	
Age (mean, (sd))	8.07 (4.64)	7.90 (4.68)	9.8 (3.9)	10.21 (3.90)	**1.09 (1.03, 1.16)**	**1.11 (1.04, 1.17)**	**0.002**	**<0.001**
Age Category (%)								
0 - <5	94 (32.9)	97.7 (34.0)	10 (13.2)^	9.0 (12.9)	ref	ref		
5 - <13	139 (48.6)	137.2 (47.7)	50 (65.8)	44.0 (63.5)	**3.97 (1.79, 8.78)**	**3.50 (1.63, 7.50)**	**0.001**	**<0.001**
13- < 17	56 (18.5)	52.5 (18.3)	16 (21.1)	16.3 (23.5)	**3.62 (1.45, 9.02)**	**3.25 (1.35, 7.84)**	**0.020**	**0.009**
PaedsCTAS (%)								
1 (requires resuscitation)	12 (4.2)^	4.9 (1.7)	6 (7.9)	2.5 (3.6)	ref	ref		
2	41 (14.3)	24.2 (8.4)	12 (15.8)	5.7 (8.3)				
3	47 (15.7)	42.8 (14.9)	15 (19.7)	11.0 (15.9)	0.91 (0.41, 2.03)	0.95 (0.34, 2.63)	1.000	0.920
4	108 (37.8)	130.1 (45.3)	29 (38.2)	34.6 (49.9)	0.61 (0.32, 1.16)	0.86 (0.38, 1.97)	0.250	0.720
5 (non-urgent)	8 (2.8^)	7.3 (2.6)	1 (1.3)	1.2 (1.8)				
Missing	73 (24.8)	76.9 (26.8)	13 (17.1)	14.2 (20.6)				

	Followed up	Followed Up - Weighted	Lost to Follow-up	Lost to Follow-up Weighted	OR (95% CI)	OR (95% CI) - Weighted**	p Value	p Value - weighted
Income Quintile (%)								
1 (lowest income quintile)	34 (11.9)	35.8 (12.5)	15 (19.7)^	14.3 (20.6)	ref	ref		
2	31 (10.8)	31.3 (10.9)	7 (9.2)^	6.1 (8.8)	0.47 (0.16, 1.37)	0.49 (0.17, 1.42)	0.198	0.188
3	58 (20.3)	57.8 (20.1)	12 (15.8)^	10.6 (15.3)	0.52 (0.22, 1.24)	0.46 (0.189, 1.13)	0.090	0.090
4	54 (18.9)	52.9 (18.4)	16 (21.1)	13.9 (20.0)	0.68 (0.29, 1.58)	0.66 (0.28, 1.54)	0.344	0.335
5 (highest income quintile)	98 (34.3)	97.7 (34.0)	19 (25.0)	17.5 (25.3)	0.43 (0.19, 0.95)	0.45 (0.20, 1.00)	0.039	0.050
Missing	14 (3.8)	11.8 (4.1)	7 (9.2)	6.9 (10.0)				
Nature of Injury (%)								
Minor External Injury	109 (38.1)	130.5 (45.4)	27 (35.5)	32.1 (46.4)	0.89 (0.53, 1.51)	1.03 (0.61, 1.75)	0.664	0.908
Upper Extremity Fracture	67 (23.4)	66.4 (23.1)	12 (15.8)^	10.6 (15.3)	0.61 (0.31, 1.20)	0.60 (0.29, 1.22)	0.151	0.156
Lower Extremity Fracture	35 (11.9)	27.7 (9.6)	12 (15.8)^	7.4 (10.6)	1.38 (0.68, 2.82)	1.11 (0.47, 2.62)	0.372	0.814
Head Injury	37 (12.6)	38.3 (13.3)	11 (14.5)^	11.8 (17.0)	1.17 (0.57, 2.43)	1.33 (0.65, 2.72)	0.672	0.432
Major Trauma	21 (7.3)	9.5 (3.3)	7 (9.2)^	2.9 (4.2)	1.28 (0.52, 3.12)	1.27 (0.33, 4.88)	0.594	0.727
Other	18 (6.3)	13.9 (4.8)	7 (9.2)^	4.5 (6.5)	1.50 (0.60, 3.75)	1.36 (0.45, 4.08)	0.380	0.580
Missing	2 (0.3)	1.2 (0.4)	0 (0.0)	0.0 (0.0)				
Motor Vehicle Collision (%)								
Yes	16 (5.6)	9.0 (3.1)	10 (13.2)	4.9 (7.1)	ref			
No	265 (91.6)	271.9 (94.6)	62 (81.6)	61.1 (88.2)	0.37 (0.16, 0.86)	0.41 (0.13, 1.28)	0.023	0.124
Missing	8 (2.8)	6.5 (2.3)	4 (5.3)	3.3 (4.7)				

* Values in bold indicate statistical significance at alpha of 0.05
** OR from unadjusted, unweighted logistic regression - modeling odds of being lost to follow-up
*** OR from unadjusted, weighted logistic regression - modeling odds of being lost to follow-up
**** ref = reference category for odd ratios
^ low base, use caution in the interpretation of statistics and inferences

When the entire baseline population was compared to the entire population of injured children seen at BCCH during the study period, study participants had significantly higher odds of being in the highest income quintile relative to the lowest (OR 1.91, 95% CI (1.37, 2.66), $p < 0.001$) (Table 3.4) and had higher odds of being older than those in the broader population (OR 1.05, 95% CI (1.02, 1.07), $p < 0.001$). None of these relationships were statistically significantly different when the comparison was limited to the study population that was not lost to follow-up (data not shown). The intentional over sampling of hospitalized children was reflected with children in our study having 3.1 times the odds of being hospitalized relative to the entire injured child population in the unweighted sample, a relationship that is no longer present in the weighted sample (Table 3.4).

Table 3.4 Parent-report study population compared to all children presenting to hospital with injury during study period, significant findings bolded in red*

Study Population	Unweighted Study Population	Weighted Study Population	All injuries Population	Unweighted OR (95% CI)	Weighted OR (95% CI)	Unweighted p value	Weighted p Value
Sex n (%)							
Male	229 (62.7)	226.18 (61.6)	8308 (58.3)	ref	ref		
Female	136 (37.2)	141.02 (38.4)	5933 (41.7)	0.83 (0.67, 1.03)	0.87 (0.71, 1.08)	0.077	0.181
Income Quintile n (%)							
1	49 (13.5)	51.33 (14.0)	2,743 (19.8)	ref	ref		
2	38 (10.5)	38.35 (10.5)	2,591 (18.8)	0.82 (0.52, 1.26)	0.79 (0.52, 1.21)	0.359	0.279
3	70 (19.3)	70.01 (19.2)	2,607 (18.9)	**1.5 (1.04, 2.17)**	1.44 (1, 2.07)	**0.031**	0.054
4	70 (19.3)	68.29 (18.7)	2,584 (18.9)	**1.52 (1.05, 2.19)**	1.41 (0.98, 2.04)	**0.027**	0.066
5	117 (32.3)	117.96 (32.3)	3,302 (23.9)	**1.98 (1.42, 2.78)**	**1.91 (1.37, 2.66)**	**<0.001**	**<0.001**
Hospitalized n (%)							
ED	258 (71.0)	324.77 (87.9)	12,617 (88.8)	ref	ref		
Admitted	107 (29.0)	42.43 (12.1)	1,624 (11.2)	**3.22 (2.56, 4.06)**	1.01 (0.73, 1.39)	**<0.001**	0.674
Age (Mean ± SD) (range 0 – < 17 years)	8.42 ± 4.5	8.33 (4.6)	7.24 ± 5.2	**1.05 (1.02, 1.07)**	**1.04 (1.02, 1.07)**	**<0.001**	**<0.001**

* OR (95% CI) = Odds ratio and 95% confidence interval from logistic regression modeling odds for study population relative to all injury group; ref = reference category for odds ratios

Despite losses to follow-up, there was representation across all categories of all variables with a minimum of 7% of children (n > 16) remaining at each time point with the exception of: levels one and five of PaedsCTAS and children who sustained their injury in MVC. For analysis, PaedsCTAS categories one and five were collapsed with the category below and above, respectively for modelling in the following chapters, the sample size of children involved in MVCs was too small to include in this variable modelling (Table 3.5).

Table 3.5 Parent-report, unweighted and weighted demographic and injury related characteristics at each time point*

	Baseline		One-month		Four-months		Twelve-months	
	Unweighted	Weighted	Unweighted	Weighted	Unweighted	Weighted	Unweighted	Weighted
n	354		266		240		225	
Baseline PedsQL total scale score (median [IQR])	92.39 [83.70, 97.83]	92.37 [83.70, 97.83]	92.86 [84.75, 98.22]	92.39 [84.78, 98.61]	92.86 [84.78, 97.83]	92.39 [84.78, 98.02]	93.48 [85.48, 98.81]	93.48 [84.78, 98.81]
Sex (%)								
Male	222 (62.7)	214.2 (61.6)	165 (62.4)	161.2 (60.7)	149 (62.4)	149.0 (61.7)	143 (64.0)	136.8 (61.8)
Female	132 (37.3)	135.1 (38.4)	101 (37.6)	104.6 (39.3)	91 (37.6)	92.4 (38.3)	82 (36.0)	84.6 (38.2)
Hospitalization Status (%)								
Emergency Department	252 (71.2)	307.4 (88.1)	196 (74.1)	237.8 (89.5)	179 (75.1)	217.1 (89.9)	162 (72.5)	196.4 (88.7)
Hospitalized	102 (28.8)	42.0 (11.9)	70 (25.9)	28.0 (10.5)	61 (24.9)	24.3 (10.1)	63 (27.5)	25.1 (11.3)
Age (mean, (sd))	8.36 (4.56)	8.36 (4.63)	8.16 (4.62)	8.04 (4.69)	8.12 (4.64)	8.00 (4.71)	7.93 (4.57)	7.89 (4.63)
Age Category (%)								
0 - <5	102 (28.8)	104.2 (30.0)	82 (31.2)	85.5 (32.2)	81 (34.2)	83.4 (34.6)	73 (32.9)	74.5 (33.6)
5 - <13	181 (51.1)	174.7 (50.3)	131 (49.8)	130.7 (49.2)	109 (46.0)	110.3 (45.7)	108 (48.6)	105.9 (47.8)
13 - < 17	71 (20.1)	70.4 (19.7)	53 (19.0)	49.7 (18.7)	50 (19.8)	47.6 (19.7)	44 (18.5)	41.1 (18.6)
PaedsCTAS (%)								)
1 (requires resuscitation)	18 (5.1)	7.4 (2.1)	11 (4.2)^	4.5 (1.7)	10 (4.2)^	4.1 (1.7)	8 (3.6)^	3.3 (1.5)
2	52 (14.7)	29.5 (8.5)	36 (13.7)	21.3 (8.0)	32 (13.5)	20.4 (8.5)	34 (15.3)	19.7 (8.9)
3	59 (16.7)	52.6 (14.9)	45 (16.3)	41.1 (15.5)	38 (15.2)	35.8 (14.8)	36 (15.3)	32.6 (14.7)
4	132 (37.3)	159.4 (45.9)	101 (38.4)	121.6 (45.7)	96 (40.5)	115.5 (47.8)	81 (36.5)	98.0 (44.2)
5 (non urgent)	9 (2.5)^	8.6 (2.5)	8 (3.0)^	7.3 (2.8)	6 (2.5)^	5.7 (2.4)	8 (3.6)	7.3 (3.3)
Missing	84 (23.4)	89.5 (25.8)	65 (24.0)	68.8 (25.9)	58 (23.6)	58.6 (24.3)	57 (25.2)	59.4 (26.8)
Income Quintile (%)								
1 (lowest income quintile)	48 (13.6)	48.9 (14.1)	30 (11.4)	31.7 (11.9)	24 (10.1)	23.6 (9.8)	20 (9.0)	19.5 (8.8)
2	36 (10.2)	35.8 (10.3)	29 (11.0)	28.9 (10.9)	27 (11.4)	28.9 (12.0)	23 (10.4)	24.0 (10.8)
3	69 (19.5)	68.0 (19.6)	51 (19.4)	52.5 (19.8)	47 (19.8)	47.6 (19.7)	46 (20.7)	46.4 (21.0)
4	68 (19.2)	64.4 (18.5)	50 (19.0)	49.7 (18.7)	44 (18.6)	44.0 (18.2)	45 (20.3)	42.8 (19.3)
5 (highest income quintile)	112 (31.6)	111.6 (32.1)	93 (35.4)	92.4 (34.8)	86 (36.3)	87.1 (36.1)	81 (36.5)	81.8 (36.9)
Missing	21 (5.9)	20.8 (5.4)	13 (3.8)	10.6 (4.0)	12 (3.8)	10.2 (4.2)	10 (3.2)	6.9 (3.1)

	Baseline	One-month	Four-months	Twelve-months				
	Unweighted	**Weighted**	**Unweighted**	**Weighted**	**Unweighted**	**Weighted**	**Unweighted**	**Weighted**
Nature of Injury (%)								
Minor External Injury	133 (37.9)	159.0 (45.8)	97 (36.9)	115.9 (43.6)	91 (38.4)	108.6 (45.0)	83 (37.4)	98.8 (44.6)
Upper Extremity Injury	78 (22.2)	76.6 (22.0)	63 (24.0)	63.9 (24.0)	56 (23.6)	55.4 (22.9)	56 (25.2)	55.4 (25.0)
Lower Extremity Injury	45 (12.3)	33.1 (9.5)	31 (11.8)	25.7 (9.7)	28 (11.4)	23.2 (9.6)	27 (11.7)	21.2 (9.6)
Head Injury	45 (12.5)	47.2 (13.6)	37 (13.7)	39.1 (14.7)	31 (12.7)	32.6 (13.5)	28 (12.2)	28.9 (13.0)
Major Trauma	28 (8.0)	12.3 (3.6)	20 (7.6)	9.0 (3.4)	17 (7.2)	7.8 (3.2)	16 (7.2)	6.6 (3.0)
Other	24 (6.8)	18.0 (5.2)	15 (5.7) ^	11.0 (4.1)	15 (6.3)	12.6 (5.2)	13 (5.9)^	9.4 (4.2)
Missing	2 (0.3)	2.4 (0.4)	2 (0.4)	1.2 (0.5)	2 (0.4)	1.2 (0.5)	1 (0.5)	1.2 (0.6)
Motor Vehicle Collision (%)								
Yes	26 (7.4)	13.9 (4.0)	16 (6.1)	9.0 (3.4)	11 (4.6)^	7.0 (2.9)	10 (4.5)^	4.9 (2.2)
No	324 (91.5)	331.4 (94.8)	241 (90.5)	249.1 (93.7)	220 (91.6)	227.5 (94.2)	210 (93.2)	212.1 (95.8)
Missing	4 (1.1)	4.1 (1.2)	9 (3.4)	7.7 (2.9)	9 (3.8)	6.9 (2.9)	5 (2.3)	(2.0)

* weighted frequencies have been back calculated from weighted percentages to represent the actual study size

^ low base, use caution in the interpretation of statistics and inferences

3.4.2 Study population – child-report

A total of 245 children reported their HRQoL for at least a single time point. At baseline there were 233 self-report responses with 168 (72.1%), 149 (63.9%) and 140 (60.1%) responses at one-, four- and 12-months, respectively. Of the 245 child-reporters, 61 provided the PedsQL total scale score at a single time point and were deemed lost to follow-up (56 only provided baseline surveys, and 5 provided a single response at another time point). There were 105 (42.6%) children with complete PedsQL total scale score at all time points, 24 had complete data to four-months post-injury but did not return the 12-month survey, 17 had just baseline and one-month follow-up surveys. For a full description of participant follow-up see Figures 3.3 and 3.4 and Table 3.6 for a description of the pattern of missingness.

Table 3.7 displays the unweighted and weighted distribution of demographic and injury related variables for the population of children with self-response HRQoL comparing those with a single survey returned (lost to follow-up) to those with data available at more than one time point (followed up). The only statistically significant differences between children lost to follow-up and those followed up were that those lost to follow-up had lower baseline HRQoL (OR 0.97, 95% CI (0.95, 0.99)) and lower odds of having an upper extremity fracture relative to those not lost to follow-up (OR 0.34, 95% CI (0.15, 0.81)). There was representation across all categories of all variables at all time points with less than 5% representation in the highest and lowest PaedsCTAS categories, children with major trauma and in children injured in MVC (Table 3.8). For this reason, as previously mentioned, PaedsCTAS was collapsed into 3 categories for modelling and MVC was not included in modelling.

Table 3.6 Pattern of missing child reported PedsQL total scale score

	Baseline	One-month	Four-months	Twelve-months	n
	✓	✓	✓	✓	105
	✓	✓	✓		24
	✓	✓			17
	✓				56
	✓		✓	✓	8
	✓	✓		✓	14
		✓	✓	✓	5
			✓	✓	2
			✓		1
	✓		✓		4
	✓			✓	5
		✓			3
				✓	1
Total	233	168	149	140	245

* ✓ indicates data are present, shading indicates missing data, n is the number of reporters with the given pattern of missing data

Figure 3.3 Child self-report, study population disposition

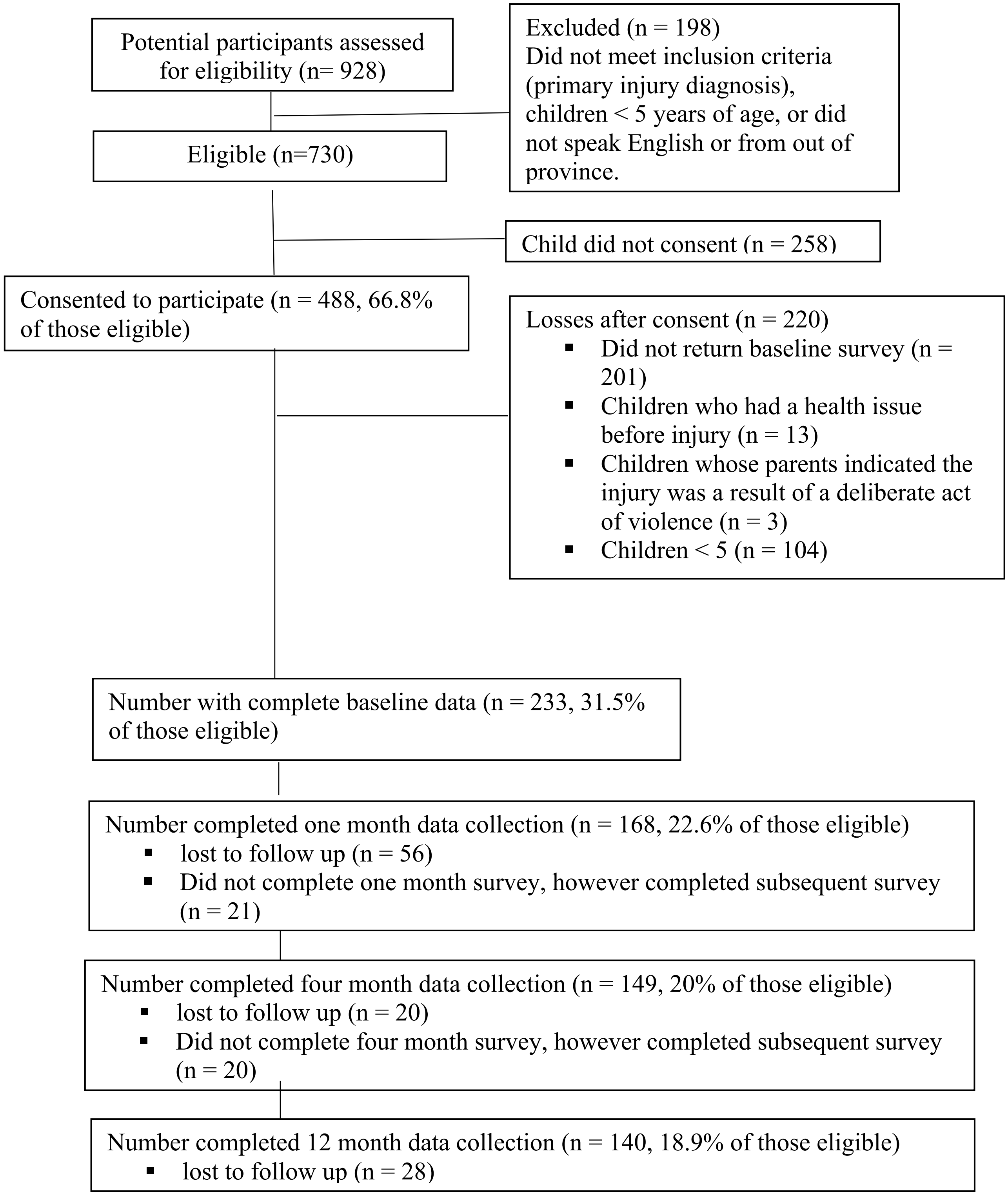


Figure 3.4 Child self-report, unadjusted, weighted mean total scale score by dropout time, 95% CI

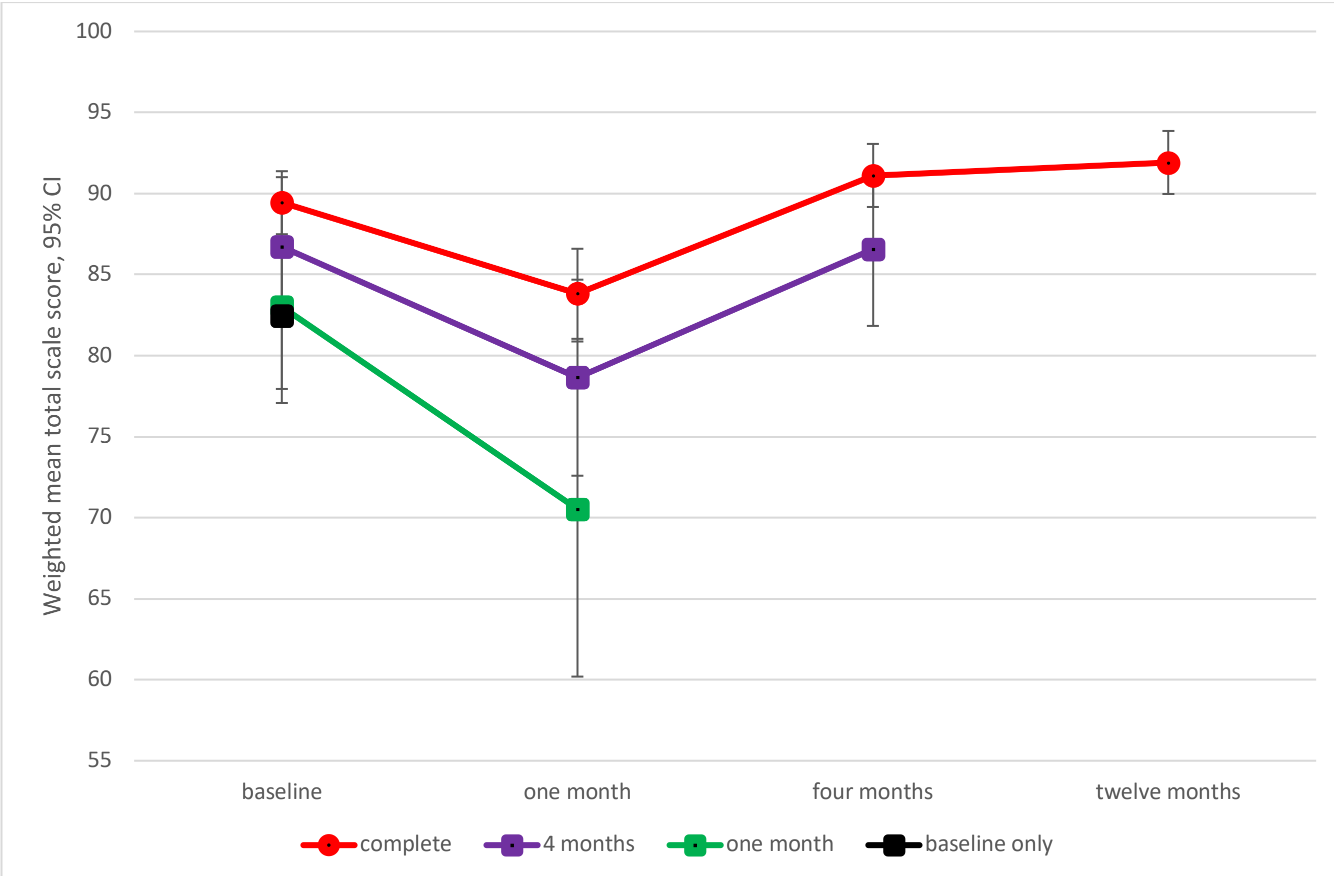


Table 3.7 Child self-report, weighted and unweighted demographic and injury related characteristics by follow-up*

	Followed up	Followed Up - Weighted	Lost to Follow-up	Lost to Follow-up Weighted	OR (95% CI)**	OR (95% CI) - Weighted***	p Value	p Value - weighted
n	184	182.41	61	56.63				
Baseline HRQoL (median [IQR])	90.22 [82.61, 95.65]	90.22 [82.61, 95.65]	84.78 [75.82, 97.75]	85.50 [75.53, 97.78]	**0.97 (0.95, 0.99)**	**0.97 (0.95, 0.99)**	**0.006**	**0.014**
Sex (%)								
Male	113 (61.4)	108.7 (59.6)	33 (54.1)	30.6 (54.0)	ref****			
Female	71 (38.6)	73.7 (40.4)	28 (45.9)	26.1 (46.0)	1.38 (0.77, 2.48)	1.28 (0.70, 2.34)	0.284	0.417
Hospitalization Status (%)								
Emergency Department	132 (71.7)	161.0 (88.3)	39 (63.9)	47.6 (84.0)	ref	ref		
Hospitalized	52 (28.3)	21.4 (11.7)	22 (36.1)	9.1 (16.0)				
Length of Stay days (mean (sd))	5.46 (7.43)		4.88 (5.72)		1.02 (0.97, 1.07)		0.432	
Age (mean, (sd))	10.50 (3.30)	10.59 (3.29)	11.15 (3.23)	11.23 (3.19)	1.07 (0.98, 1.17)	1.08 (0.98, 1.18)	0.139	0.109
Age Category (%)								
5 - <13	134 (72.8)	132.7 (72.8)	43 (70.5)	38.7 (68.4)	ref	ref		
13 - < 17	50 (27.2)	49.7 (27.2)	18 (29.5)	17.9 (31.6)	1.19 (0.63, 2.27)	1.29 (0.67, 2.47)	0.590	0.443
PaedsCTAS (%)								
1 (requires resuscitation)	7 (3.8)^	2.9 (1.6)	3 (4.9)^	1.2 (2.2)	ref	ref		
2	28 (15.2)	17.2 (9.4)	11 (18.0)	5.3 (9.4)				
3	26 (14.1)	22.0 (12.1)	12 (19.7)	9.8 (17.3)	1.25 (0.49, 3.17)	1.41 (0.44, 4.51)	0.638	0.562
4	65 (35.3)	77.7 (42.6)	21 (34.4)	24.8 (43.8)	0.72 (0.35, 1.48)	0.88 (0.34, 2.28)	0.369	0.798
5 (non-urgent)	7 (3.8)^	6.1 (3.4)	1 (1.6)^	1.2 (2.2)				
Missing	51 (27.7)	56.5 (31.0)	13 (21.3)	14.2 (25.1)				
Income Quintile (%)								
1 (lowest income quintile)	21 (11.4)	22.4 (12.3)	11 (18.0)	9.4 (16.6)	ref	ref		
2	21 (11.4)	21.6 (11.8)	4 (6.6)	4.1 (7.2)	0.36 (0.10, 1.33)	0.45 (0.12, 1.66)	0.126	0.231
3	36 (19.6)	35.0 (19.2)	12 (19.7)	10.6 (18.7)	0.64 (0.24, 1.69)	0.72 (0.26, 2.02)	0.366	0.534
4	32 (17.4)	31.0 (17.0)	10 (16.4)	9.8 (17.3)	0.60 (0.22, 1.65)	0.75 (0.26, 2.15)	0.320	0.597
5 (highest income quintile)	65 (35.3)	63.9 (35.0)	20 (32.8)	17.9 (31.7)	0.59 (0.24, 1.42)	0.67 (0.27, 1.69)	0.239	0.395
Missing	9 (4.9)	8.6 (4.7)	4 (6.6)	4.9 (8.6)				

	Followed up	Followed Up - Weighted	Lost to Follow-up	Lost to Follow-up Weighted	OR (95% CI)**	OR (95% CI) - Weighted***	p Value	p Value - weighted
Nature of Injury (%)								
Minor External Injury	65 (35.3)	76.9 (42.1)	23 (37.7)	28.1 (49.5)	1.07 (0.59, 1.95)	1.07 (0.59, 1.95)	0.823	0.823
Upper Extremity Fracture	51 (27.7)	51.7 (28.3)	9 (14.8)	6.9 (12.3)	**0.44 (0.20, 0.95)**	**0.34 (0.15, 0.81)**	**0.038**	**0.015**
Lower Extremity Fracture	26 (14.1)	22.0 (12.1)	11 (18.0)	7.8 (13.7)	1.36 (0.63, 2.97)	1.16 (0.48, 2.79)	0.434	0.744
Head Injury	17 (9.2)	17.5 (9.6)	7 (11.5)	6.9 (12.2)	1.33 (0.52, 3.40)	1.32 (0.52, 3.38)	0.553	0.562
Major Trauma	14 (7.6)^	5.8 (3.2)	6 (9.8) ^	2.5 (4.4)	1.29 (0.47, 3.53)	1.37 (0.30, 6.28)	0.615	0.684
Other	9 (4.9)^	6.1 (3.4)	5 (8.2)^	4.5 (7.9)	1.70 (0.55, 5.27)	2.43 (0.69, 8.53)	0.361	0.167
Missing	2 (1.1)	2.4 (1.3)	0 (0.0)	0.0 (0.0)				
Motor Vehicle Collision (%)								
Yes	13 (7.1)^	6.2 (3.4)	6 (9.8)^	3.3 (5.8)	ref	ref		
No	167 (90.8)	173.0 (94.8)	54 (88.5)	52.9 (93.5)	0.71 (0.26, 1.97)	0.71 (0.26, 1.97)	0.514	0.514
Missing	4 (2.2)	3.3 (1.8)	1 (1.6)	0.4 (0.7)				

* Values in bold indicate statistical significance at alpha of 0.05
** OR from unadjusted, unweighted logistic regression - modeling odds of being lost to follow-up
*** OR from unadjusted, weighted logistic regression - modeling odds of being lost to follow-up
**** ref = reference category for odd ratios
^ low base, use caution in the interpretation of statistics and inferences

Table 3.8 Child self-report, weighted and unweighted demographic and injury related characteristics at each time point

	Baseline		One-month		Four-months		Twelve-months	
	Unweighted	Weighted	Unweighted	Weighted	Unweighted	Weighted	Unweighted	Weighted
n	233	228.82	168	169.36	149	150.23	140	139.25
Baseline HRQoL (median [IQR])	90.22 [80.43, 95.65]	89.13 [80.49, 95.65]	90.22 [82.61, 95.65]	90.22 [82.61, 95.65]	91.30 [84.78, 95.65]	91.30 [83.79, 95.65]	92.39 [84.51, 96.74]	91.30 [82.80, 95.85]
Sex (%)								
Male	137 (58.8)	133.2 (57.7)	103 (61.3)	151.2 (89.3)	88 (59.1)	87.1 (58.0)	89 (63.6)	85.1 (61.1)
Female	96 (41.2)	97.7 (42.3)	65 (38.7)	18.1 (10.7)	61 (40.9)	63.1 (42.0)	51 (36.4)	54.1 (38.9)
Hospitalization Status (%)								
Emergency Department	167 (72.2)	203.7 (88.2)	124 (73.8)	150.0 (89.7)	110 (73.8)	134.2 (89.3)	101 (72.1)	123.2 (88.5)
Hospitalized	66 (27.8)	27.2 (11.8)	44 (26.2)	17.3 (10.3)	39 (26.2)	16.1 (10.7)	39 (27.9)	16.1 (11.5)
Age (mean, (sd))	10.67 (3.27)	10.71 (3.27)	10.51 (3.28)	10.58 (3.29)	10.71 (3.37)	10.75 (3.38)	10.50 (3.42)	10.56 (3.39)
Age Category (%)								
5 - <13	168 (73.0)	165.3 (71.6)	123 (73.2)	122.6 (72.4)	103 (69.1)	104.6 (69.6)	99 (70.7)	99.7 (71.6)
13 - < 17	65 (27.0)	65.5 (28.4)	45 (26.8)	46.8 (27.6)	46 (30.9)	45.6 (30.4)	41 (29.3)	39.5 (28.4)
PaedsCTAS (%)								
1 (requires resuscitation)	8 (3.5)^	3.3 (1.4)	5 (3.0)^	2.1 (1.2)	5 (3.4)^	2.1 (1.4)	4 (2.9)	1.6 (1.2)
2	35 (15.2)	20.1 (8.7)	24 (14.3)	15.5 (9.2)	22 (14.8)	14.7 (9.8)	23 (16.4)	14.3 (10.3)
3	37 (15.2)	31.4 (13.6)	24 (14.3)	20.4 (12.0)	21 (14.1)	19.2 (12.7)	18 (12.9)	16.3 (11.7)
4	83 (36.1)	99.6 (43.2)	62 (36.9)	74.0 (43.7)	55 (36.9)	65.5 (43.6)	49 (35.0)	59.0 (42.3)
5 (non-urgent)	7 (3.0) ^	6.1 (2.6)	7 (4.2)^	6.1 (3.6)	5 (3.4) ^	4.5 (3.0)	6 (4.3)	4.9 (3.5)
Missing	63 (27.0)	70.4 (30.5)	46 (27.4)	51.3 (30.3)	41 (27.5)	44.4 (29.5)	40 (28.6)	43.1 (31.0)
Income Quintile (%)								
1 (lowest income quintile)	29 (12.4)	29.7 (12.9)	18 (10.7)	19.5 (11.5)	15 (10.1)	15.1 (10.0)	16 (11.4)	16.3 (11.7)
2	24 (10.3)	25.2 (10.9)	19 (11.3)	20.8 (12.3)	17 (11.4)	19.1 (12.7)	15 (10.7)	15.9 (11.4)
3	47 (20.2)	45.2 (19.6)	32 (19.0)	31.8 (18.8)	28 (18.8)	27.7 (18.4)	26 (18.6)	25.2 (18.1)
4	41 (17.6)	39.5 (17.1)	30 (17.9)	29.3 (17.3)	26 (17.4)	26.1 (17.3)	21 (15.0)	21.6 (15.5)
5 (highest income quintile)	80 (34.3)	78.2 (33.9)	60 (35.7)	59.4 (35.1)	54 (36.2)	53.7 (35.8)	56 (40.0)	55.4 (39.8)
Missing	12 (5.2)	13.0 (5.6)	9 (5.4)	8.6 (5.1)	9 (6.0)	8.6 (5.7)	6 (4.3)	4.9 (3.5)
Nature of Injury (%)								
Minor External Injury	87 (37.8)	103.7 (45.3)	60 (35.7)	70.8 (41.8)	54 (36.2)	63.4 (42.2)	50 (35.7)	58.6 (42.1)
Upper Extremity Injury	58 (25.2)	57.0 (24.9)	48 (28.6)	48.9 (28.8)	40 (26.8)	40.7 (27.1)	40 (28.6)	41.5 (29.8)
Lower Extremity Injury	33 (14.2)	26.5 (11.5)	25 (14.9)	21.6 (12.8)	21 (14.1)	19.2 (12.7)	18 (12.9)	15.5 (11.1)
Head Injury	23 (9.9)	24.0 (10.4)	15 (8.9)	15.9 (9.4)	14 (9.4)	14.7 (9.8)	14 (10.0)	13.8 (9.9)
Major Trauma	17 (7.3)	7.0 (3.0)	11 (6.5)^	4.5 (2.7)	11 (7.4)^	4.5 (3.0)	11 (7.9)	4.5 (3.3)
Other	13 (5.6)^	10.2 (4.4)	7 (4.2) ^	5.3 (3.1)	7 (4.7)^	5.3 (3.5)	6 (4.3)	4.1 (2.9)
Missing	2 (0.4)	2.4 (1.1)	2 (1.2)	2.4 (1.4)	2 (1.3)	2.4 (1.6)	1 (0.7)	1.2 (0.9)

	Baseline Unweighted	One-month Weighted	Four-months Unweighted	Twelve-months Weighted	Unweighted	Weighted	Unweighted	Weighted
Motor Vehicle Collision (%)								
Yes	16 (7.0)	8.2 (3.6)	9 (5.4)	4.5 (2.7)	8 (5.4)	4.1 (2.7)	8 (5.7)	4.1 (2.9)
No	214 (91.7)	219.8 (95.2)	156 (92.9)	162.0 (95.7)	137 (91.9)	143.7 (95.6)	128 (91.4)	131.9 (94.7)
Missing	3 (1.3)	2.9 (1.2)	3 (1.8)	2.9 (1.6)	4 (2.7)	2.5 (1.6)	4 (2.9)	3.3 (2.3)

* weighted frequencies have been back calculated from weighted percentages to represent the actual study size
^ low base, use caution in the interpretation of statistics and inferences

3.4.3 HRQoL trajectory and distribution

On average, the parent reported PedsQL total scale score following injury demonstrated a statistically significant decrease from baseline to one-month post-injury (baseline weighted total scale score mean of 90.5, and one-month weighted total scale score mean of 81.3, paired t-test $p < 0.001$). This was followed by a return to baseline at four-months post-injury with the four-month weighted total scale score mean being no longer clinically or statistically different from baseline. There was minimal change from four to 12 months. The 12-month weighted mean total scale score, was not statistically or clinically significantly different from the weighted mean at baseline or four-months post-injury (Table 3.9 crude, Table 3.10 weighted and Figure 3.5).

The parent-reported weighted physical and psychosocial health summary scores were statistically significantly different from each other at all time points (paired t tests $p < 0.001$, at all time points). The weighted mean physical health summary score started out significantly greater than the psychosocial health summary score at baseline (mean of 92.9 and 87.1 for physical and psychosocial health summary scores respectively), dipping lower at one-month post-injury (77.8 and 83.3), and raising higher again at four- and 12-months post-injury (Table 3.10, Figure 3.5).

A similar pattern was observed with the child self-reported weighted PedsQL total scale score with a statistically significant decrease from baseline to one-month post-injury in the weighted mean total scale score (paired t-test $p <0.001$) and returned to baseline at four-months (paired t-test of baseline and four-months total scale score $p = 0.220$). The weighted mean score at 12-months was similar to baseline and four-months (Table 3.11 crude, Table 3.12 weighted, Figure 3.6), but increased compared to one-month.

The weighted mean child-reported physical and psychosocial health summary scores were only statistically significantly different from each other at four- and 12-months post-injury.

At four- and 12-months post-injury, the weighted mean physical health summary score was higher than the psychosocial health summary score (paired t-test $p = 0.04$ and <0.001 for 4 and twelve-months, respectively) Figures 3.7 and 3.8.

For the same population of children, the weighted mean parent-reported PedsQL total scale score was not statistically significantly different from the weighted mean child-reported PedsQL total scale score at baseline, four- or 12-months post-injury. However, the weighted mean parent-reported PedsQL total scale score was statistically significantly lower at one-month post-injury relative to the weighted mean child reported PedsQL total scale score at the same time point (paired t test $p = 0.006$) (Table 3.12, Figure 3.6). This pattern was followed by both the physical and psychosocial health summary scores, with the parent-reported weighted means being not statistically significantly different from the child-reported at baseline, four- or 12-months post-injury and being statistically significantly lower than the child weighted means at one-month post-injury (paired t-test $p = 0.004$ and $p=0.030$ for the weighted physical and psychosocial summary health scores respectively) Figures 3.7 and 3.8.

