The role of comorbidities on outcomes after traumatic brain injury

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Abstract

Traumatic brain injury (TBI) is a leading cause of disability and mortality worldwide resulting in a myriad of difficulties including cognitive impairment, functional disability, postconcussion syndrome (PCS) symptoms and diminished quality of life, that have been known to last many years. The epidemiological transition coinciding with rising trends in both TBIs and chronic health conditions, requires greater attention to be placed on understanding the outcomes of those with TBI who are increasingly also likely to have a health condition or comorbidity. In doing so, it furthers our current limited understanding about the additional mediating and/or moderating role that comorbidities are likely to play on delayed recovery and difficulties experienced after TBI. In the measurement of such outcomes, detailed examination of the psychometric properties of scales using modern methods such as Rasch analysis plays a central role. Psychometric analysis not only ensures that outcome measures uphold validity and reliability for use in the intended populations, but also contributes to precision medicine by increasing measurement accuracy of scales.

The aims of this thesis were twofold. The first objective was to apply Rasch analysis to evaluate the performance of the Cumulative Illness Rating Scale (CIRS), Rivermead Postconcussion Questionnaire (RPQ), as well as the WHO Quality of Life Questionnaire-BREF (WHOQoL-BREF) and its shorter derivatives in TBI and orthopaedic populations. The second objective was to develop and test a conceptual and empirically-derived model that illustrates the structural relationships between the presence of comorbidities and injury characteristics, and their impact on PCS symptoms and quality of life in TBI and orthopaedic samples. These study aims were achieved using an age-sex matched case-control sample consisting of n=109 TBI and n=114 orthopaedic patients recruited from the Midland Trauma Registry in the Waikato district of New Zealand. Participants were assessed via telephone interviews regarding their health history, ongoing symptoms and current quality of life at six months to six years post-injury.

Results from the first study using Rasch analysis demonstrated that the RPQ and WHOQoL-BREF scales are reliable and unidimensional measures of persistent postconcussion symptoms and quality of life, respectively, that can be used for assessment in individuals with either TBI or orthopaedic injuries. Shorter versions such as the EUROHIS-QOL-8 and the development of a new 12-item WHOQoL version

were also shown to be reliable measures especially useful in time-restrained settings, or where minimising respondent burden is a priority.

In the second study, multivariate linear regression identified that individuals with TBI or orthopaedic injuries, and with a history of neurological or psychiatric problems were at increased risk of reporting prolonged PCS symptoms and diminished quality of life. Findings from structural equation modelling also revealed that the persistence of post-injury psychological, neurological and musculoskeletal difficulties influenced long-term symptoms and quality of life in both groups. Previous research has misattributed PCS symptoms to the presence of a TBI, whereas a notable finding arising from these findings is that these symptoms are a significant predictor of post-injury quality of life in TBI and orthopaedic patients alike.

This thesis has made practical contributions to psychometric research, adhering to best practice guidelines with the provision of ordinal-to-interval conversion tables for improving clinical assessment. The development of a conceptual model that highlights the impact of comorbidities on injury outcomes serves as an important prognostic tool that can be useful for clinicians to identify high-risk individuals who are likely to have persisting difficulties. Prognostic modelling can therefore enable rehabilitation practitioners to modify treatment and tailor rehabilitation strategies from an early stage according to a patient's individual needs.

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Attestation of Authorship

I hereby declare that this submission is my own work, and that to the best of my knowledge and belief, contains no material previously published or written by another person (unless appropriately referenced in text).

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Shivanthi Balalla 09/09/2019

Co-authored Works

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Ethical Approval

For the conduct of this research ethical approval was sought and obtained from the Auckland University of Technology Ethics Committee (ref. 15/454) on 1 December 2015, New Zealand Health and Disability Ethics Committee (ref. 15/NTA/173) on 17 December 2015, and the Waikato District Health Board (ref. RD015127) on 26 January 2016.

Abbreviations

CFI – Comparative Fit Index

CI – Confidence Interval

CIRS – Cumulative Illness Rating Scale

DIF – Differential Item Functioning

EENT – Eyes, ears, nose, throat

GCS – Glasgow Coma Scale

GI – Gastrointestinal

GU – Genitourinary

HRQoL – Health-related quality of life

ISS – Injury Severity Score

LOS – Length of stay

NZ – New Zealand

PCS – Postconcussion Syndrome

QoL – Quality of life

RMSEA – Root Mean Square Error of Approximation

RPQ – Rivermead Postconcussion Questionnaire

SD – Standard deviation

SEM – Structural Equation Modelling

TBI –Traumatic Brain Injury

WHOQoL-BREF – World Health Organisation Quality of Life-BREF

Chapter 1 Epidemiology and classification of traumatic brain injury

1.1 Epidemiology and burden of TBI