Figure 3.5 Parent-report PedsQL total scale, physical health summary and psychosocial health summary scores, weighted mean with 95% CI

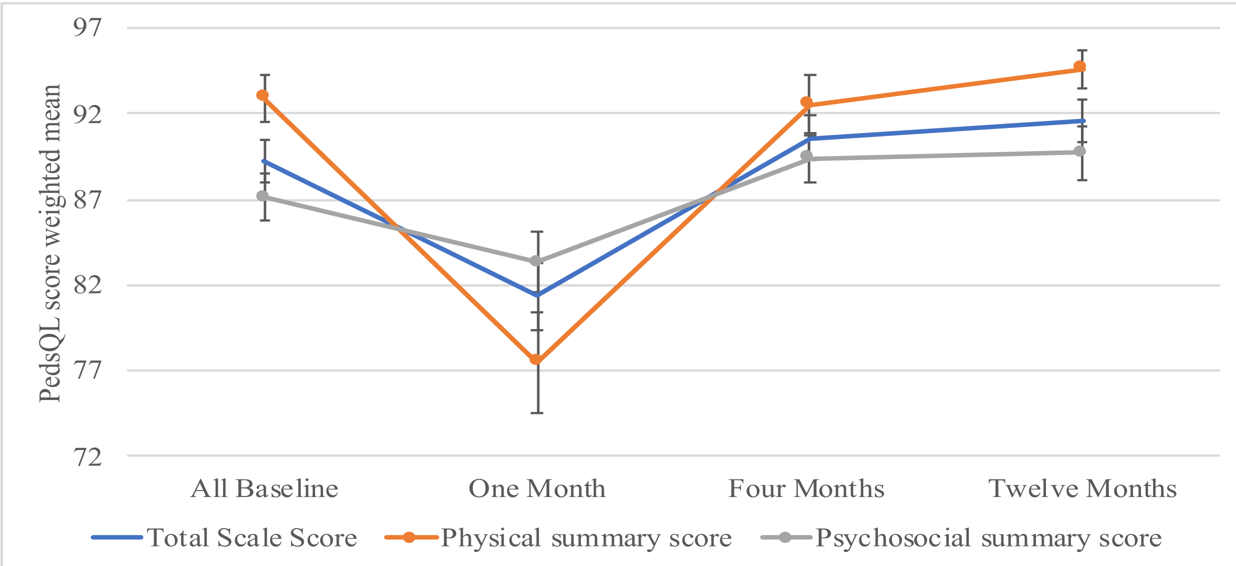


Figure 3.6 Child and parent sub-population PedsQL total scale score, weighted mean with 95% CI

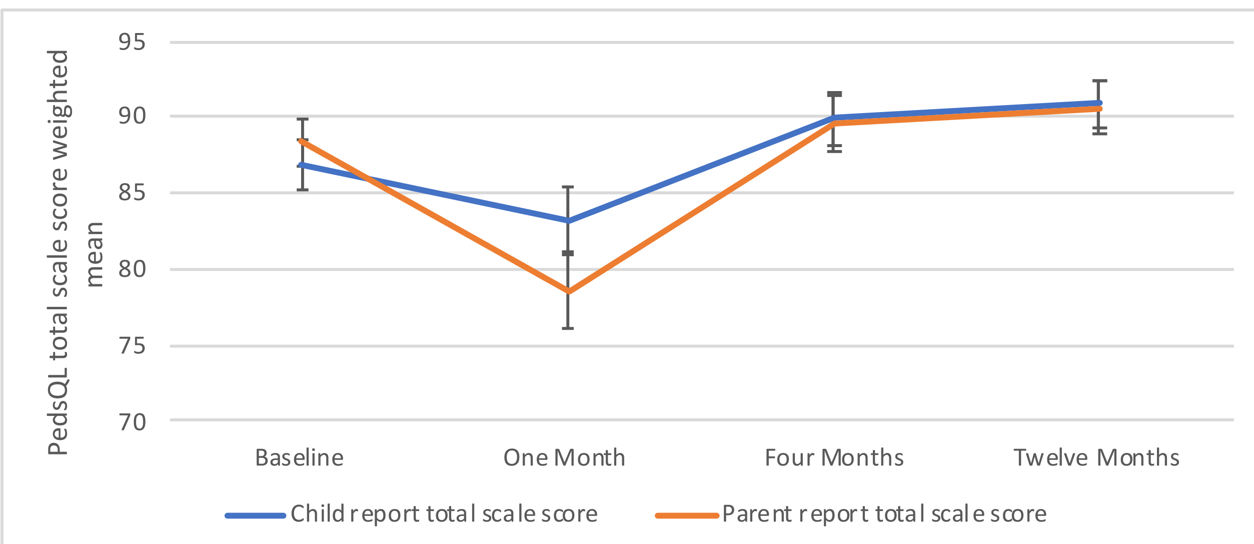


Figure 3.7 Child and parent sub-population physical health summary score, weighted mean with 95% CI

Figure 3.8 Child and parent sub-population psychosocial health summary score, weighted mean with 95% CI

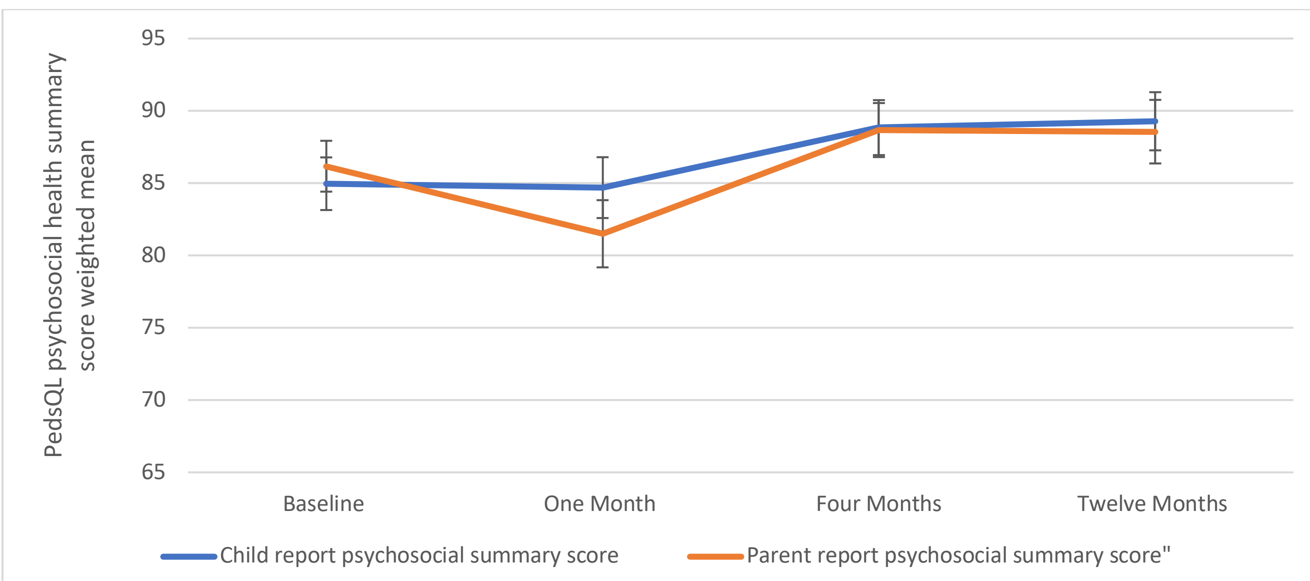


Table 3.9 Distribution of parent report PedsQL scores by time point (children 0 -16 years) - unweighted

	n	mean	SD	median	IQR	MIN	MAX	# 100	% with 100
Total scale score									
All Baseline	354	89.25	11.90	92.39	14.13	22.83	100	68	19.21
One-month	266	78.55	18.01	82.61	25.00	18.48	100	27	10.27
Four-months	240	90.31	10.57	92.86	13.04	34.78	100	53	22.36
Twelve-months	225	91.46	9.65	94.57	13.08	55.43	100	63	27.48
Physical Heath Summary Score									
All Baseline	352	92.84	13.44	96.88	9.38	9.38	100	170	48.29
One-month	265	73.24	26.77	81.25	37.5	0.00	100	59	22.05
Four-months	240	91.84	14.16	97.22	9.38	0.00	100	118	49.79
Twelve-months	225	94.25	9.27	100	9.38	46.88	100	119	52.70
Psychosocial Health Summary Score									
All Baseline	354	87.25	13.17	90.38	18.33	25.00	100	84	23.36
One-month	265	81.55	15.27	85.00	21.67	28.33	100	33	12.45
Four-months	239	89.38	10.70	91.67	15.38	51.39	100	65	27.20
Twelve-months	225	89.84	11.79	94.23	16.67	43.33	100	70	31.11

Table 3.10 Distribution of parent report PedsQL scores by time point (children 0 -16 years) - weighted

	n	mean	SD	median	IQR	MIN	MAX	# 100	% with 100
Total scale score									
All Baseline	349.36	90.49	11.81	92.39	14.13	22.82	100.00	66.77	19.22
One-month	267.88	81.34	16.64	85.68	28.74	18.48	100.00	31.32	11.78
Four-months	243.44	91.06	10.47	92.86	12.15	34.78	100.00	58.99	24.44
Twelve-months	223.53	91.86	9.56	94.57	14.14	55.43	100.00	59.86	27.03
Physical Health Summary Score									
All Baseline	349.36	92.93	13.08	96.88	9.38	9.38	100.00	163.29	47.01
One-month	267.88	77.81	24.60	87.36	37.50	0.00	100.00	67.51	25.39
Four-months	243.44	92.57	13.96	100.00	9.38	0.00	100.00	126.96	52.59
Twelve-months	223.53	94.62	8.63	100.00	6.25	46.88	100.00	117.67	53.13
Psychosocial Health Summary Score									
All Baseline	349.36	87.14	13.30	90.38	18.33	25.00	100.00	81.43	23.45
One-month	267.88	83.35	14.65	86.54	20.08	28.33	100.00	38.63	14.53
Four-months	243.44	89.38	11.18	91.67	16.67	45.45	100.00	70.39	28.99
Twelve-months	223.53	89.75	11.97	93.33	16.67	43.33	100.00	69.22	30.52

Table 3.11 Distribution of child-report & parent report PedsQL scores by time point (children 5 -16) – unweighted

	n	Mean	SD	median	IQR	MIN	MAX	# 100	% with 100
Total scale score									
All Baseline -child-report	233	86.80	12.69	90.22	15.22	21.74	100	34	14.78
All Baseline – parent-report	228	88.32	12.42	91.30	14.13	33.73	100	36	15.79
One-month -child- report	168	81.20	15.70	84.78	22.83	34.78	100	17	10.30
One-month – parent-report	163	76.67	17.39	79.35	26.09	18.48	100	13	7.98
Four-months – child-report	149	89.35	11.53	93.48	15.12	42.39	100	32	21.92
Four-months – parent-report	144	89.44	11.41	91.85	13.04	34.78	100	30	20.83
Twelve-months – child-report	140	90.95	9.71	94.02	11.96	61.96	100	33	23.91
Twelve-months – parent-report	136	90.71	10.29	94.02	13.48	55.43	100	34	25.00
Physical health summary score									
All Baseline	230	90.35	15.53	96.88	12.50	3.12	100	95	41.30
All Baseline – parent-report	228	92.03	15.19	96.88	9.38	9.38	100	110	48.25
One-month – child-report	165	77.48	24.41	87.5	37.50	6.25	100	43	26.06
One-month – parent-report	163	69.80	26.39	71.88	40.10	0.00	100	28	17.18
Four-months – child-report	146	90.96	14.18	93.75	12.50	0.00	100	64	43.84
Four-months – parent-parent	144	90.60	16.45	96.88	9.38	0.00	100	70	48.61
Twelve-months – child-report	138	93.84	8.58	96.88	9.38	56.25	100	66	47.83
Twelve-months -parent-report	136	93.93	9.84	100.00	9.38	46.88	100	74	54.41
Psychosocial health summary score									
All Baseline child-report	230	84.67	14.28	88.33	20.00	31.67	100	40	17.39
All Baseline – parent-report	228	86.22	13.49	89.17	20.00	35.00	100	46	20.18
One-month – child-report	160	83.36	14.19	86.67	21.67	36.67	100	24	15.00
One-month – parent-report	163	80.39	15.53	83.33	21.67	28.33	100	16	9.82
Four-months – child-report	146	88.55	11.91	91.67	16.67	50.00	100	38	26.03
Four-months – parent-report	144	88.81	11.18	90.83	15.42	53.33	100	36	25.00
Twelve-months – child-report	138	89.38	11.87	93.33	16.67	46.67	100	38	27.54
Twelve-months – parent-report	136	88.96	12.73	93.33	18.33	43.33	100	39	28.68

Table 3.12 Distribution of child self-report & parent report PedsQL scores by time point (children 5 -16) - weighted

	mean	SD	median	IQR	MIN	MAX	# 100	% with 100
Total scale score								
Baseline – child-report	87.05	12.33	89.70	15.16	21.74	100	34	14.86
Baseline - parent-report	88.41	12.12	91.30	14.03	33.73	100	36	15.73
One-month – child-report	83.47	14.71	86.96	22.83	34.78	100	17	10.16
One-month – parent-report	78.57	16.62	80.43	22.82	18.48	100	13	7.77
Four-months – child-report	90.22	11.17	93.48	13.04	42.39	100	32	21.60
Four-months – parent-report	89.52	11.56	92.02	13.76	34.78	100	30	20.25
Twelve-months – child-report	91.09	9.76	93.48	12.49	61.96	100	33	23.84
Twelve-months – parent-report	90.62	10.23	93.38	13.00	55.43	100	34	24.56
Physical health summary score								
Baseline – child-report	90.36	15.27	93.75	12.5	3.12	100	95	41.52
Baseline - parent-report	92.08	14.58	96.88	9.38	9.38	100	110	48.07
One-month – child-report	80.83	22.79	88.86	29.63	6.25	100	43	25.70
One-month – parent-report	77.70	24.96	75.00	37.07	0.00	100	28	16.73
Four-months – child-report	92.06	13.60	96.88	12.50	0.00	100	64	43.19
Four-months – parent-report	91.06	16.56	98.91	9.38	0.00	100	70	47.24
Twelve-months – child-report	93.75	8.40	96.88	9.38	56.25	100	66	47.68
Twelve-months – parent-report	93.78	8.92	100.00	9.38	46.88	100	74	53.46
Psychosocial health summary score								
Baseline – child-report	85.06	14.09	88.33	18.34	31.67	100	40	17.48
Baseline - parent-report	86.17	13.55	88.33	20.00	35.00	100	46	20.10
One-month – child-report	84.81	13.58	88.33	18.33	36.67	100	24	14.34
One-month – parent-report	81.50	15.13	85.00	20.78	28.33	100	16	9.56
Four-months – child-report	89.08	11.72	91.67	16.67	50.00	100	38	25.55
Four-months – parent-report	88.67	11.44	90	18.27	53.33	100	36	24.20
Twelve-months – child-report	89.28	12.05	93.33	16.67	46.67	100	38	27.45
Twelve-months – parent-report	89.30	13.08	93.33	18.33	43.33	100	39	28.18

PedsQL total scale scores were negatively skewed at all times for both the parent-report and child-report and demonstrated a ceiling effect at all time points with the exception of one-month post-injury. At baseline, one, four- and 12-months post-injury, 19%, 12%, 24%, and 27% of parent-reporters provided a score of 100 for the total scale score, respectively (Figures 3.9 and 3.10, Table 3.9). A similar pattern was observed among the child-reporters (Figures 3.11 and 3.12, Table 3.12). At one, four and 12 months post-injury, there were two, one and four parents who indicated that their child was still affected by their injury while reporting the upper bound of 100 on the PedsQL total scale score.

Figure 3.9 Histograms of parent report PedsQL total scale score at each time point - unweighted

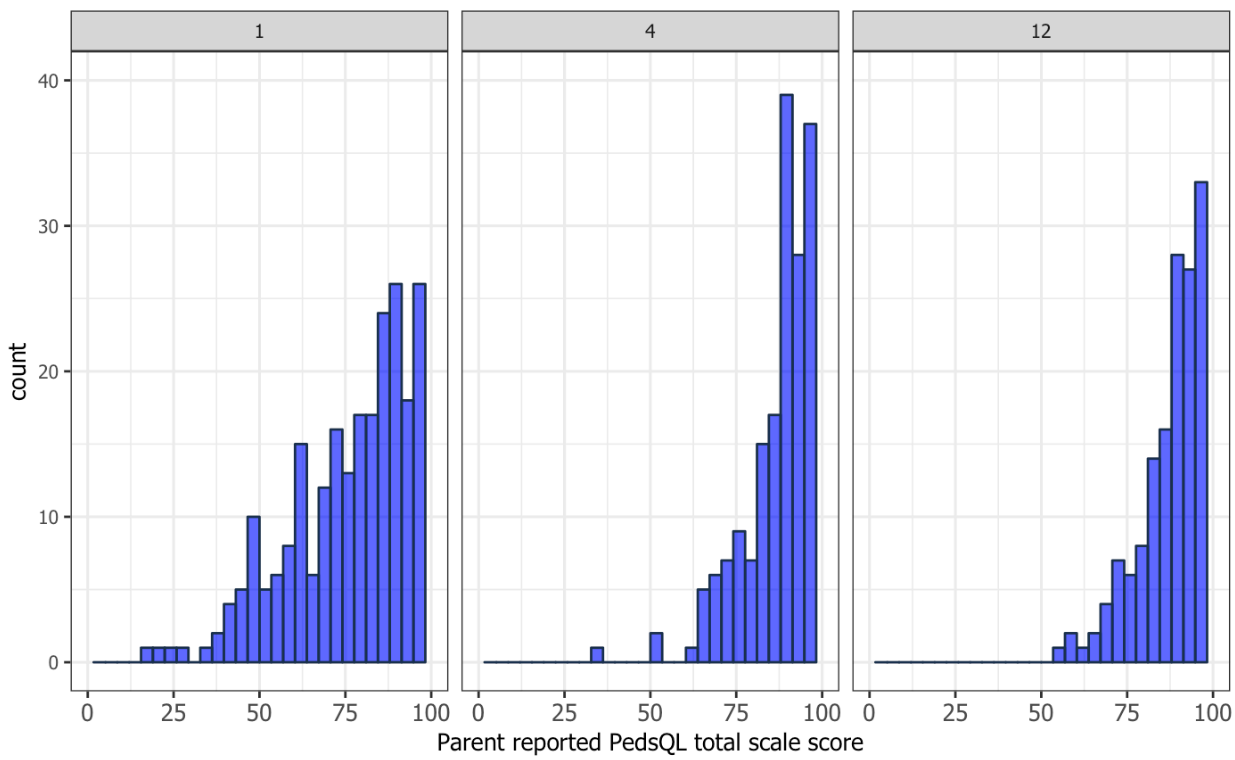


Figure 3.10 Boxplots of parent report PedsQL total scale score by time following injury

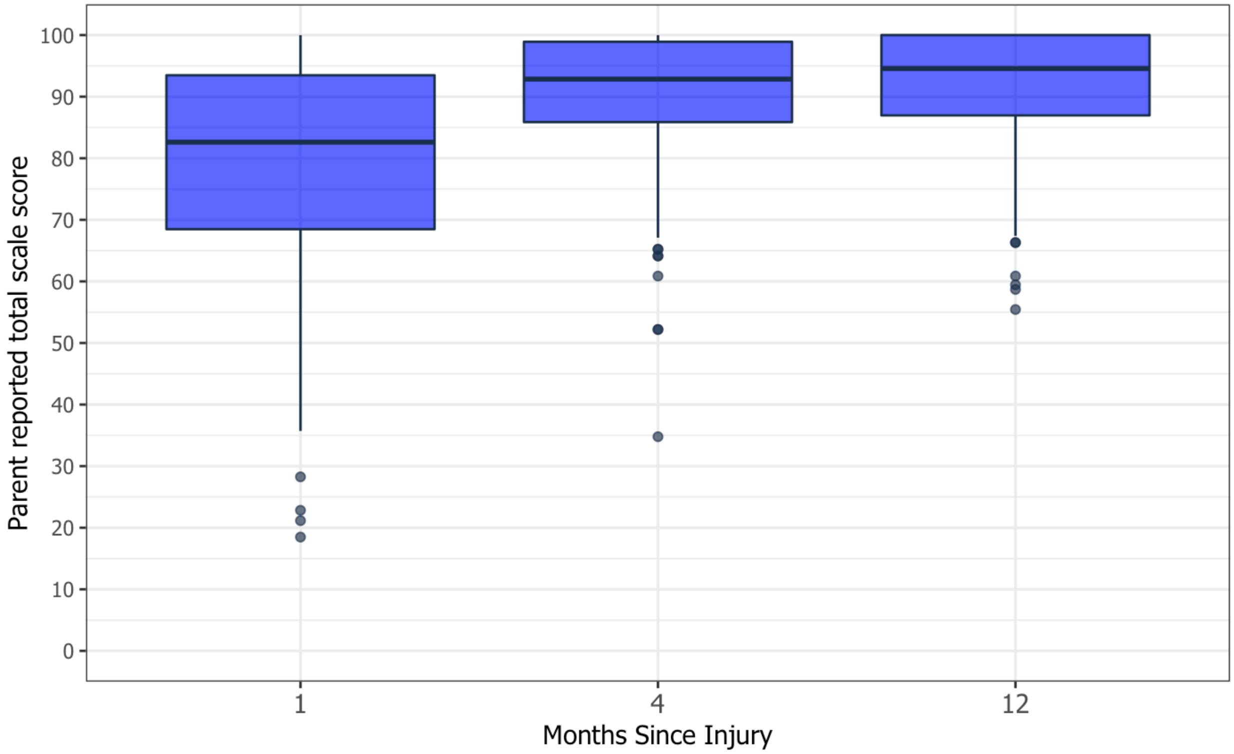


Figure 3.11 Histograms of child self-report PedsQL total scale score at each time point – unweighted

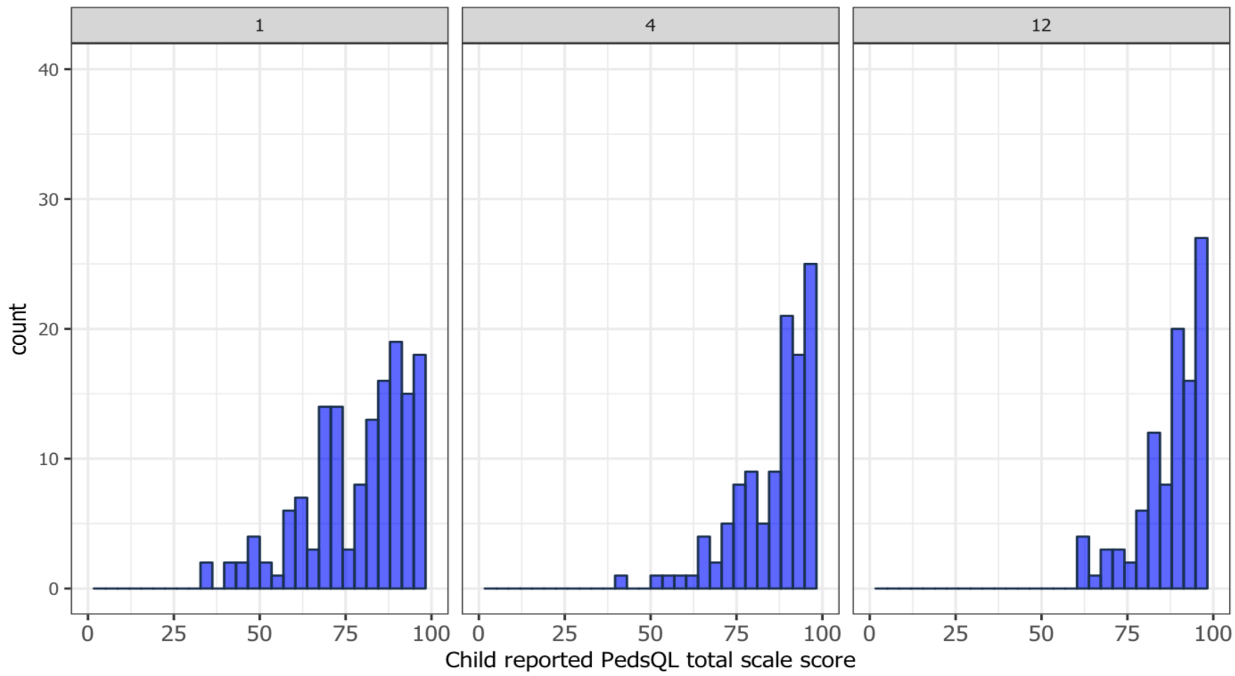
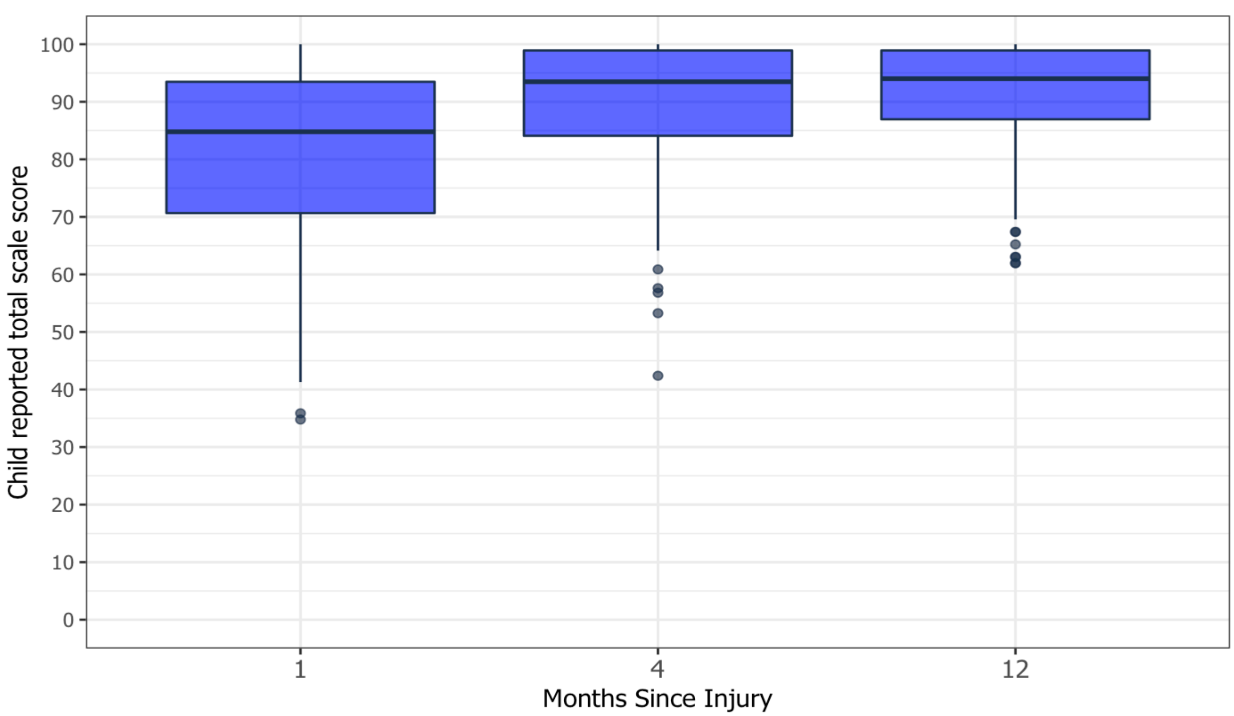


Figure 3.12 Boxplots of child self-report PedsQL total scale score at each time point – unweighted



3.5 Discussion

3.5.1 Study population and missing data

The first objective of this chapter was to describe the CYBOI study population, examine how representative the population is of the target population, explore patterns of data missingness and investigate demographic and injury related variables associated with loss to follow-up. Relative to the general injury population presenting to BCCH during the study period, the study participants had significantly higher odds of being in the highest income quintile relative to the lowest, higher odds of being older and higher odds of having been hospitalized. The higher odds of having been hospitalized, with 29% of children in the study population being hospitalization as a result of their injury, and 11% in the general injury population, was a direct result of the intentional over sampling of hospitalized children to allow for a mix of injury severities. The average age of the study population was approximately one year older than that of the general injury population, despite this there is representation across all age categories in the study population including those < 5 thus an examination of the impact of age will be possible. The under representation of the lowest income quintile is in line with research from other developed countries that has found that families with disadvantageous socioeconomic backgrounds tend to be underrepresented in health research (103,104). It is possible that being from a lower income bracket could be associated with a detrimental impact on HRQoL recovery, which may not be captured with these data due to small sample size. However, income was not identified as a predictive factor for HRQoL following childhood injury in any of the studies included in the literature review in Chapter 2. In accordance with other studies of childhood injury, the study population was over 60% male, as was seen in the preceding literature review where over half of the studies, (n=17) had populations that were 60% or more male.

Although the study sample represents only 44% of the eligible population approached for study participation, a wide breadth of injuries was sampled and the over-sampling of injuries that required hospitalization was achieved. To be used in mixed effects models all variables must have representation across all time points, this was realized with the exception of the proportion of children in MVC and the highest PaedsCTAS scores. To address this issue, PaedsCTAS scores in subsequent chapters were collapsed for modelling and MVC was not investigated as a predictor of HRQoL. The follow-up rate of 64% for parent-report and 60% for child-report at 12 months post-injury is within the range of follow-up for other studies of HRQoL among injured children, although it is at the lower end. In Chapter 2, the literature review found five of the 27 studies had follow-up rates less than 70%.

The missing outcome data (PedsQL total scale score) in the CYBOI data were primarily observed to be monotone and missingness was not MCAR given the association of follow-up with both income quintile and baseline HRQoL. It is possible data were MNAR with missing HRQoL data being associated with the HRQoL of the individual at that time point given the borderline significance of hospitalization with missingness in the unweighted sample. There is some evidence that missing data were MAR, as it was observed that the mean HRQoL at the time point before being lost to follow-up was not statistically significantly different across individuals at different drop out times. However, given the majority of attrition occurred from baseline to the first follow-up the possibility of differential loss to follow-up cannot be ruled out. Inherent in the definitions, there is no way to test if data are MAR or MNAR without collecting additional data. In some cases, it is possible to follow-up on a group of the non-responders to ask a few key questions and compare responses from those who answered the study to those who did not, this type of follow-up was not possible for the CYBOI study. When follow-up is not possible, plausible assumptions are often made based on patterns of missingness and associations of missingness with available variables; however, sensitivity analyses have been recommended for many years (105). The National Research Council's Panel on Handling Missing Data in Clinical Trials recommends that, "*examining sensitivity to the assumptions about the missing data mechanism should be a mandatory component of reporting*" (106). Given the possibility of data being MNAR with informative drop-out, a sensitivity analysis with imputed values systematically lower than those expected under the assumption of MAR will be explored in the next chapter.

3.5.2 HRQoL distribution and trajectory

The second and third objectives of this chapter describe the distribution and trajectory of self-reported and parent-reported child HRQoL in the year following injury as measured by the PedsQL. It was found that on average children's total scale scores had returned to baseline by four-months post-injury as reported both by parents and children. The trajectory of HRQoL appeared nonlinear, with a curve from one-month to 12 months. In addition, a ceiling effect was observed with the PedsQL for the total scale score and both the physical health and psychosocial health summary scores at all time points with the exception of the psychosocial score at one-month post-injury. Varni et al observed a ceiling effect in only the physical health score in a sample of healthy children aged 2-18 years with 39.6% reporting a perfect score (98). However, the authors pointed out these ceiling effects may have been attenuated in their research given their study population (98). A ceiling effect was observed in the physical health summary score of the PedsQL among 150 injured children at six and 12 months post-injury by Gabbe et al, but not with the psychosocial score (30). This difference may be explained by their sample, where only children who were admitted to hospital with a length of stay of greater than three days were included. Stevens et al observed a ceiling effect of the total scale score and both the physical health and psychosocial health summary scores of the PedsQL among children 2-18 years with minor injuries at baseline and at one to two weeks post-injury (31).

Apparent ceiling effects in HRQoL data are difficult to interpret as it is possible that the highest possible score represents a scale constraint or it may represent an individual with the highest possible self-perceived HRQoL (107). A 2017 study of adults examined EQ5D-5L results among the general population to discern if the highest possible score truly represented an individual with “no problems” or was more often a result of a constraint of the tool. The study found that the highest possible score was strongly related to morbidity, indicating that “no problems” might represent truly healthy participants (107). No similar study was found among children. In this chapter it was found that 95% of parents reporting a score of 100 on the PedsQL total scale score for their child also indicated that their child was not impacted by their injury. This suggests that it is possible the apparent ceiling effect is largely representative of individuals with no residual problems, with a small proportion of individuals having problems not captured by the PedsQL, either due to reporter inconsistencies or a true ceiling effect. Regardless, it is acknowledged that the negatively skewed distribution of the HRQoL data and the proportion of individuals with the greatest possible score in this study will need to be taken into consideration when conducting statistical analyses (e.g. regression models).

The Tobit regression model is one method of analyzing censored data and can be used for data with a ceiling effect (108). The model assumes scores beyond one are theoretically possible, and therefore, when used on HRQoL data the tool is erroneous in bounding the distribution at one (109). As discussed above, the upper bound is in fact an appropriate measure for some individuals HRQoL, as much of the time values at the upper bound represent individuals who view themselves as having no problems with their HRQoL. For this reason, the Tobit model may not be the best solution for the ceiling effect of HRQoL data (109). Another approach is to use a model that is robust to normality assumptions and data skewness, while using a nonlinear form that describes the data as approaching an asymptote. Nonlinear quantile mixed models (NLQMM) are an attractive solution as they provide interpretable parameter estimates, do not require the normality assumptions of ordinary least squares (OLS) regression models, and are valid in the presence of skewness and outliers (110). Further discussion and application of modelling techniques for this data can be found in the next chapter.

3.6 Conclusion

In this chapter HRQoL data following childhood injury has been described, both as reported by a parent proxy and by the child. It was found that most children recovered to baseline HRQoL scores as reported by both proxy and self-report by four-months post-injury. The skewed distribution and ceiling effect present in the HRQoL variable was identified as was the predominantly monotone pattern of missingness in this data. Understanding the distribution of the variables and pattern of missingness allows for appropriate considerations in future analyses. The next steps with these data will be longitudinal modelling of HRQoL data to identify variables associated with HRQoL following childhood injury.

Chapter 4: Longitudinal Modelling HRQoL Variables

4.1 Introduction

Given the sheer magnitude of childhood injuries, it is important to understand the pattern and timeframe of recovery to allow for the appropriate provision of resources and support throughout recovery. It has been recommended that longitudinal studies with multiple assessments over time be conducted in general injury populations, with specific interest on the impact of injuries on children (48). Such longitudinal research allows for investigation into both the pattern of recovery and insight into any permanent consequences of injury. As found in Chapter 2, the literature on HRQoL following childhood injury is growing, but there are still a limited number of studies that have investigated factors associated with recovery applying appropriate longitudinal analyses that account for correlation over time and allow for multivariable analysis. In addition, more studies have been called for that include less serious injuries, such as those presenting to the ED, and studies that collect and analyze the HRQoL of children following injury from both the child's and the parent's perspectives (111).

Parent and child perspectives of children's HRQoL are different outcome measures; both are important in their own right and both should be gathered when possible. Parent perception of children's HRQoL is a driving factor behind health care utilization (37–39) and children's perspective should be the outcome of interest in providing healthcare as it is their health and well-being that is in question. As stated by another group of investigators, the question is not which perspective is accurate, but what each contributes to the understanding of pediatric HRQoL (112). Parental reports may be gathered to get a deeper understanding of a child's HRQoL from another perspective, in which case differences in parent-proxy and child self-report HRQoL measures may not be relevant (113). In other instances, children are unwilling to or cannot provide their own response, and as such, parent-report may be the only measure available.

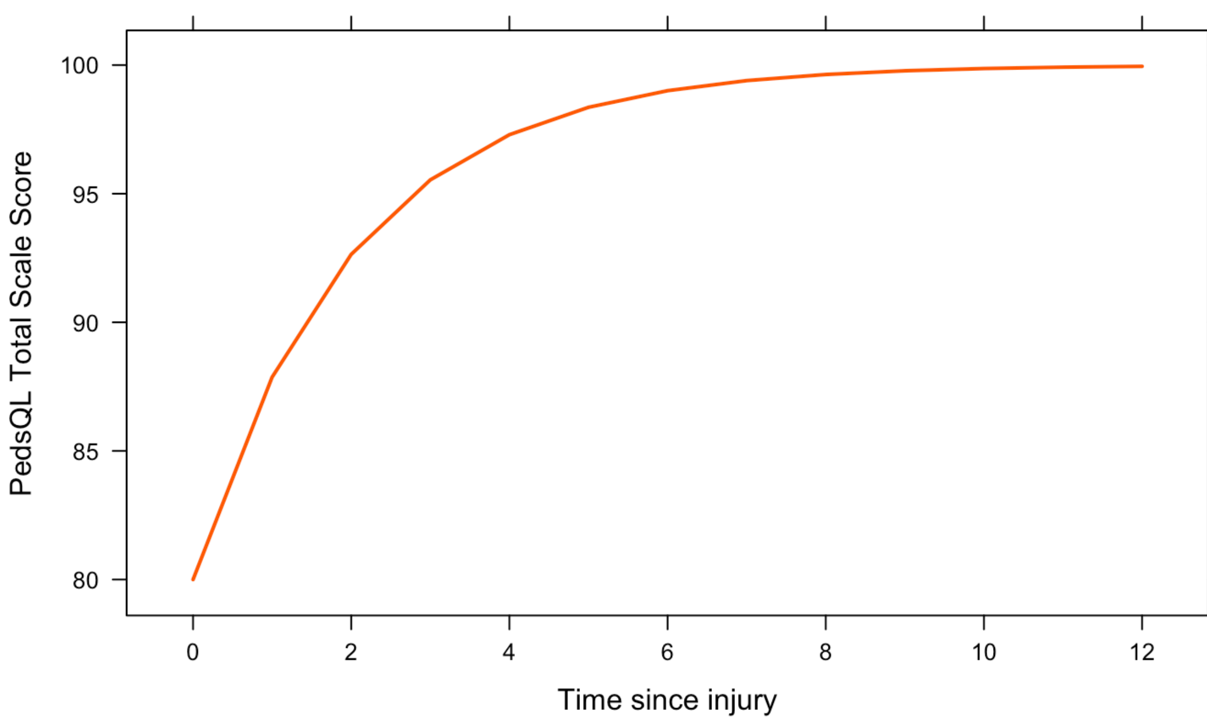
In these situations, it is helpful to understand where differences in parent- and child-reported HRQoL lie and to what extent parent-reports are an appropriate proxy for children's experiences. The conclusion of a 2016 systematic review on the agreement between parent- and child-reported HRQoL reinforced that while self-report should be gathered whenever possible, parent proxy as a secondary outcome can provide important additional information (36). These findings were further validated in the most recent systematic literature on the topic explored in Chapter 2 of this dissertation.

With regards to multivariable modelling, there are a number of techniques that can be applied to longitudinal data that address the correlation between time points in different situations. Each technique has its own set of assumptions regarding the data being examined, which must be met for it to be valid. The challenge is to choose an appropriate statistical model; one that is suitable in terms of the distributional assumptions on the error, accounts for the correlation of repeated measurements, accounts for the boundedness of the outcome and, in the case of the CYBOI, accounts for nonlinear temporal trajectories (114). The challenges of choosing such a model are compounded by the inherent need to convey the derived information to a variety of stakeholders in a concise and understandable manner, many of whom may have limited statistical understandings. Past analyses of longitudinal HRQoL data have varied across all of the literature, and often do not take into account the correlated nature of longitudinal data and/or data missingness as demonstrated in Chapter 2. Another example of this issue is found in a review by the, "Setting International Standards in Analysing Patient-Reported Outcomes and Quality of Life endpoints data" (SISAQOL) group, working toward standardizing analysis of QoL data in randomized cancer clinical trials. In their review on the quality of statistical methods for analyzing QoL data in cancer randomized controlled trails, the authors found that, of 33 studies, eight (24%) used methods suitable for repeated measures (115). The review did not discuss the suitability of the analyses used based on the distribution of HRQoL data.

Even when techniques that account for data correlation are applied in longitudinal analyses, there can be issues in the analytical processes. For example, the commonly applied multivariable analysis of variance is a form of a complete case analysis which, in addition to making the assumption that the covariance structure of the data is compound symmetric (also known as exchangeable), requires data be MCAR. However, even if data are MCAR this analysis can produce biased estimates due to unbalanced designs (45). Linear mixed-effects models (LME), another potential approach, apply maximum likelihood methods that allow data to be the more realistic MAR. In these mixed models both individual-level patterns of change (individual random effects) and population-level averages (fixed effects) can be estimated. The variance-covariance structure of the random effects addresses the correlation between repeated measures in these models. One way of addressing the issue of nonlinearity (as seen in the data from the CYBOI study) is to include time as a categorical variable, especially within a contained set of time-specific event captures. This is possible with the CYBOI data given the small number of follow-up points. This method can be effective; however, it does increase the number of parameters in the model, which may be an issue in model building and lead to overparameterization and overfitting, potentially resulting in misleading results. In addition, LME assumes a normal error distribution. This is not the case with bounded HRQoL data, a situation that especially becomes an issue when a ceiling effect is present as is the case with the CYBOI data. Transformations can be used to address both nonlinearity and bounded outcomes although this method leads to parameter estimates that are less directly interpretable and may overfit to specific datasets, limiting their representativeness.

Nonlinear mixed-effects models (NLME) address the issue of nonlinearity while providing parameter estimates with clear interpretations, although it is also subject to the normality assumption on the error. In the case of NLME, a function that fits the nonlinear relationship between time and HRQoL must be identified. In the CYBOI study, the number of nonlinear models that can be explored are limited by the small number of follow-up points. Given the trajectory seen in the CYBOI data, an asymptotic regression function may be a good candidate (see Figure 4.1). This model has the form: $\mathrm{A} + (\mathrm{R} - \mathrm{A})e^{-bx}$ where A is the horizontal asymptote (in this case 100, the maximum value on the PedsQL), R is the intercept and b is the rate of the curve. Because the horizontal asymptote is fixed at 100, the intercept and rate are the variables that would be predicted by injury related and demographic variables.

Figure 4.1 Theoretical asymptotic regression function



If the assumption of normal errors is violated, a different approach is required to avoid standard errors being underestimated. The application of quantile regression for longitudinal data allows for modelling of any quantile of interest, is not restricted by assumptions regarding residuals, and is robust to outliers and outcome skewness (110). Quantile regression can be used longitudinally as a mixed model accounting for data correlation and can follow a linear or nonlinear form.

This chapter addresses a gap in the literature regarding how HRQoL evolves in the year following childhood injury from both parent's and children's perspectives, including identifying factors associated with the changes observed. In addition, given the unique attributes of the HRQoL outcome and the lack of literature applying appropriate analyses in this area, the impact of different models on the parameter and error estimates is examined through the application of linear mixed effects models (LME), nonlinear mixed effects models (NLME), non-linear quantile mixed models (NLQMM), and generalized liner mixed models (GLMM) with a binary distribution and logit link. The specific aim of this chapter is to address the following questions: 1) What demographic and injury related variables are predictive of decreased HRQoL in the year following childhood injury? 2) What longitudinal modelling method best fits the data given the attributes identified in the previous chapter?

4.2 Objectives

4.2.1 Primary

1. Identify demographic and injury related variables associated with lower PedsQL total scale scores reported by parents in the year following injury using data collected in the CYBOI study.

2. Identify demographic and injury related variables associated with lower PedsQL total scale scores reported by children in the year following injury using data collected in the CYBOI study.

4.2.2 Secondary

1. Compare results of longitudinal modelling methods predicting the PedsQL total scale scores in the year following childhood injury. Examine variables included and the direction, magnitude and significance of parameter estimates.
2. Compare results of the longitudinal models of the PedsQL total scale score between child and parent population response (parents who had children who provided self-response HRQoL) in terms of significant variables, and direction, magnitude and significance of parameter estimates

4.3 Methods

The study population and data collection are described in Chapter 3.

4.3.1 Statistical methods

4.3.1.1 Outcomes

The primary outcomes included in this analysis were parent- and child-reported children's HRQoL as determined by the total scale score from the PedsQL at one, four- and 12-months post-injury. In addition, a dichotomous variable was created to represent recovery. Children were considered "recovered" if their total scale score was within the minimally clinically important difference (MCID) of their baseline total scale score (a score that is greater than or equal to their baseline total scale score minus 4.4 points for self-report and 4.5 points for parent-report (32)). A sub analysis of parents whose children provided their own responses to the PedsQL (children > 5 years) was performed to allow for comparison of parent and child results, this population is referred to as the parent sub-population from this point forward.

4.3.1.2 Potential predictive variables

The variables that were explored as possible predictors of the outcomes described above included: child's age at the time of injury, explored continuously and as a categorical variable based on the PedsQL categories < 5 years, 5- <8 years, 8- <13 years, 13- <17 years old; child's sex; hospitalization status; PaedsCTAS (three levels 1, 2 and 3 as described previously with PaedsCTAS of 1 and 2 combined, and 4 and 5 combined due to low bases); parents income quintile (ordered categorical variable 1 lowest quintile, 2, 3, 4, 5 highest quintile); parents highest level of education (ordered categorical variable: some high school/ graduated high school or some trade school/college/university; diploma from trade school or college; university degree; post-graduate degree); injury category (minor external; upper extremity fracture; lower extremity fracture; head injury; major trauma; other); and child's baseline total scale score on the PedsQL.

4.3.1.3 Bivariable analysis

All descriptive analyses and bivariable statistics reported are weighted due to the over sampling of hospitalized children, where the weights were calculated at each time point to account for attrition. All modelling was on the crude data, where the over sampling of hospitalized children was controlled for by the inclusion of hospitalization status as a covariate in the models. Analyses were performed using R version 3.5.2, Vienna, Austria (116), in the integrated development environment RStudio version 1.0.153, Boston, MA (117). Additional packages used are cited as appropriate.

The intercept, slope and distribution of the total scale score as reported both by parents and children have been visualized in the form of trellis plots with a random sample of 36 participants (R package Lattice: multivariate Data Visualization with R)(118), spaghetti plots and box plots by age category, gender and hospitalization status (the variables most often found to be significant predictors of HRQoL in Chapter 2).

The total scale score and the dichotomous recovery outcome, were described by all of the potential predictive variables listed above at each time point by median and IQR, and by frequencies and percentages. Bivariable associations between the potential predictive variables with the median total scale score at each time point were investigated by Mann-Whitney-U and Kruskal-Wallis tests. Based on the central limit theorem, t-tests and one-way ANOVA are robust to non-normality when the sample size is large but given the highly skewed nature of these outcome in the CYBOI data, medians were a better representation of central tendency. Significant Kruskal-Wallis test results were followed by a post-hoc Dunn-Bonferroni test to determine where differences in medians existed. This test compares all possible pairs of medians with a correction to the alpha to account for multiple testing.

4.3.1.4 Model building

Models identifying predictors of decreased HRQoL over time were built for the parent- and child-response total scale score and for the parent sub-population. To allow for direct comparison of child response and parent sub-population models, the parent sub-population models included the same variables as the child-response models, regardless of significance testing. Four different mixed effects models were fit to the data: 1) linear mixed effects models (LME), 2) non-linear mixed effects models (NLME), 3) non-linear quantile mixed model (NLQMM), and 4) generalized liner mixed model (GLMM) with a binary distribution and logit link. In all models where time was continuous, the variable was centered on one-month, where time was categorical one-month was used as the reference category. In addition, baseline total scale score was centered on the mean. Centering was performed to allow the intercept to be interpreted as the mean total scale score at one-month post-injury in the LME and NLME and the median in the NLQMM.

For the LME, the R package lme4: Linear Mixed-Effects Models using 'Eigen' and S4 was used (119). The first model built was the empty means, random intercept model, to only account for the random effect of study participants (120). This model was then compared to a model including a fixed effect for time. A significant result for this variable indicates, on average, there is change in the outcome over time. The model with a fixed effect for time was then compared to one with a random effect of time (i.e. a random slope). A significant result for the random effects model indicates individuals differ in their rates of change in the outcome over time. The significance of additional fixed effects was evaluated via associated Wald test p-values. The significance of random effects was evaluated via associated likelihood ratio tests (LRT) and information criteria (Akaike Information Criterion (AIC) and Bayesian Information Criterion (BIC)) between models with the same fixed effects, where smaller values indicate a better fitting model (121). All models were estimated using maximum likelihood.

After the appropriate model for time was determined, the relationship between the outcome and the eight demographic and injury related variables identified as potential predictive variables (age, sex, hospitalization status, PaedsCTAS, baseline total scale score, injury type, income quintile and highest education of parent(s)) was examined. Each of these time invariant predictors were added to the appropriate model of time independently first as a fixed effect, and if significant, as a modifier of the random effects in the model. Each variable determined to be significant in the bivariable model was added in order of significance based on bivariable model p-values to the final model and retained if Wald test or LRT had a p value < 0.05. Potential interaction terms deemed relevant from the empirical literature were tested for significance in the final model. Collinearity was assessed by the covariance correlation matrix and, if present, the variable that had the stronger relationship with the outcome as determined by the bivariable model was included in the final model.

The intraclass correlation (ICC) or rho (ρ) was calculated from the empty means random intercept model and for the final model for each outcome as follows:

$$ICC = \frac{\text{(between person variation (the random intercept variance)}}{\text{(between person (random intercept variation) + within person variation (residual))}}$$

The ICC represents the proportion of intercept variation due to between-person differences in the intercept and can be interpreted as "the proportion of the variance explained by the grouping structure in the population" (122). The ICC is useful as it can provide information about whether the outcome is a trait that does not vary within an individual on various occasions but varies across individuals, or is it a state that does not vary across individuals but does vary across occasions. An ICC closer to 1 indicates most of the variation in the outcome is due to differences between people (cross sectional differences) relative to within person variation (longitudinal differences). R^2 was calculated and interpreted as the proportion of the variance in the outcome explained by the given model but was not used for intra-model comparisons. The marginal R^2 describes the proportion of total variance explained by the fixed effects, and the conditional R^2 describes the proportion of the total variance explained by the fixed and random effects. Although the R^2 is not a measure of model fit, it provides information on how much of the variation in the outcome is explained by the model; a small R^2 indicates a large proportion of the variation in the outcome is left unexplained by the model.

For the NLME the R package nlme: Linear and Nonlinear Mixed Effects Models was used (123). The asymptotic NLME had the form:

$$(A + (R_0 - A) * e^{(-e(LRC*time))}$$

Where A is the asymptote fixed at 100, R_0 is the intercept and LRC is the logarithm of the rate constant (the non-linear rate of approach to asymptote). The logarithm of the rate constant was used to ensure the estimate for the rate is positive (124). Model building of the NLME followed a similar pattern to the LME. First, the appropriate model for time was determined by comparing the empty means, random intercept model which included a fixed effect for both intercept and rate holding the asymptote at 100, with a model with a random effect for both intercept and rate. Random effects significance was again based on LRT results ($p < 0.05$), and fixed effects significance was based on Wald test p values ($p < 0.05$ was considered significant). After the appropriate model for time was determined, bivariable models for each of the eight predictors individually were built. Each predictor was added as a function of the rate and then intercept. If the predictor was significant, it was then tested as a random effect modifier. Each significant predictor in the bivariable model was added in order of significance based on bivariable model p-values to the final model and retained if Wald test or LRT was < 0.05. Once all variables to be included in the final model were identified, all possible combinations of interaction terms were included in the model one at a time and tested for significance. As in the LME, the ICC was calculated for the empty means random intercept models and the final models by dividing the between group variance by the total variance. The R^2 is inappropriate for non-linear models as it tends to be uniformly high across a set of models (125).

The NLQMM was built using the R coding and methodology suggested and made available by Geraci (110). The NLQMM was built using the asymptotic function and the covariates identified in the NLME. Bootstrap standard errors with n=199 replications were calculated, setting a seed for each model to allow for reproducibility of results (110).

LME and NLME model residuals have been visualized via quantile-quantile (QQ) plots (also known as normal probability plots) to assess normality of the distribution of residuals. In addition, fitted values have been plotted against residuals, to examine the assumption of constant variance. When residuals are normally distributed the data in a QQ plot should follow a diagonal line, whereas non-normality is indicated by deviation from the diagonal line. When there is constant variance, the residual versus fitted plot data should form a horizontal band around the 0 line. For both the LME and NLME Levene's test for homogeneity of variance across groups was calculated for the significant predictor variables in the models (126). A significant p-value (i.e. $p<0.05$) for this test indicates the null hypothesis (the assumption of equal variances across groups) is not met. Fitted versus observed scatter plots for the fixed effects and fixed and random effects models (all participants) were visualized. In addition, fixed and random components model trajectories for a random sample of 36 participants were visualized separately. There are currently no documented model diagnostics or measures of goodness of fit for the NLQMM.

Finally, a GLMM with a binary distribution and logit link was fitted to estimate variance parameters for study ID (the random effect) and log-odds parameters for the covariates (the fixed effects). GLMMs are an extension of LME that allow for response variables from different distributions, depending on the link function applied. As described above, HRQoL was dichotomized into children who were fully recovered and those who were not. Odds ratios and 95% CIs for recovery were estimated and model building followed the same pattern as described above, with variables being added to the model in order of significance according to bivariable analysis and retained if the LRT p-value was < 0.05. The ICC_{GLMM} was calculated for the empty means, random intercept models and for the final models, and the marginal and conditional R^2_{GLMM} (127) have been calculated for the final models.

4.3.1.5 Sensitivity analysis

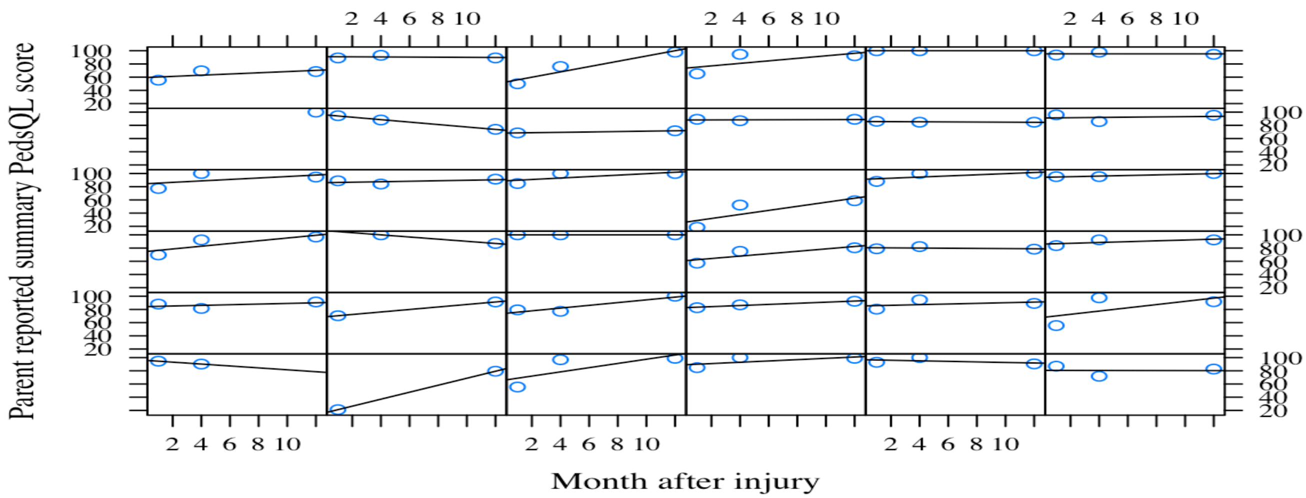
Multiple imputation, generating 10 imputed data sets (i.e. m=10) was used to impute values for all missing data using the R package Multivariate Imputation by Chained Equations ('mice'), which applies fully conditional specification (128). Variables with missing data imputed included baseline total scale score, total scale score at each follow-up time point, PaedsCTAS score, QAIPPE score and parents' highest level of education. The imputation models were based on the variable type: continuous data used predictive mean matching; binary data used logistic regression; unordered categorical data used polytomous logistic regression; and ordered categorical data used proportional odds. Imputation of all missing data was conditioned on all available and relevant variables. An MNAR sensitivity analysis was then carried out as suggested by van Buuren (129) subtracting a given amount from all imputed values for HRQoL scores, a method known as a delta(δ)-adjustment, where a delta of 0 assumes MCAR. Given the possibility that individuals with lower HRQoL were lost to follow-up after baseline (based on the association of loss to follow-up and baseline HRQoL) values of 5, 10 and 15 were subtracted from all imputed values for HRQoL creating three new datasets and three new models to compare to the all available analyses.

4.4 Results

4.4.1 Bivariable

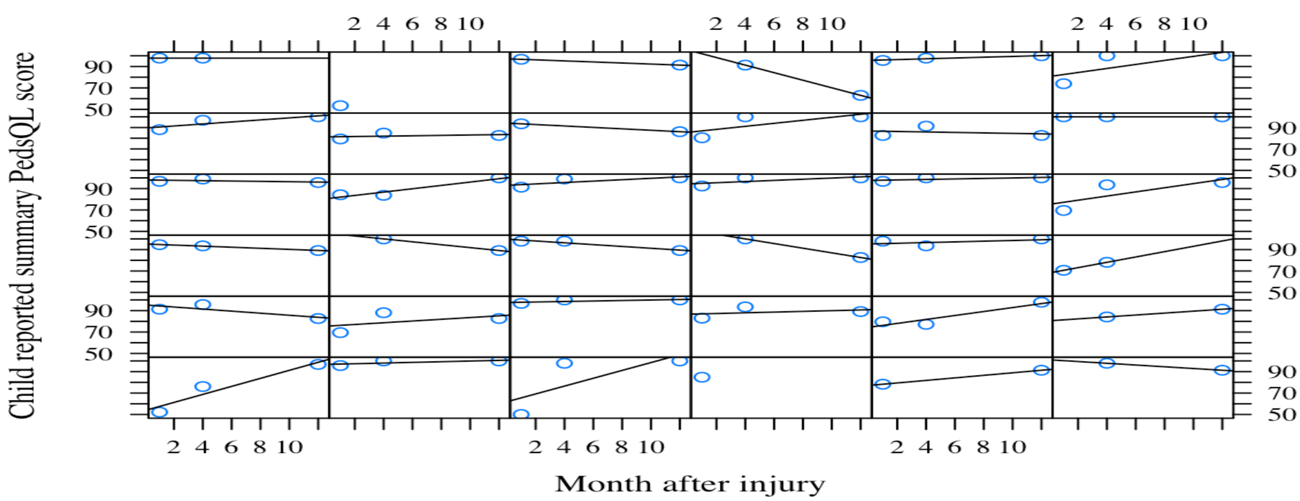
The study population was described in Chapter 3. The trellis plots of a random sample of 36 study participants (Figures 4.2 and 4.3) and the spaghetti plots (Figures 4.4 and 4.5) of the total scale scores depict clear variability in parent and child reported total scale scores across individuals in both intercept and slope. This indicates that a random effects models should be considered for both the parent and child data. In addition, the spaghetti plots (Figure 4.4 and 4.5) illustrate the non-linear relationship between time and HRQoL.

Figure 4.2 Trellis plots of parent reported total scale score at one-, four- and 12-months post-injury for a random sample of 36 study participants*



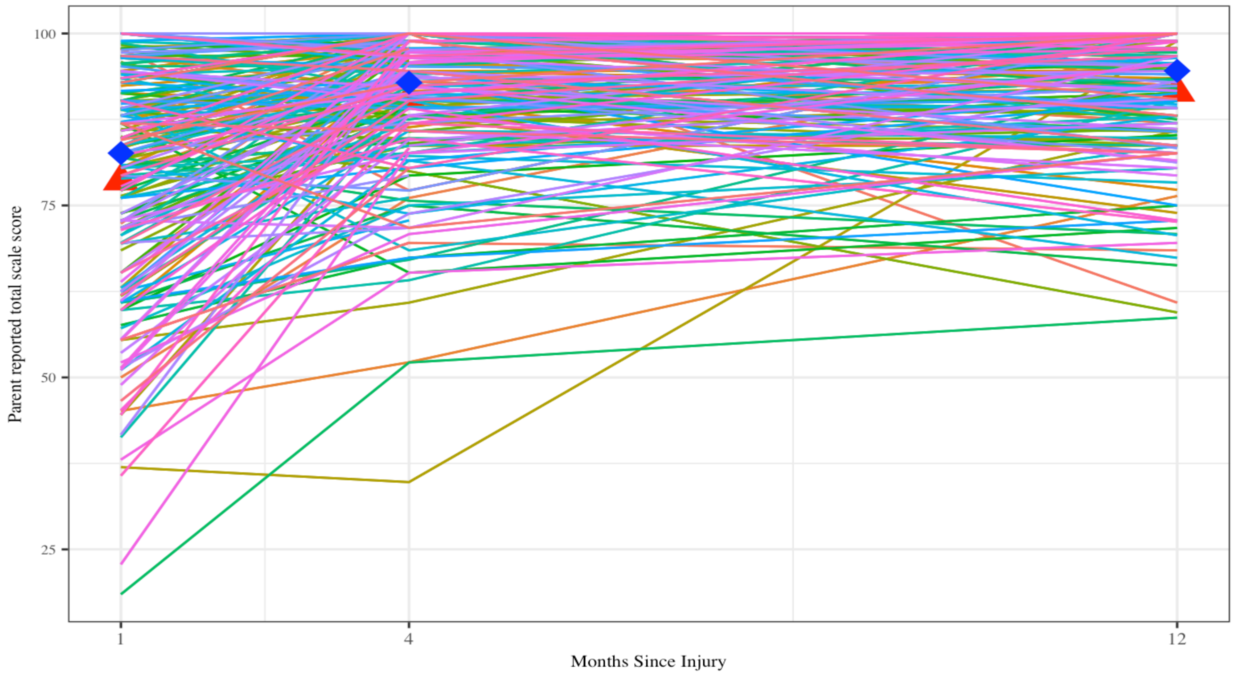
* Each square represents one of the 36 randomly selected study participants; dots represent the total scale score at the associated time points; the line is the line of best fit for that individual across time

Figure 4.3 Trellis plots of child reported PedsQL total scale score at one-, four- and 12-months post-injury for a random sample of 36 study participants*



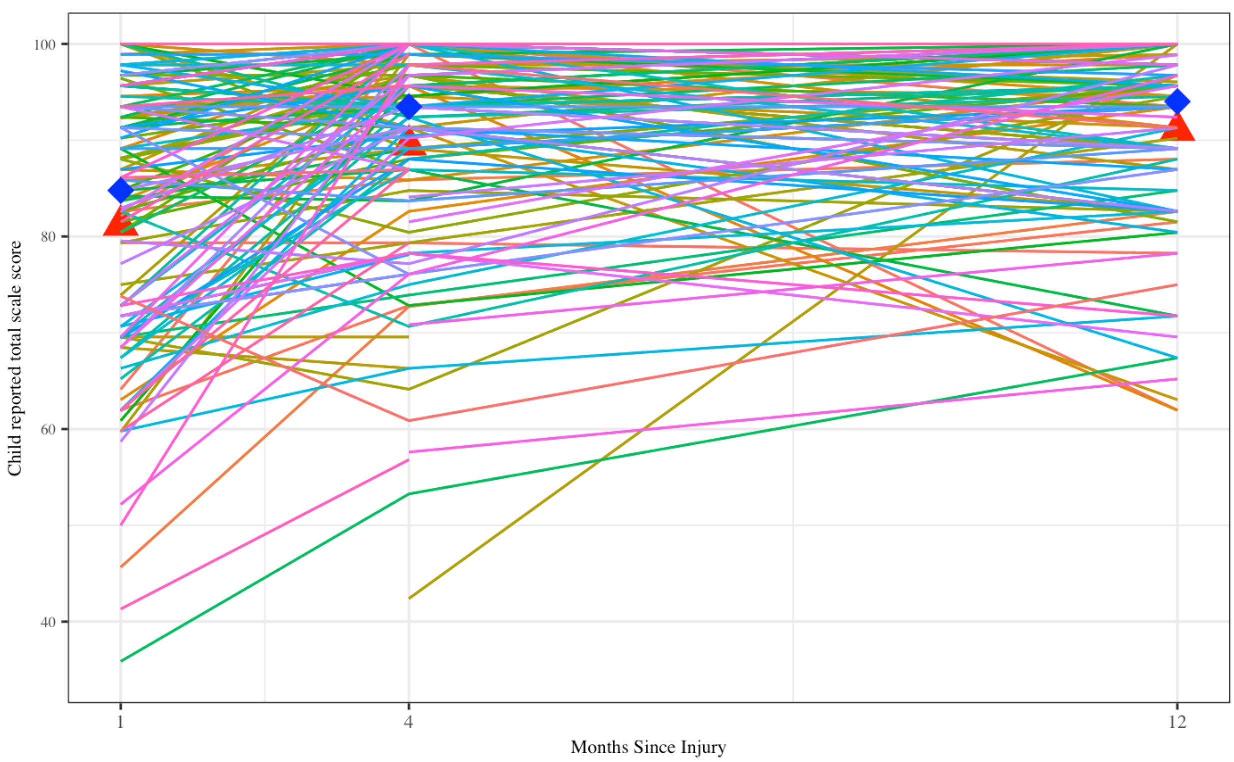
* Each square represents one of the 36 randomly selected study participants; dots represent the total scale score at the associated time points; the line is the line of best fit for that individual across time

Figure 4.4 Spaghetti plot of parent reported total scale score



* Each line represents the trajectory of an individual participants total scale score over time, blue diamonds represent median score at each time point, red triangles represent mean score at each time point

Figure 4.5 Spaghetti plot of child reported total scale score*



* Each line represents the trajectory of an individual participants total scale score over time, blue diamonds represent median score at each time point, red triangles represent mean score at each time point

At one-month post-injury the parent-reported median total scale score was statistically significantly different by age group (Kruskal Wallis $p<0.001$), injury type (Kruskal Wallis $p<0.001$) and hospitalization status (Mann Whitney-U $p<0.001$) (Table 4.1). Similarly, for the child-reported median total scale score, there were statistically significant differences at one-month post-injury by hospitalization status and injury type, but not by age category (Table 4.2). There were no statistically significant differences at four or 12 months post-injury for either parent- or child-reported total scale score for any of these variables.

4.4.1.1 Age category

A post hoc Dunn-Bonferroni test found significant differences in parent-reported median total scale scores between children less than five years old and those eight to 13 years old ($p < 0.001$) and from 13 to 17 years old ($p < 0.001$). Older children (greater than five years of age) had lower median total scale scores reported by their parents relative to their younger counterparts (Table 4.1). Overall, the pattern of recovery was not observed to be distinctly different by age (Figures 4.6, 4.7 and 4.8 and Table 4.1). Due to no clear linear relationship observed between total scale score and age (Figure 4.6), age has been examined categorically for the purpose of modelling.

Figure 4.6 Scatter plot of parent reported total scale score by age and time since injury

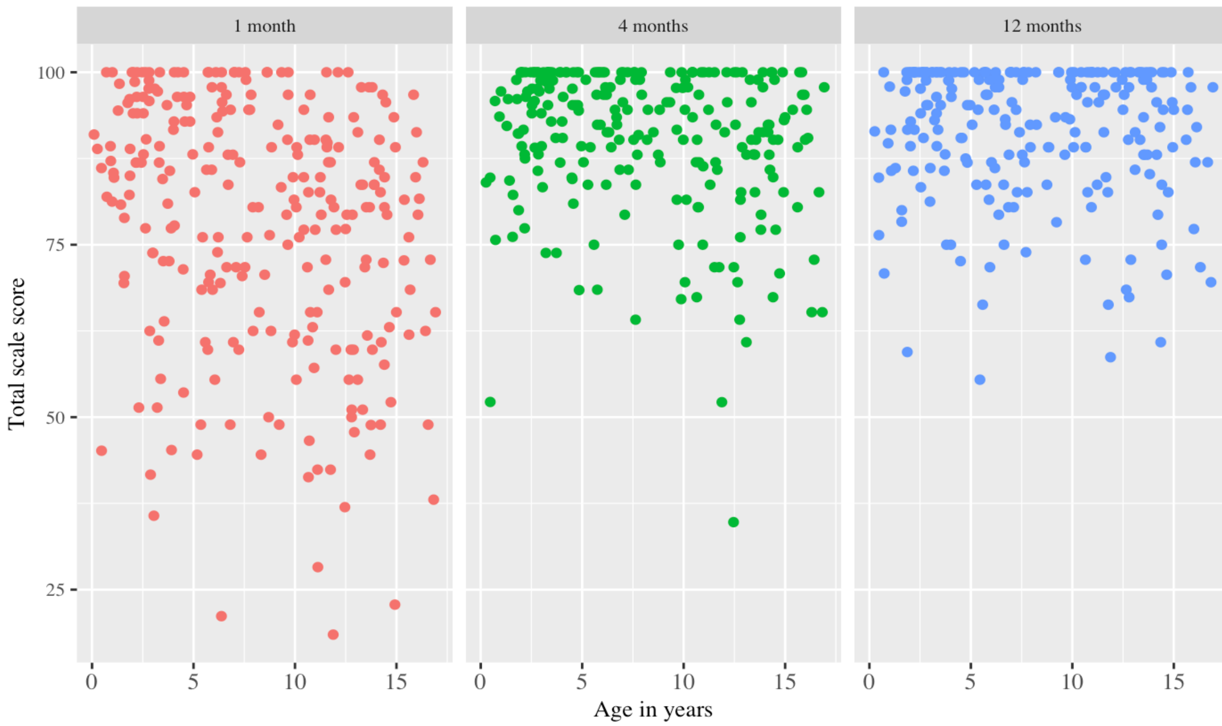


Figure 4.7 Spaghetti plot parent reported total scale score by age category

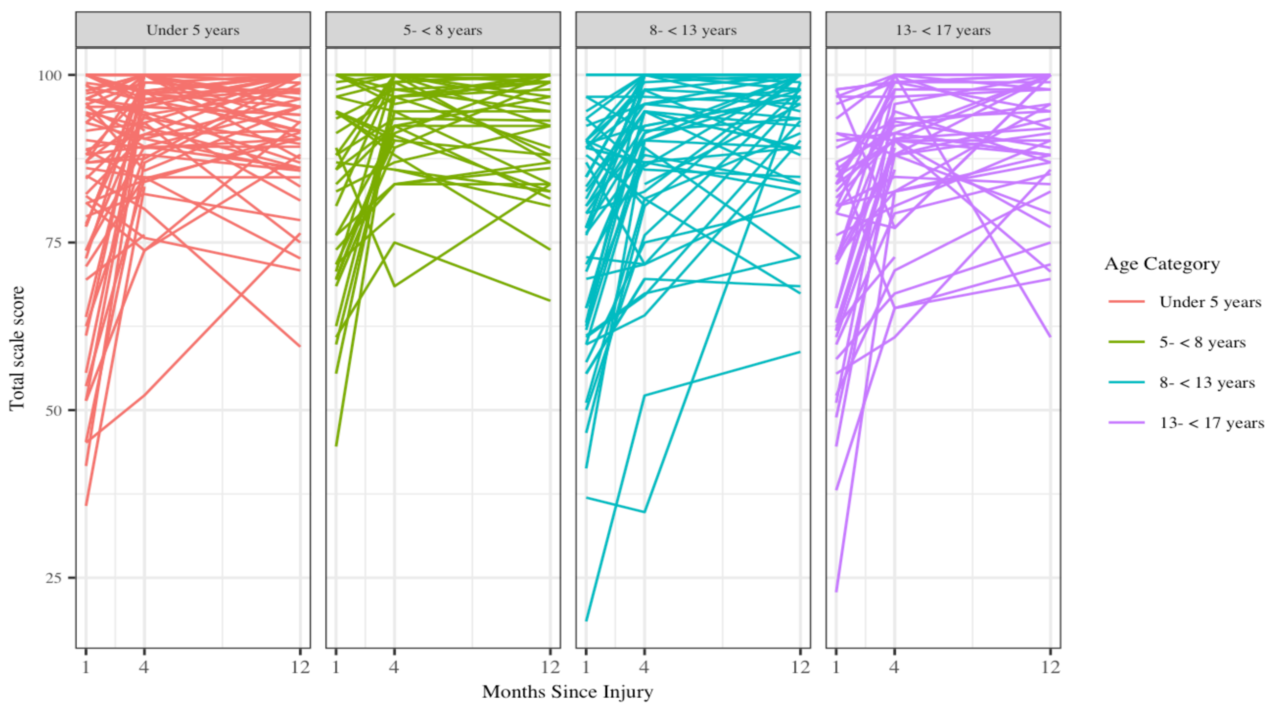
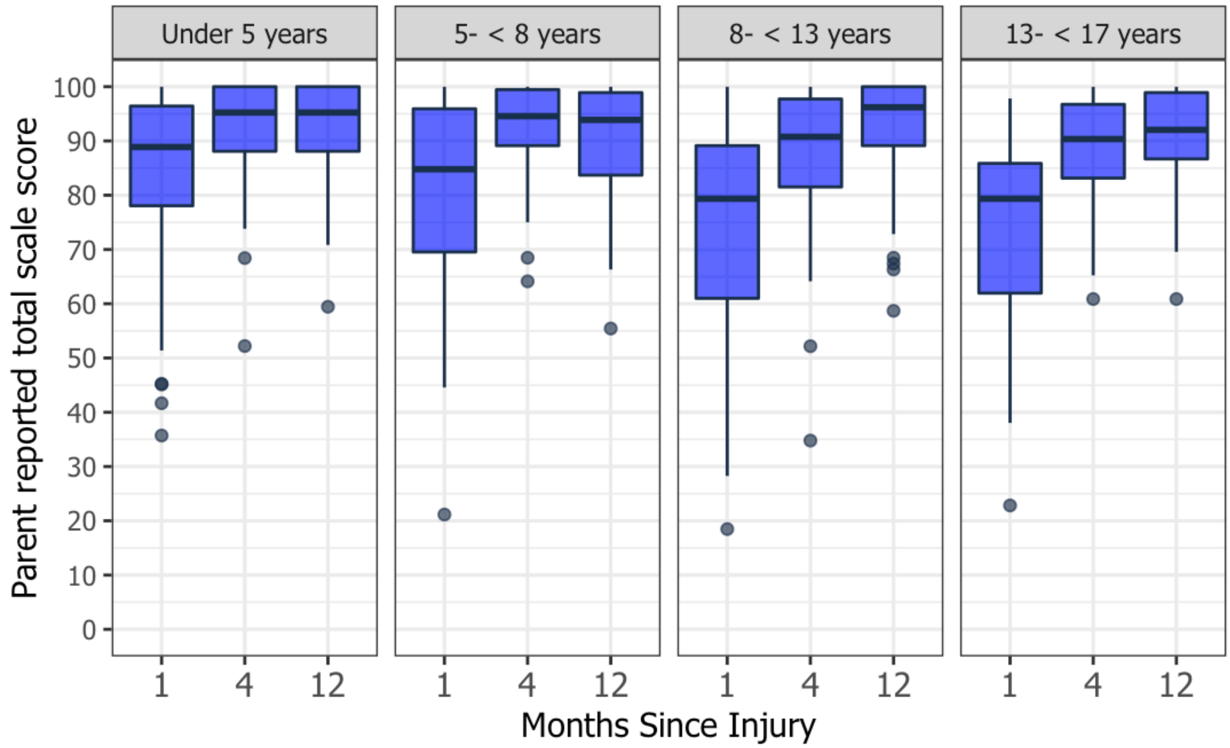


Figure 4.8 Boxplot of parent reported total scale score by age category



4.4.1.2 Hospitalization status

At one-month post-injury, parents of children who had been hospitalized rated their children's total scale score lower than those seen in the ED with median total scale score of 65.22 and 86.96 respectively ($p < 0.001$). Similarly, for child-reported total scale score, there was a statistically significant relationship between hospitalization status and median total scale score at one-month post-injury with scores of 72.83 and 88.04 for those seen in the ED and hospitalized children respectively ($p<0.001$) (a difference of 15.21 points, Table 4.2). For the same population of children (children > 5 years of age), the difference in parent-reported total scale scores for those seen in the ED and those hospitalized was similar at one-month post-injury (17.39 points). However, parent-reported scores were lower (median score of 65.22 and 82.61 for children who were hospitalized and those seen in the ED respectively (Table 4.3)). All median total scale scores were comparable regardless of hospitalization status by four-months post-injury (Table 4.1, Table 4.2 and Table 4.3).

4.4.1.3 Injury type

Parent-reported total scale score medians for injury type were significantly higher at one-month post-injury for children with minor external injuries relative to upper extremity fractures ($p=0.004$), lower extremity fractures ($p<0.001$), and major trauma ($p <0.001$). Parent-reported total scale score medians were also significantly higher for children with upper extremity injuries ($p<0.001$) and head injuries ($p<0.001$) relative to lower extremity fractures, and for children with head injuries relative to major trauma ($p=0.001$). Likewise, injury type had a statistically significant relationship with child-reported total scale score at one-month post-injury. Children who had experienced major trauma or lower extremity fractures had lower self-reported median total scale scores relative to children with other injuries (major trauma compared to minor external $p <0.001$, compared to upper extremity fracture $p = 0.01$, and compared to head injuries $p = 0.001$; lower extremity fractures compared to minor external $p <0.001$, compared to upper extremity fractures $p = 0.003$, and compared to head injuries $p <0.001$) (Tables 4.1, 4.2 and 4.3).

Table 4.1 Parent reported total scale score by demographic and injury related variables**

	One-month					Four-months					Twelve-months				
		Unweighted		Weighted			Unweighted		Weighted			Unweighted		Weighted	
	n	Median	IQR	Median	IQR	n	Median	IQR	Median	IQR	n	Median	IQR	Median	IQR
Sex															
Male	165	82.61	24.38	85.44	28.26	149	91.67	13.04	91.93	14.08	143	93.48	14.01	93.16	13.89
Female	101	83.70	31.55	86.34	23.91	91	94.57	12.44	94.48	13.04	82	95.45	12.09	96.16	10.87
Hospitalization Status															
Emergency Department	196	86.96	20.97	**86.96**	**24.44**	179	93.06	13.34	92.96	13.04	162	94.57	11.96	94.57	11.96
Hospitalized	70	65.22	30.09	**65.22**	**48.62**	61	92.22	12.50	91.76	14.10	63	94.57	17.39	94.57	15.74
Age Category															
<5 years old	82	88.89	18.37	**90.72**	**15.24**	81	95.24	11.90	95.24	10.80	73	95.24	11.90	95.24	10.71
5 - < 8 years old	52	84.78	26.39	86.89	28.28	47	94.57	10.33	95.09	10.37	50	93.87	15.21	94.54	13.07
8 - <13 years old	79	79.35	28.14	**79.35**	**36.96**	62	90.76	16.21	90.22	18.48	58	96.20	10.87	94.94	10.87
13 - <17 years old	53	79.35	23.91	**80.43**	**35.48**	50	90.35	13.59	90.39	15.03	44	92.05	12.23	91.80	12.46
PaedsCTAS (%)															
1 (requires resuscitation)	11^	71.43	24.80	**65.61**	**41.21**	10^	89.60	9.01	88.10	12.65	8^	94.57	18.21	89.13	7.42
2	36	71.54	29.53	**73.53**	**39.83**	32	91.85	11.43	90.24	14.43	34	93.12	16.03	90.50	14.19
3	45	80.43	23.67	**84.09**	**29.09**	38	90.22	14.95	90.22	17.39	36	96.58	13.25	95.66	11.96
4	101	85.71	21.43	**85.36**	**25.00**	96	92.39	13.35	92.39	14.13	81	94.05	11.39	93.57	12.37
5 (non-urgent)	8^	82.61	17.44	**83.68**	**19.47**	6^	96.15	6.78	94.57	7.89	8^	91.30	9.87	91.30	9.60
Missing	65	87.47	29.08	**89.13**	**22.83**	58	95.65	10.87	95.74	10.76	58	95.24	11.96	95.30	10.87
Income Quintile (%)															
1 (lowest income quintile)	30	80.62	30.90	81.24	37.50	24	91.30	15.31	92.38	15.91	20	97.28	16.58	95.30	12.75
2	29	80.43	22.95	81.29	28.26	27	90.22	14.99	90.03	15.38	23	93.48	15.79	92.93	14.53
3	51	86.96	24.02	88.47	16.28	47	95.83	11.68	96.87	9.19	46	95.45	11.68	96.01	9.73
4	50	83.51	21.43	85.19	25.50	44	95.24	9.81	94.79	10.75	45	94.05	12.80	92.03	12.26
5 (highest income quintile)	93	80.43	29.81	80.86	31.99	86	92.31	11.90	91.31	14.13	81	94.05	10.87	93.43	12.82
Missing	13	81.67	17.14	89.91	19.67	12	92.62	5.20	92.15	9.52	10	94.39	12.50	95.15	8.00

	One-month					Four-months					Twelve-months				
		Unweighted		Weighted			Unweighted		Weighted			Unweighted		Weighted	
	n	Median	IQR	Median	IQR	n	Median	IQR	Median	IQR	n	Median	IQR	Median	IQR
Injury															
Minor external	97	89.13	16.79	**89.13**	**19.57**	91	94.57	14.67	94.51	15.22	83	94.57	12.77	94.31	12.80
Upper extremity fracture	63	77.38	20.73	**77.57**	**30.43**	56	93.27	10.85	92.92	11.22	56	94.02	11.62	94.20	11.96
Lower extremity fracture	32	53.41	25.85	**61.79**	**50.49**	28	90.56	16.02	90.45	18.85	27	95.24	8.64	93.90	10.70
Head injury	37	87.14	15.99	**88.04**	**18.39**	31	93.48	10.93	93.49	10.73	28	95.45	10.75	95.51	8.52
Major trauma	20	60.45	18.13	**61.09**	**40.22**	17	91.11	12.02	91.73	12.18	16	95.11	19.02	94.57	13.30
Other	15	86.96	18.03	**92.46**	**15.19**	15	92.22	6.86	91.76	11.96	13	88.04	12.23	88.57	18.27
Missing	2	96.20	1.63	**94.57**	**4.26**	2	88.59	11.41	77.17	14.61	2	98.91	1.09	97.83	1.39
Parents Highest Education*															
1	9^	70.45	19.02	69.47	28.80	8^	95.11	6.49	89.41	8.38	7^	89.13	21.36	76.03	28.26
2	23	84.78	35.33	85.67	22.49	18	91.85	13.16	91.68	11.36	20	92.57	12.48	91.67	11.96
3	48	77.52	28.06	83.66	25.66	43	93.48	14.16	93.99	17.39	46	95.45	11.68	94.56	11.13
4	91	85.87	25.93	86.94	25.00	83	94.05	10.84	94.57	10.71	76	94.90	12.23	95.54	11.90
5	85	84.52	22.31	84.78	20.76	81	92.39	13.20	92.00	14.61	72	94.57	13.35	93.26	13.89
Missing	10	77.72	26.63	80.47	25.93	7	80.95	18.48	80.52	8.70	4	72.83	10.87	66.30	6.52
Overall	266	82.61	25.00	85.68	28.26	240	92.86	13.04	92.86	13.83	225	94.57	13.04	94.57	12.70

* Parent highest education categories: 1 = graduated high school, 2 = some trade school, college or university, 3 = Diploma from trade school or college, 4 = University degree, 5 = Post-graduate degree (Master's and/or Doctorate)

** Bolded medians are statistically significantly different from each other at alpha of 0.05 based on Mann-Whitney U or Kruskal Wallis test followed by Dunn-Bonferroni post hoc as appropriate

^ Use caution when interpreting statistics and inferences associated with categories with low bases

Table 4.2 Child reported total scale score by demographic and injury related variables**

	One-month					Four-months					Twelve-months				
		Unweighted		Weighted			Unweighted		Weighted			Unweighted		Weighted	
	n	Median	IQR	Median	IQR	n	Median	IQR	Median	IQR	n	Median	IQR	Median	IQR
Sex															
Male	103	84.21	24.46	86.96	23.91	88	93.48	15.39	93.48	14.13	89	94.57	12.80	94.57	15.22
Female	65	85.87	20.65	86.80	16.15	61	91.30	15.22	93.22	10.87	51	93.48	11.96	93.48	11.96
Hospitalization Status															
Emergency Department	124	88.10	22.09	**88.04**	**21.84**	110	93.48	11.96	93.48	11.96	101	93.48	10.87	93.48	10.87
Hospitalized	44	72.83	22.93	**72.83**	**23.08**	39	91.30	19.57	91.30	19.57	39	95.65	13.04	94.57	13.04
Age Category															
5 - <8 years old	52	86.53	22.28	86.96	21.76	46	92.3913	10.87	91.30	13.04	48	91.30	10.42	92.13	10.87
8 - <13 years old	71	84.21	25.54	85.87	25.74	57	92.3913	19.57	92.22	19.57	51	95.65	11.41	95.11	11.96
13 - < 17 years old	45	83.70	21.74	88.06	21.25	46	94.31	11.14	94.23	8.70	41	95.65	9.78	94.57	15.22
PaedsCTAS (%)															
1 (requires resuscitation)	5^	77.17	29.55	63.59	3.06	5^	81.52	14.13	79.35	14.13	4^	92.39	9.78	89.13	9.04
2	24	75.54	28.56	81.46	26.37	22	92.39	13.02	90.93	10.87	23	95.65	14.13	94.98	13.04
3	24	77.12	19.57	81.86	21.82	21	93.48	9.78	92.19	9.78	18	95.11	9.51	93.48	15.22
4	62	88.04	22.28	88.04	22.29	55	93.48	13.59	92.93	11.96	49	94.57	10.87	93.65	10.87
5 (non-urgent)	7^	93.48	13.04	93.48	12.44	5^	100.00	8.70	100.00	8.70	6^	93.48	12.59	92.13	10.87
Missing	46	86.96	21.74	88.00	19.90	41	95.65	16.30	95.48	14.13	40	93.48	11.14	93.48	11.96
Income Quintile (%)															
1 (lowest income quintile)	18	82.61	19.84	82.24	19.57	15	93.48	14.67	92.39	10.87	16	94.02	11.96	93.48	8.70
2	19	90.22	13.59	89.67	11.89	17	89.13	10.87	89.34	10.87	15	95.65	9.24	95.48	9.78
3	32	85.87	26.39	91.65	24.78	28	95.65	13.32	95.65	8.70	26	92.39	12.28	91.30	17.39
4	30	83.70	19.29	85.87	18.38	26	91.85	19.02	90.55	17.39	21	95.65	15.22	91.66	15.22
5 (highest income quintile)	60	84.50	23.91	85.70	23.07	54	93.48	15.93	93.48	13.04	56	93.48	13.04	93.48	13.04
Missing	9	93.48	17.08	93.48	5.46	9	95.65	3.26	95.11	10.87	6	95.65	9.78	94.64	12.16

	One-month					Four-months					Twelve-months				
		Unweighted		Weighted			Unweighted		Weighted			Unweighted		Weighted	
	n	Median	IQR	Median	IQR	n	Median	IQR	Median	IQR	n	Median	IQR	Median	IQR
Injury															
Minor external	60	91.30	19.84	**89.14**	**20.92**	54	93.48	12.77	93.44	13.25	50	93.48	14.67	93.48	14.78
Upper extremity fracture	48	85.33	16.58	**86.66**	**15.14**	40	95.65	12.23	94.90	11.96	40	95.11	10.60	94.57	9.78
Lower extremity fracture	25	65.22	19.57	**67.39**	**24.74**	21	89.13	22.83	91.04	22.83	18	94.02	9.78	94.23	10.87
Head injury	15	93.48	14.50	**94.55**	**10.10**	14^	93.48	4.70	91.30	5.49	14^	92.39	9.78	92.80	10.87
Major trauma	11^	69.57	12.50	**65.70**	**13.78**	11^	81.52	13.04	79.89	14.13	11^	95.65	15.22	93.48	19.57
Other	7^	85.71	10.87	**88.40**	**9.36**	7^	95.65	10.87	88.72	13.04	6^	92.93	13.86	91.30	11.96
Missing	2	98.37	0.54	**97.83**	**0.70**	2	98.91	1.09	97.83	2.17	1	91.30	0.00	91.30	0.00
Parents Highest Education*															
1	4^	75.72	22.00	68.48	22.41	3^	95.65	1.09	94.57	0.00	4^	76.09	27.17	62.29	1.09
2	13^	89.13	14.13	89.31	10.87	13^	95.65	11.96	95.48	10.87	15	95.65	9.24	95.65	5.43
3	29	81.52	22.83	84.94	21.30	28	91.30	22.83	90.55	27.17	26	95.65	9.47	93.40	9.91
4	56	86.96	21.47	88.04	21.74	46	95.11	11.68	94.94	11.96	43	95.65	13.47	94.73	13.04
5	62	85.25	21.74	85.82	22.00	56	91.30	13.86	91.30	13.04	48	92.39	15.22	91.30	13.04
Missing	4	77.17	19.02	78.59	12.88	3	78.26	16.30	71.74	32.61	4	91.30	10.87	91.72	2.17
Overall	168	84.78	22.83	86.96	23.91	149	93.48	14.82	93.48	11.96	140	94.02	11.96	93.48	11.96

* Parent highest education categories: 1 = graduated high school, 2 = some trade school, college or university, 3 = Diploma from trade school or college, 4 = University degree, 5 = Post-graduate degree (Master's and/or Doctorate)

** Bolded medians are statistically significantly different from each other at alpha of 0.05 based on Mann-Whitney U or Kruskal Wallis test followed by Dunn-Bonferroni post hoc as appropriate

^ Use caution when interpreting statistics and inferences associated with categories with low bases

Table 4.3 Parent reported total scale score by demographic and injury related variables, children > 5 years

	One-month					Four-months					Twelve-months				
		Unweighted		Weighted			Unweighted		Weighted			Unweighted		Weighted	
	n	Median	IQR	Median	IQR	n	Median	IQR	Median	IQR	n	Median	IQR	Median	IQR
Sex															
Male	102	80.43	25.00	81.64	22.83	87	90.48	13.59	90.26	14.13	88	93.33	15.49	92.05	14.13
Female	68	79.35	28.13	80.43	28.26	59	94.57	11.41	94.57	11.96	54	96.20	11.41	96.74	10.87
Hospitalization Status															
Emergency Department	125	82.61	23.91	**82.61**	**23.91**	112	92.39	13.32	92.39	13.10	103	93.48	11.41	93.48	11.96
Hospitalized	45	65.22	33.70	**65.22**	**33.70**	34	91.30	9.51	91.30	9.78	39	95.65	16.85	95.11	17.39
Age Category															
5 – 8 years old	50	84.78	26.99	87.07	27.17	42	95.11	10.60	96.44	10.87	46	94.57	15.22	94.57	11.96
8 – < 13 years old	71	79.35	27.22	79.35	27.17	57	91.30	16.30	91.30	16.30	55	96.74	10.87	94.66	11.96
13 – < 17 years old	49	79.35	24.46	80.43	27.17	47	90.22	13.04	90.27	14.13	41	92.05	11.96	91.42	10.87
PaedsCTAS (%)															
1 (requires resuscitation)	5^	59.78	22.83	54.35	22.83	3^	88.10	3.26	88.07	6.52	2^	89.67	10.33	79.35	20.65
2	24	78.80	28.26	76.09	26.09	20	90.76	10.60	89.13	16.30	23	94.57	15.76	95.23	13.69
3	25	71.74	25.00	71.57	29.35	22	90.76	15.22	90.22	16.30	20	97.28	14.13	96.36	17.39
4	62	80.43	19.78	80.43	20.21	56	91.30	14.33	91.30	15.12	51	92.39	10.87	92.39	10.87
5 (non-urgent)	6^	78.80	11.29	81.60	20.85	4^	96.15	5.36	94.57	11.96	6^	91.30	6.52	91.30	6.52
Missing	48	84.60	31.25	88.12	28.26	41	94.57	11.96	95.52	11.96	40	95.11	11.14	94.57	10.87
Income Quintile (%)															
1 (lowest income quintile)	17	80.43	27.17	81.05	34.78	14^	95.11	9.51	93.48	9.78	13^	97.83	9.78	96.33	16.30
2	20	78.31	22.92	78.70	18.48	16	89.13	11.96	88.79	15.22	15	90.22	17.39	90.84	16.30
3	34	85.33	26.03	87.44	26.28	27	92.39	13.04	96.46	10.87	27	96.74	15.22	96.74	10.87
4	29	82.61	18.48	82.61	21.74	25	92.39	9.63	92.39	10.87	25	92.39	16.30	89.13	18.48
5 (highest income quintile)	61	77.17	27.72	78.41	28.26	56	91.30	12.50	90.22	14.13	55	93.48	10.33	92.39	10.87
Missing	9	81.67	17.14	83.91	18.48	8	91.43	9.24	90.48	10.87	7	100.00	5.61	98.37	3.26

	One-month					Four-months					Twelve-months				
		Unweighted		Weighted			Unweighted		Weighted			Unweighted		Weighted	
	n	Median	IQR	Median	IQR	n	Median	IQR	Median	IQR	n	Median	IQR	Median	IQR
Injury															
Minor external Injury	62	85.33	19.27	**84.78**	**20.21**	56	91.30	16.30	90.22	16.30	52	92.39	15.49	92.38	16.30
Upper extremity fracture	47	80.43	20.65	**77.68**	**21.74**	40	93.27	9.98	93.06	9.78	41	94.57	11.96	94.40	11.96
Lower extremity fracture	25	55.43	25.89	**61.60**	**21.74**	19	90.22	15.22	87.46	16.30	6^	91.30	13.32	94.20	12.60
Head injury	15	88.04	21.74	**88.04**	**22.83**	13	93.48	8.70	94.30	8.70	20	95.11	9.67	96.78	6.82
Major trauma	11^	59.78	20.06	**57.61**	**23.81**	9^	88.10	9.78	88.07	9.78	12^	97.28	7.10	90.22	15.22
Other	8^	89.67	10.14	**92.46**	**7.61**	7^	91.30	5.43	90.76	6.52	9^	94.57	15.22	89.13	19.57
Missing	2	96.20	1.63	**94.57**	**3.26**	2	88.59	11.41	77.17	22.83	2	98.91	1.09	97.83	2.17
Highest Education*															
1	4^	75.00	19.84	68.48	22.83	2^	92.93	2.72	90.22	1.64	3^	77.27	14.13	72.60	5.53
2	15	83.70	42.93	84.36	30.43	12^	90.22	13.56	90.26	14.03	14^	91.85	13.53	90.22	11.96
3	31	72.83	29.89	78.09	28.02	29	91.30	15.22	91.30	17.39	28	94.02	10.87	92.47	11.96
4	57	81.52	29.10	81.88	27.17	46	92.39	9.51	92.39	10.87	47	96.74	12.50	96.74	8.70
5	61	80.43	21.74	80.43	22.83	57	92.39	13.04	91.47	14.13	49	94.57	11.96	93.00	11.96
Missing	2	64.67	16.85	59.45	0.00	0	0.00	0.00	0.00	0.00	1	66.30	0.00	66.30	0.00
Overall	170	80.43	27.17	81.56	25.00	146	92.03	13.04	92.17	13.04	142	94.57	13.04	93.48	11.96

* Parent highest education categories: 1 = graduated high school, 2 = some trade school, college or university, 3 = Diploma from trade school or college, 4 = University degree, 5 = Post-graduate degree (Master's and/or Doctorate)

** Bolded medians are statistically significantly different from each other at alpha of 0.05 based on Mann-Whitney U or Kruskal Wallis test followed by Dunn-Bonferroni post hoc as appropriate

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4.4.2 Linear mixed effects models total scale score

The empty means, random intercept models are the simplest models explored (Appendix G). The ICC for the parent model was calculated as 0.31 indicating that 31% of the variance in the parent-response total scale score outcome is between person variance, whereas 69% is within person variance over time or, put another way, 31% of the variation in total scale score is cross-sectional and 69% is longitudinal. The ICC for the child-response model was similar, but higher, at 0.42, indicating 42% of the variance in the child-response total scale score outcome is between person and 58% is within person variance over time. The intercept model with time (Appendix G) includes parameter estimates for the mean total scale score at each time point with a fixed intercept of 78.61, 80.83 and 76.39 at one-month post-injury in the parent, child-response and parent sub-population models respectively. The mean total scale score was estimated to increase by 11.14 at four-months post-injury and 12.36 at 12 months post-injury for parent reported scores, by 7.91 and 9.02 for child-response and by 12.19 and 13.57 in the parent sub-population model. Although parents mean total scale score at one-month post-injury was lower than that of the children with greater increase at four- and 12-months, these results are not clinically or statistically different from the child model. The Wald test p-value for the fixed time variables was significant ($p<0.001$). A model testing a random time variable (random slope) was explored but was not possible due to low sample size.

The next models examined included the following covariates: age category, baseline total scale score, hospitalization status (with ED as the reference category), PaedsCTAS collapsed into the three previously described categories with levels one and two combined, and levels four and five combined, sex, parent’s highest education, injury type and income quintile (not presented) as fixed effects and as interaction terms with time.

For the parent-response model age category, PaedsCTAS, baseline total scale score, hospitalization status and injury type all resulted in models with smaller AIC relative to the time only model, with significant Wald test p-values (age category $p < 0.001$, baseline total scale score $p<0.001$, hospitalization status $p<0.001$, injury type $p< 0.001$, PaedsCTAS = 0.035, sex $p=0.578$, parent's highest education $p=0.149$ and income quintile $p=0.78$). Baseline total scale score was the only significant modifier of the random intercept ($p<0.001$). This variable means that the random intercept variance is now predicted as a function of baseline total scale score or, in other words, baseline total scale score is a significant predictor of heterogeneity of random incept variance.

The final LME model for parent-response included age category, baseline total scale score, hospitalization status, and injury type, added in that order based on bivariable model p-values, as well as baseline total scale score as a modifier of the random intercept. Hospitalization status, age category and injury type were also included as interaction terms with time given significant Wald test p-values associated with these terms when they added to the model with the other significant covariates (Table 4.4).

From the final parent-response LME for total scale score (Table 4.4) the intercept represents the mean total scale score when all variables included in the model are held at their reference values. Thus, at one-month post-injury for children less than five years of age, who visited the ED, with a minor external injury, and mean baseline total scale score the mean total scale score at one-month post-injury was estimated at 88.43 (95% CI 85.68, 91.18). This score was estimated to increase by 3.10 points at four-months (95% CI -0.15, 6.36), and 2.08 points at 12 months (95% CI -1.25, 5.41) post-injury relative to one-month post-injury (Table 4.4). The mean total scale score was statistically significantly lower at one-month post-injury for the oldest group of children relative to children under five years old (estimate -6.87, 95% CI (-10.57, -3.22), p<0.001), for children hospitalized relative to those who visited the ED (estimate -13.16, 95% CI (-16.77, -9.52), p<0.001), for children with lower extremity fractures (estimate -21.93, 95% CI (-26.64, -17.28), p<0.001), upper extremity fractures (estimate -4.72 95% CI (-8.17, -1.27) p=0.007) or major trauma relative to minor external injuries (estimate -7.97, 95% CI (-14.10, -1.88), p=0.010). For each one point increase in baseline total scale score, there was a corresponding estimated 0.50 (95% CI 0.37, 0.64) point increase in one-month total scale score.

The interactions with time indicate that total scale score at four- and 12-months post-injury change in a differential manner from one-month by age group, hospitalization status and injury type. For children who were hospitalized (with reference values in all other categories), their estimated mean total scale score at one-month post-injury is 13.16 points lower than children seen in the ED. Hospitalized children's total scale score is then estimated to increase from one to four-months post-injury by 15.14 points (estimate for four-months + estimate for interaction term) relative to children seen in the ED whose scores simply increase by 3.10 from one to four-months post-injury (Table 4.4). The ICC of this final model indicated that 18% of the variance was due to between person variation. The decrease in ICC from the empty means model to the final model indicates that the variables in the model explained proportionally more of the between person variance of total scale score relative to the longitudinal variance as would be expected. The marginal R^2 indicates that 45.5% of variation in total scale score is explained by the fixed effects of the model. The conditional R^2 indicates that 67.2% of variation in total scale score is explained by the fixed and random effects of the model (random intercept and modification of random intercept by baseline total scale score) (Table 4.4).

Table 4.4 Final linear mixed effects model for parent-response total scale score **

Predictors	*Estimates*	*95% CI*	*p*
(Intercept)	**88.43**	**85.68, 91.18**	**<0.001**
Time			
1 month	ref		
4 months	3.10	-0.15, 6.36	0.062
12 months	2.08	-1.25, 5.41	0.221
Age Category			
< 5 years old	ref		
5 - < 8 years old	-2.40	-6.06, 1.24	0.196
8 - <13 years old	-3.09	-6.57, 0.32	0.076
13 - <17 years old	**-6.87**	**-10.57, -3.22**	**<0.001**
Baseline total scale score	**0.50**	**0.37, 0.64**	**<0.001**
Hospitalization Status			
Emergency Department	ref		
Hospitalized	**-13.16**	**-16.77, -9.52**	**<0.001**
Injury Type			
Upper extremity fracture	**-4.72**	**-8.17, -1.27**	**0.007**
Lower extremity fracture	**-21.93**	**-26.64, -17.28**	**<0.001**
Head injury	1.58	-2.54, 5.68	0.455
Major Trauma	**-7.97**	**-14.10, -1.88**	**0.010**
Other	3.52	-2.38, 9.38	0.243
Hospitalized * Time			
4 months * hospitalized	**12.04**	**7.76, 16.54**	**<0.001**
12 months * hospitalized	**12.16**	**7.64, 16.45**	**<0.001**
Injury Type * Time			
4 months * Upper extremity fracture	**6.39**	**2.17, 10.60**	**0.003**
12 months * upper extremity fracture	**5.74**	**1.52, 9.95**	**0.008**
4 months * Lower extremity fracture	**18.52**	**12.88, 24.16**	**<0.001**
12 months * Lower extremity fracture	**24.32**	**18.61, 30.03**	**<0.001**
4 months * Head	-0.66	-5.66, 4.35	0.798
12 months * Head	1.88	-3.24, 7.01	0.471
4 months * Major Trauma	5.37	-1.99, 12.75	0.152
12 months * Major Trauma	**9.06**	**1.48, 16.63**	**0.019**
4 months * Other	-2.70	-9.92, 4.54	0.465
12 months * Other	-6.08	-13.55, 1.38	0.110
Age category * time			
4 months * 5- ,8 years old	1.86	-2.59, 6.31	0.412
12 months * 5- <8 years old	0.39	-4.03, 4.81	0.862
4 months 8- <13 years old	-0.40	-4.59, 3.81	0.856
12 months * 8 - <13 years old	4.20	-0.02, 8.44	0.051
4 months * 13 - <17 years old	4.08	-0.31, 8.47	0.068
12 months * 13 - <17 years old	**4.95**	**0.42, 9.48**	**0.032**
Random Effects			
Residual variance	69.04		
Random intercept variance	15.55		
Baseline total scale score	0.35		
ICC	0.18		
# observations	707		
Marginal R^2 = 0.465	Conditional R^2 = 0.680		

** Bolded parameter estimates are statistically significant at alpha of 0.05 in the model, ref = reference category, CI = confidence interval, p = p-value associated with parameter estimate, ICC = interclass correlation

For the final child-response LME model baseline total scale score, injury type and hospitalization status were retained as fixed effects and as interaction terms with time. Given the smaller sample size of the child-response population, baseline total scale score could not be included as a modifier of the random intercept (Table 4.5).

In the child-response LME for total scale score, being hospitalized relative to being seen in the ED (estimate -9.48, 95% CI (-14.24, -4.73), $p<0.001$), having a lower extremity fracture (estimate -16.18, 95% CI (-20.85, -9.21), $p<0.001$) or having major trauma relative to minor external injury (estimate -10.13, 95% CI (-20.85, -9.21), $p=0.024$) were statistically significantly associated with a lower total scale score at one-month post-injury. In addition, baseline total scale score had a positive direct relationship with total scale score at one-month post-injury (estimate 0.50, 95% CI 0.34, 0.67), $p<0.001$) (Table 4.5). Children who were hospitalized saw greater gains in total scale score at four and 12 months post-injury relative to those seen in the ED as reflected by the significant interaction between hospitalization status with time (four month estimate 8.44, 95% CI (3.08, 13.81), $p=0.002$, 12 month estimate 7.98, 95% CI (2.51, 13.45), $p=0.004$), as did children with lower extremity fractures (four month estimate 11.31, 95% CI (5.07, 17.57), $p<0.001$), 12 month estimate 20.81, 95% CI (14.12, 27.49), $p<0.001$).

Relative to the child-response model, the model of the parent sub-population reflected a significantly lower estimated mean total scale score at one-month post-injury (parameter estimate did not fall within the 95% confidence intervals of the estimate in the child model) and larger parameter estimates (indicating greater increase in mean total scale score) at four and 12 months post-injury (Table 4.5).

Table 4.5 Final linear mixed effect model for child-response total scale score and parent sub population**

	Child			Parent sub population		
Predictors	*Estimates*	*95% CI*	*p*	*Estimates*	*95% CI*	*p*
(Intercept)	**85.55**	**82.74, 88.36**	**<0.001**	**81.82**	**78.81, 84.83**	**<0.001**
Time						
One-month	ref			ref		
4 months	3.58	0.49, 6.66	**0.023**	**6.73**	**3.26, 10.21**	**<0.001**
12 months	2.24	-0.97, 5.46	0.171	**6.66**	**3.11, 10.20**	**<0.001**
Baseline total scale score	**0.50**	**0.34, 0.67**	**<0.001**	**0.64**	**0.44, 0.83**	**<0.001**
Injury Type						
Minor External	ref			ref		
Upper extremity fracture	-1.29	-5.60, 3.03	0.560	-2.75	-7.34, 1.84	0.240
Lower extremity fracture	**-16.18**	**-20.85, -9.21**	**<0.001**	**-22.45**	**-28.56, -16.35**	**<0.001**
Head injury	2.23	-3.19, 9.06	0.493	6.15	-0.66, 12.96	0.077
Major Trauma	**-10.13**	**-19.94, -1.32**	**0.024**	-7.92	-17.26, 1.41	0.096
Other	3.32	-5.58, 12.23	0.464	7.30	-2.10, 16.70	0.128
Hospitalization Status						
Emergency Department	ref			ref		
Hospitalized	**-9.48**	**-14.24, -4.73**	**<0.001**	**-9.35**	**-14.41, -4.29**	**<0.001**
Baseline HRQoL * Time						
4 months*baseline	-0.06	-0.21, 0.18	0.866	**-0.27**	-0.50, -0.04	**0.022**
12 months * baseline	-0.02	-0.24, 0.13	0.538	-0.15	-0.38, 0.09	0.221
Hospitalized * Time						
4 months * hospitalized	8.44	3.08, 13.81	**0.002**	**9.65**	**3.60, 15.69**	**0.002**
12 months * hospitalized	7.98	2.51, 13.45	**0.004**	**8.26**	**2.13, 14.39**	**0.008**
Injury Type * Time						
4 months * upper extremity fracture	2.63	-2.16, 7.43	0.282	4.50	-0.85, 9.85	0.099
12 months * upper extremity fracture	4.70	-0.14, 9.55	0.057	5.08	-0.32, 10.49	0.065
4 months * lower extremity fracture	**11.32**	**5.07, 17.57**	**<0.001**	**18.23**	**11.15, 25.32**	**<0.001**
12 months * lower extremity fracture	**20.81**	**14.12, 27.49**	**<0.001**	**26.42**	**18.87, 33.96**	**<0.001**

	Child			Parent sub population		
Predictors	*Estimates*	*95% CI*	*p*	*Estimates*	*95% CI*	*p*
4 months * head injury	0.21	-7.64, 5.71	0.952	0.42	-7.47, 8.31	0.916
12 months * head injury	0.05	-7.30, 6.19	0.988	0.12	-7.91, 8.14	0.977
4 months * Major trauma	4.36	-10.30, 18.45	0.384	2.57	-8.32, 13.46	0.644
12 months * major trauma	**14.62**	**-1.01, 28.10**	**0.004**	9.01	-2.07, 20.09	0.111
4 months * other	-3.20	-14.94, 6.44	0.436	-8.36	-20.02, 3.31	0.160
12 months * other	-2.29	-15.80, 7.87	0.512	-9.08	-20.95, 2.79	0.134
Random Effects						
Residual variance	65.44			80.55		
Random intercept variance	56.55			54.95		
ICC	0.46			0.41		
# observations	428			428		
Marginal R^2 = 0.378 Conditional R^2 = 0.666				Marginal = 0.436 Conditional R^2 = 0.665		

** Bolded parameter estimates are statistically significant in the model at alpha of 0.05, those in green are statistically significant from the child-response model, ref = reference category, CI = confidence interval, p = p-value associated with parameter estimate

4.4.2.1 LME model diagnostics

Figures 4.9 and 4.10 display a QQ plot of residuals and residuals against predicted values respectively of the parent response total scale score model. These plots demonstrate the assumptions of normality and homogeneity of error variance for the model are not met, and the model has been miss-specified. The QQ plot demonstrates a significant deviation from normal, with residuals deviating from the diagonal line at the tails of the distribution (Figure 4.9). The residual vs. predicted plot demonstrates heteroscedasticity with less variance of residuals at higher levels compared to the lower levels of the predicted values (Figure 4.10). The misspecification may be due to the form of the data (under dispersion due to too many scores of 100) or due to a missing predictor. It is possible being unable to include slope as a random effect is limiting the ability to correctly specify this model. Similar observations were made of the child-response and parent sub-population final LME models (Appendix I). A log-linear model with a transformed outcome of log (total scale score) was explored in an attempt to reduce the skewness of residuals (130), however issues in both residual normality and heteroscedasticity were not improved (data not shown). Despite the violations of model assumptions, the model trajectories plotted as the fitted versus observed in Figure 4.11 followed a relatively uniform diagonal path.

Figure 4.9 Quantile-quantile plot for parent-response for total scale score linear mixed effects model

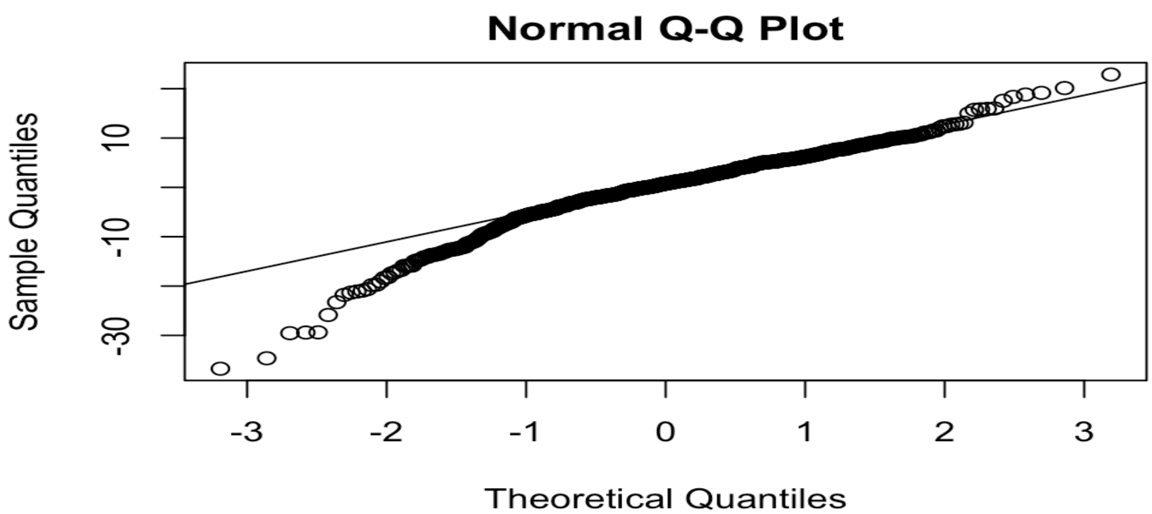


Figure 4.10 Residual vs predicted plot for parent-response total scale score linear mixed effects model

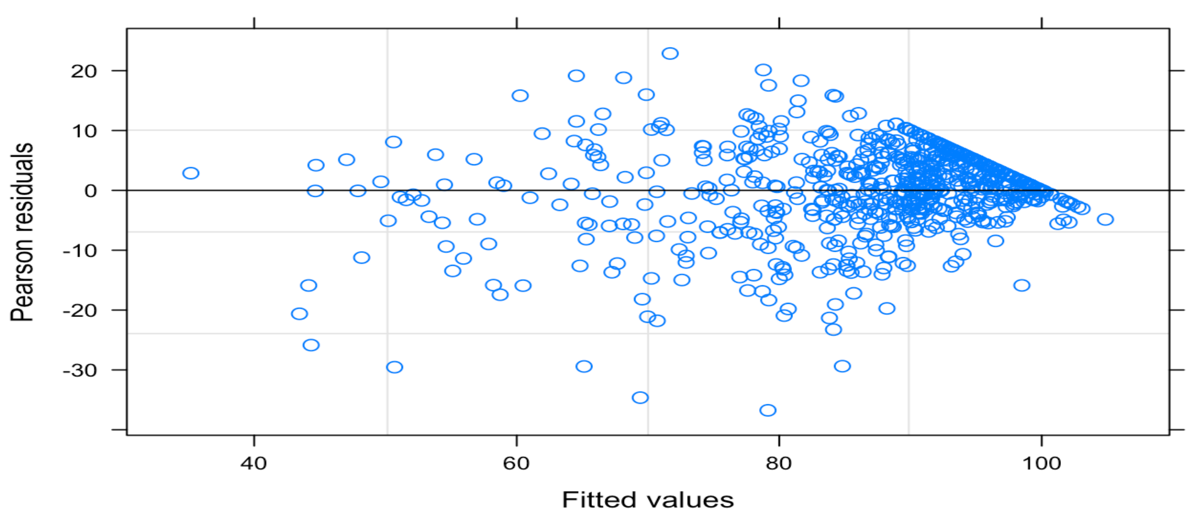
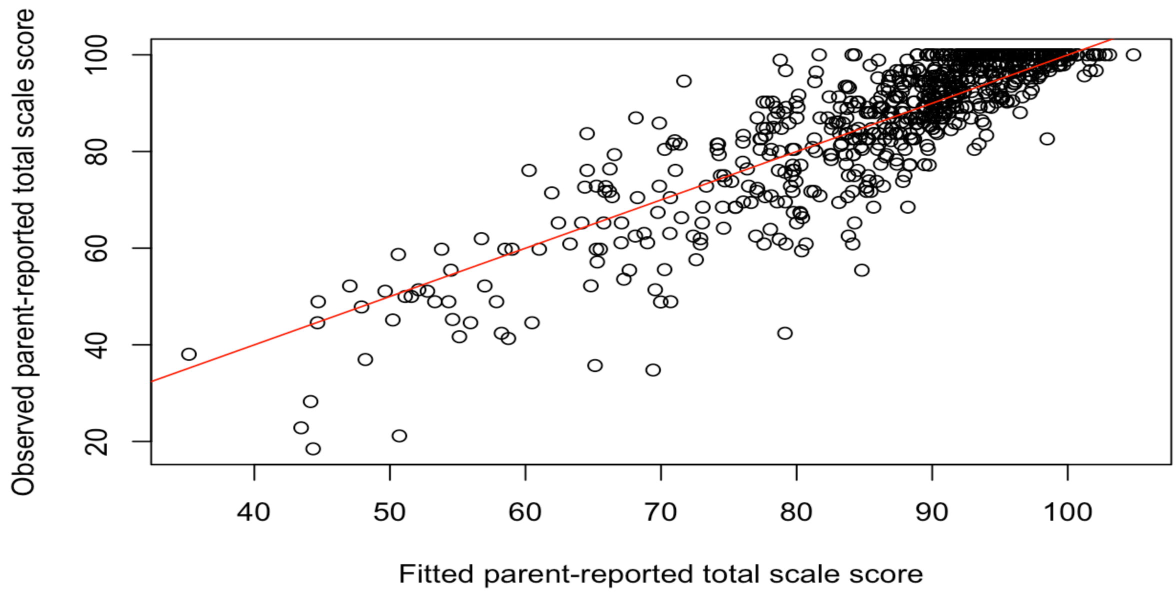


Figure 4.11 Overall quality of fixed effects fitted values with random effects against observed total scale score, parent response total scale score model



4.4.3 Non-linear mixed effects model

The NLME with asymptotic form, treated time continuously. A random effect for both intercept and rate were explored. In both the parent-and child-response models, random rate had a very small variance (p<0.0001), indicating it did not account for much of the variation in the model. It was not included in model building.

The first model presented is the fixed intercept and fixed LRC, random intercept model used to obtain starting values for subsequent models (Appendix H). The ICC of the NLME for parents, children and the parent sub-population were found to be consistent across models with values of 0.58, 0.57 and 0.54 respectively. These values indicate that 58%, 57% and 54% of the variance in the total scale score is due to between person variation, or variation in the random intercept with the remainder being due to within person differences overtime. The asymptote for these models was fixed at 100 based on the upper bound of the total scale score. In the parent-response model, the estimate for the fixed intercept was 81.14 (95% CI 79.31, 82.97) and for the

LRC it is exp(-2.46) = 0.085, indicating that at one-month post-injury, the estimated mean total scale score was 81.14 with an estimated non-linear average rate of approach to the asymptote (100) of 0.085 points/month (Appendix H). The fixed intercept in the child and parent sub-population models were 83.02 (95% CI 80.92, 85.02) and 79.15 (76.85, 81.46) respectively. The parent sub-population intercept was statistically significantly lower than that of the child-response model (parent sub-population intercept does not fall in the 95% confidence intervals for the child response intercept) (Appendix H).

The next models examined included the following covariates individually: age category, baseline total scale score, hospitalization status (with ED as the reference category), PaedsCTAS collapsed into the three previously described categories, sex, parent's highest education, injury type and income quintile (not presented) as fixed effects for intercept and log rate (data not presented).

For the parent-response model, age category ($p<0.001$), PaedsCTAS ($p=0.001$), hospitalization status ($p<0.001$), parent's highest education ($p=0.020$), baseline total scale score ($p<0.001$) and injury type ($p<0.001$) were significant fixed effects associated with the intercept. PaedsCTAS ($p=0.005$), hospitalization status ($p<0.001$), income quintile (0.019), injury type ($p=0.002$) and baseline total scale score ($p<0.001$) were significantly associated with the LRC on the Wald test p-values. These variables were added to the model one at a time in order of bivariable model significance. Age category, hospitalization status, injury type and baseline total scale score were retained for the intercept and hospitalization status, baseline total scale score and injury type were retained for the LRC.

Next, variables that were included as fixed effects were explored for their role in explaining part of the random effect variability. Based on a significant LRT baseline total scale score (p<0.001) was included as a random effect modifier. None of the interaction terms were found to be significant when added as fixed effects and therefore were not included.

Table 4.6 presents the final NLME asymptotic model for parent-response total scale score. From this model, the estimated mean total scale score at one-month post-injury for children < 5 years of age, seen in the ED, with a minor external injury and mean baseline total scale score was 89.21 (95% CI 86.42, 92.00). Older children relative to those < 5 years of age (estimate for children 13 - < 16 years old -5.34, 95% CI (-9.01, -1.67), p<0.001), those hospitalized relative to those seen in the ED (estimate -12.93, 95% CI (-16.94, -8.92), p<0.001), those with lower extremity fractures (estimate -20.31, 95% CI (-25.55, -15.07), p<0.001) and upper extremity fractures (estimate -4.54, 95% CI (-8.22, -0.86) relative to those with minor external injury, and those with lower baseline total scale score relative to those with higher baseline total scale score (estimate 0.46, 95% CI (0.28, 0.63), p<0.001) all had statistically significantly lower total scale score at one-month post-injury.

The estimated rate of approach to the asymptote for children under five years old, seen in the ED, with minor external injuries and mean baseline total scale score was 0.03 (i.e. exp(-3.49)). Children who were hospitalized relative to those seen in the ED (estimate 0.91, 95% CI (0.56, 1.26), p<0.001), those with higher baseline total scale score (estimate 0.05, 95% CI (0.04, 0.07), p<0.001), and those with upper extremity fractures (estimate 1.29, 95% CI (0.59, 2.00), p<0.001) or lower extremity fractures (estimate 1.32, 95% CI (0.63, 2.01), p<0.001) relative to those with minor external injuries all had estimated greater rate of approach to the asymptote (i.e. greater recovery in terms of total scale score in the same period of time).

The ICC for this model was 0.55, indicating 55% of the variance was due to between person variation, or variation in the random intercept. The time invariant predictors in this model explained an additional 66% of the total outcome variance relative to the time only model as given by:

$$\frac{(residual\ variance\ +\ random\ intercept\ variance\ +\ variance\ explained\ by\ baseline\ total\ scale\ score\ in\ the\ model\ in\ Table\ 4.6)}{residual\ variance + random\ intercept\ variance\ in\ model\ in\ Appendix\ G}$$

The NLME asymptotic model for child-reported total scale score can be found Table 4.7. Consistent with the parent-response total scale score model, children with lower baseline total scale score (estimate 0.41, 95% CI (0.19, 0.63), p<0.001), those hospitalized relative to those seen in the ED (estimate -10.34, 95% CI (014.79, -5.90), p<0.001) and those with lower extremity fractures (estimate (-12.95, 95% CI (-18.10, -7.80), p<0.001) or major trauma (estimate -9.12, 95% CI (-17.83, -0.40), p=0.043) relative to those with minor external injuries had statistically significantly lower total scale score at one-month post-injury. In addition, children with greater baseline total scale scores (estimate 0.05, 95% CI (0.02, 0.07), p<0.001) and those who were hospitalized (estimate 1.21, 95% CI (0.67, 1.75), p<0.001) had a greater estimated LRC relative to those with lower baseline total scale score and children seen in the ED. The time invariant predictors in this model explained an additional 61% of the total outcome variance relative to the time only model. Similar relationships were observed in the parent sub-population NLME model (Table 4.7), but the total scale score at one-month post-injury in the parent sub-population model was statistically significantly lower than in the child-response model (parent estimate 82.83, 95% CI (79.85, 85.81), p<0.001, child estimate 87.90, 95% CI (85.33, 90.47), p <0.001) Table 4.7.

Table 4.6 Parent response asymptotic non-linear fixed effects model*

Predictors	*Estimates***	*95% CI*	*p*
R0 intercept	**89.21**	**86.42, 92.00**	**<0.001**
R0 – Age Category			
< 5 years old	ref		
5 - 8 years old	-1.82	-5.49, 1.85	0.336
8 - 13 years old	-2.68	-6.17, 0.80	0.136
13 - <17 years old	**-5.34**	**-9.01, -1.67**	**0.005**
R0 – Hospitalization Status			
Emergency Department	ref		
Hospitalized	**-12.93**	**-16.94, -8.92**	**<0.001**
R0 – Injury Type			
Minor External	ref		
Upper extremity fracture	**-4.54**	**-8.22, -0.86**	**0.017**
Lower extremity fracture	**-20.31**	**-25.55, -15.07**	**<0.001**
Head injury	1.68	-2.58, 5.95	0.445
Major Trauma	-5.25	-11.99, 1.49	0.132
Other	2.80	-3.05, 8.65	0.354
R0 – Baseline total scale score	**0.46**	**0.28, 0.63**	**<0.001**
LRC intercept	**-3.49**	**-4.11, -2.87**	**<0.001**
LRC – Hospitalization Status			
Emergency Department	ref		
Hospitalized	**0.91**	**0.56, 1.26**	**<0.001**
LRC – Baseline total scale score	**0.05**	**0.04, 0.07**	**<0.001**
LRC – Injury Type			
Minor External	ref		
Upper extremity fracture	**1.29**	**0.59, 2.00**	**0.001**
Lower extremity fracture	**1.32**	**0.63, 2.01**	**<0.001**
Head injury	0.68	-0.23, 1.58	0.149
Major Trauma	0.60	-0.19, 1.38	0.141
Other	0.11	-0.96, 1.19	0.839
Random Effects			
Residual variance	8.44		
Random intercept variance	6.08		
Random intercept modifier	0.74		
ICC	0.55		
# observations	707		

* Bolded parameter estimates are statistically significant in the model at alpha of 0.05, ref = refence category for that variable, 95% *CI* = 95% confidence interval associated with parameter estimate, R0 = fixed intercept, LRC = log rate constant

**Estimates associated with LRC have not been exponentiated

Table 4.7 Child response asymptotic NLME, and parent sub population*

	Child			Parent sub population		
Predictors	*Estimates*	*95% CI*	*p*	*Estimates*	*95% CI*	*p*
R0 – (Intercept)	**87.90**	**85.33, 90.47**	**<0.001**	**82.83**	**79.85, 85.81**	**<0.001**
R0 – Baseline total scale score	**0.41**	**0.19, 0.63**	**<0.001**	**0.57**	**0.32, 0.82**	**<0.001**
Hospitalization Status						
Emergency Department	ref			ref		
Hospitalized	**-10.34**	**-14.79, -5.90**	**<0.001**	**-11.08**	**-16.49, -5.66**	**<0.001**
Injury Type						
Minor external	ref			ref		
Upper extremity fracture	-1.61	-5.24, 2.02	0.389	-0.58	-4.99, 3.82	0.797
Lower extremity fracture	**-12.95**	**-18.10, -7.80**	**<0.001**	**-15.54**	**-21.59, -9.48**	**<0.001**
Head injury	0.91	-4.16, 5.98	0.728	**6.70**	**0.12, 13.28**	**0.049**
Major Trauma	**-9.12**	**-17.83, -0.40**	**0.043**	-5.40	-15.24, 4.43	0.287
Other	2.68	-4.25, 9.62	0.452	4.94	-4.12, 14.00	0.290
LRC intercept	**-3.18**	**-3.64, -2.71**	**<0.001**	**-2.55**	**-2.84, -2.26**	**<0.001**
LRC – Baseline total scale score	**0.05**	**0.02, 0.07**	**<0.001**	**0.04**	**0.02, 0.07**	**<0.001**
LRC – Hospitalization Status						
Emergency Department	ref			ref		
Hospitalized	**1.21**	**0.67, 1.75**	**<0.001**	**0.97**	**0.55, 1.39**	**<0.001**
Random Effects						
Residual variance	8.36			9.46		
Random intercept variance	3.72			5.89		
Random intercept modifier	0.84			0.76		
ICC	0.65			0.59		
# observations	418			418		

* Bolded parameter estimates are statistically significant in the model at alpha of 0.05, ref = reference category for that variable, 95% *CI* = 95% confidence interval associated with parameter estimate, R0 = fixed intercept, LRC = log rate constant, variables that are green are statistically significantly different from the child-response model

4.4.3.1 Model diagnostics

The pattern of the residuals for all three of the asymptotic NLME models improved from the LME models (parent-response model residual plots presented) in terms of normality with less deviation from the expected linear diagonal line in the normal probability (QQ plot) (Figure 4.12.) Although more linear, there is still evidence of poor model specification at the tails of the residuals (Figure 4.12), and there is heteroscedasticity present, but to a lesser degree, in the scatter plot of the standardized residuals versus fitted total scale score values plot (Figure 4.13). Figures 4.14, 4.15, and 4.16 demonstrate the model parameter estimates predict the total scale score well, with the predicted versus observed trajectories generally following a linear line, and the individual level predictions matching the observed values well. Although the trajectories of the predicted models were well matched to the observed data, the model assumption violations suggest another step is required. An appropriate transformation of the outcome data could be explored to try to coerce a linear relationship between continuous time and total scale score or a model that does not have the same assumptions regarding the distribution of the residuals could be applied such as quantile regression (110).

Figure 4.12 Quantile - Quantile plot parent-response total scale score non-linear mixed effects asymptotic model

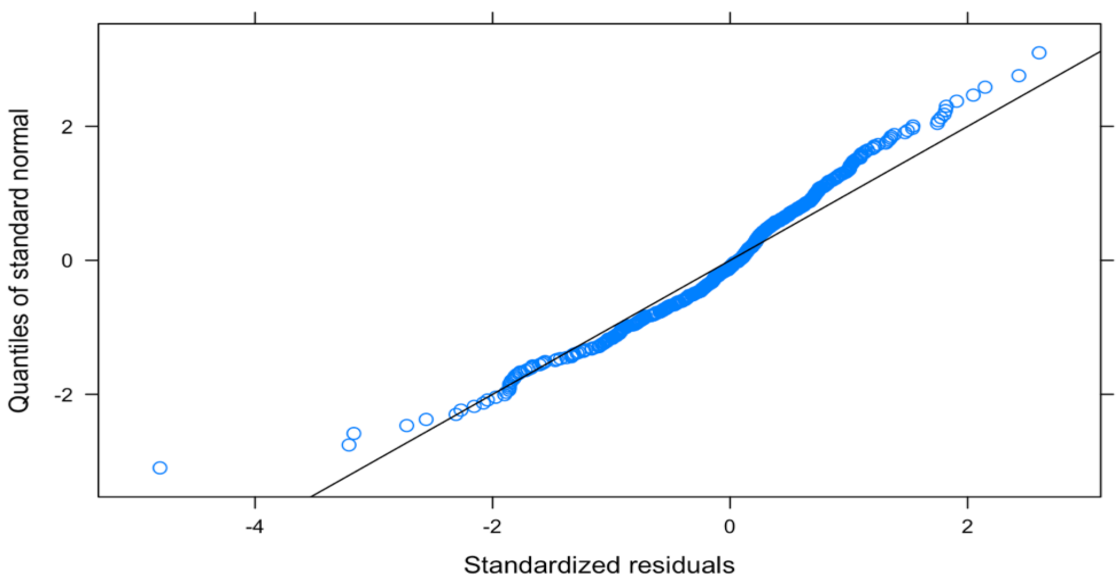


Figure 4.13 Standardized residuals vs fitted parent-response total scale score values for parent-responses non-linear mixed effects asymptotic model

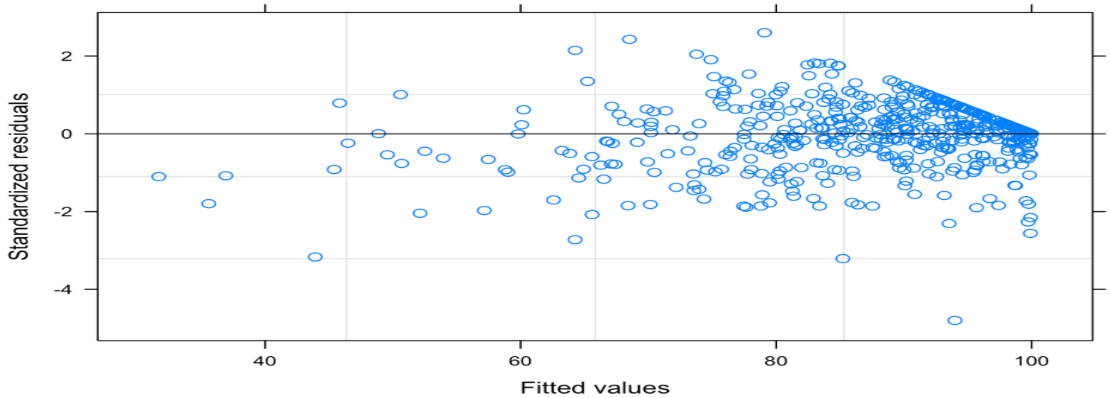


Figure 4.14 Overall quality of fixed effects fitted values without random effects against observed values for parent-response total scale score model

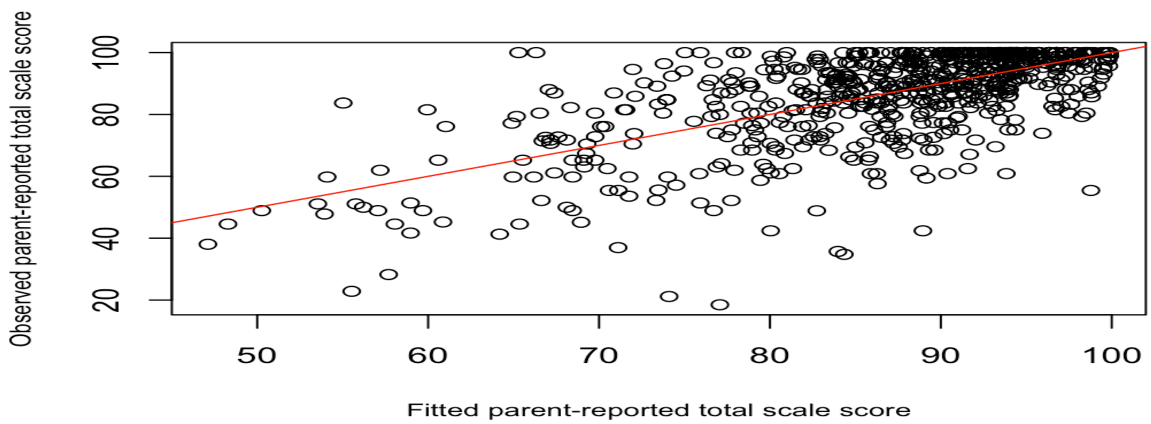


Figure 4.15 Overall quality of fixed effects fitted values with random effects against observed response for the parent-response total scale score model

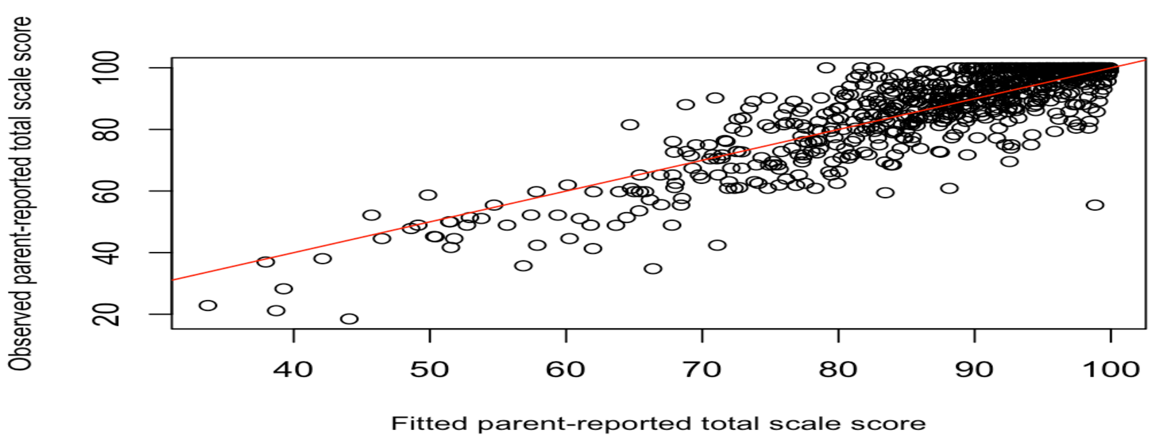
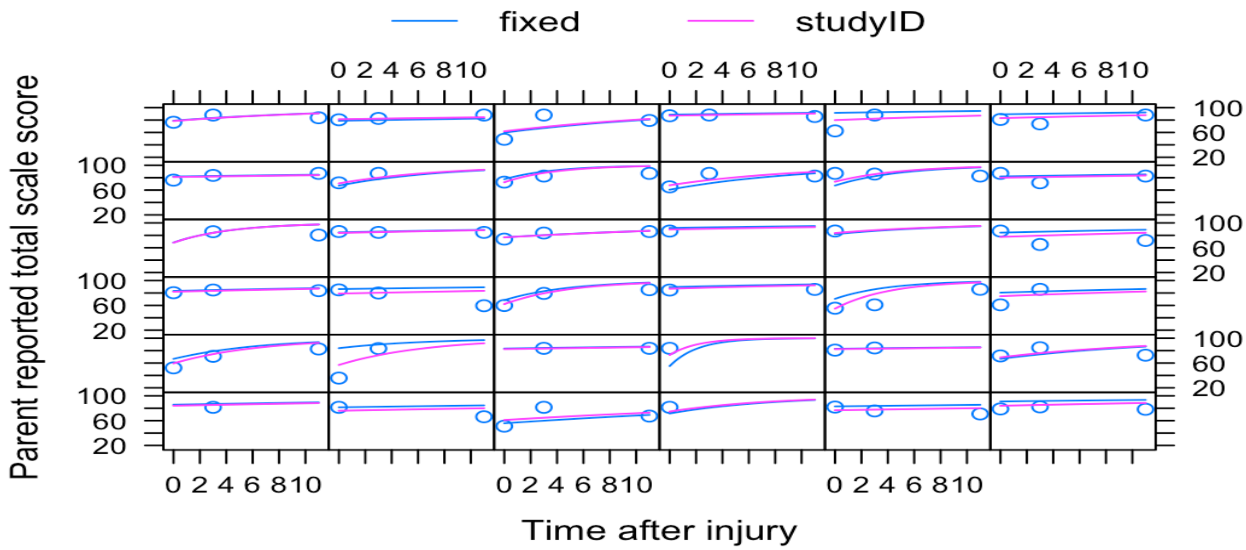


Figure 4.16 Study ID specific (study ID, random effect) and population average (fixed) predicted total scale scores obtained from final parent-response non-linear mixed effects model*



* Each square represents one study ID, blue dots are the observed values for parent-reported total scale score, blue line is the fitted regression line from the non-linear mixed effects model for fixed effects, pink line represents the regression line accounting for random effects

4.4.4 Non-linear quantile mixed model

The NLQMM with the same form and covariates as the asymptotic NLME models were built next. The final NLQMM for parent-response, child-response and parent sub-population can be found in Tables 4.8 and 4.9. The underlined model coefficients in these tables represent those estimates that are statistically significantly different from their NLME OLS analogues (i.e. they fall outside the 95% confidence intervals of the OLS estimate). The interpretation of these models is in line with that of the NLME however instead of population means, population medians have been estimated.

For the parent-response NLQMM model in Table 4.14, the median total scale score at one-month post-injury for children < 5 years of age, seen in the ED, with minor external injuries and mean baseline total scale score was estimated as 89.32 (95% CI 83.05, 95.59). Similar to the other models, hospitalized children (estimate -10.70, 95% CI (-17.04, -4.35), p<0.001) and those with lower extremity fractures (estimate -26.93, 95% CI (-53.39, -0.48), p=0.046) had statistically significantly lower median total scale score relative to children seen in the ED and those with minor injuries. Every one-point increase in baseline total scale score was associated with a 0.47 (95% CI 0.19, 0.75), p=0.001) increase in total scale score at one-month post-injury. The variance estimate for the random intercept in this model was very small (<0.01) indicating variance in the intercepts across individuals (between person variation) did not account for a significant amount of the overall variation in this model. Due to the extremely small random intercept variance estimate, the ICC for this model was not calculated.

In the child-response NLQMM both baseline total scale score (estimate 0.63, 95% CI (0.32, 0.93), p<0.001) and being hospitalized (estimate -11.52, 95% CI (-20.92, -2.12), p=0.016), were associated with statistically significantly lower total scale score at one-month post-injury. No other variables were significant in this model. The parent sub-population NLQMM for total scale score had no statistically significantly different parameter estimates from their child-response model analogues. The variance estimates for the random intercept in these models was again very small (<0.01), consistent with the parent response model, indicating variance in the intercepts across individuals did not account for a significant amount of the overall variation in these models. Due to the extremely small random intercept variance estimates, the ICC for these models was not calculated.

Table 4.8 Parent-response total scale score non-linear quantile mixed effects model*

Predictors	*Estimates*	*95% CI*	*p*
R0 intercept	**89.32**	**83.05, 95.59**	**<0.001**
R0 - Age Category			
< 5 years old	ref		
5 - < 8 years old	0.48	-5.95, 6.91	0892
8 - <13 years old	-0.69	-6.98, 5.50	0837
13 - <17 years old	-3.10	-8.74, 2.54	0.284
R0 - Hospitalization Status			
Emergency Department	ref		
Hospitalized	**-10.70**	**-17.04, -4.35**	**0.001**
R0 – Injury Type			
Minor External	ref		
Upper extremity fracture	-3.26	-20.18, 13.66	0.719
Lower extremity fracture	<u>**-26.93**</u>	**-53.39, -0.48**	**0.046**
Head injury	3.10	-20.68, 26.89	0.810
Major Trauma	<u>-13.80</u>	-32.11, 4.51	0.140
Other	4.22	-8.73, 17.18	0.533
R0 – Baseline total scale score	**0.47**	**0.19, 0.75**	**0.001**
LRC intercept	<u>-5.50</u>	-14.78, 3.77	0.247
LRC – Hospitalization Status			
Emergency Department	ref		
Hospitalized	1.18	-4.45, 6.81	0.695
LRC – Baseline HRQoL	<u>0.48</u>	-1.44, 2.41	0.635
LRC – Injury Type			
Minor External	Ref		
Upper extremity fracture	<u>4.52</u>	-4.22, 13.25	0.315
Lower extremity fracture	<u>6.19</u>	-14.75, 27.12	0.574
Head injury	1.50	-19.30, 22.29	0.896
Major Trauma	<u>8.03</u>	-13.30, 29.35	0.470
Other	<u>-0.44</u>	-31.99, 31.12	0.980
Random Effects			
Residual variance	3.84		
Random intercept variance	<0.01		
# observations	707		

* Parameter estimates bolded are statistically significant in the model at alpha of 0.05, ref = reference category for that variable, 95% *CI* = 95% confidence interval associated with parameter estimate, *p* = p-value associated with parameter estimate, R0 = fixed intercept, LRC = log rate constant, estimates that are underlined are statistically significantly different from their NLME analogue

Table 4.9 Child and parent sub-population total scale score non-linear quantile mixed effects model*

	Child			Parent sub population		
Predictors	*Estimates*	*95% CI*	*p value*	*Estimates*	*95% CI*	*p value*
R0 - (Intercept)	**88.38**	**82.05, 95.59**	**<0.001**	**84.90**	**77.27, 92.53**	**<0.001**
R0 - Baseline HRQoL	**0.63**	**0.32, 0.93**	**<0.001**	**0.52**	**0.09, 0.94**	**0.017**
Hospitalization Status						
ED	ref					
Hospitalized	**-11.52**	**-20.92, -2.12**	**0.016**	**-9.80**	**-19.25, -0.34**	**0.042**
Injury Type						
Minor external	ref					
Upper extremity fracture	-0.18	-9.68, 9.32	0.973	-0.26	-13.93, 13.41	0.973
Lower extremity fracture	-11.29	-27.97, 5.39	0.186	-17.59	-43.39, 8.21	0.182
Head injury	0.75	-11.34, 12.84	0.911	8.98	-11.49, 29.46	0.397
Major Trauma	-12.87	-26.97, 0.82	0.065	-6.12	-22.60, 10.37	0.476
Other	2.45	-12.41, 17.31	0.760	6.36	-8.49, 21.22	0.408
LRC intercept	-2.91	-8.40, 2.58	0.303	-1.84	-11.08, 7.40	0.709
LRC - Baseline HRQoL	0.03	-2.43, 2.49	0.983	<u>0.10</u>	-5.11, 5.32	0.972
LRC – Hospitalization Status						
ED	Ref					
Hospitalized	<u>1.83</u>	-11.60, 15.25	0.802	<u>0.32</u>	-12.29, 12.92	0.964
Random Effects						
Residual variance	3.86			4.17		
Random intercept variance	<0.01			<0.01		
# observations	418			418		

* Parameter estimates bolded are statistically significant in the model at alpha of 0.05, ref = reference category for that variable, 95% *CI* = 95% confidence interval associated with parameter estimate, *p* = p-value associated with parameter estimate, R0 = fixed intercept, LRC = log rate, estimates that are underlined are statistically significantly different from their NLME analogue, estimates that are in green are statistically significantly different from the child-response analogue

4.4.5 GLMM outcome and models

Forty four percent of children (n=113) were identified as "recovered" based on the parent-reported total scale score (the score was within the MCID of 4.4 points) at one-month post-injury, with 78.0% (n = 181) and 81.6% (n = 182) recovered at four and 12 months post-injury respectively. Based on bivariable logistic regression, statistically significant differences in the odds of recovery were observed by hospitalization status at one and four-months post-injury with 13.4% (n = 9), 68.4% (n = 39) and 82.3% (n = 51) of hospitalized children recovered at one, four and 12 months, respectively, while 45.6% (n = 87), 81.1% (n = 142), and 81.4% (n = 131) of children seen in the ED were recovered at each time point (one-month OR = 0.13 (95% CI = 0.06, 0.28), p<0.001, four-months OR = 0.50 (95% CI = 0.26-0.99, p=0.046)) (Appendix J). There were also statistically significant differences in the odds of recovery by age category with the older two age groups having lower odds of recovery at one and four-months relative to the youngest age group (at one-month 8-<13 years OR = 0.28 (95% CI = 0.14, 0.54), p<0.001, 13-<17 years old OR = 0.25 (95% CI = 0.12-0.53), p<0.001; at four-months 8<13 years OR = 0.36 (95% CI = 0.16, 0.84), p=0.019, 13<17 years old OR = 0.33 (95% CI = 0.14-0.79), p=0.012) (Table 4.16). In addition, children who had upper extremity fractures (OR = 0.23 (95% CI 0.12, 0.46), <0.001), lower extremity fractures (OR = 0.02 (95% CI 0.00, 0.16), p<0.001) and major trauma (OR = 0.11, (95% CI 0.03, 0.39), p<0.001) had lower odds of recovery relative to children with minor external injuries at one-month post-injury (Appendix J). Finally, PaedsCTAS was also associated with odds of recovery at one-month post-injury with children with PaedsCTAS of 4 or 5 having higher odds of recovery relative to those with scores of 1 or 2 (OR 2.98 (95% CI 1.35–6.62), p=0.001).

Consistent with the results for the parent-response, hospitalization status, PaedsCTAS and injury type were all associated with the odds of recovery at one-month post-injury for child-response total scale score (Appendix K). At one-month post-injury children who were hospitalized relative to being seen in the ED (OR = 0.22, 95% CI 0.10, 0.48, p<0.001), those with a PaedsCTAS of 4 or 5 relative to 1 or 2 (OR 3.57, 95% CI 1.35, 9.47, p=0.011), and those who had a lower extremity fracture (OR 0.11, 95% CI 0.04, 0.35, $p<0.001$) or major trauma (OR = 0.12, 95% CI 0.02, 0.61, $p=0.011$) relative to minor external injuries, had lower odds of recovery. No variables were statistically significantly associated with child-response recovery at four- or 12- months post-injury (Appendix K). It should be noted that there are many small frequencies (< 15) across the categories in both the parent and child response data for this dichotomous variable. Limited data reduce the ability to make valid inferences and should be interpreted with caution.

4.4.6 Generalized linear mixed models

Four variables were found to be statistically significant in the dichotomous parent response GLMM model when each variable was entered into the model independently based on LRT: hospitalization status ($p < 0.001$); baseline total scale score ($p=0.040$); injury type ($p <0.001$); and age category ($p<0.001$). When each variable was added to the final model in order of bivariable significance, hospitalization status, age category and injury type were retained, based on LRT. There was a statistically significant interaction term between hospitalization status and time. Reflecting the loss of data and power caused by dichotomizing a continuous variable, the 95% CI inflated to infinity for some parameters indicating the model did not appropriately converge due to overparameterization when an interaction between injury and time was included in the model, having the potential for misleading results. For this reason, this interaction was not retained in the final model (Table 4.10).

The odds of recovery were greater at four- and 12-months post-injury relative to one-month post-injury (OR for four-months 6.96, 95% CI (3.61, 13.41), $p<0.001$, OR for 12 months 6.75, 95% CI (3.47, 13.14), $p<0.001$). Hospitalization (OR 0.08, 95% CI (0.02, 0.27), $p<0.001$), older age (OR 8- < 13 years old OR 0.36, 95% CI (0.16, 0.80), $p<0.012$, OR 13-<17 years old 0.19, 95% CI (0.08, 0.47), $p<0.001$) and having a lower extremity fracture (OR 0.29, 95% CI

(0.10, 0.83), p=0.021) were associated with lower odds of recovery relative to being seen in the ED, age less than five years old and having a minor external injury. Hospitalization was also associated with greater odds of recovery at four- and 12-months post-injury relative to being seen in the ED (4 month OR 23.47, 95% CI (5.33, 103.33), p<0.001, 12 month OR 6.84, 95% Ci (1.77, 26.45), p=0.005). However, due to the width of the 95% CI, not much can be concluded from the parameter estimate.

Table 4.10 Parent-response total scale score GLMM**

Predictors	Odds Ratios	95% CI	p
(Intercept)	**3.12**	**1.51, 6.43**	**0.002**
Time			
1 month	ref		
4 months	**6.96**	**3.61, 13.41**	**<0.001**
12 months	**6.75**	**3.47, 13.14**	**<0.001**
Hospitalization Status			
Emergency Department	ref		
Hospitalized	**0.08**	**0.02, 0.27**	**<0.001**
Age Category			
< 5 years old	ref		
5 - < 8 years old	0.49	0.21, 1.17	0.109
8 - <13 years old	**0.36**	**0.16, 0.80**	**0.012**
13 - <17 years old	**0.19**	**0.08, 0.47**	**<0.001**
Injury Type			
Minor External	ref		
Upper extremity fracture	0.62	0.29, 1.35	0.228
Lower extremity fracture	**0.29**	**0.10, 0.83**	**0.021**
Head injury	1.68	0.60, 4.71	0.325
Major Trauma	0.37	0.09, 1.52	0.168
Other	1.32	0.31, 5.52	0.705
Time * Hospitalization status			
4 months * hospitalized	**23.47**	**5.33, 103.33**	**<0.001**
12 months * hospitalized	**6.84**	**1.77, 26.45**	**0.005**
Random Effects			
Residual variance	3.29		
Random intercept variance	2.53		
ICC	0.43		
Marginal R^2	0.345		
Conditional R^2	0.630		
# Observations	707		

** Bolded parameter estimates statistically significant in the model at alpha of 0.05, ref = referent category, 95% CI = 95% confidence intervals associated with parameter estimate, *p* = p-value associated with parameter estimate, Odd Ratio = Odds of having recovered as defined by total scale score at each time point being within the MCID of the PedsQL tool of the total scale score at baseline

For the child-response model hospitalization status (p<0.001), baseline total scale score (p<0.001), PaedsCTAS category (p=0.017), and injury type (p=0.028) were statistically significant based on the LRT when included independently with categorical time. Injury type, hospitalization status and baseline total scale score were retained in the final model (Table 4.19). Consistent with the parent response model, there was a statistically significant interaction between hospitalization status and time. Again, similar to the parent-response model, the odds of recovery were higher at four and 12 months post recovery relative to one-month (four month OR 2.68, 95% CI (1.29, 5.58), p=0.008, 12 month OR 2.80, 95% CI (1.36, 5.77), p=0.005), and upper extremity fractures were associated with lower odds of recovery relative to minor external injuries (OR 0.29, 95% CI (0.11, 0.77), p=0.013) (Table 4.11).

In the parent sub-population GLMM the odds of recovery at one-month were statistically significantly lower relative to the child response model (parent response OR 0.74, 95% CI (0.38, 1.43), p=0.369, child response OR 2.70, 95% CI (1.46, 4.98), p=0.002). In contrast the odds of recovery at four- and 12-months were statistically significantly greater in the parent response GLMM relative to the analogous estimates from the child-response model (Table 4.11)

Table 4.11 Child and parent sub-population total scale score GLMM**

	Child			Parent		
Predictors	**Odds Ratios**	**95% CI**	**p**	**Odds Ratios**	**95% CI**	**p**
(Intercept)	**2.70**	**1.46, 4.98**	**0.002**	0.74	0.38, 1.43	0.369
Time						
1 month	ref			ref		
4 months	**2.68**	**1.29, 5.58**	**0.008**	**10.25**	**4.33, 24.24**	**<0.001**
12 months	**2.80**	**1.36, 5.77**	**0.005**	**7.77**	**3.47, 17.42**	**<0.001**
Injury Type						
Minor External	ref			ref		
Upper extremity fracture	0.82	0.39, 1.73	0.607	0.83	0.35, 1.98	0.679
Lower extremity fracture	**0.29**	**0.11, 0.77**	**0.013**	0.33	0.10, 1.08	0.067
Head injury	1.97	0.58, 6.72	0.278	2.16	0.54, 8.59	0.276
Major Trauma	0.58	0.13, 2.51	0.466	0.24	0.04, 1.51	0.128
Other	2.62	0.42, 16.50	0.304	1.11	0.17, 7.38	0.913
Hospitalization Status						
Emergency Department	ref			ref		
Hospitalized	**0.18**	**0.06, 0.54**	**0.003**	**0.11**	**0.02, 0.51**	**0.005**
Baseline HRQoL	**0.95**	**0.92, 0.98**	**0.003**	1.00	0.96, 1.03	0.912
Time * Hospitalization status						
Four-months * hospitalized	**11.34**	**2.26, 56.84**	**0.003**	**13.94**	**2.01, 96.59**	**0.008**
Twelve-months * hospitalized	3.47	0.84, 14.27	0.084	5.75	1.00, 32.89	0.050
Random Effects						
Residual variance	3.29			3.29		
Random intercept variance	0.97			2.12		
ICC	0.23			0.39		
Marginal R^2	0.242			0.330		
Conditional R^2	0.414			0.593		
# Observations	418			418		

** Bolded values statistically significant in the model at alpha of 0.05, ref = referent category, CI = 95% confidence intervals associated with parameter estimate, *p* = p-value associated with parameter estimate, variables green are statistically significantly different from the child model, Odd Ratio = Odds of having recovered as defined by total scale score at each time point being within the MCID of the PedsQL tool of the total scale score at baseline

4.4.7 Missing data sensitivity analysis

Models relating to the missing data sensitivity analysis are described in Tables 4.12 and 4.13. The NLME models were used for this sensitivity analysis. The first model presents the results of MI under MAR in the parent-response NLME model compared to the all available data parent-response NLME model (Table 4.12). There was only one parameter estimate that was statistically significantly different across these two models.

In the sensitivity analysis models applying the adjustment for possible MNAR, estimates that lie outside the 95% confidence intervals of the all available data model are underlined in tables 4.12 and 4.13. In Table 4.13, an increasing number of estimates were statistically significantly different from the all available data model as the amount of bias increased. When MI values for HRQoL at all time points were biased downwards by five points, only one estimate was statistically significantly different from the all available data model. In the moderately biased model, where MI estimates were decreased by 10 points, four estimates were statistically significantly different from the all available data model. In the most heavily biased model, where MI estimates where biased downwards by 15 points, ten of the 19 estimates were statistically significantly different from the all available data model (Table 4.13).

Table 4.12 Multiple imputation under missing at random assumption for parent-response total scale score non-linear mixed effects models (NLME)*

	Parent-response NLME all available data			MI under MAR model		
Predictors	*Estimates*	*95% CI*	*p*	*Estimate*	*95% CI*	*p*
R0 intercept	**89.21**	**86.42, 92.00**	**<0.001**	**89.55**	**86.54, 92.56**	**<0.001**
Age Category						
< 5 years	ref			ref		
5-8 years	-1.82	-5.49, 1.85	0.336	-2.77	-6.39, 0.85	0.134
8-13 years	-2.68	-6.17, 0.80	0.136	**-3.76**	**-7.23, -0.28**	**0.034**
13-16 years	**-5.34**	**-9.01, -1.67**	**0.005**	**-4.59**	**-8.35, -0.83**	**0.017**
Hospitalization Status						
Emergency Department	ref					
Hospitalized	**-12.93**	**-16.94, -8.92**	**<0.001**	**-11.48**	**-17.11, -5.86**	**<0.001**
Injury Type						
	ref			ref		
Upper extremity fracture	**-4.54**	**-8.22, -0.86**	**0.017**	-3.76	-7.91, 0.39	0.076
Lower extremity fracture	**-20.31**	**-25.55, -15.07**	**<0.001**	**-21.44**	**-28.13, -14.75**	**<0.001**
Head injury	1.68	-2.58, 5.95	0.445	0.01	-5.03, 5.04	0.999
Major Trauma	-5.25	-11.99, 1.49	0.132	**-9.12**	**-18.08, -0.15**	**0.046**
Other	2.80	-3.05, 8.65	0.354	2.69	-4.08, 9.45	0.445
Baseline HRQoL	**0.46**	**0.28, 0.63**	**<0.001**	**0.45**	**0.28, 0.62**	**<0.001**
LRC intercept	**-3.49**	**-4.11, -2.87**	**<0.001**	**-3.53**	**-4.25, -2.81**	**<0.001**
Hospitalization Status						
Emergency Department	ref			ref		
Hospitalized	0.91	0.56, 1.26	<0.001	**0.81**	**0.15, 1.46**	**0.016**
Baseline total scale score	**0.05**	**0.04, 0.07**	**<0.001**	0.02	-0.01, 0.04	0.121
Injury Type						
Minor external	ref			ref		
Upper extremity fracture	**1.29**	**0.59, 2.00**	**0.001**	**0.93**	**0.09, 1.76**	**0.030**
Lower extremity fracture	**1.32**	**0.63, 2.01**	**<0.001**	**1.55**	**0.63, 2.47**	**0.001**
Head injury	0.68	-0.23, 1.58	0.149	0.66	-0.43, 1.76	0.238
Major Trauma	0.60	-0.19, 1.38	0.141	1.05	-0.21, 2.31	0.102
Other	0.11	-0.96, 1.19	0.839	0.15	-1.25, 1.54	0.850
Random Effects						
Residual variance	8.44			88.36		
Random intercept variance	6.08			51.14		
ICC	0.42			0.37		
Random slope variance	0.74			0.93		
# observations	707			1095		

* Variables bolded are statistically significant in the model at alpha of 0.05, variables underlined are statistically significantly different from the all available data model, ref = referent category, 95% CI = 95% confidence intervals associated with parameter estimate, *p* = p-value associated with parameter estimate, MI = multiple imputation, MAR = missing at random

Table 4.13 Parent-response NLME with MI with imputations for parent-response total scale score at each time point biased downwards by deltas of 5, 10, 15

	Parent-response NLME all available data			MI model Delta of -5			MI model Delta of -10			MI model Delta of -15		
Predictors	*Beta*	*95% CI*	*p*	*Beta*	*95% CI*	*p*	*Beta*	*95% CI*	*p*	*Beta*	*95% CI*	*p*
R0 intercept	**89.21**	**86.42, 92.00**	**<0.001**	**90.35**	**87.25, 93.45**	**<0.001**	**92.28**	**88.99, 95.58**	**<0.001**	**94.02**	**90.78, 97.27**	**<0.001**
Age Category												
< 5 years	ref											
5-8 years	-1.82	-5.49, 1.85	0.336	-1.47	-5.31, 2.36	0.460	-1.30	-5.44, 2.83	0.548	-0.70	-4.96, 3.56	0.761
8-13 years	-2.68	-6.17, 0.80	0.136	-1.27	-4.88, 2.34	0.501	0.29	-3.53, 4.11	0.891	1.68	-2.19, 5.56	0.402
13-16 years	**-5.34**	**-9.01, -1.67**	**0.005**	**-3.92**	**-7.64, -0.21**	**0.038**	-3.51	-7.68, 0.66	0.099	-3.08	-7.38, 1.21	0.160
Hospitalization Status												
ED	ref											
Hospitalized	**-12.93**	**-16.94, -8.92**	**<0.001**	**-10.07**	**-14.86, -5.28**	**<0.001**	**-10.16**	**-14.70, -5.61**	**<0.001**	**-9.61**	**-14.99, -4.23**	**<0.001**
Injury Type												
Minor external	ref											
Upper extremity fracture	**-4.54**	**-8.22, -0.86**	**0.017**	**-4.96**	**-9.07, -0.84**	**0.018**	**-7.07**	**-11.70, -2.43**	**0.003**	**-8.24**	**-14.27, -2.21**	**0.007**
Lower extremity fracture	**-20.31**	**-25.55, -15.07**	**<0.001**	**-22.79**	**-29.13, -16.46**	**<0.001**	**-21.29**	**-28.30, -14.28**	**<0.001**	**-24.14**	**-31.26, -17.01**	**<0.001**
Head injury	1.68	-2.58, 5.95	0.445	0.82	-4.27, 5.91	0.766	0.24	-4.63, 5.12	0.928	0.85	-4.13, 5.84	0.751
Major Trauma	-5.25	-11.99, 1.49	0.132	**-12.08**	**-20.07, -4.09**	**0.003**	**-12.00**	**-20.68, -3.33**	**0.007**	**-13.21**	**-21.54, -4.88**	**0.002**
Other	2.80	-3.05, 8.65	0.354	4.36	-1.63, 10.34	0.154	4.03	-3.23, 11.29	0.280	3.36	-4.24, 10.95	0.393
Baseline HRQoL	**0.46**	**0.28, 0.63**	**<0.001**	**0.45**	**0.26, 0.64**	**<0.001**	**0.45**	**0.23, 0.66**	**<0.001**	**0.41**	**0.22, 0.60**	**<0.001**
LRC intercept	**-3.49**	**-4.11, -2.87**	**<0.001**	**-3.31**	**-3.99, -2.63**	**<0.001**	**-3.48**	**-4.22, -2.73**	**<0.001**	**-4.45**	**-7.61, -1.30**	**0.006**
Hospitalization Status												
ED	ref											
Hospitalized	0.91	0.56, 1.26	<0.001	**0.84**	**0.25, 1.43**	**0.005**	**0.94**	**0.46, 1.42**	**<0.001**	1.52	-2.07, 5.11	0.414
Baseline HRQoL	**0.05**	**0.04, 0.07**	**<0.001**	0.02	-0.01, 0.05	0.119	0.01	-0.03, 0.05	0.767	0.01	-0.07, 0.07	0.981

	Parent-response NLME all available data			MI model Delta of -5			MI model Delta of -10			MI model Delta of -15		
Injury Type												
Minor external	ref											
Upper extremity fracture	**1.29**	**0.59, 2.00**	**0.001**	**1.07**	**0.18, 1.95**	**0.018**	**1.52**	**0.59, 2.45**	**<0.001**	<u>2.55</u>	-0.84, 5.94	0.141
Lower extremity fracture	**1.32**	**0.63, 2.01**	**<0.001**	**1.61**	**0.73, 2.50**	**<0.001**	**1.80**	**0.86, 2.74**	**<0.001**	<u>2.96</u>	-0.21, 6.13	0.066
Head injury	0.68	-0.23, 1.58	0.149	0.67	-0.42, 1.75	0.231	0.82	-0.36, 1.99	0.173	0.92	-1.77, 3.61	0.513
Major Trauma	0.60	-0.19, 1.38	0.141	**1.20**	**0.16, 2.24**	**0.023**	**<u>1.52</u>**	**0.27, 2.77**	**0.017**	<u>2.30</u>	-0.09, 4.69	0.059
Other	0.11	-0.96, 1.19	0.839	-0.09	-1.41, 1.24	0.907	0.24	-1.39, 1.86	0.786	0.65	-2.98, 4.29	0.737
Residual variance	8.44			99.86			116.53			130.49		
Random intercept variance	6.08			65.55			93.42			141.69		
Random slope variance	0.74			0.89			1.21			1.95		
ICC												
# obs	707											

* NLME = non-linear mixed effect model, underlined estimates are statistically significantly different from the all available data model, ref = referent category, 95% CI = 95% confidence intervals associated with parameter estimate, *p* = p-value associated with parameter estimate, variables bolded are statistically significant in the model at alpha of 0.05

4.5 Discussion

4.5.1 Variables associated with HRQoL

The primary objective of this chapter was to investigate factors associated with decreased PedsQL total scale score reported by parents and children in the year following injury, and the secondary objective was to compare results across longitudinal modelling methods. Of the eight possible predictor variables included in this study, hospitalization status, injury type, age category, and baseline total scale score were the only variables retained the final models of the primary outcomes for parent- and child-reported total scale score (Tables 4.14 and 4.15). Neither of the measures of socioeconomic status (income quintile and parent's highest education) nor child's sex or PaedsCTAS were found to significantly contribute to these models. Hospitalization status and injury type were included in all eight of the models of the primary outcomes (parent and child LME, NLME, NLQMM and GLMM). Being hospitalized and sustaining a lower extremity fracture were consistently associated with a parameter estimate indicating lower total scale score or lower odds of recovery relative to children who were seen in the ED and those with minor external injuries respectively. Hospitalization status was significant across all eight models, and the lower extremity fracture parameter estimate was significant across in all but the child response GLMM. Age category was retained in all of the parent models (and none of the child) with the oldest two age categories always associated with lower HRQoL/lower odds of recovery relative to children under five years of age. The only parent-response model in which age was not significant was the NLQMM. Baseline total scale score was included and significant in all but the parent GLMM, with a one-point increase in baseline total scale score being consistently associated with an increase of approximately half that in follow-up total scale score (across time in the LME and for the intercept in the NLME and NLQMM).

Table 4.14 Final parent-response models*

LME			NLME			NLQMM			GLMM		
Predictors	*Est*	*95% CI*	*Predictors*	*Est*	*95% CI*	*Predictors*	*Est*	*95% CI*	*Predictors*	*Est*	*95% CI*
(Intercept)	**88.43**	**85.68, 91.18**	R0 intercept	**89.21**	**86.42, 92.00**	R0 intercept	**89.32**	**83.05, 95.59**	(Intercept)	**3.12**	**1.51, 6.43**
Time									Time		
1 month	ref								1 month	ref	
4 months	3.1	-0.15, 6.36							4 months	**6.96**	**3.61, 13.41**
12 months	2.08	-1.25, 5.41							12 months	**6.75**	**3.47, 13.14**
Age Category (years of age)			R0 – Age Category (years of age)			R0 - Age Category (years of age)			Age Category (years of age)		
< 5	ref		< 5	ref		< 5	ref		< 5	ref	
5 - < 8	-2.4	-6.06, 1.24	5 - 8	-1.82	-5.49, 1.85	5 - < 8	0.48	-5.95, 6.91	5 - < 8	0.49	0.21, 1.17
8 - <13	-3.09	-6.57, 0.32	8 - 13	-2.68	-6.17, 0.80	8 - <13	-0.69	-6.98, 5.50	8 - <13	**0.36**	**0.16, 0.80**
13 - <17	**-6.87**	**-10.57, -3.22**	13 - <17	**-5.34**	**-9.01, -1.67**	13 - <17	-3.10	-8.74, 2.54	13 - <17	**0.19**	**0.08, 0.47**
Baseline total scale score	**0.5**	**0.37, 0.64**	R0 – Baseline total scale score	**0.46**	**0.28, 0.63**	R0 – Baseline total scale score	**0.40**	**0.19, 0.75**			
Hospitalization Status			R0 – Hospitalization Status			R0 - Hospitalization Status			Hospitalization Status		
ED	Ref		ED	ref		ED	ref		ED	ref	
Hospitalized	**-13.16**	**-16.77, -9.52**	Hospitalized	**-12.93**	**-16.94, -8.92**	Hospitalized	**-10.70**	**-17.04, -4.35**	Hospitalized	**0.08**	**0.02, 0.27**
Injury Type			R0 – Injury Type			R0 – Injury Type			Injury Type		
Minor External	ref		Minor External	ref		Minor External	Ref		Minor External	ref	
Upper extremity fracture	**-4.72**	**-8.17, -1.27**	Upper extremity fracture	**-4.54**	**-8.22, -0.86**	Upper extremity fracture	-3.26	-20.18, 13.66	Upper extremity fracture	0.62	0.29, 1.35
Lower extremity fracture	**-21.93**	**-26.64, -17.28**	Lower extremity fracture	**-20.31**	**-25.55, -15.07**	Lower extremity fracture	**-26.93**	**-53.39, -0.48**	Lower extremity fracture	**0.29**	**0.10, 0.83**
Head injury	1.58	-2.54, 5.68	Head injury	1.68	-2.58, 5.95	Head injury	0.23	-20.68, 26.89	Head injury	1.68	0.60, 4.71
Major Trauma	**-7.97**	**-14.10, -1.88**	Major Trauma	-5.25	-11.99, 1.49	Major Trauma	-5.12	-32.11, 4.51	Major Trauma	0.37	0.09, 1.52
Other	3.52	-2.38, 9.38	Other	2.8	-3.05, 8.65	Other	4.39	-8.73, 17.18	Other	1.32	0.31, 5.52
			LRC intercept	**-3.49**	**-4.11, -2.87**	LRC intercept	-5.5	-14.78, 3.77			
			LRC – Baseline total scale score	**0.05**	**0.04, 0.07**	LRC – Baseline HRQoL	0.48	-1.44, 2.41			

	LME			NLME			NLQMM			GLMM	
Predictors	*Est*	*95% CI*	*Predictors*	*Est*	*95% CI*	*Predictors*	*Est*	*95% CI*	*Predictors*	*Est*	*95% CI*
Hospitalized * Time			LRC – Hospitalization Status			LRC – Hospitalization Status			Hospitalized * Time		
4 months * hospitalized	**12.04**	**7.76, 16.54**	ED	ref		ED	Ref		4 months * hospitalized	**23.47**	**5.33, 103.33**
12 months * hospitalized	**12.16**	**7.64, 16.45**	Hospitalized	**0.91**	**0.56, 1.26**	Hospitalized	1.18	-4.45, 6.81	12 months * hospitalized	**6.84**	**1.77, 26.45**
Injury Type * Time			LRC – Injury Type			LRC – Injury Type					
4 months * Upper extremity fracture	**6.39**	**2.17, 10.60**	Minor External	ref		Minor External	Ref				
12 months * upper extremity fracture	**5.74**	**1.52, 9.95**	Upper extremity fracture	**1.29**	**0.59, 2.00**	Upper extremity fracture	4.52	-4.22, 13.25			
4 months * Lower extremity fracture	**18.52**	**12.88, 24.16**	Lower extremity fracture	**1.32**	**0.63, 2.01**	Lower extremity fracture	6.19	-14.75, 27.12			
12 months * Lower extremity fracture	**24.32**	**18.61, 30.03**	Head injury	0.68	-0.23, 1.58	Head injury	1.50	-19.30, 22.29			
4 months * Head	-0.66	-5.66, 4.35	Major Trauma	**0.6**	**-0.19, 1.38**	Major Trauma	8.03	-13.30, 29.35			
12 months * Head	1.88	-3.24, 7.01	Other	0.11	-0.96, 1.19	Other	-0.44	-31.99, 31.12			
4 months * Major Trauma	5.37	-1.99, 12.75									
12 months * Major Trauma	**9.06**	**1.48, 16.63**									
4 months * Other	-2.7	-9.92, 4.54									
12 months * Other	-6.08	-13.55, 1.38									
Age category * time											
4 months * 5- <8	1.86	-2.59, 6.31									
12 months * 5- <8	0.39	-4.03, 4.81									

LME			NLME			NLQMM			GLMM		
Predictors	*Est*	*95% CI*	*Predictors*	*Est*	*95% CI*	*Predictors*	*Est*	*95% CI*	*Predictors*	*Est*	*95% CI*
4 months * 8- <13	-0.4	-4.59, 3.81									
12 months * 8 - <13	4.2	-0.02, 8.44									
4 months * 13 - <17	4.08	-0.31, 8.47									
12 months * 13 - <17	**4.95**	**0.42, 9.48**									
Random Effects			Random Effect			Random Effects			Random Effects		
Residual variance	69.04		Residual variance	8.44		Residual variance	3.84		Residual variance	3.29	
Random intercept variance	15.55		Random intercept variance	6.08		Random intercept variance	<0.01		Random intercept variance	2.53	
Random slope variance	0.35		Random slope variance	0.74							
ICC	0.18		ICC						ICC	0.43	
# observations	707		# observations	707		# observations	707		# observations	707	

* LME = linear mixed effects model, NLMM = non-linear mixed effects model, NLQMM = non-linear quantile mixed effects model, GLMM = generalized logistic mixed model, ref = referent category for that variable, Est = parameter estimate, 95% CI = 95% confidence interval, bolded values are significant in the respective model at alpha of 0.05, red box indicates variable that is significant across all four models, ED = emergency department, underlined parameter estimates indicate a statistically significant difference from the NLME analogue

Table 4.15 Final child response and parent sub population linear mixed effects, non-linear mixed effects and non-linear quantile mixed effects models

	LME					NLME				NLQMM			
	Child		Parent sub population			Child		Parent sub population		Child		Parent sub population	
	Est	*95% CI*	*Est*	*95% CI*		*Est*	*95% CI*	*Est*	*95% CI*	*Est*	*95% CI*	*Est*	*95% CI*
Intercept	**85.55**	**82.74, 88.36**	81.82	**78.81, 84.83**	R0 – Intercept	**87.9**	**85.33, 90.47**	82.83	79.85, 85.81	**88.4**	**82.05, 95.59**	**84.90**	**77.27, 92.53**
Time													
One-month	ref		ref										
4 months	**3.58**	**0.49, 6.66**	**6.73**	**3.26, 10.21**									
12 months	2.24	-0.97, 5.46	**6.66**	**3.11, 10.20**									
Baseline	**0.5**	**0.34, 0.67**	**0.64**	**0.44, 0.83**	**R0 – Baseline**	**0.41**	**0.19, 0.63**	**0.57**	**0.32, 0.82**	**0.63**	**0.32, 0.93**	**0.52**	**0.09, 0.94**
Injury Type					**Injury**								
Minor External	ref		ref		Minor external	ref		ref		ref			
Upper extremity fracture	-1.29	-5.60, 3.03	-2.75	-7.34, 1.84	Upper extremity fracture	-1.61	-5.24, 2.02	-0.58	-4.99, 3.82	-0.18	-9.68, 9.32	-0.26	-13.93, 13.41
Lower extremity fracture	**-16.18**	**-20.85, -9.21**	**-22.45**	**-28.56, -16.35**	Lower extremity fracture	**-13**	**-18.10, -7.80**	-15.5	-21.59, -9.48	**-11.3**	**-27.97, 5.39**	-17.59	-43.39, 8.21
Head injury	2.23	-3.19, 9.06	6.15	-0.66, 12.96	Head injury	0.91	-4.16, 5.98	**6.7**	**0.12, 13.28**	0.75	-11.34, 12.84	8.98	-11.49, 29.46
Major Trauma	**-10.13**	**-19.94, -1.32**	-7.92	-17.26, 1.41	Major Trauma	**-9.12**	**-17.83, -0.40**	-5.4	-15.24, 4.43	-12.9	-26.97, 0.82	-6.12	-22.60, 10.37
Other	3.32	-5.58, 12.23	7.3	-2.10, 16.70	Other	2.68	-4.25, 9.62	4.94	-4.12, 14.00	2.45	-12.41, 17.31	6.36	-8.49, 21.22
Hospitalization Status													
ED	ref		ref		ED	ref				ref			
Hosp	**-9.48**	**-14.24, -4.73**	**-9.35**	**-14.41, -4.29**	Hosp	**-10.3**	**-14.79, -5.90**	**-11.1**	**-16.49, -5.66**	**-11.5**	**-20.92, -2.12**	**-9.80**	**-19.25, -0.34**
Baseline HRQoL * Time					LRC intercept	**-3.18**	**-3.64, -2.71**	**-2.55**	**-2.84, -2.26**	-2.91	-8.40, 2.58	-1.84	-11.08, 7.40
4 months* baseline	-0.06	-0.21, 0.18	-0.27	-0.50, -0.04	**LRC – Baseline**	**0.05**	**0.02, 0.07**	**0.04**	**0.02, 0.07**	0.03	-2.43, 2.49	0.10	-5.11, 5.32
12 months * baseline	-0.02	-0.24, 0.13	-0.15	-0.38, 0.09									

	LME					NLME				NLQMM			
	Child		Parent sub population			Child		Parent sub population		Child		Parent sub population	
	Est	*95% CI*	*Est*	*95% CI*		*Est*	*95% CI*	*Est*	*95% CI*	*Est*	*95% CI*	*Est*	*95% CI*
Hospitalized * Time					**LRC – Hospitalization Status**								
4 months * hospitalized	**8.44**	**3.08, 13.81**	**9.65**	**3.60, 15.69**	ED	ref		ref		ref			
12 months * hospitalized	**7.98**	**2.51, 13.45**	**8.26**	**2.13, 14.39**	Hosp	**1.21**	**0.67, 1.75**	**0.97**	**0.55, 1.39**	1.83	-11.60, 15.25	0.32	-12.29, 12.92
Injury Type * Time													
4 months * upper extremity fracture	2.63	-2.16, 7.43	4.5	-0.85, 9.85									
12 months * upper extremity fracture	4.7	-0.14, 9.55	5.08	-0.32, 10.49									
4 months * lower extremity fracture	**11.32**	**5.07, 17.57**	**18.23**	**11.15, 25.32**									
12 months * lower extremity fracture	**20.81**	**14.12, 27.49**	**26.42**	**18.87, 33.96**									
4 months * head injury	0.21	-7.64, 5.71	0.42	-7.47, 8.31									
12 months * head injury	0.05	-7.30, 6.19	0.12	-7.91, 8.14									
4 months * Major trauma	4.36	-10.30, 18.45	2.57	-8.32, 13.46									
12 months * major trauma	14.62	-1.01, 28.10	9.01	-2.07, 20.09									
4 months * other	-3.2	-14.94, 6.44	-8.36	-20.02, 3.31									
12 months * other	-2.29	-15.80, 7.87	-9.08	-20.95, 2.79									
Random Effects					**Random Effects**								

Residual variance	65.44	80.55	Residual variance	8.36	9.46	3.86	4.2
Random intercept variance	56.55	54.95	Random intercept variance	3.72	5.89	<0.01	<0.01
			Random slope variance	0.84	0.76		
ICC	0.46	0.41	ICC				
# obs	428	428	# obs	418	418	418	418

* LME = linear mixed effects model, NLMM = non-linear mixed effects model, NLQMM = non-linear quantile mixed effects model, GLMM = generalized logistic mixed model, ref = referent category for that variable, Est = parameter estimate, 95% CI = 95% confidence interval, bolded values are significant in the respective model at alpha of 0.05, red box indicates variable that is significant across all four models, ED = emergency department, underlined parameter estimates indicate a statistically significant difference from the NLME analogue, green parameter estimates indicate a statistically significant difference from the child-response analogue

Table 4.16 Child response and parent sub population generalized linear mixed model

	Child		Parent sub population	
Predictors	*Est*	*95% CI*	*Est*	*95% CI*
(Intercept)	**2.70**	**1.46, 4.98**	0.74	**0.38, 1.43**
Time				
1 month	ref		ref	
4 months	**2.68**	**1.29, 5.58**	10.25	**4.33, 24.24**
12 months	**2.8**	**1.36, 5.77**	7.77	**3.47, 17.42**
Baseline HRQoL	**0.95**	**0.92, 0.98**	1.00	**0.96, 1.03**
Injury Type				
Minor External	ref		**ref**	
Upper extremity fracture	0.82	0.39, 1.73	**0.83**	**0.35, 1.98**
Lower extremity fracture	**0.29**	**0.11, 0.77**	**0.33**	**0.10, 1.08**
Head injury	1.97	0.58, 6.72	**2.16**	**0.54, 8.59**
Major Trauma	0.58	0.13, 2.51	**0.24**	**0.04, 1.51**
Other	2.62	0.42, 16.50	**1.11**	**0.17, 7.38**
Hospitalization Status				
ED	ref		**ref**	
Hospitalized	**0.18**	**0.06, 0.54**	**0.11**	**0.02, 0.51**
Time * Hospitalization status				
Four-months * hospitalized	**11.34**	**2.26, 56.84**	**13.94**	**2.01, 96.59**
Twelve-months * hospitalized	3.47	0.84, 14.27	**5.75**	**1.00, 32.89**
Random Effects				
Residual variance	3.29		**3.29**	
Random intercept variance	0.97		**2.12**	
ICC	0.23		**0.39**	
# Observations	418		**418**	

* ref = referent category for that variable, Est = parameter estimate, 95% CI = 95% confidence interval, bolded values are significant in the respective model at alpha of 0.05, ICC = intraclass correlation

Hospitalization status was retained as a factor associated with rate of recovery, represented as an interaction term in the LME and GLMM, and as a fixed effect of the log rate of approach to the asymptote in the NLME and NLQMM, in all of the models, with children who were hospitalized experiencing a greater recovery in terms of outcome in the same time period relative to children seen in the ED. The parameter estimate associated with this term was significant in all but the parent and child NLQMM models. These findings indicate that children who were hospitalized experienced a greater immediate impact to their HRQoL with larger gains in HRQoL from one to twelve-months post-injury relative to their less injured peers.

These findings are consistent with the literature where studies with varying populations and injury types/severity have found associations between lower HRQoL following injury and hospitalization status (42,65), older age (41,60,62) and extremity fractures (62,65). In addition, hospitalization may have acted as a proxy for injury severity in the current study. Although PaedsCTAS was investigated as an objective measure of the severity of presenting condition, there was a large amount (25%) of missing data in this variable due to a change in hospital electronic record keeping during the course of the study, and the gold standard of injury severity score (ISS) was not collected. Studies have found that more severe injury as measured by the ISS, is associated with lower HRQoL scores in hospitalized children from one-month to 24 months post-injury (41,62,71).

4.5.2 Discussion of modelling techniques

A comparison of the different models used in our study is shown in table 4.17. The LME and GLMM models are the most commonly used in the literature and the most interpretable across audiences. One limitation of the LME with the CYBOI data is that the non-linear relationship meant that time had to be represented categorically, thereby limiting the ability to allow this parameter to be included as a random effect due to the increase in parameters and small sample size. In addition, this model is not designed for skewed, bounded data. This limitation is reflected in the model diagnostics which resulted in non-normality and heteroscedasticity of the residuals for the models. Although violations of distributional assumptions should not bias parameter estimates in OLS modelling, the estimated standard errors are usually incorrect (109).

The primary drawback of the GLMM for the CYBOI data is the information surrounding the variability of a continuous variable is lost when the outcome variable is dichotomised and possibly divided into heterogeneous categories. There were many small frequencies ($n < 15$) across variable categories with this outcome, indicating this model is not best suited for these data. That said, the use of being within the MCID of the total scale score at each time point relative to baseline to indicate recovery is an interpretable and meaningful cut point. By definition the MCID represents the change in the tool that is clinically important and this cut point has been used in the literature before (131). Another issue with this measure of recovery is that it is based on the retrospective measure of baseline HRQoL. A recent systematic review demonstrated consistently higher retrospectively measured pre-injury HRQoL scores relative to population norms (89). It is possible that a retrospective measure of pre-injury health is not equivalent to a prospective measure due to recall bias and response shift. In this situation, where pre-injury HRQoL is inflated, patients who might actually be recovered to their true pre-injury HRQoL may be defined as not recovered based on an inflated retrospective baseline measure. More prospective research on HRQoL and injury is required to help clarify this issue.

Table 4.17 Comparison of modelling techniques

	Linear Mixed Effects Model	Non-linear Mixed Effects Model	Non-linear quantile mixed effects model	Generalized linear mixed model with a logit link
Meaning of estimates	Mean change in outcome on a continuous/linear scale for different categories/values of the associated independent variable. Advantage: Widely understood and interpretable	Mean change in the intercept and the log rate constant for different categories/values of the associated independent variable. Different independent variables can be included in the model as a function of each of the intercept and log rate constant. Disadvantage: Parameter estimates associated with the log rate of approach to the asymptote have limited direct interpretability to individuals not familiar with the model.	Median change in the intercept and log rate constant for different categories/values of the associated variable Advantage: Good for skewed data and/or data with outliers where the median may be considered a better/more relevant representation of central tendency. In addition, this model can estimate quantiles throughout the distribution. This is valuable if different relationships between independent variables and outcome is expected/possible at tails of distribution. Disadvantage: Parameter estimates associated with the log rate of approach to the asymptote have limited direct interpretability to individuals not familiar with the model.	Log odds of the outcome for different levels/values of the associated independent variable. Advantage: Widely understood and interpretable.
Relationship between exposure and outcome	Linear relationship between independent and dependent variables. Based on the descriptive analysis of the CYBOI data this assumption was clearly violated. The work around with this model was to include time as a categorical variable. Disadvantage: Increased number of parameters with time as a categorical variable	The relationship between independent and dependent variables and outcome matches the proposed equation. In the case of this research an asymptotic form was applied based on the trajectory of the outcomes determined in the descriptive analysis. This form allowed for modelling the intercept and log rate constant.	The relationship between the independent and dependent variables matches the proposed equation. In the case of this research an asymptotic form was applied based on the trajectory of the outcomes determined in the descriptive analysis.	A linear relationship between the independent variables and the log odds of the outcome.

	Linear Mixed Effects Model	Non-linear Mixed Effects Model	Non-linear quantile mixed effects model	Generalized linear mixed model with a logit link
Normality of residuals	Model residuals should have a normal distribution Residuals were viewed on a quantile quantile (normal probability) plot and a light tailed distribution with violation of normality at the extremes of the outcome distribution was observed. Parameter estimates have been demonstrated to be robust to violations of normality of residuals however this violation does impact the validity of error estimates. Specifically, it may lead to the underestimation of standard errors increasing the risk of type I error.	Model residuals should have a normal distribution Violation of normality was apparent on the quantile quantile plot, to a lesser degree relative to the LME. Violation of normality of residuals may impact the validity of error estimates. Specifically, it may lead to the underestimation of standard errors increasing the risk of type I error.	No assumptions regarding the distribution of residuals.	No assumption regarding normality of residuals.
Homogeneity of residual variance	Homoscedasticity of residuals (aka homogeneity of variance). Evidence of this assumption being violated due to the ceiling effect was observed. Similar to above, this violation can invalidate error estimates.	Homoscedasticity of residuals. Evidence of this assumption being violated due to the ceiling effect was observed. Similar to above, this violation can invalidate error estimates.	No assumptions regarding the distribution of residuals.	No assumption regarding homogeneity of variance.

The NLME model was found to fit the data better than the LME model, with the asymptotic form addressing the upper bound of the data. However, there was still violations of normality and presence of heteroscedasticity in the residuals which were likely to lead to errors in the standard error estimates. If standard errors are underestimated the risk of a type I error (rejection of a true null hypothesis) increases. The NLQMM model was found to be the best suited model to our type of data: robust to skewness, outliers, and with no requirements regarding the distribution of the errors (110). The trade off in making no assumptions about error is larger standard errors result, as was demonstrated in the NLQMM models used for this research, and thus requires a larger sample size to make valid inferences (110). It is worth noting that mean regression can be prone to underestimating uncertainty if the normality assumptions are violated as was the case here(109). For the majority of parameter estimates there was not a statistically significant difference between in the NLQMM and NLME. The differences that did exist could be attributed to the wide confidence intervals of the NLQMM which limit the interpretability and meaning of the associated parameter estimates. In addition, the variance associated with the random intercept was very small for all of the NLQMM models, this is possibly due to modelling the median versus the mean. As was demonstrated in Chapter 3, the HRQoL outcome was highly skewed thus the mean was not a good representation of central tendency and one would expect large variance. It is possible that because the median has significantly less variance the estimated between person intercepts have significantly lower variance. Currently, there is no way to visualize these models thus it was not possible to test this hypothesis. In addition to the requirement for larger sample size and the lack of model goodness of fit tests or visualization techniques, a final drawback of the NLQMM model is the computation expense of running these models with bootstrapped standard errors.

When analyzing HRQoL, the distributional assumptions of OLS models are often violated by the non-normal distribution, with a left-skew and apparent truncation (or a ceiling effect) at the upper bound (1 or 100) leading to non-normal residuals and/or heteroscedasticity (109). In this chapter, NLQMM model was used to address the lack of normality and heteroscedasticity of the residuals observed in model diagnostics with LME and NLME models as it does not have any restrictions regarding residuals and it is robust to skewness (132). The asymptotic form was applied as it was found to fit the data appropriately and address the upper bound in the NLME model. The NLQMM model produces interpretable results without the need for transformation.

Tobit regression is an alternative method to addressing the unique form of HRQoL (108). Tobit regression has been demonstrated to be superior to OLS models in providing unbiased estimates when the distribution of HRQoL on the regressors is normal with uniform variance. However, when the variance of the conditional distribution is not uniform (i.e. heteroscedastic) the performance of the Tobit model is worse than that of OLS (133). In addition, if the truncation at the upper bound is appropriate, the theoretical underpinning the Tobit model does not apply.

Another longitudinal method robust to data and error distributions is the generalized estimating equation (GEE) (134). GEE is used to provide population level estimates as the variance covariance matrix is treated as a nuisance variable. This differs from mixed effects models where the variance is a variable to be defined and modelled and thus mixed models produce individual level estimates. Although the literature favours mixed models in terms of quantity, there has recently been more interest in the application of GEE models primarily because they are more flexible model with no assumptions regarding distribution (135). However, there is some controversy around their application. Specifically, it has been argued that parameter estimates are robust to misspecification of the working correlation structure (the within-subject covariance) (135), but there is some research that suggests otherwise. In a recent abstract from the 2018 Society for Research on Educational Effectiveness conference it was demonstrated that mixed models outperformed GEE in all parameter estimations in terms of bias, consistency and validity. In addition, the consistency and efficiency of parameter estimates in GEE models was demonstrated to be dependent on the working correlation structure (136). A further consideration of these models is that data are assumed to be MCAR, and estimates will not be valid if this assumption is violated. GEE with weights, multiple imputation or both (doubly robust estimation) is possible in order to allow for modelling data that are MAR if the extraneous data to apply these methods validly is available to the researcher (45). For the CYBOI data it is also of note that, although GEE models are more flexible in terms of distribution assumptions, they still assume a linear relationship between the covariates and the response variable (or a transformation of the response). Also, it is still a model of the mean, which in the case of these data is not the best representation of central tendency. For these reasons, this model was not pursued for the purpose of this research, although it may be of interest to explore GEE models in future analysis of HRQoL data.

4.5.3 Comparison of parent and child results

An important exploratory objective of this research was to compare results between child-response models and the comparable parent population response model. Across the child and parent sub-population models for total scale scores there were no statistically significant differences in parameter estimates for the NLQMM model (Table 4.15). In the other three models, the only consistent statistically significant difference between the parent sub-population-response and child-response parameter estimates were the estimates associated with each time point. The parameter estimate for total scale score at one-month post-injury in the parent models was statistically significantly lower in the LME and NLME and the parent GLMM model had statistically significantly lower odds of recovery at one-month post-injury. The estimates associated with four- and 12-months post-injury in the LME were statistically significantly higher in the parent model, as were the odds ratios in the GLMM for these variables. This may indicate that although parents rated children's total scale score lower than the children themselves at one-month post-injury (controlling for hospitalization status, injury type and baseline total scale score), this difference was mediated at four- and 12-months post-injury. Interestingly, the models of the exploratory outcomes demonstrated a statistically and clinically significant difference in parameter estimates in the intercept for the NLME model between parent and child-reported physical health summary score, indicating that, controlling for all variables in the model, parents rated their children's physical health lower than children themselves at one month post injury. However, this was not the case for the psychosocial health score NLME models.

Studies of parent and child agreement on HRQoL tend to vary in their results. However, a 2017 study of children 11-16 years newly diagnosed with a chronic condition found that baseline (the time of diagnosis) differences between parent and child report of HRQoL were largest with smaller differences as time from diagnosis increased (137). Sluys et al.'s 2015 study among five to 18 year old children and their parents six years after hospitalization for injury found no significant differences in parent versus self-report of HRQoL, as measured by the PedsQL (73). Gabbe et al published the only study identified that looked at parent-child agreement in HRQoL longitudinally in a sample of 37 parent-child dyads of children 13-17 years admitted to hospital with an injury as a principal diagnosis over the year following injury (138). This study found significant difference between parent and child reports of HRQoL up to six months after injury, and agreement improved with time post-injury. It has been speculated that these differences may be caused by children inflating their HRQoL due a positive illusory bias, by parents underestimating the HRQoL of children due to depression distortion, or by a condition having a less negative impact from the child's perspective of their life than perceived by parents, which is referred to as the disability paradox (137). Further research is required to investigate the complexity and multifaceted nature of reasons behind these differences.

4.5.4 Missing data

The substantial attrition in this study and possibility that data that are MNAR are the largest limitations of this research. Regardless of the form (MCAR, MAR or MNAR), missing data must be addressed in analyses. Previous studies of HRQoL and childhood injury have primarily employed complete case analysis (41,56,65,70,71) in which all cases with one or more missing values are deleted. This method can be quite wasteful with large proportions of data being deleted, reducing the ability to detect effects of interest (129). In addition, if data are not MCAR, complete case analysis will introduce bias (94,139). Mean imputation is a method in which missing data are replaced with the mean. The major issues with this method are that it underestimates variance, can change relationships between variables and, similar to complete case analysis, if not MCAR leads to biased estimates (128). Last observation carried forward (LOCF) is an approach to missing data in which the last non-missing value is used as the value for all subsequent missing scores. Similar to the previous two methods, MCAR is necessary but not sufficient for unbiased estimates (140). Another assumption of LOCF is that individual responses would have remained constant from the time of the last observation to the end of the study. LOCF can underestimate error and provide biased estimates that go in either direction (129) and this method has been strongly criticized (141). An alternative approach that is valid under the much more common case of data that are assumed to be MAR is multiple imputation (MI). In MI *m* sets of values for the missing data are created based on the conditional distribution of the unobserved outcomes, given the observed ones, resulting in *m* full data sets (each with slightly different values) (45,129,140). Each data set is analyzed, and results are combined or pooled, including a calculation of the variation across parameter estimates for each data set. The advantages of MI are that it is valid under MAR and it does not underestimate error. In addition, it is applicable to different variable types (continuous, discrete and categorical). However, this technique can still be problematic if it is not correctly implemented (142).

There are cases where none of the above methods are required. Maximum likelihood, in which all available data are used, is the parameter estimation method used in mixed effects models (along with others) and the estimates are unbiased if data are MAR and the model is correctly specified (143). Thus, in the case where only variables with repeated measures are missing in mixed models, MI is redundant (144). However, where time invariant predictors are missing, individuals would be excluded from mixed models, this is a situation where MI can be of use. In addition, if the assumption of MAR is under question (that is, data may be MNAR) as is the case in this study, MI provides a means for a sensitivity analysis using a constant shift between the distributions of the observed and missing values.

The missing data sensitivity analysis in this study using MI demonstrated that the models would change substantially, and meaningfully, if all of the missing HRQoL data were 15 points below what would be expected under MAR conditions. The increasing change across the sensitivity analysis models with increasing amounts of bias showed that the model is sensitive to a change in HRQoL, which is a good sign. If the model was not sensitive to a change in the outcome it would suggest the model and associated parameter estimates were not very meaningful. This issue highlights the importance of attention to subject retention and taking steps to reduce missing data. All efforts were taken at the time of data collection to minimize non-response bias: inclusion of personalized notes with mailed and emailed surveys (all participants received both); and repeated email and phone follow-up, including contacting parents at different times of day and days of week.

4.5.5 Strengths and limitations

This research contributes to the literature as a large, longitudinal study of HRQoL following childhood injury. The results are consistent with some previous research findings, with older age, lower extremity fractures and hospitalization being associated with lower HRQoL immediately following injury. This study included a large volume of less severe injuries that have not been included in previous studies. Other strengths include the nature of the data collected, presented and analysed: inclusion of a baseline measure of HRQoL; three follow-up points in the year following injury; both parent- and child-report of HRQoL; two measures of SES with representation across injury types.

The inclusion of an internationally recognized measure of injury severity would have been of benefit to this study. The ISS is the most commonly used measure of injury severity and was not able be captured in this study due to limited resources. PaedsCTAS was instead collected and used as a measure of injury severity. Unfortunately, this variable was not collected consistently throughout the course of the study limiting the use of PaedsCTAS for this research.

Finally, although a wide breadth of modelling options were pursued in the analysis of these data, the analyses applied do not represent all possibilities. Analytic techniques not applied could have provided more and different information regarding the relationships that exist within the CYBOI data. Specifically, applying the NLQMM model across the distribution of HRQoL from the 10th percentile to the 90th, for example, would provide information about how variables are associated with having the lowest and highest HRQoL scores at each time point and this information could be used to inform future interventions. In addition, multivariate regression and/or structural equation modelling with both parent and child report HRQoL as the dependent variables would have allowed for the ability to conduct tests of the coefficients across both outcomes simultaneously.

4.6 Conclusions

This study is unique as it examined the longitudinal recovery of children in the year following injury through a variety of statistical methodologies to account for known limitations found in prior research, as described in Chapter 2. To our knowledge, this is the first study to truly assess the merits and drawbacks of the unique approaches to longitudinal and missing data in this manner with regards to children's' HRQoL. The findings indicate that very few injuries have a long-lasting impact on children's HRQoL, demonstrating children's resilience to physical trauma. This research contributes to and expands upon the current literature on recovery from childhood injury by including a wide age-range of children, looking at a longer time period post-injury, and using a reliable and validated pediatric tool to measure HRQoL. It can be concluded that, while most children recovered quickly following injury, children who were older, with lower extremity fractures and who were hospitalized due to their injuries were at higher risk of greater immediate deficits in the their HRQoL relative to their injured peers, and specifically their physical HRQoL. The consistency of these findings across studies demonstrates that these results are robust to analysis method, study design and population. Parameter estimates across the models used were, for the most part, in the same direction, the error estimates, on the other hand, were likely underestimated in the OLS models (the LME and NLME models). The NLQMM model was found to be an appropriate model for these data and should be considered as analytic technique in future analyses of HRQoL outcomes, especially with skewed distributions.

Chapter 5: Exploratory Outcomes, Physical and Psychosocial Health Summary Scores

A single HRQoL score that summarizes responses to several domains is a useful outcome measure to allow for comparison across studies and populations and to identify factors associated with overall lower HRQoL. Examining the finer levels of HRQoL, such as the physical and psychosocial health summary scores from the PedsQL, can provide more nuanced insight into where deficits lie, and where resources could be used to improve overall HRQoL. In studies where both physical and psychosocial components of HRQoL are reported, there is evidence of greater dips in physical versus psychosocial HRQoL among children following injury (27,43,59,62). No studies were identified that reported on the predictors of physical and psychosocial health following childhood injury, as identified from multivariable modelling separately. This chapter reports the results of models that examined the physical and psychosocial health summary scores from the PedsQL as separate outcomes.

5.1 Objective

To investigate factors associated with PedsQL physical health and psychosocial health summary scores reported by parents and children in the year following injury.

5.2 Methods

The study population and data collection are described in Chapter 3.

5.2.1 Statistical methods

5.2.1.1 Outcomes

The exploratory outcomes included in this chapter were the physical health and psychosocial health summary scores, as reported by parents and children at one-, four- and 12-months post-injury.

5.2.1.2 Potential predictive variables

The variables that were explored as possible predictors of the outcomes are as described in Chapter 4: child's age at the time of injury explored continuously and as a categorical variable based on the PedsQL categories < 5 years, 5- <8 years, 8- <13 years, 13- <17 years old; child's sex; hospitalization status; PaedsCTAS (three levels 1, 2 and 3 as described previously with PaedsCTAS of 1 and 2 combined, and 4 and 5 combined due to low bases); parents income quintile (ordered categorical variable 1 lowest quintile, 2, 3, 4, 5 highest quintile); parents highest level of education (ordered categorical variable, 4 categories: some high school/ graduated high school or some trade school/college/university, diploma from trade school or college, university degree, post-graduate degree); injury category (six categories: minor external, upper extremity fracture, lower extremity fracture, head injury, major trauma, other); and child's baseline total scale score.

5.2.1.3 Bivariable analysis

As in the previous chapter, all descriptive analyses and bivariable statistics reported are weighted due to the over sampling of hospitalized children, where the weights were calculated at each time point to account for attrition. All modelling was on the crude data, where the over sampling of hospitalized children was controlled for by the inclusion of hospitalization status as a covariate in the models. Analyses were performed using R version 3.5.2, Vienna, Austria (116), in the integrated development environment RStudio version 1.0.153, Boston, MA (117). Additional packages used are cited as appropriate.

The physical health and psychosocial health summary scores were described by all of the potential predictive variables listed above at each time point by median and IQR and by frequencies and percentages. Bivariable associations between the potential predictive variables with the median total scale score at each time point were investigated by Mann-Whitney-U and

Kruskal-Wallis tests. Based on the central limit theorem t-tests and one-way ANOVA are robust to non-normality when the sample size is large but given the highly skewed nature of these outcome in the data there was more interest in comparing medians. Significant Kruskal-Wallis test results were followed by a post-hoc Dunn-Bonferroni test to determine where differences in medians existed. This test compares all possible pairs of medians with a correction to the alpha to account for multiple testing.

5.2.1.4 Model building

Models identifying predictors of decreased physical and psychosocial health over time were built as described in the previous chapter. Two different mixed effects models were fit to these outcomes: 1) non-linear mixed effects models (NLME) and 2) a non-linear quantile mixed model (NLQMM). In all models, time was centered on one-month and baseline total scale score was centered on the mean. Centering was performed to allow the intercept to be interpreted as the mean (or median) HRQoL score at one-month post-injury.

5.3 Results

5.3.1 Physical health summary scores

Based on Mann Whitney U tests the median physical health summary score for parent-response at one-month post-injury was statistically significantly different for children hospitalized compared to children seen in the ED with medians of 87.50, 53.13, respectively ($p<0.001$) (Table 5.1). In addition, older children had lower parent-reported medians relative to younger age groups. At one-month post-injury children eight to 13 years of age (median of 75.00) and 13 to 17 years of age (median of 68.75) had lower parent-reported medians relative to children less than five year of age (median of 93.75) ($p<0.001$ for both). At four-months post-injury children eight to 13 years of age (median of 93.75) had a statistically significantly lower median relative to those five to eight years of age (median of 100.00, $p=0.010$), and children 13 to 17 years of age (median of 93.75) relative to those under five (median of 100.00) and those five to eight years of age (median of 100.00, $p<0.001$ for both). PaedsCTAS and injury type were also statistically significantly associated with median parent-response physical health summary score at one-month post-injury (Table 5.1). Upper extremity fractures, lower extremity fractures and major trauma were found to have statistically significantly lower medians relative to minor external injuries and head injuries ($p<0.001$), lower extremity fractures had a statistically significantly lower median relative to upper extremity fractures and other injuries ($p<0.001$). At four-months post-injury the median physical health summary score was statistically significantly lower for children with lower extremity injuries relative to children with minor external injuries and upper extremity fractures ($p=0.010$) (Table 5.1).

Table 5.1 Parent-response physical health summary score over time*

	One-month					Four-months					Twelve-months				
		Unweighted		Weighted			Unweighted		Weighted			Unweighted		Weighted	
	N	Median	IQR	Median	IQR	N	Median	IQR	Median	IQR	N	Median	IQR	Median	IQR
Sex															
Male	164	81.25	34.38	87.50	34.38	149	100.00	9.38	100.00	6.25	143	100.00	6.25	100.00	6.25
Female	101	81.25	45.83	84.38	34.38	91	96.88	10.94	96.88	9.38	82	98.44	9.38	99.98	8.37
Hospitalization Status															
ED	195	**87.50**	**31.25**	**87.50**	**31.25**	179	**100.00**	**8.33**	**100.00**	**8.33**	162	100.00	6.25	100.00	6.25
Hospitalized	70	**53.13**	**39.84**	**53.13**	**40.93**	61	**93.75**	**13.89**	**93.75**	**12.50**	63	100.00	12.50	98.44	9.38
Age Category															
<5	81	**93.75**	**25.00**	**93.75**	**15.82**	81	**100.00**	**6.25**	**100.00**	**6.25**	73	97.22	6.25	97.05	6.25
5-8	52	**87.50**	**35.16**	**87.50**	**31.31**	47	**100.00**	**3.13**	**100.00**	**3.13**	50	100.00	8.59	100.00	6.25
8-13	79	**71.88**	**42.19**	**75.00**	**40.63**	62	**95.31**	**12.50**	**93.75**	**12.50**	58	100.00	8.59	100.00	6.25
> 13	53	**65.63**	**37.50**	**68.75**	**32.37**	50	**93.75**	**14.84**	**93.75**	**12.50**	44	96.88	13.28	96.88	10.81
PaedsCTAS (%)															
1 (requires resuscitation)	11^	**62.50**	**18.75**	**56.25**	**28.86**	10^	87.50	8.42	87.50	9.05	8^	96.88	10.94	93.75	4.00
2	36	**59.38**	**51.56**	**64.53**	**35.94**	32	96.88	9.38	96.88	6.25	34	96.88	9.38	96.88	7.30
3	45	**75.00**	**34.38**	**82.24**	**29.46**	38	93.75	12.50	93.75	12.50	36	100.00	12.50	96.88	12.50
4	101	**84.38**	**31.25**	**84.88**	**31.25**	96	100.00	8.59	100.00	7.04	81	100.00	6.25	97.69	6.25
5 (non urgent)	8^	**72.74**	**33.59**	**68.23**	**31.77**	6^	98.44	5.47	98.95	2.58	8^	100.00	13.28	100.00	3.91
Missing	64	**89.06**	**41.41**	**93.75**	**25.00**	58	100.00	9.38	100.00	6.25	58	100.00	6.25	100.00	6.25
Income Quintile (%)															
1 (lowest income quintile)	30	76.56	48.96	78.13	35.36	24	96.88	16.41	96.88	9.38	20	96.88	10.94	94.80	7.39
2	29	65.63	43.75	70.19	34.38	27	93.75	12.50	93.75	9.46	23	96.88	10.94	96.35	7.02
3	51	90.63	31.25	91.47	25.00	47	100.00	6.25	100.00	2.78	46	100.00	8.59	100.00	3.57
4	49	78.13	34.38	81.68	25.43	44	100.00	8.59	100.00	6.25	45	100.00	9.38	100.00	6.03
5 (highest income quintile)	93	81.25	46.88	82.24	34.38	86	96.88	12.50	96.88	12.50	81	100.00	6.25	100.00	6.25
Missing	13	84.38	36.43	86.95	16.80	12^	95.31	13.54	94.79	9.99	10	100.00	16.41	100.00	9.51

	One-month					Four-months					Twelve-months				
		Unweighted		Weighted			Unweighted		Weighted			Unweighted		Weighted	
	N	Median	IQR	Median	IQR	N	Median	IQR	Median	IQR	N	Median	IQR	Median	IQR
Injury															
Minor external Injury	97	93.75	25.00	93.75	22.74	91	**100.00**	**8.85**	**100.00**	**9.38**	83	100.00	6.25	100.00	6.25
Upper extremity fracture	63	71.88	28.13	75.00	30.40	56	**100.00**	**6.25**	**100.00**	**6.25**	56	100.00	6.25	100.00	4.39
Lower extremity fracture	32	25.00	39.84	43.75	40.63	28	**90.63**	**26.56**	**90.63**	**22.89**	27	96.88	7.81	97.38	6.25
Head injury	36	90.63	25.00	92.68	20.18	31	**100.00**	**10.94**	**100.00**	**8.34**	28	98.44	12.50	98.95	12.18
Major trauma	20	50.00	25.00	50.00	40.92	17	**90.63**	**15.63**	**90.63**	**13.43**	16	96.88	15.63	93.75	11.90
Other	15	90.63	28.13	94.17	10.03	15^	**94.44**	**7.81**	**97.19**	**6.25**	13^	100.00	9.38	99.10	8.45
Missing	2	93.75	6.25	87.50	8.00	2	**87.50**	**12.50**	**75.00**	**16.00**	2^	100.00	0.00	100.00	0.00
Highest Education**															
1	9^	84.38	47.22	89.00	13.31	8^	96.88	7.81	93.75	6.25	7^	100.00	10.94	84.57	14.85
2	23	78.13	62.50	82.77	31.25	18	98.44	11.72	99.98	6.25	20	100.00	3.91	100.00	3.13
3	47	68.75	42.19	82.71	42.99	43	100.00	10.94	100.00	9.90	46	100.00	6.08	100.00	4.88
4	91	87.50	39.06	87.50	35.44	83	96.88	9.38	97.16	6.25	76	98.61	9.38	99.98	6.25
5	85	81.25	32.99	81.25	28.13	81	96.88	12.50	96.88	9.93	72	100.00	8.59	100.00	9.29
Missing	10^	71.88	42.97	80.90	37.50	7^	93.75	25.00	83.36	16.40	3^	84.38	1.56	81.25	1.63
Overall	265	81.25	37.50	87.50	36.20	240	96.88	9.38	100.00	9.38	225	100.00	9.38	100.00	6.25

* Bolded medians are statistically significantly different from each other at alpha of 0.05 based on Mann-Whitney U or Kruskal Wallis test followed by Dunn-Bonferroni post hoc as appropriate

** Parent highest education categories: 1 graduated high school, 2 some trade school, college or university, 3 = Diploma from trade school or college, 4 = University degree, 5 = Post-graduate degree (Master's and/or Doctorate)

^ Use caution when interpreting statistics and inferences associated with categories with low bases

For child-response physical health summary score at one- and four-months post-injury, being hospitalized was associated with lower median physical summary score relative to have being seen in the ED ($p<0.001$). Injury type was also associated with median physical health summary score at one- and four-months post-injury.

At one-month post-injury children with lower extremity fractures and major trauma had statistically significantly lower median physical summary scores relative to children with minor external injuries and head injuries ($p<0.001$, major trauma had a low base n = 11, this should be interpreted with caution), lower extremity fractures were also associated with lower median physical summary scores relative to upper extremity fractures ($p=0.002$). At four-months post-injury, children with lower extremity fractures and major trauma had statistically significantly lower median physical summary scores relative to those with upper extremity fractures ($p=0.040$, and $p=0.020$ respectively) (Table 5.2).

Sex, age category, PaedsCTAS, income quintile and parent's highest education were not statistically significantly associated with child-reported physical health summary score median at any time point.

Table 5.2 Child-response physical health summary score over time

	One-month					Four-months					Twelve-months				
		Unweighted		Weighted			Unweighted		Weighted			Unweighted		Weighted	
	N	Median	IQR	Median	IQR	N	Median	IQR	Median	IQR	N	Median	IQR	Median	IQR
Sex															
Male	100	85.68	20.42	88.29	19.56	88	91.67	16.67	91.67	16.67	89	93.33	16.67	93.33	16.62
Female	63	88.33	17.50	90.00	15.77	61	91.67	15.00	91.67	15.95	51	93.33	15.00	93.33	16.67
Hospitalization Status															
ED	119	**90.00**	**16.89**	**90.00**	**16.67**	110	**91.67**	**16.67**	**91.67**	**16.67**	101	93.33	16.67	93.33	16.67
Hospitalized	44	**76.67**	**20.67**	**76.67**	**21.13**	39	**93.33**	**19.17**	**93.33**	**20.00**	39	93.18	14.17	91.59	13.73
Age Category															
5-8	47	86.67	20.00	89.39	17.28	46	90.00	15.83	90.00	16.67	48	90.00	14.17	93.29	13.33
8-13	71	85.00	20.00	85.00	18.33	57	91.67	20.00	91.67	18.84	51	95.00	13.33	94.17	13.33
> 13	45	90.00	20.00	91.37	17.26	46	94.17	13.33	94.99	12.83	41	96.67	15.00	93.33	16.25
PaedsCTAS (%)															
1 (requires resuscitation)	5^	76.67	28.93	65.83	7.94	5^	83.33	13.33	81.67	5.29	4^	90.00	12.50	85.00	0.54
2	23	80.00	22.18	86.67	22.22	22	91.67	17.08	89.76	14.29	23	93.33	18.33	92.77	15.57
3	24	80.00	24.36	80.00	24.11	21	91.67	13.33	89.75	12.04	18	96.67	12.92	95.01	13.92
4	62	87.50	17.92	86.67	16.25	55	91.67	16.67	90.83	16.67	49	93.33	16.67	93.33	16.67
5 (non-urgent)	7^	93.33	7.50	91.67	9.07	5^	100.00	6.67	100.00	1.72	6^	92.50	14.58	91.09	11.53
Missing	42	90.00	21.25	42.00	90.00	41	95.00	18.33	94.72	16.67	40	93.26	12.50	93.33	14.11
Income Quintile (%)															
1 (lowest income quintile)	18	80.00	22.92	78.87	23.78	15^	90.00	16.67	90.00	14.95	16	93.33	14.58	93.33	13.76
2	19	91.67	17.50	91.39	18.13	17	90.00	13.33	90.27	12.55	15^	93.33	10.00	93.33	7.86
3	31	90.00	25.80	90.26	20.90	28	94.17	15.00	96.60	13.33	26	93.33	19.58	93.33	20.00
4	29	85.00	16.67	84.82	13.17	26	90.83	22.08	88.90	20.79	21	93.33	16.67	89.20	16.43
5 (highest income quintile)	58	87.50	19.92	89.43	17.12	54	92.50	16.67	91.67	16.67	56	93.33	13.33	93.33	13.33
Missing	8	87.50	14.17	89.97	10.42	9^	93.33	8.33	93.33	8.52	6^	94.17	14.17	92.20	11.75

	One-month					Four-months					Twelve-months				
		Unweighted		Weighted			Unweighted		Weighted			Unweighted		Weighted	
	N	Median	IQR	Median	IQR	N	Median	IQR	Median	IQR	N	Median	IQR	Median	IQR
Injury															
Minor external Injury	59	**90.00**	**23.33**	**90.00**	**24.55**	54	**92.50**	**16.25**	**91.67**	**16.67**	50	93.33	19.17	93.33	18.70
Upper extremity fracture	46	**88.33**	**13.33**	**88.33**	**11.86**	40	**95.00**	**16.67**	**93.90**	**16.30**	40	93.33	13.33	93.33	11.29
Lower extremity fracture	25	**75.00**	**16.67**	**76.67**	**14.85**	21	**86.67**	**21.67**	**89.42**	**17.69**	18	95.00	11.25	96.08	10.00
Head injury	15	**90.00**	**14.17**	**91.65**	**11.41**	14^	**90.00**	**6.22**	**90.00**	**7.52**	14^	90.00	12.92	91.08	13.43
Major trauma	11^	**73.33**	**13.85**	**71.67**	**12.74**	11^	**83.33**	**14.64**	**81.67**	**15.92**	11^	95.00	15.77	92.50	9.31
Other	5^	**90.00**	**5.00**	**90.80**	**1.78**	7^	**96.67**	**16.67**	**82.79**	**15.65**	6^	90.00	21.67	86.67	11.81
Missing	2	**98.33**	**0.00**	**98.33**	**0.00**	2^	**100.00**	**0.00**	**100.00**	**0.00**	1^	86.67	0.00	86.67	0.00
Highest Education**															
1	3^	76.67	10.83	79.10	0.00	3^	93.33	1.67	93.87	0.00	4^	72.50	25.83	60.00	19.75
2	13^	86.67	16.67	85.83	18.22	13^	96.67	11.67	96.10	12.61	15	93.33	10.00	93.33	5.81
3	29	81.67	24.36	85.77	20.86	28	89.17	20.42	87.79	17.44	26	93.33	14.58	93.28	15.97
4	55	88.33	16.67	90.00	15.04	46	93.33	16.67	93.33	12.34	43	96.67	13.33	95.28	11.20
5	59	88.33	22.50	88.33	23.14	56	91.67	16.67	90.56	16.67	48	92.50	17.08	90.56	17.72
Missing	4	77.50	23.75	79.94	10.46	3	73.33	15.00	70.00	0.00	3^	86.67	12.50	87.21	0.00
Overall	163	86.67	20.83	88.33	18.33	149	91.67	16.67	91.67	16.67	140	93.33	16.67	93.33	16.67

* Bolded medians are statistically significantly different from each other at alpha of 0.05 based on Mann-Whitney U or Kruskal Wallis test followed by Dunn-Bonferroni post hoc as appropriate

** Parent highest education categories: 1 graduated high school, 2 some trade school, college or university, 3 = Diploma from trade school or college, 4 = University degree, 5 = Post-graduate degree (Master's and/or Doctorate)

^ Use caution when interpreting statistics and inferences associated with categories with low bases

Seven variables were independently significant for the fixed intercept in the bivariable parent-response asymptotic NLME model for physical health summary score: hospitalization status, PaedsCTAS, age category, income quintile, parents' level of education, injury type and sex (all with p values < 0.001 on the Wald test). Hospitalization status, baseline total scale score, age category, income quintile and sex were statistically significantly associated with the fixed effect LRC in the bivariable models (Wald p values < 0.001 for all).

In the final NLME model, being hospitalized relative to being seen in the ED (estimate -20.26, 95% CI (-26.64, -13.88), p<0.001), being in an older age category relative to those under five years old (estimate for eight to 13 years old -7.95, 95% CI (-13.77, -2.14), p=0.008, estimate for 13 to 17 years old -10.76, 95% CI (-17.01, -4.51), p=0.001), having an upper extremity fracture (estimate -11.22, 95% CI (-17.22, -4.51), p<0.001), lower extremity fracture (estimate -37.07, 95% CI (-45.13, -29.01), p<0.001), or major trauma (estimate -14.58, 95% CI (-25.20, -3.96), p=0.008) relative to minor external injuries and being female relative to male (estimate (-5.82, 95% CI (-10.32, -1.32), p=0.013) were all associated with statistically significantly lower physical health summary scores at one-month post-injury (Table 5.3). The LCR in the parent-response physical health summary score NLME model was statistically significantly greater for children with higher baseline total scale score (estimate 0.02, 95% CI (0.01, 0.03), p=0.002), those who were hospitalized relative to those seen in the ED (estimate 0.57, 95% CI (0.24, 0.91), p=0.001), and those with an upper extremity fracture (estimate 1.65, 95% CI (1.18, 2.13), p<0.001), lower extremity fracture (estimate 0.88, 95% CI (0.44, 1.32), p <0.001), or major trauma (estimate 0.94, 95% CI (0.39, 1.49), p<0.001) relative to minor external injuries.

The parameter estimate associated with head injuries was statistically significantly greater in the parent-response NLQMM for physical health summary score relative to the analogous NLME (NLQMM estimate -13.80, 95% CI (-53.96, 26.36), p=0.511, NLME estimate 1.30, 95% CI (-5.73, 8.32), p=0.721). In addition, the parameter estimates associated with the LRC intercept, and the following predictors of LRC: baseline total scale score, hospitalization status, upper extremity fracture, lower extremity fracture, major trauma, and age categories five to eight years old and eight to 13 years old were all statistically significantly greater in the NLQMM relative to the NLME (Table 5.3).

Table 5.3 Parent-response NLME and NLQMM for physical summary score*

	NLME asymptotic model			NLQMM model		
Predictors	Estimates	95% CI	*p*	Estimate	95% CI	*p*
R0 intercept	**94.95**	**90.00, 99.89**	**<0.001**	**95.45**	**81.60, 109.30**	**<0.001**
Hospitalization Status						
Emergency Department	ref					
Hospitalized	**-20.26**	**-26.64, -13.88**	**<0.001**	**-23.72**	**-32.89, -14.55**	**<0.001**
Age Category						
< 5 years old	ref					
5 - <8 years old	-1.54	-7.85, 4.78	0.638	-0.60	-17.94, 16.75	0.951
8 - <13 years old	**-7.95**	**-13.77, -2.14**	**0.008**	-3.38	-18.92, 12.17	0.683
13 - < 17 years old	**-10.76**	**-17.01, -4.51**	**0.001**	-8.00	-18.89, 2.90	0.151
Injury Type						
Minor external	ref					
Upper extremity fracture	**-11.22**	**-17.22, -4.51**	**<0.001**	-12.40	45.75, 20.95	0.476
Lower extremity fracture	**-37.07**	**-45.13, -29.01**	**<0.001**	-42.14	-84.52, 0.24	0.051
Head injury	1.30	-5.73, 8.32	0.721	<u>-13.80</u>	-53.96, 26.36	0.511
Major Trauma	**-14.58**	**-25.20, -3.96**	**0.008**	-12.87	-44.63, 18.89	0.435
Other	2.06	-7.98, 12.11	0.691	3.65	-16.49, 23.79	0.736
Sex						
Male	ref					
Female	**-5.82**	**-10.32, -1.32**	**0.013**	-1.21	-7.35, 4.93	0.712
LRC (Intercept)	**-2.43**	**-2.89, -1.96**	**<0.001**	<u>0.43</u>	-9.62, 10.49	0.938
Baseline HRQoL	**0.02**	**0.01, 0.04**	**0.002**	<u>0.44</u>	-0.36, 1.24	0.287
Hospitalization Status						
Emergency Department	ref					
Hospitalized	**0.57**	**0.24, 0.91**	**0.001**	<u>6.29</u>	-4.99, 17.56	0.278
Injury Type						
Minor external	ref					
Upper extremity fracture	**1.65**	**1.18, 2.13**	**<0.001**	<u>5.35</u>	-11.76, 22.45	0.551
Lower extremity fracture	**0.88**	**0.44, 1.32**	**<0.001**	<u>11.18</u>	-6.59, 28.95	0.220
Head injury	-0.10	-0.81, 0.60	0.776	-0.16	-27.70, 27.39	0.992
Major Trauma	**0.94**	**0.39, 1.49**	**0.001**	<u>3.04</u>	-25.48, 31.56	0.845
Other	0.47	-0.31, 1.25	0.243	**<u>23.04</u>**	**6.07, 40.01**	**0.008**
Age Category						
< 5 years old	ref					
5 - <8 years old	0.31	-0.17, 0.78	0.217	<u>2.35</u>	-14.96, 19.66	0.803
8 - <13 years old	0.02	-0.37, 0.41	0.915	<u>2.24</u>	-16.71, 21.19	0.828
13 - < 17 years old	-0.28	-0.64, 0.09	0.141	-0.53	-17.13, 16.06	0.954
Random Effects						
Residual variance	10.22			4.54		
Random intercept variance	15.50			<0.01		
# observations	706			706		

* Parameter estimates bolded are statistically significant in the model at alpha of 0.05, ref = reference category for that variable, 95% *CI* = 95% confidence interval associated with parameter estimate, *p* = p-value associated with parameter estimate, R0 = fixed intercept, LRC = log rate, estimates that are in blue and underlined are statistically significantly different from their NLME analogue

For the child-response physical health summary score NLME, hospitalization status, injury type and PaedsCTAS were statistically significantly associated with the fixed intercept, and baseline total scale score, parent's education and injury type were statically significantly associated with the LRC in the bivariable NLME models (data not shown). In the final child-response NLME model, physical health summary score at one-month post-injury was statistically significantly lower for children who were hospitalized (estimate -10.87, 95% CI (-18.82, -2.93), p=0.008), children with lower extremity fractures (estimate -33.22, 95% CI (-42.87, -23.58), p<0.001), and major trauma (estimate -19.41, 95% Ci (-34.38, -4.44, p=0.013) relative to those with minor external injuries. The LRC was statistically significantly greater for children with higher baseline total scale score (estimate 0.03, 95% CI (0.02, 0.05), p<0.001), and for children whose parents had university degrees (estimate 0.66, 95% CI(0.10, 1.21, p=0.022) and those with post graduate degrees (estimate 0.96, 95% CI 0.45, 1.47), p<0.001) relative to those who had graduated high school or had some trade school, college or university education (Table 5.4). The only difference in the parent sub-population NLME for physical health summary score relative to that for child-response model was that the parameter estimate for the intercept was statistically significantly lower in the parent response model (parent estimate 80.11, 95% CI (74.83, 85.38), p <0.001, child estimate 86.61, 95% CI (81.85, 91.37), p<0.001).

Table 5.4 Child-response and parent sub-population NLME physical health summary score*

	Child			Parent sub-population		
Predictors	Estimates	95% CI	p	Estimates	95% CI	p
R0.(Intercept)	**86.61**	**81.85, 91.37**	**<0.001**	**80.11**	**74.83, 85.38**	**<0.001**
Hospitalization Status						
ED	ref					
Hospitalized	**-10.87**	**-18.82, -2.93**	**0.008**	**-11.90**	**-20.71, -3.10**	**0.009**
Injury Type						
Minor external	ref					
Upper extremity fracture	-3.61	-10.87, 3.65	0.335	-4.59	-12.53, 3.54	0.278
Lower extremity fracture	**-33.22**	**-42.87, -23.58**	**<0.001**	**-37.79**	**-48.45, -27.13**	**<0.001**
Head injury	6.69	-4.14, 17.52	0.231	6.21	-5.76, 18.18	0.315
Major Trauma	**-19.41**	**-34.38, -4.44**	**0.013**	-11.51	-28.02, 4.99	0.177
Other	5.42	-9.26, 20.10	0.474	10.39	-5.89, 26.68	0.217
LRC (Intercept)	**--2.06**	**-2.49, -1.62**	**<0.001**	**-2.03**	**-2.45, -1.61**	**<0.001**
Baseline total scale score	**0.03**	**0.02, 0.05**	**<0.001**	**0.02**	**0.00, 0.04**	**0.038**
Parents Highest Education**						
1	ref					
2	0.07	**-0.46, 0.61**	0.788	0.49	-0.02, 1.00	0.065
3	**0.66**	**0.10, 1.21**	**0.022**	**1.29**	**0.74, 1.83**	**<0.001**
4	**0.96**	**0.45, 1.47**	**<0.001**	**0.80**	**0.29, 1.30**	**0.002**
Random Effects						
Residual variance (σ^2)	9.75			11.97		
Random intercept variance ($\tau_{00\ studyID}$)	16.15			16.95		
# observations	414			414		

* ref = referent category, 95% CI = 95% confidence intervals associated with parameter estimate, *p* = p-value * Parameter estimates bolded are statistically significant in the model at alpha of 0.05, ref = reference category for that variable, 95% *CI* = 95% confidence interval associated with parameter estimate, *p* = p-value associated with parameter estimate, R0 = fixed intercept, LRC = log rate, estimates that are in green are statistically significantly different from their NLME analogue, estimates in italics are statistically significantly different from the corresponding child response model estimate
** Parent highest education categories: 1 graduated high school or some trade school, college or university, 2 = Diploma from trade school or college, 3 = University degree, 4 = Post-graduate degree (Master’s and/or Doctorate)

The majority of the parameter estimates from the child and parent sub-population NLQMM for physical health summary score were not statistically significantly different from the analogous NLMEs. The only differences in the child-response model were for the parameter estimates for the middle two parent's education categories for LRT which were statistically significantly greater in the NLQMM relative to the NLME (Table 5.5). In the parent response model, the parameter estimate for the intercept was greater in the NLQMM (NLQMM estimate 87.48, 95% CI (75.03, 99.93), $p < 0.001$), NLME estimate (80.11, 95% CI (74.83, 85.38), $p<0.001$), as were the estimates for the LRC (NLQMM estimate 1.28, 95% CI (-16.98, 19.53) $p=0.889$, NLME estimate -2.03, 95% CI (-2.45, -1.61) $p<0.001$) and for all of the covariates associated with the LRC: baseline total scale score and parents highest education (Table 5.5). There were no statistically significant differences in parameter estimates between the parent sub-population and child-response NLQMM models for physical health summary score.

Table 5.5 Child-response and parent sub-population physical health summary score NLQMM

Predictors	Child Estimate	Child 95% CI	Child p	Parent sub-population Estimate	Parent sub-population 95% CI	Parent sub-population p
R0.(Intercept)	**91.40**	**84.50, 98.31**	**<0.001**	**87.48**	**75.03, 99.93**	**<0.001**
Hospitalization Status						
Emergency Department	ref					
Hospitalized	**-18.74**	**-31.55, -5.93**	**0.004**	-19.15	--31.88, -6.42	0.003
Injury Type						
Minor external	ref					
Upper extremity fracture	-3.91	-29.12, 21.31	0.774	**-12.48**	-42.35, 17.40	0.421
Lower extremity fracture	**-38.28**	**-80.20, 3.63**	**0.073**	-40.61	-84.43, 3.22	0.069
Head injury	8.57	-24.96, 42.09	0.629	6.25	-34.53, 47.03	0.777
Major Trauma	-22.70	-54.03, 8.63	0.156	-5.85	-42.91, 31.21	0.770
Other	8.54	-18.02, 35.10	0.539	9.37	-20.37, 39.11	0.9548
LRC (Intercept)	-1.65	-20.34, 17.05	0.873	1.28	-16.98, 19.53	0.889
Baseline total scale score	0.03	-8.22, 8.27	0.996	0.60	-5.06, 6.27	0.845
Parents Highest Education**						
1	**ref**					
2	0.87	-59.97, 61.71	0.980	6.81	-39.92, 53.54	0.788
3	1.78	-51.76, 55.32	0.953	9.54	-45.25, 64.33	0.746
4	0.77	-41.15, 42.49	0.974	5.51	-25.65, 36.66	0.742
Random Effects						
Residual variance (σ^2)	4.47			5.02		
Random intercept variance ($\tau_{00\ studyID}$)	<0.01			<0.01		
# observations	414			414		

*ref = referent category, 95% CI = 95% confidence intervals associated with parameter estimate, *p* = p-value * Parameter estimates bolded are statistically significant in the model at alpha of 0.05, ref = reference category for that variable, 95% *CI* = 95% confidence interval associated with parameter estimate, *p* = p-value associated with parameter estimate, R0 = fixed intercept, LRC = log rate, estimates that are underlined are statistically significantly different from their NLME analogue, estimates in italics are statistically significantly different from the corresponding child response model estimate
** Parent highest education categories: 1 graduated high school or some trade school, college or university, 2 = Diploma from trade school or college, 3 = University degree, 4 = Post-graduate degree (Master's and/or Doctorate

5.3.2 Psychosocial health summary scores

There were no statistically significant differences in median psychosocial health summary score for parent or child report at any time for sex, income quintile, PaedsCTAS or parent's highest education. At one-month post-injury, for both parent- and child-response, the median psychosocial health summary score was statistically significantly lower for hospitalized children relative to those seen in the ED ($p < 0.001$). The median psychosocial health summary was not statistically significantly different between children admitted to hospital relative to those seen in the ED at four- or 12-months post-injury (Table 5.6 and 5.7). At one-month post-injury, for both parent- and child-response, children who experienced major trauma (child $p=0.020$, parent $p<0.001$) and those with lower extremity fractures (child $p=0.010$, parent $p<0.001$), had statistically significantly lower psychosocial summary scores relative to children who experienced minor external injuries. For parent-response only, at one-month post-injury children who experienced lower extremity fractures had statistically significantly lower median psychosocial summary scores relative to children who experienced an upper extremity fracture ($p=0.010$) and to children who experienced a head injury ($p<0.001$). Finally, for parent-response, children who were eight to years of age had statistically significantly lower median psychosocial health summary scores relative to those less than five years ($p=0.010$). There were no statistically significant differences in median psychosocial summary score at four- or 12-months (Table 5.6).

Table 5.6 Parent response psychosocial health summary score over time*

	One-month					Four-months					Twelve-months				
		Unweighted		Weighted			Unweighted		Weighted			Unweighted		Weighted	
	N	Median	IQR	Median	IQR	N	Median	IQR	Median	IQR	N	Median	IQR	Median	IQR
Sex															
Male	165	83.33	21.67	85.00	21.60	148	91.51	16.67	90.00	17.00	143	92.31	17.58	91.67	16.67
Female	100	88.33	22.08	90.00	20.00	91	94.23	15.00	94.08	14.61	82	95.00	15.42	95.00	11.54
Hospitalization Status															
Emergency Department	196	**88.25**	**20.00**	**88.16**	**20.00**	178	91.67	16.67	91.67	16.67	162	93.78	16.67	93.33	16.67
Hospitalized	69	**73.08**	**21.67**	**72.37**	**21.89**	61	92.31	13.21	91.99	13.28	63	95.00	19.17	94.17	17.87
Age Category															
< 5 years old	82	88.46	19.09	90.24	17.19	81	94.23	13.46	94.23	13.46	73	94.23	13.46	94.23	12.14
5 - <8 years old	51	85.00	23.75	85.25	25.44	47	93.33	12.98	94.71	13.66	50	93.33	18.33	93.33	18.33
8 - <13 years old	79	**81.67**	**22.50**	**83.33**	**21.67**	61	90.00	21.67	87.53	23.14	58	95.00	15.83	95.00	16.66
13 - < 17 years old	53	83.33	23.33	85.00	20.19	50	88.33	16.25	88.33	16.39	44	91.67	17.98	91.11	17.21
PaedsCTAS															
1 (requires resuscitation)	11^	73.08	24.20	65.29	25.90	10^	89.84	12.50	88.33	12.40	8^	94.17	20.00	88.33	7.82
2	35	78.33	18.75	79.16	21.23	32	92.21	13.33	91.67	13.42	34	91.86	19.58	88.92	18.89
3	45	81.67	21.60	82.17	19.58	38	88.33	18.27	88.33	18.53	36	94.62	15.31	93.34	14.66
4	101	86.67	20.00	86.67	18.33	96	91.67	17.08	91.67	15.87	81	92.31	16.67	92.31	16.67
5 (non urgent)	8^	92.50	15.83	93.30	11.53	6^	97.44	11.10	96.67	12.09	8^	94.17	13.45	90.01	7.42
Missing	65	88.46	25.00	90.00	21.41	57	96.15	15.00	97.07	13.70	58	94.62	12.29	95.00	11.67
Income Quintile															
1 (lowest income quintile)	30	74.48	32.47	77.17	32.86	24	91.99	20.00	91.11	16.98	20	97.37	19.17	95.56	15.30
2	28	87.50	18.56	88.32	16.17	27	88.33	13.33	86.95	16.13	23	90.00	17.50	90.00	16.35
3	51	85.00	25.35	87.88	20.14	47	96.15	12.92	96.79	10.57	46	94.62	12.29	95.00	11.67
4	50	85.83	18.81	86.67	15.71	44	93.27	12.28	91.88	12.50	45	92.31	16.19	91.26	15.24
5 (highest income quintile)	93	80.77	20.77	81.92	20.00	85	91.67	18.33	90.00	18.33	81	93.33	16.67	92.49	16.54
Missing	13^	90.38	16.67	92.13	13.33	12^	91.99	8.75	91.88	9.40	10	97.50	11.25	98.31	5.06

	One-month					Four-months					Twelve-months				
		Unweighted		Weighted			Unweighted		Weighted			Unweighted		Weighted	
	N	Median	IQR	Median	IQR	N	Median	IQR	Median	IQR	N	Median	IQR	Median	IQR
Injury															
Minor external Injury	97	90.00	19.74	89.41	19.73	91	92.31	16.67	91.99	16.67	83	95.00	15.83	94.44	15.91
Upper extremity fracture	63	83.33	19.58	83.49	21.04	56	91.03	13.21	90.13	13.46	56	93.78	18.33	93.33	16.56
Lower extremity fracture	32	**69.17**	**22.29**	**75.00**	**20.32**	28	91.99	16.60	90.03	19.89	27	95.00	14.17	91.96	15.26
Head injury	37	85.00	18.33	86.36	17.87	30	91.89	12.29	92.17	11.52	28	96.15	10.28	96.78	9.52
Major trauma	19	**75.00**	**22.95**	**75.80**	**28.81**	17	91.35	15.00	92.30	12.66	16	94.17	19.17	93.33	13.70
Other	15^	90.00	14.84	91.14	5.80	15^	92.31	7.69	91.77	11.01	13^	88.33	17.31	88.60	14.72
Missing	2^	97.50	0.83	96.67	1.07	2^	89.17	10.83	78.33	13.87	2^	98.33	1.67	96.67	2.13
Highest Education**															
1	9^	71.67	22.50	70.00	28.98	8^	92.08	8.22	89.38	10.56	1^	98.33	0.00	98.33	0.00
2	22	83.33	25.02	86.62	15.85	18	90.00	10.20	89.44	10.41	7^	88.33	21.91	78.14	15.83
3	48	79.42	23.94	85.00	21.91	43	92.31	16.88	91.41	20.28	20	89.17	17.50	88.33	17.12
4	91	86.67	22.29	89.59	20.77	83	92.31	15.00	93.33	14.66	46	95.58	16.01	94.50	14.43
5	85	85.00	20.00	85.84	20.00	80	90.87	18.56	90.00	19.60	76	94.62	13.85	95.00	11.66
Missing	10^	73.33	15.61	74.94	14.76	7^	80.00	17.63	74.46	18.13	72	93.33	16.67	92.66	16.67
Overall	265	85.00	21.73	86.54	20.99	239	91.67	16.67	91.67	16.67	225	94.23	16.67	93.48	16.67

* Bolded medians are statistically significantly different from each other at alpha of 0.05 based on Mann-Whitney U or Kruskal Wallis test followed by Dunn-Bonferroni post hoc as appropriate

** Parent highest education categories: 1 graduated high school, 2 some trade school, college or university, 3 = Diploma from trade school or college, 4 = University degree, 5 = Post-graduate degree (Master's and/or Doctorate)

^ Use caution when interpreting statistics and inferences associated with categories with low bases

Table 5.7 Child response psychosocial health summary score over time*

	One-month					Four-months					Twelve-months				
		Unweighted		Weighted			Unweighted		Weighted			Unweighted		Weighted	
	N	Median	IQR	Median	IQR	N	Median	IQR	Median	IQR	N	Median	IQR	Median	IQR
Sex															
Male	103	84.38	37.50	90.63	25.00	87	96.88	10.94	100.00	9.38	89	100.00	6.25	98.46	6.25
Female	65	87.50	34.38	87.50	24.54	61	93.75	12.50	93.75	12.50	51	93.75	12.50	93.75	12.50
Hospitalization Status															
Emergency Department	124	**92.19**	**21.88**	**90.63**	**21.88**	109	96.88	9.38	96.88	9.38	101	96.88	9.38	96.88	9.38
Hospitalized	44	**60.94**	**32.03**	**59.38**	**30.74**	39	93.75	20.31	92.19	19.49	39	100.00	6.25	100.00	6.25
Age Category															
5 - <8 years old	52	90.63	25.00	93.75	18.75	46	100.00	6.25	100.00	6.25	48	100.00	12.50	93.75	9.01
8 - <13 years old	71	82.14	46.88	88.96	37.01	57	93.75	12.50	91.15	12.50	51	96.88	7.81	96.88	6.63
13 - < 17 years old	45	81.25	37.50	81.25	28.13	45	93.75	12.50	96.31	9.38	41	96.88	9.38	96.39	9.38
PaedsCTAS															
1 (requires resuscitation)	5^	50.00	21.88	50.00	24.58	5^	84.38	9.38	81.25	4.96	4^	96.88	4.69	96.88	1.01
2	24	71.88	32.81	76.00	27.82	22	93.75	10.94	93.75	9.82	23	100.00	12.50	100.00	6.25
3	24	76.56	46.88	81.25	40.87	21	93.75	9.38	93.75	9.38	18	98.44	9.38	92.75	9.92
4	62	87.50	17.97	87.50	18.75	54	96.88	11.72	96.88	9.96	49	93.75	9.38	93.75	7.85
5 (non urgent)	7^	93.75	29.69	93.75	24.29	5^	100.00	0.00	100.00	0.00	6^	100.00	0.00	100.00	0.00
Missing	46	95.31	29.69	96.88	21.88	41	96.88	12.50	96.88	9.88	40	100.00	6.25	98.96	6.25
Income Quintile															
1 (lowest income quintile)	18	81.25	25.00	81.25	25.00	14^	100.00	8.59	100.00	6.25	16	96.88	10.94	96.88	10.49
2	19	90.63	20.31	92.17	18.94	17	93.75	12.50	93.75	12.50	15^	93.75	9.38	93.75	7.13
3	32	87.50	41.41	93.75	25.97	28	95.31	10.16	97.89	7.27	26	95.31	6.25	93.75	6.25
4	30	84.38	32.81	87.50	19.50	26	93.75	12.50	93.75	12.50	21	100.00	6.25	100.00	6.25
5 (highest income quintile)	60	82.81	45.31	87.44	33.68	54	96.88	12.50	97.87	9.38	56	100.00	9.38	97.93	9.38
Missing	9	93.75	28.13	93.22	10.77	9^	100.00	6.25	98.95	6.25	6^	98.44	3.13	96.88	3.62

	One-month					Four-months					Twelve-months				
		Unweighted		Weighted			Unweighted		Weighted			Unweighted		Weighted	
	N	Median	IQR	Median	IQR	N	Median	IQR	Median	IQR	N	Median	IQR	Median	IQR
Injury															
Minor external Injury	60	93.75	18.75	93.75	18.75	53	96.88	9.38	96.88	9.38	50	93.75	9.38	93.75	9.38
Upper extremity fracture	48	81.70	25.00	87.50	18.98	40	98.44	9.38	98.95	6.48	40	100.00	10.16	96.89	8.97
Lower extremity fracture	25	**50.00**	**34.38**	**50.49**	**30.20**	21	87.50	28.57	90.08	20.20	18	98.44	8.59	100.00	9.79
Head injury	15	100.00	9.38	100.00	1.76	14^	100.00	8.59	100.00	8.08	14^	100.00	5.47	100.00	5.59
Major trauma	11^	**50.00**	**17.19**	**50.00**	**21.14**	11^	87.50	17.19	85.94	10.48	11^	93.75	14.06	93.75	7.35
Other	7^	93.75	32.81	94.77	5.77	7^	100.00	3.13	100.00	0.00	6^	100.00	0.00	98.98	0.71
Missing	2	98.44	1.56	96.88	2.00	2	96.88	3.13	93.75	4.00	1	100.00	0.00	100.00	0.00
Highest Education**															
1	4^	81.03	35.60	65.63	22.65	3^	93.75	3.13	93.75	3.26	4^	82.81	29.69	66.68	23.14
2	13	93.75	40.63	94.26	14.87	13^	93.75	9.38	95.29	6.25	15^	96.88	6.25	97.38	3.13
3	29	78.13	43.75	82.75	31.25	28	95.31	18.75	93.75	17.91	26	100.00	6.25	100.00	6.69
4	56	87.50	32.03	90.63	25.00	45	96.88	6.25	100.00	6.25	43	96.88	12.50	93.75	12.50
5	62	87.50	30.47	87.50	24.91	56	93.75	12.50	93.75	12.50	48	96.88	7.03	93.75	6.25
Missing	4	76.56	14.84	75.00	16.61	3	87.50	18.75	75.00	0.00	3	100.00	7.81	92.19	0.00
Overall	168	87.50	38.28	89.37	27.84	148	93.75	12.50	96.88	9.38	140	96.88	9.38	96.88	9.38

** Bolded medians are statistically significantly different from each other at alpha of 0.05 based on Mann-Whitney U or Kruskal Wallis test followed by Dunn-Bonferroni post hoc as appropriate

** Parents highest education categories: 1 graduated high school, 2 some trade school, college or university, 3 = Diploma from trade school or college, 4 = University degree, 5 = Post-graduate degree (Master's and/or Doctorate)

^ U se caution when interpreting statistics and inferences associated with categories with low bases

The variables found to be significant for the fixed intercept in the NLME model for parent-response psychosocial summary score were hospitalization status, baseline total scale score and age category (Table 5.8). Children who were hospitalized (estimate -10.08, 95% CI (-13.62, -6.54), p<0.001) and the oldest two groups of children were found to have significantly lower mean psychosocial summary scores at one-month post-injury relative to those seen in the ED and children < 5 years of age (estimate for children eight to 13 -4.39, 95% CI (-8.30, -0.47), p=0.030, estimate for children 13 to 17 -4.53, 95% CI (-8.79, -0.26), p=0.040). For every one-point increase in baseline total scale score there was an estimated corresponding 0.64 (95% CI 0.47, 0.81) point increase in psychosocial health summary score. The LRT was statistically significantly greater for children who were hospitalized relative to those seen in the ED (estimate 2.44, 95% CI (1.38, 3.49), p<0.001), those with higher baseline total scale score (estimate 0.14, 95% CI 0.09, 0.20), p<0.001)) and for those with a PaedsCTAS score of three relative to those with a score of one or two (estimate 1.38, 95% CI (0.53, 2.24), p=0.002). Children from higher income quintiles had significantly lower LRC (estimate for quintile 3 -3.12, 95% CI (-4.50, -1.74), p<0.001, estimate for quintile 4 -2.49, 95% CI (-3.68, -1.30), p<0.001), and estimate for quintile 5 -1.35, 95% CI (-2.24, -0.47), p=0.003

In the NLQMM model the estimate for LRC was statistically significantly lower than that of the analogous NLME (NLQMM estimate -10.92, 95% CI -22.74, 0.89, p=0.701, NLME estimate -3.34, 95% CI (-4.59, -2.09), p<0.001) (Table 4.29). The parameter estimates for baseline total scale score (NLQMM 0.62, 95% CI -1.51, 2.75, p=0.905), income quintiles 3 (estimate 7.25, 95% CI -11.91, 26.42), p=0.978) and 4 (estimate 0.95, 95% CI (-11.95, 13.85), p=0.399), and PaedsCTAS (estimate for level 2 4.35, 95% CI (-3.70, 12.39), p=0.737, estimate for level 3 3.72, 95% CI (-10.94, 18.37), p = 0.653) were statically significantly greater in the NLQMM relative to the NLME (Table 5.8).

Table 5.8 Parent-response non-linear mixed effects model (NLME) and non-linear quantile mixed effects model (NLQMM) psychosocial summary score

	NLME asymptotic model			NLQMM model		
Predictors	Estimates	95% CI	p	Estimate	95% CI	p
R0.(Intercept)	**87.68**	**85.05, 90.30**	**<0.001**	88.09	**77.84, 98.34**	**<0.001**
Hospitalization Status						
ED	ref					
Hospitalized	**-10.08**	**-13.62, -6.54**	**<0.001**	-7.01	**-24.56, 10.55**	**<0.001**
Baseline total scale score	**0.64**	**0.47, 0.81**	**<0.001**	0.76	**0.52, 1.00**	**<0.001**
Age Category						
< 5 years old	ref					
5 - <8 years old	-2.48	-6.66, 1.71	0.253	0.30	-5.34, 5.94	0.801
8 - <13 years old	**-4.39**	**-8.30, -0.47**	**0.030**	-5.50	-12.66, 1.66	0.285
13 - < 17 years old	**-4.53**	**-8.79, -0.26**	**0.040**	-3.10	-9.72, 3.52	0.557
LRC (Intercept)	**-3.34**	**-4.59, -2.09**	**<0.001**	-10.92	-22.74, 0.89	0.701
Hospitalization Status						
Emergency Department	ref					
Hospitalized	**2.44**	**1.38, 3.49**	**<0.001**	5.17	-16.06, 26.41	0.182
Baseline total scale score	**0.14**	**0.09, 0.20**	**<0.001**	0.62	-1.51, 2.75	0.905
Income Quintile						
1	ref					
2	-4.25	-8.80, 0.30	0.071	0.10	-20.50, 20.69	0.770
3	**-3.12**	**-4.50, -1.74**	**<0.001**	7.25	-11.91, 26.42	0.978
4	**-2.49**	**-3.68, -1.30**	**<0.001**	0.95	-11.95, 13.85	0.399
5	**-1.35**	**-2.24, -0.47**	**0.003**	-0.39	-36.41, 35.64	0.652
PaedsCTAS						
1	ref					
2	**1.38**	**0.53, 2.24**	**0.002**	4.35	-3.70, 12.39	0.737
3	0.43	-0.61, 1.47	0.424	3.72	-10.94, 18.37	0.653
Random Effects						
Residual variance	7.77			3.77		
Random intercept variance	8.99			<0.01		
# observations	515			515		

* Parameter estimates bolded are statistically significant in the model at alpha of 0.05, ref = reference category for that variable, 95% *CI* = 95% confidence interval associated with parameter estimate, *p* = p-value associated with parameter estimate, R0 = fixed intercept, LRC = log rate, estimates that underlined are statistically significantly different from their NLME analogue

Consistent with the parent-response, hospitalization status and baseline total scale score were significantly associated with mean psychosocial summary score at one-month post-injury in the child NLME model. Hospitalized children were found to have lower mean psychosocial summary score at one-month post-injury relative to those seen in the ED (estimate -5.29, 95% CI (-8.68, -1.90), p=0.003) and there was an estimated mean increase of 0.62 (95% CI 0.46, 0.78) in the mean psychosocial health summary score at one-month post-injury for every one point increase in baseline total scale score (Table 5.9). There were no statistically significant differences in the parent sub-population and child response NLME models for psychosocial health summary score. (Table 5.9).

The parameter estimate for baseline total scale score predicting the intercept was statistically significantly greater in the NLQMM model relative to the NLME for child-reported psychosocial health summary score (NLQMM estimate 0.91, 95% CI (0.52, 1.29, p<0.001, NLME estimate 0.61, 95% CI (0.46, 0.78), p<0.001). There were no statistically significant differences between the parent sub-population and child-response NLQMM models for the psychosocial health summary score Table 5.9 and 5.10).

Table 5.9 Child-response and parent sub-population non-linear mixed effects model psychosocial health summary score

	Child population			Parent sub-population		
Predictors	Estimates	95% CI	p	Estimates	95% CI	p
R0.(Intercept)	**85.97**	**84.11, 87.84**	**<0.001**	**83.81**	**81.64, 85.98**	**<0.001**
Hospitalization Status						
ED	ref					
Hospitalized	**-5.29**	**-8.68, -1.90**	**0.003**	**-6.02**	**-10.10, -1.95**	**0.004**
Baseline total scale score	**0.62**	**0.46, 0.78**	**<0.001**	**0.58**	**0.38, 0.77**	**<0.001**
LRC (aIntercept)	**-3.99**	**-4.80, -3.19**	**<0.001**	**-3.43**	**-4.00, -2.86**	**<0.001**
Baseline total scale score	0.03	-0.04, 0.11	0.391	**0.09**	**0.02, 0.15**	**0.015**
Random Effects						
Residual variance	8.70			9.37		
Random intercept variance	7.65			9.28		
# observations	418			418		

*ref = referent category, 95% CI = 95% confidence intervals associated with parameter estimate, *p* = p-value associated with parameter estimate, Parameter estimates bolded are statistically significant in the model at alpha of 0.05

Table 5.10 Child-response and parent sub-population non-linear quantile mixed effects model psychosocial health summary score

	Child model			Parent sub-population		
Predictors	Estimate	95% CI	p	Estimate	95% CI	p
R0.(Intercept)	**86.33**	**83.52, 89.13**	**<0.001**	**85.41**	**82.66, 88.17**	**< 0.001**
Hospitalization Status						
Emergency Department	ref					
Hospitalized	-4.03	-11.50, 3.43	0.293	-9.78	-16.86, -2.70	0.329
Baseline total scale score	**0.91**	**0.52, 1.29**	**<0.001**	**0.91**	**0.41, 1.42**	**<0.001**
LRC (Intercept)	-2.79	-41.91, 36.33	0.897	-2.28	-52.54, 47.99	0.935
Baseline total scale score	0.05	-12.60, 12.71	0.994	0.12	-36.34, 36.58	0.995
Random Effects						
Residual variance	4.04			4.29		
Random intercept variance	<0.01			<0.01		
# observations	418			418		

*ref = referent category, 95% CI = 95% confidence intervals associated with parameter estimate, *p* = p-value associated with parameter estimate, estimates underlined are statistically significantly different from the corresponding child response model estimate, Parameter estimates bolded are statistically significant in the model at alpha of 0.05

5.4 Discussion

The exploratory objective of this research was to investigate factors associated with PedsQL physical and psychosocial health summary scores reported by parents and children in the year following injury. The analysis of these exploratory outcomes demonstrated hospitalized and lower extremity fractures were both associated with a negative impact on children's physical health summary score at one-month post-injury as reported by both parents and children. In the parent-response models older age was also associated with lower one-month physical health summary scores. The parent-response physical health summary score NLME model was the only model where sex was significant, with females being estimated to have 5.8 points lower physical health summary score at one-month post-injury relative to males.

Similar to the physical health summary score models, hospitalization was also linked to lower psychosocial health summary scores at one-month post-injury as reported by both parents and children. Unlike the total scale score models and the physical health summary score models, injury type was not a significant variable in the psychosocial health summary score models for either parent- or child-response. The parent-response psychosocial health summary score model was the only model where income quintile was significant, with higher quintiles being associated with a faster rate of approach to the asymptote (i.e. greater gains in the outcome in the same time period) relative to the smallest income quintile.

These findings indicate that that parents perceive female's physical health to be more impacted by injury relative to males (controlling for hospitalization status, age category and injury type), and that parents perceive older children to be more impacted in their physical wellbeing relative to their younger counterparts. The differences across the physical and psychosocial health summary score results highlight the importance of investigating these as independent outcomes. While the HRQoL summary score provides a clean endpoint that is easily compared across studies and disease states, the domain summary scores provide further insight into the child's experience during recovery from injury. With this in mind future research could look further at the PedsQL sub-scales and school functioning to further drill down differences.

Chapter 6: Discussion

6.1 Relevance

Childhood injuries are one of the leading threats to paediatric health and well-being accounting for a large proportion of childhood hospitalizations in Canada and around the world (4,8). Understanding the trajectory of children's recovery from unintentional injuries across health domains, and the factors that are associated with recovery, can help inform injury prevention and management by healthcare providers and parents. The purpose of this thesis was to describe the impact of childhood injury on HRQoL and identify factors associated with decreased HRQoL following childhood injury. Secondary aims were to examine the utility of different longitudinal analysis methods for HRQoL following childhood injury, to discuss the impact of analysis method and identify appropriate statistical models that could be used in future research in this field.

To address the goals of this thesis, the results of a systematic review and analysis of primary research on HRQoL following childhood injury from the CYBOI study have been presented. This research has addressed identified gaps in the literature and advanced knowledge in terms of content area and methodology. In this final chapter, I have summarized how I have addressed the objectives of this research, the overall findings and the strengths and limitations of this thesis. I have also made recommendations for future research based on the findings from my work.

6.2 Objective 1

The first objective of this thesis was to describe the trajectory of, and identify factors associated with, children's HRQoL in the year following injury, as reported by both the child and parent.

The trajectory of HRQoL across studies in the systematic review in Chapter 2 was as varied as the tools and methods used in the studies themselves. Due to the limitations in analyses used and the variability in study methodology it was difficult to derive much knowledge about the trajectory of HRQoL following childhood injury over all. The same number of studies reported children recovered quickly (within one year and most within six months) as reported long term deficits in HRQoL beyond one-year post-injury (n=8 for each group). There were some factors that stood out as significant predictors of HRQoL post-injury despite the variation in study design and methods. Older children, children with more severe injuries and females were reported in multiple studies to suffer greater HRQoL deficits relative to those younger, with less severe injuries and male.

The average trajectory of HRQoL following injury in the CYBOI study demonstrated a significant dip at one-month post-injury and a return to baseline by four-months post-injury as measured by both the mean and median PedsQL total scale score. The physical health summary score demonstrated a larger dip at one-month post-injury relative to the psychosocial health score; both recovered to baseline by 4 months post-injury. On average, parent-reported HRQoL was equivalent to the child's own report at baseline, four- and twelve-months post-injury, but parents rated their children's HRQoL lower than children themselves at one-month post-injury. Although the average HRQoL scores were equivalent with baseline at four- and 12-months post-injury, some children were identified as not having recovered based on the MCID of the summary score. Over half of children were not recovered based on MCID at one-month post-injury, with 22% and 18% being classified as "not recovered" at four- and 12-months post-injury. These findings highlight how focusing on averages as the only outcome of interest can be misleading and the benefit of looking at an outcome in multiple ways.

The factors identified as significant predictors of HRQoL in the CYBOI study were hospitalization status, injury type and age. Children who were hospitalized, relative to those seen in the ED, older (over eight years old) relative younger children (under five years of age), and those with lower extremity injuries relative to minor external injuries were identified as having lower mean HRQoL, and greater odds of not being recovered at one-month post-injury.

6.3 Objective 2

The second objective of this thesis was to explore longitudinal models that can be used for the analysis of HRQoL data following childhood injury; to apply a selection of models to data gathered through primary research; and to discuss the impact of modelling technique on results.

Of the 30 studies included in the systematic review in Chapter 2, four studies applied longitudinal models, with the remaining examining data by time point, half with multivariable models, and half with no modelling at all. This suggests there is a need to provide information and direction on the analysis of HRQoL as an outcome in the context of childhood injury.

In the analyses in Chapter 4, it was found that the LME and NLME provided appropriate trajectories of the observed vs fitted data, indicating valid parameter estimates. However, model assumptions were violated with non-linear and heteroscedastic residuals. The violation of assumptions means the standard errors of these models are likely not valid. The use of the GLMM as an additional model in analyzing HRQoL as an outcome offered an interesting perspective. By dichotomizing the outcome, it was possible to identify the specific attributes of the children who had outstanding deficits at each time point. That said, dichotomizing a continuous outcome is associated with a significant loss of data and decrease in variability and efficiency. This resulted in small bases ($n < 15$) for many categories across predictor variables increasing the error associated with model estimates demonstrating the need for larger sample size for this type of analysis.

The NLQMM is robust to assumptions regarding the distribution of the error meaning and estimates population medians rather than means, which is a more appropriate measure of central tendency given the distribution of the outcomes. For these reasons, this model was deemed the best fitting to the CYBOI data. Although the NLQMM provided the best fit to the data it requires a larger sample size to make inferences, which was demonstrated by the wider confidence intervals relative to the analogous NLME.

6.4 Public Health Applications

The findings of this thesis can be used to inform clinical care and future research. Understanding the children at greatest risk of deficits in their HRQoL following injury provides direction for where resources could be focused to help attenuate these affects. Children who are at higher risk of short-term deficits in HRQoL could be linked with affiliate health care providers such as physiotherapists, occupational therapists, and psychologists to help mediate these effects. They could also be followed up more systematically via in person appointments or telephone calls to ensure all required supports are in place. These types of supports should be evaluated in future research to determine their effectiveness, and cost-effectiveness, in mediating the effects of injury on HRQoL in those at highest risk of large deficits (older children, those hospitalized and children with lower extremity injuries).

In terms of methodology, a number of weaknesses were identified in the analysis methods used in previous research in this field. The findings from my work, and the results of surveys of high impact public-health and medical journal editors suggests that authors need to pay more attention to presenting full descriptive results, addressing clustering of data in analyses, attending to assumptions behind statistical methods applied, and describing and addressing missing data appropriately (44,145). Reporting guidelines, such as those made available by the EQUATOR (enhancing the quality and transparency of health research) network “Statistical Analyses and Methods in Published Literature” (SAMPL) Guidelines can provide a framework for ensuring appropriate reporting of statistical methods (146).

The application of different models with the CYBOI data allowed for the demonstration of some of the issues that can arise when model assumptions are not met. The use of longitudinal quantile regression addresses many of the issues associated with HRQoL data and should be considered in future research. Quantile regression is widely used in finance and economics and is becoming more popular in medical and public health research (147). Although a 2010 study illustrated the effectiveness of quantile regression with cross sectional HRQoL data (148), only one study was found that applied longitudinal quantile regression to HRQoL (149). This may be due to the ability to perform longitudinal quantile regression, and specifically on non-linear data, with pre-defined packages only recently been made available.

In addition to being agnostic to the distribution of errors, and being robust to outliers and skewed outcomes, another important strength of quantile regression, when examining HRQoL as an outcome, is the ability to predict the tails of the distribution. This feature allows the consideration of the impact of a covariate on the entire distribution of an outcome, not just the conditional mean. This aspect of longitudinal quantile regression should be explored in future research of HRQoL in general, and specifically in the context of childhood injury.

The findings from this research provide an example of the importance of understanding model assumptions, running diagnostics, and understanding the implications of violations of these assumptions prior to settling on a final model. HRQoL is increasingly being used as an endpoint in epidemiologic and clinical studies and it presents unique challenges as an analytic outcome being bounded and often left skewed. The analyses applied, diagnostics run and findings from this thesis can help inform future analysis of HRQoL data in the context of childhood injury and beyond.

6.5 Strengths and Limitations

The strengths of this thesis include the focus on statistical methods both within the systematic review and in the primary research and the representation of the study population across ages, and mild to moderate injury types. The limitations include missing data and lack of representation of the study population in some sub groups.

The focus on statistical methods in this thesis allowed for an understanding of the limitations of previous research and provides knowledge on how analyses could be approached in the future. Where the previous systematic reviews on HRQoL and childhood injury did not rigorously address the limitations in analyses of the included studies, the systematic review performed in this thesis demonstrated the need for more research that applies thorough and robust statistical methods. This includes exploring the distribution of the outcome and ensuring the analyses used are appropriate for the given distribution, appropriate modelling that takes into account clustering by time, and quantifying, describing and addressing missing data. Through the analyses performed on the CYBOI data, the value of a thorough descriptive analysis to understand the nuances of the data was provided, as well as methods to approach describing missing data. Four different longitudinal models were put forth as possibilities to model longitudinal HRQoL data. The strengths and weakness were presented, along with the impact on error estimates when assumptions are not met. These results can help guide and inform future analyses on HRQoL. The limitations in the CYBOI data were highlighted in the descriptive analysis focusing on the significant amount of missing data, and a thorough approach to dealing with missing data was presented. That said, no analysis can truly remedy missing data, but only provide insight into the possible impact on model estimates given different situations (e.g., MAR vs MNAR) thus the missing data in the CYBOI study remains a limitation to this work.

A second strength of my research is the representation across mild to moderate injury types in the CYBOI study. Although there was limited representation of the most severely injured children (PaedsCTAS level 1 (requires resuscitation) n=12 at baseline and n=8 at 12 months). there was good representation at PaedsCTAS level two (n = 41 at one-month, 34 at 12 months) as well as the less severely injured levels three and four. With the composition of the CYBOI study population in mind, the results can be generalized to children suffering unintentional injuries of minor to moderate severity presenting at hospital (PaedsCTAS 2, 3 and 4); however, caution should be used when generalizing to the most seriously injured children. The population included in my research is an important population to study as it represents a large part of the injury pyramid that is often overlooked by research focusing only on more serious injuries.

In addition to having minimal representation of the most seriously injured children, it should also be noted that the study population excluded individuals who did not speak English. Given the first language in BC is English, the inability to speak English could conceivably impact the recovery of a child following injury and these results should not be generalized to this vulnerable population. Similarly, geographic areas (urban vs rural) were not examined as factors that might impact recovery, and again caution should be used when considering a specifically rural population.

Heterogeneity in the study populations allows for comparisons across injury types in terms of the impact of injury on HRQoL. However, it also reduces the statistical power to examine factors associated with recovery within specific injury groups; this is where a more homogenous population would be of value. There is a separate literature for some childhood injuries including, but not limited to, HRQoL among children who have sustained burns (150,151), traumatic brain injuries (152,153) and spinal cord injuries (154,155). These studies, with a more homogenous population, can describe the nuances of recovery within these injury types and specific factors that may be unique to these injuries.

6.6 Recommendations For Future Research

Based on the results of this work it is recommended that future research investigate how factors associated with decreased HRQoL following childhood injury may vary across the distribution of HRQoL scores by modelling different quantiles using quantile regression. The use of GEE with HRQoL outcomes could be explored and compared to the results of other modelling techniques. It would be prudent to explore the potential benefits of providing affiliate healthcare resources including physiotherapy, occupational therapy and psychology to children at highest risks of immediate HRQoL deficits following childhood injury. In addition, examining the impact of childhood injury on the individual domains of HRQoL (i.e. from the PedsQL: physical functioning, emotional functioning, social functioning and school functioning) could provide more nuanced information about how children are affected by their injuries, and what resources might be best suited to help them. Finally work on HRQoL following childhood injury should explore the impact of being part of a vulnerable population; non-English speaking individuals should be included in study populations and the impact of living and recovering in more rural areas should be explored.

6.7 Conclusion

This research indicates that most mild to moderately injured children regain HRQoL baseline status by four-months post-injury. Older children, those hospitalized, and children with lower extremity fractures were at higher risk of having lower HRQoL in the early part of recovery relative to younger children, those seen in the ED and children with other types of injuries. Future research in this area should be sure to follow statistical reporting guidelines paying special attention to descriptive analyses, dealing with missing data and clustering of data. Non-linear quantile regression is a promising modelling technique for HRQoL outcomes given it is robust to skewness and outliers and free from any assumptions regarding the distribution of errors, however, requires larger sample sizes relative to OLS regression.

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Appendices

Appendix A Literature search strategy for MEDLINE using the OVIDSP interface

1. exp child/ or exp "congenital, hereditary, and neonatal diseases and abnormalities"/ or exp infant/ or adolescent/ or exp pediatrics/ or child, abandoned/ or exp child, exceptional/ or child, orphaned/ or child, unwanted/ or minors/ or (pediatric* or paediatric* or child* or newborn* or congenital* or infan* or baby or babies or neonat* or pre-term or preterm* or premature birth* or NICU or preschool* or pre-school* or kindergarten* or kindergarden* or elementary school* or nursery school* or (day care* not adult*) or schoolchild* or toddler* or boy or boys or girl* or middle school* or pubescen* or juvenile* or teen* or youth* or high school* or adolesc* or pre-pubesc* or prepubesc*).mp. or (child* or adolesc* or pediat* or paediat*).jn.
2. *quality of life/
3. (health related quality of life or health-related quality of life).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
4. (quality-of-life or quality of life or QoL).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms
5. Health Status/
6. health status disparities.mp. or Health Status Disparities/
7. self-perceived health status.mp.
8. functional status.mp.
9. health status indicator.mp. or Health Status Indicators/
10. pedsql.mp.
11. (child health questionnaire or CHQ).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
12. (health utilities index or HUI).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
13. KIDSCREEN.mp.
14. (euroqol or eq5d or eq-5d* or eq-5d-y).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
15. *"Wounds and Injuries"/
16. (traumatic injury or general injury).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
17. 15 or 16
18. 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14
19. 1 and 17 and 18
20. personal satisfaction/
21. life satisfaction.mp.
22. well being.mp.
23. 18 or 20 or 21 or 22
24. 1 and 17 and 23

Appendix B Quality assessment tool

	Yes	No	NR/NA
1. Was the research question or objective in this paper clearly stated?			
2. Was the study population clearly specified and defined?			
3. Was the participation rate of eligible persons at least 50%?			
4. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?			
5. Was a sample size justification, power description, or variance and effect estimates provided?			
6. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?			
7. Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?			
Was this study ≥ 12 month?			
8. For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (e.g., categories of exposure, or exposure measured as continuous variable)?			
Was injury severity captured?			
Were both hospitalized, and children seen in the ED included?			
9. Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?			
10. Was the exposure(s) assessed more than once over time?			
11. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?			
12. Were the outcome assessors blinded to the exposure status of participants?			
13. Was loss to follow-up after baseline 20% or less?			
14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?			
Age			
Sex			
Baseline HRQoL			
Injury severity			
Injury type			
Quality Rating (Good, Fair, or Poor) (based on NIH guidance)			

Appendix C Data extraction tool

1. Study ID (01 plus surname of first author and year first full report was published)
2. First author
3. Year of publication
4. Country in which the study was conducted
5. Aim of study
6. Longitudinal (Y/N)
7. Type of study
8. Population description (from which study participants are drawn)
9. Inclusion Criteria
10. Exclusion Criteria
11. Age Range (at time of injury) mean (SD)
12. Method of recruitment
13. sampling technique
14. Number eligible
15. Number enrolled n (% of eligible)
16. Sex of participants (% Male)
17. Mechanism of injury (%)
18. Types of injury (%)

19 HRQoL Outcome measure(s) (range of instrument)

20. Who reported HRQoL
21. Other outcome measures
22. study start date (recruitment started)
23. study end date (recruitment finished)
24. Number of follow ups/points of data collection
25. Time of follow up (from time of injury) (response rates)
26. Follow up rates at each time point
27. HRQoL Summary Score at each time point available
28. HRQoL Domain scores at each time point available
29. % hospitalized
30. % PICU
31. % ER
32. Other?
33. Length of hospitalization (range, mean, median)
34. measure of injury severity (range)
35. Injury severity distribution
36. Baseline measure of HRQoL (describe)
37. Predictors of HRQoL examined

38 Significant Predictors for HRQoL (and direction of relationship)

39. Comparison Group
40. When did HRQoL return to baseline/population norm
41. Analysis Method - bivariable as applied to HRQoL (specify parametric or non-parametric)
42. Analysis Method - model with HRQoL data as outcome
43. Method of addressing missing data/missing data assumptions

44. Measure/observed ceiling effect
45. Measure/report distrubtion of HRQoL data
46. Reported mean sd, median IQR, both
47. In both mean and median reported - is there a difference in these values?
48. Strengths
49. Limitations
50. Key conclusions

Appendix D Predictors of HRQoL

ISS / MISS	Valadka - At an average of 4.4 years post-injury, higher ISS had higher odds of disability	Sluys - Higher ISS was associated with higher self-reported scores in social functioning	Vollrath - At one month & one-year post-injury, higher MISS was associated with lower HRQoL scores	Holbrook 2007 - at 24 months follow-up, ISS group > 16 was strongly associated with significant QoL deficient	Schweer - at 1 and 6 months postinjury higher ISS was significantly associated with lower physical health summary score
Sex	Vollrath - At one-month post-injury, being female was significantly associated with worse HRQoL, however this association was no longer significant at 1 year	Holbrook 2007 - at 24 months follow-up female sex was strongly associated with significant QOL deficits	Polinder - at 9 months post-injury girls had 3 times the odds of suboptimal function as measured by the EQ5D relative to boys	Sluys – Female sex was associated with higher proxy scores in psychosocial health	
Age group	Herz - over the first year after injury, each year above 12 years of age was associated with a 1 point decreased in Total QOL score	Schneeberg - Older children had significantly worse HRQoL over the year following injury relative to younger children. In addition, children who were older had a steeper slope to recovery relative to younger children	Sluys - 6 years after injury higher current age of the child was associated with higher self-reported scores in emotional function and social function and lower self-reported scores in school functioning	Holbrook 2007 - at 24 months follow-up older age was strongly associated with significant QOL deficits	Schweer - At 6 months post-injury older age was significantly associated with lower physical health summary score

PTS/PTSD post-injury	Landolt - A higher post-traumatic stress symptoms score at 1 month were associated with lower HRQoL	Zatzick - PTSD reaction index scores of 38 or higher were associated with significantly lower CHQ-87 bodily pain and mental health subscale scores in the year following injury				
Hospitalization	Polinder - at 9 months post-injury children who were hospitalized had statistically significantly greater odds for suboptimal function as measured by the EQ5D relative to those who were not hospitalized	Schneeberg - Hospitalized children had significantly worse HRQoL over the year following injury relative to those who were not hospitalized. In addition, children who were hospitalized had a steeper slope to recovery relative to children seen in the ED.	Sturms 2005 - Children hospitalized reported lower HRQoL scores on the motor functioning and autonomy scales compared with outpatients			

Injury mechanism	Sturms 2005 - Children who had been in a motor vehicle accident had lower motor functioning scores during follow-up relative to those not in a motor vehicle accident				
Baseline HRQoL	Schneeberg - Baseline HRQoL was positively correlated to HRQoL over the year following injury	Vollrath- at one year post-injury, the strongest predictor of the 1 year TACQOL composite score was the score at one month	Landolt - Overall quality of life as measured by the TACQOL at one month was positively correlated with TACQOL score at 1 year	Zatzick - baseline CHQ-87 subscale scores * results not stated	
Type of injury	Valadka - At an average of 4.4 years post-injury, truncal and leg injury had higher odds of disability relative to other injuries	Dekker - All other injuries vs fractures of the extremities - - the odds of unfavourable outcome for injuries not concerning an extremity fracture was 3.3 times higher than for those with a fracture of the extremities	Schweer - at 1 and 6 months postinjury injury to an extremity was significantly associated with lower physical health summary score whereas injury to head/neck was significantly associated with lower psychosocial summary score	Sturms 2005 - children with lower extremity fractures reported on average less motor functioning and lower autonomy scores compared with children with upper extremity fractures or without an extremity fracture	

Multiple injuries	Holbrook 2007 - at 24 months follow-up three of more body regions injured was strongly associated with significant QoL deficits				
Race	Herz - in the year following injury being of non-white race was associated with a 5.2 point decrease in QOL	Zatzick * results not stated			

Appendix E Baseline study survey for parents of children 8-12 years of age

7 0

Child and Youth
Burden of Injury Research Study

Questionnaire 1:
Baseline Assessment for PARENTS
Thank you for your help with the Child and Youth Burden of Injury research study. This is the first Questionnaire of up to 4 that you will receive over the span of one year. It asks a series of questions about your child's health before the injury. We would be grateful if you would be willing to complete this questionnaire and send it back to us in the prepaid addressed envelope within the next 3-4 days. To thank you there is a $2 gift voucher in the envelope.

You also have the option to complete the questionnaire online. Simply go to the website: www.tinyurl.com/parent-8 and follow the instructions. Your Web ID for the online questionnaire is found at the top, right hand corner of this page.

We have also enclosed a package for your child to fill out. If your child is unable to complete this on their own, we would appreciate that you help the child complete their questionnaire.
In about 1 month, we will send you Questionnaire 2 to complete.

If you have any questions about the study please contact me at XXX-XXX-XXXX

Thank you very much for taking part in this study.

Dr. Mariana Brussoni
Assistant Professor
Director, BC Canadian Hospitals Injury Reporting and Prevention Program
University of British Columbia
Child & Family Research Institute
Developmental Neuroscience & Child Health
BC Injury Research & Prevention Unit
L-408 4480 Oak Street,
Vancouver, BC V6H 3V4

Today's Date: _________________ (dd/mm/yyyy)

PART 1

1. Child's Birth Date: ________________ (dd/mm/yyyy)

2. Is the child: male ☐ female ☐

The following questions ask about where and how your child's injury occurred.

3. What type of activity was your child doing when they were injured? (Please tick one box only)

Education?	☐
Sports or exercise at a school?	☐
Sports or exercise at a club/ gym?	☐
General leisure/entertainment/shopping?	☐
Paid work?	☐
Unpaid/ Voluntary work?	☐
Housework (e.g. home and garden maintenance)?	☐
Other? Please specify: ____________________	☐

Please provide further details of what your child was doing at the time of the injury. For example: fell down stairs at home, cut hand with saw at work, pushed off swing in playground

Where did the injury happen? (Please tick one box only)

At School	☐
In your own home	☐
In some other person's home	☐
In a residential home	☐
At work	☐
On a public road or on a pavement	☐
In an entertainment area (e.g. cinema, café)	☐
Countryside (e.g. open land, beach and sea)	☐
Sports grounds/ centres	☐
Public buildings (e.g. shops, library)	☐
Some other area, please give details:	☐

Was a motor vehicle involved in your child's accident?

Yes ☐ No ☐

If yes, was your child a…? (tick one box only)

Pedestrian	☐
Driver	☐
Passenger	☐
Cyclist	☐
Other road user	☐

Was your child's injury caused by an…? (Please tick one box only)

Accident	☐
Deliberate violence	☐
Uncertain if accident or deliberate	☐
Unknown	☐

a. Were you with your child when he or she was injured?

Yes ☐ No ☐

Please provide further details:

a. Were you also injured during the same incident?

Yes ☐ No ☐

Please provide further details:

Please think about the events that led to your child's injury and answer the following questions.

10. Would you say this incident was a "freak event"?

Yes ☐ No ☐

11. How much control did you feel you had to stop the event from happening?

_________	_________	_________	_________	_________	_________	_________
1 Uncontrollable	2	3	4	5	6	7 Totally controllable

12. How much of a chance do you think the event could happen to your child again?

_________	_________	_________	_________	_________	_________	_________
1 Very low	2	3	4	5	6	7 Very high

13. In general, the chance of your child being injured again in the future is:

_________	_________	_________	_________	_________	_________	_________
1 Very low	2	3	4	5	6	7 Very high

The next group of questions are about your child's health before the injury.

14. Before your child's injury did they suffer from a disability or long term health problem that limited their normal activities?

Yes ☐ No ☐

15. In the 4 weeks before your child was injured on how many days did ill health restrict their normal activities? _________ days

In the 4 weeks before your child was injured on how many days did they miss attending school or some other form of education because of ill health?

_________ days

PART 2

By placing a tick in one box in each group below, please indicate which statements best describe your child’s health state on the day before they were injured.

EQ-5D questionnaire here

PART 3

PedsQL tool here

PART 4

To enable us to access your child's Medical Services Plan and PharmaCare data, we require your child's Personal Health Number. Please enter it in the spaces below:

— — — —   — — —   — — —

We would like to examine the long term effect of injury in people with different backgrounds. Your answers to these questions would greatly help us to understand how injury affects different groups and communities and would be very much appreciated. All answers will be treated as strictly confidential and will be held securely and will not be stored with information that can identify your name or address.

If you do not wish to answer any of these questions then please leave that question blank.

1. Are you the injured child's…..

mother ☐

father ☐

other caregiver (please give details) ☐

____

2. Currently, you and the child's other parent are:

Living together and legally married or in common-law relationship ☐

No longer living together, but have previously been married or common-law partners ☐

Living apart and have never lived together as a couple ☐

Never had a relationship as a couple ☐

Other parent is deceased ☐

3. Your child lives: (please choose one)

With both parents ☐

Mostly with mother ☐

Mostly with father ☐

Equally with each parent ☐
(e.g., shared custody)

4. Do you currently rent or own your home?

Rent ☐

Own ☐

5. How many people usually live at your address, including yourself?
Number of people: ___________

6. What is the primary language/s that you speak at home? (For example: French, Mandarin, Urdu)

____

7. What is the highest grade or level of education you have attended or completed?

Some high school ☐

Graduated high school ☐

Some - trade school, college or university ☐

Diploma from trade school or college ☐

University degree ☐
(e.g., Bachelor's or undergraduate degree)

Post-graduate degree ☐
(e.g., Master's and/or Doctorate degree)

8. What is the highest grade or level of education the child's other parent attended or completed?

Some high school ☐

Graduated high school ☐

Some - trade school, college or university ☐

Diploma from trade school or college ☐

University degree ☐
(e.g., Bachelor's or undergraduate degree)

Post-graduate degree ☐
(e.g., Master's and/or Doctorate degree)

9. What is your best estimate of the total income of all members of your household from all sources last year before taxes and deductions? Was the total household income….

$14,999 or less ☐

between $15,000 and $ 29,999 ☐

between $ 30,000 and $ 59,999 ☐

between $ 60,000 and $ 79,999 ☐

$ 80,000 or greater ☐

10. Has your injured child had any other injuries in the last 12 months that required medical attention by a doctor, nurse, or dentist?

Yes ☐ No ☐

If yes, how many injuries? __________

Please describe the most serious injury and how it happened:

Thank you!

Thank you very much for your help. Please return this questionnaire and consent form in the prepaid envelope by the end of the week. We look forward to hearing from you.

Appendix F Injury definitions for PaedsCTAS

Mechanism of injury modifier guidelines for PaedsCTAS* adapted from (156)

Mechanism of injury	Description	CTAS level
General Trauma	MVC: ejection from vehicle, rollover, extrication time > 20 min, significant intrusion into passenger's space, death in the same passenger compartment, impact > 40 km/h (unrestrained) or impact > 60 km/h (restrained) MCC: impact with a car > 30 km/hr, especially if rider is separated from motorcycle Pedestrian or bicyclist: run over or struck by vehicle at >10 km/h Fall: from > 3 ft (> 1 m) or 5 stairs	2
Head Trauma	MVC: ejection from vehicle, unrestrained passenger striking head on windshield Pedestrian: struck by vehicle Fall: from > 3 ft (> 1 m) or 5 stairs Assault: with blunt object other than fist or feet	2
Neck Trauma	MVC: ejection from vehicle, rollover, high speed (especially if driver unrestrained) MCC: impact with a car > 30 km/hr, especially if rider is separated from motorcycle Fall: fall from > 3 ft (> 1 m) or 5 stairs Axial load to the head	2

CTAS = Canadian Emergency Department Triage and Acuity Scale; MCC = motorcyclist collision; MVC = motor vehicle collision. *This is not an exclusive list. For more information see CTAS Complaint Oriented Triage (COT) teaching/reference tool: http://ctas-phctas.ca/?page_id=294

Appendix G Empty means, Random intercept linear mixed effects models

Parent response total scale score linear mixed effects model with no predictor variables*

	Empty means, random intercept			Intercept model with time		
Predictors	*Estimates*	*95% CI*	*p*	*Estimates*	*95% CI*	*p*
(Intercept)	**86.01**	**84.69, 87.33**	**<0.001**	**78.61**	**76.98, 80.23**	**<0.001**
4 months				**11.14**	**9.29, 12.99**	**<0.001**
12 months				**12.36**	**10.48, 14.24**	**<0.001**
Random Effects						
Residual variance	152.75			106.68		
Random intercept variance	68.66			80.68		
ICC	0.31			0.43		
# observations	731			731		

* 95% CI = confidence interval for parameter estimate, *p* = p-value associated with parameter estimate, ICC = interclass correlation, bolded figures indicate significance at alpha of 0.05

Child response total scale score linear mixed effects model with no predictor variables*

	Empty means, random intercept			Intercept model with time		
Predictors	*Estimates*	*95% CI*	*P*	*Estimates*	*95% CI*	*p*
(Intercept)	**86.12**	**84.50, 87.74**	**<0.001**	**80.83**	**78.89, 82.76**	**<0.001**
4 months				**7.91**	**5.83, 9.99**	**<0.001**
12 months				**9.02**	**6.88, 11.15**	**<0.001**
Random Effects						
Residual variance	106.53			83.27		
Random intercept variance	81.99			86.74		
ICC	0.42			0.51		
# observations	457			457		

* 95% CI = confidence interval for parameter estimate, *p* = p-value associated with parameter estimate, ICC = interclass correlation, bolded figures indicate significance at alpha of 0.05

Sub-population of parent-response total scale score for parents with children who provided child-response, linear mixed effects model with no predictor variables*

	Empty means, random intercept			Intercept model with time		
Predictors	*Estimates*	*95% CI*	*P*	*Estimates*	*95% CI*	*p*
(Intercept)	**84.53**	**82.86, 86.21**	**<0.001**	**76.39**	**74.33, 78.46**	**<0.001**
4 months				**12.19**	**9.78, 14.60**	**<0.001**
12 months				**13.57**	**11.11, 16.04**	**<0.001**
Random Effects						
Residual variance	166.15			89.40		
Random intercept variance	63.95			79.56		
ICC	0.28			0.47		
# observations	457			457		

* 95% CI = confidence interval for parameter estimate, *p* = p-value associated with parameter estimate, ICC = interclass correlation, bolded figures indicate significance at alpha of 0.05

Appendix H Random intercept asymptotic non-linear mixed effects models

Random intercept asymptotic non-linear mixed effects model parent-response total scale score*

Predictors	*Estimates*	*95% CI*	*p*
intercept	**81.14**	**79.31, 82.97**	**<0.001**
Log rate	**-2.46**	**-2.62, -2.29**	**<0.001**
Random Effects			
Residual variance	9.59		
Random intercept variance	13.11		
ICC	0.58		
# of observations	731		

* CI = 95% confidence interval of parameter estimate, *p* = p-value associated with parameter estimate, values in bold are significant at alpha of 0.05, ICC = intraclass correlation

Random intercept asymptotic non-linear mixed effects model child-response total scale score*

Predictors	*Estimates*	*95% CI*	*p*
intercept	**83.02**	**80.92, 85.02**	**<0.001**
Log rate	**-2.91**	**-3.23, -2.66**	**<0.001**
Random Effects			
Residual variance	8.85		
Random intercept variance	11.70		
ICC	0.57		
# of observations	451		

* CI = 95% confidence interval of parameter estimate, *p* = p-value associated with parameter estimate, values in bold are significant at alpha of 0.05, ICC = intraclass correlation

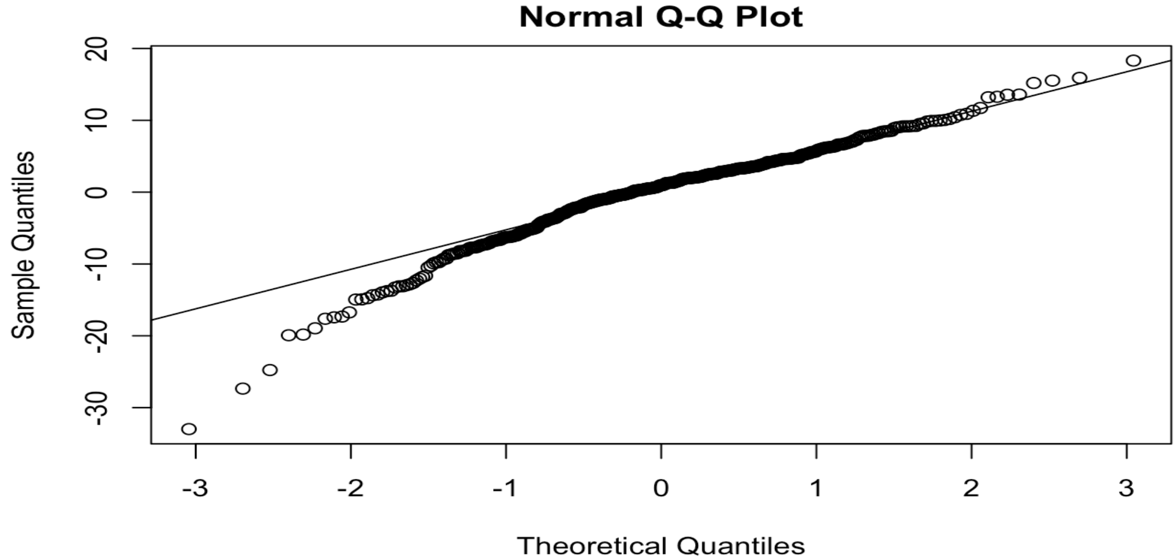
Random intercept asymptotic non-linear mixed effects model parent sub population parent-response total scale score*

Predictors	*Estimates*	*95% CI*	*p*
intercept	**79.15**	**76.85, 81.46**	**<0.001**
Log rate	**-2.50**	**-2.72, -2.28**	**<0.001**
Random Effects			
Residual variance	10.17		
Random intercept variance	12.58		
ICC	0.54		
# of observations	451		

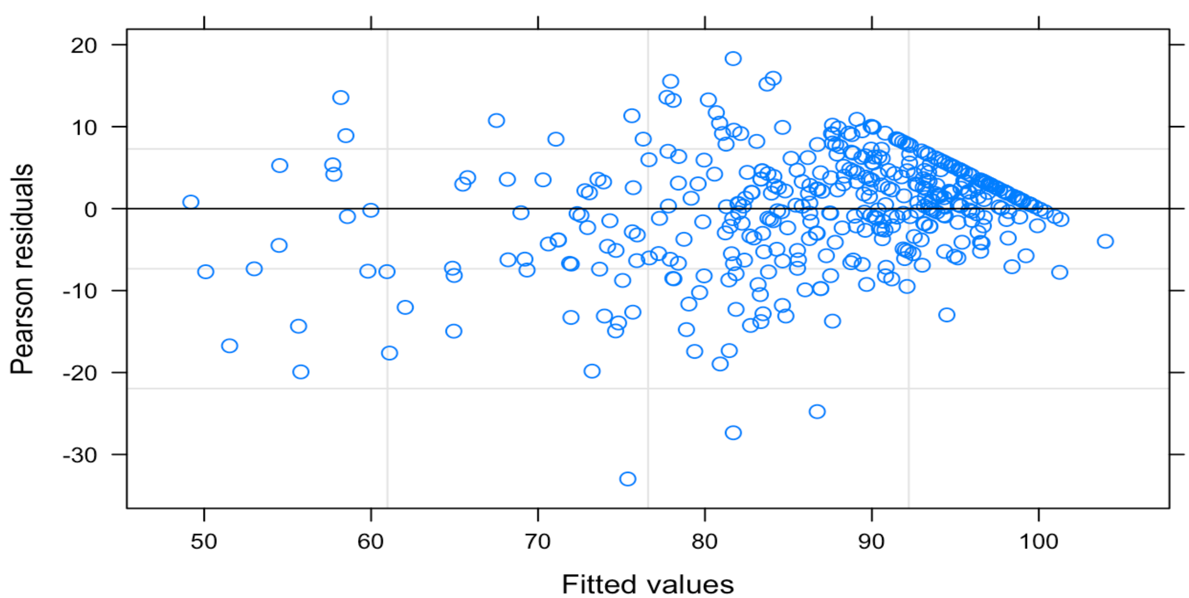
* CI = 95% confidence interval of parameter estimate, *p* = p-value associated with parameter estimate, values in bold are significant at alpha of 0.05, ICC = intraclass correlation

Appendix I Child-reported total scale score linear effect model residual plots

Quantile-quantile plot for child-response for total scale score linear mixed effects model



Residual vs predicted plot for child-response total scale score linear mixed effects model



Appendix J Parent response recovery defined by being within MCID (4.5) of baseline total scale score*

	One Months					Four-months					Twelve-months				
	Recovered		Not Recovered			Recovered		Not Recovered			Recovered		Not Recovered		
Sex	n	%	n	%	OR (95% CI)	n	%	n	%	OR (95% CI)	n	%	n	%	OR (95% CI)
Male	66	41.51	93	58.49	ref	115	79.31	30	20.69	ref	116	81.12	27	18.88	ref
Female	47	47.47	52	52.53	1.27 (0.77, 2.11)	66	75.86	21	24.14	0.82 (0.43, 1.55)	66	73.33	14	26.67	1.10 (0.54, 2.24)
Hospitalization Status															
ED	**87**	**45.55**	**104**	**54.45**	**ref**	142	81.14	33	18.86	ref	131	81.37	30	18.63	ref
Hospitalized	**9^**	**13.43**	**58**	**86.57**	**0.13 (0.06, 0.28)**	39	68.42	18	31.58	0.50 (0.26, 0.99)	51	82.26	11^	17.74	1.06 (0.50, 2.28)
Age Category															
<5 years old	50	61.73	31	38.27	ref	69	86.25	11^	13.75	ref	63	86.30	10^	13.70	ref
5 - < 8 years old	25	49.02	26	50.98	0.60 (0.29, 1.21)	38	86.36	6^	13.64	1.01 (0.35, 2.95)	36	73.47	13^	26.53	0.44 (0.18, 1.10)
8 - <13 years old	**23**	**31.08**	**51**	**68.92**	**0.28 (0.14, 0.54)**	**41**	**69.49**	**18**	**30.51**	**0.36 (0.16, 0.84)**	52	91.23	5^	8.77	1.65 (0.53, 5.13)
13 – <17 years old	**15^**	**28.85**	**37**	**71.15**	**0.25 (0.12, 0.53)**	**33**	**55.93**	**26**	**44.07**	**0.33 (0.14, 0.79)**	31	70.45	13	29.55	0.38 (0.15, 0.96)
PaedsCTAS (%)															
1 (requires resuscitation)	**2^**	**18.18**	**9^**	**81.82**	ref	8^	80.00	2^	20.00	ref	6	75.00	2^	25.00	ref
2	**8^**	**22.86**	**27**	**77.14**		22	70.97	9^	29.03		28	82.35	6^	17.65	
3	**17**	**40.48**	**25**	**59.52**	2.45 (0.96, 6.22)	24	66.67	12	33.33	0.73 (0.28, 1.95)	32	88.89	4^	11.11	1.88 (0.52, 6.86)
4	**46**	**46.94**	**52**	**53.06**	2.98	78	83.87	15	16.13	1.90	62	76.54	19	23.46	0.72
5 (non urgent)	**2^**	**25.00**	**6^**	**75.00**	(1.34, 6.62)	5^	83.33	1^	16.67	(0.79, 4.56)	5^	62.50	3^	37.50	(0.29, 1.78)
Missing	38	59.38	26	40.63		44	78.57	12	21.43		49	87.50	7^	12.50	
Income Quintile (%)															
1 (lowest income quintile)	13^	44.83	16	55.17	ref	18	75.00	6^	25.00	ref	16	80.00	4^	20.00	ref
2	10^	35.71	18	64.29	0.68 (0.24, 1.98)	19	76.00	6^	24.00	1.06 (0.29, 3.88)	18	78.26	5^	21.74	0.90 (0.21, 3.94)
3	27	52.94	24	47.06	1.38 (0.55, 3.46)	35	76.09	11^	23.91	1.06 (0.34, 3.34)	32	71.11	13^	28.89	0.62 (0.17, 2.19)
4	20	41.67	28	58.33	0.88 (0.35, 2.23)	38	88.37	5^	11.63	2.53 (0.68, 9.41)	39	86.67	6^	13.33	1.62 (0.40, 6.54)

5 (highest income quintile)	35	39.33	54	60.67	0.80 (0.34, 1.86)	61	74.39	21	25.61	0.97 (0.34, 2.76)	69	86.25	11^	13.75	1.57 (0.44, 5.57)
Injury															
Minor external Injury	**59**	**62.11**	**36**	**37.89**	ref	69	77.53	20	22.47	ref	67	80.72	16	19.28	ref
Upper extremity fracture	**17**	**27.42**	**45**	**72.58**	0.23 (0.12, 0.46)	48	87.27	7^	12.73	1.99 (0.78, 5.07)	46	82.14	10^	17.86	1.10 (0.46, 2.63)
Lower extremity fracture	**^1**	**3.33**	**29**	**96.67**	0.02 (0.00, 0.16)	16	64.00	9^	36.00	0.52 (0.20, 1.34)	22	84.62	4^	15.38	1.31 (0.40, 4.35)
Head injury	**22**	**64.71**	**12**	**35.29**	1.12 (0.49, 2.53)	26	86.67	4^	13.33	1.88 (0.59, 6.04)	25	89.29	3^	10.71	1.99 (0.52, 7.42)
Major trauma	**3^**	**15.00**	**17**	**85.00**	0.11 (0.03, 0.39)	12	70.59	5^	29.41	0.70 (0.22, 2.21)	10	62.50	6^	37.50	0.40 (0.13, 1.26)
Other	**9^**	**60.00**	**6^**	**40.00**	0.92 (0.30, 2.79)	9^	64.29	5^	35.71	0.52 (0.16, 1.73)	10	83.33	2^	16.67	1.19 (0.24, 5.99)
Highest Education**															
1	14	33.33	28	66.67	ref	28	77.78	8^	22.22	ref	21	75.00	7^	25.00	ref
2	16	33.33	32	66.67	0.64 (0.26, 1.61)	32	59.26	22	40.74	1.29 (0.44, 3.80)	41	89.13	5^	10.87	2.73 (0.77, 9.66)
3	43	47.78	47	52.22	1.18 (0.52, 2.65)	63	68.48	29	31.52	1.47 (0.55, 3.92)	62	72.09	24	27.91	1.48 (0.53, 4.15)
4	38	45.24	46	54.76	1.06 (0.47, 2.41)	67	83.75	13^	16.25	2.29 (0.82, 6.37)	58	81.69	13^	18.31	1.49 (0.52, 4.23)
Overall	113	43.8	145	56.202		181	78.02	51	21.98		182	81.61	41	18.39	

* Bolding indicates a statistically significantly association with the odds of recovery at alpha of 0.05, OR = bivariable odds ratio for odds of recovery, 95% CI = 95% confidence interval associated with parameter estimate

** Parent highest education categories: 1 graduated high school or some trade school, college or university, 3 = Diploma from trade school or college, 4 = University degree, 5 = Post-graduate degree (Master's and/or Doctorate)

^ Use caution when interpreting statistics and inferences associated with categories with low bases

Appendix K Child-response recovery defined by being within MCID (4.4) of baseline total scale score*

	One Month					Four-months					Twelve-months				
	Recovered		Not Recovered			Recovered		Not Recovered			Recovered		Not Recovered		
Sex	n	%	n	%	OR (95% CI)	n	%	n	%	OR (95% CI)	n	%	n	%	OR (95% CI)
Male	52	54.17	44	45.83	ref	64	78.05	18	21.95	ref	69	84.15	13^	15.85	ref
Female	39	60.94	25	39.06	1.32 (0.69, 2.51)	46	77.97	13^	22.03	1.00 (0.44, 2.23)	38	76.00	12^	24.00	0.60 (0.25, 1.44)
Hospitalization Status															
Emergency Department	**79**	**65.83**	**41**	**34.17**	ref	88	81.48	20	18.52	ref	79	79.80	20	20.20	ref
Hospitalized	**12^**	**30.00**	**28**	**70.00**	**0.22 (0.10, 0.48)**	22	66.67	11^	33.33	1.42 (0.49, 4.14)	28	71.79	11^	28.21	1.42 (0.49, 4.14)
Age Category															
5-8	32	65.31	17	34.69	ref	34	82.93	7^	17.07	ref	36	81.82	8^	18.18	ref
8-13	38	56.72	29	43.28	0.70 (0.33, 1.49)	41	74.55	14^	25.45	0.60 (0.22, 1.66)	42	85.71	7^	14.29	1.33 (0.44, 4.04)
> 13	21	47.73	23	52.27	0.49 (0.21, 1.12)	35	77.78	10^	22.22	0.72 (0.25, 2.11)	29	74.36	10^	25.64	0.64 (0.23, 1.84)
PaedsCTAS (%)															
1 (requires resuscitation)	1^	25.00	3^	75.00	ref	2^	66.67	1^	33.33	ref	2^	100.00	0^	0.00	ref
2	8^	40.00	12^	60.00		14^	73.68	5^	26.32		16	80.00	4^	20.00	
3	10	41.67	14^	58.33	1.19 (0.37, 3.79)	14^	66.67	7^	33.33	0.75 (0.20, 2.77)	14^	82.35	3^	17.65	1.04 (0.20, 5.41)
4	**41**	**68.33**	**19**	**31.67**	**3.57 (1.35, 9.47)**	44	81.48	10^	18.52	1.80 (0.56, 5.74)	41	83.67	8	16.33	1.11 (0.30, 4.07)
5 (non urgent)	**4^**	**66.67**	**2^**	**33.33**		4^	100.00	0^	0.00		4^	80.00	1^	20.00	
Missing	27	58.70	19	41.30		32	80.00	8^	20.00		30	76.92	9^	23.08	

	Recovered		Not Recovered			Recovered		Not Recovered			Recovered		Not Recovered		
Income Quintile (%)															
1 (lowest income quintile)	7^	43.75	9^	56.25	ref	11^	84.62	2^	15.38	ref	11^	78.57	3^	21.43	ref
2	13^	72.22	5^	27.78	3.34 (0.80,13.94)	11^	68.75	5^	31.25	0.40 (0.06, 2.52)	11^	78.57	3^	21.43	1.00 (0.16, 6.08)
3	20	62.50	12^	37.50	2.14 (0.63, 7.26)	23	85.19	4^	14.81	1.05 (0.17, 6.60)	22	88.00	3^	12.00	2.00 (0.35, 11.58)
4	14^	48.28	15^	51.72	1.20 (0.35, 4.09)	19	76.00	6^	24.00	0.58 (0.10, 3.36)	16	80.00	4^	20.00	1.09 (0.20, 5.87)
5 (highest income quintile)	32	56.14	25	43.86	1.65 (0.54, 5.03)	38	73.08	14^	26.92	0.49 (0.10, 2.51)	43	79.63	11^	20.37	1.07 (0.25, 4.49)
Injury															
Minor external Injury	42	71.19	17	28.81	ref	40	74.07	14^	25.93	ref	41	82.00	9^	18.00	ref
Upper extremity fracture	25	54.35	21	45.65	0.48 (0.21, 1.08)	32	82.05	7^	17.95	1.55 (0.56, 4.30)	30	78.95	8^	21.05	0.82 (0.28, 2.38)
Lower extremity fracture	5^	21.74	18	78.26	0.11 (0.04, 0.35)	13^	68.42	6^	31.58	0.76 (0.24, 2.38)	13^	81.25	3^	18.75	0.95 (0.22, 4.05)
Head injury	11^	78.57	3^	21.43	1.48 (0.37, 5.99)	13^	100.00	0^	0.00	NA	9^	69.23	4^	30.77	0.49 (0.12, 1.97)
Major trauma	2^	22.22	7^	77.78	0.12 (0.02, 0.61)	6^	66.67	3^	33.33	0.70 (0.15, 3.18)	8^	88.89	1^	11.11	1.76 (0.19, 15.86)
Other	4^	57.14	3^	42.86	0.54 (0.11, 2.67)	5^	83.33	1^	16.67	1.75 (0.19, 16.30)	5^	100.00	0^	0.00	NA
Highest Education**															
1	7^	46.67	8^	53.33	ref	10^	71.43	4^	28.57	ref	12^	70.59	5^	29.41	ref
2	13^	44.83	16	55.17	0.93 (0.27, 3.24)	20	71.43	8^	28.57	1.00 (0.24, 4.14)	24	92.31	2^	7.69	5.00 (0.84, 29.66)
3	29	53.70	25	46.30	1.33 (0.42, 4.17)	36	81.82	8^	18.18	1.80 (0.45, 7.22)	34	100.00		0.00	2.02 (0.54, 7.60)
4	40	66.67	20	33.33	2.29 (0.73, 7.20)	44	80.00	11^	20.00	1.60 (0.42, 6.08)	36	76.60	11^	23.40	1.36 (0.39, 4.73)
Overall	91	56.88	69	43.13		110	78.01	31	21.99		107	81.06	25	18.94	

* Bolded indicates a statistically significant association with the odds of recovery
** Parent highest education categories: 1 graduated high school or some trade school, college or university, 3 = Diploma from trade school or college, 4 = University degree, 5 = Post-graduate degree (Master's and/or Doctorate)
^ Use caution when interpreting statistics and inferences associated with categories with low bas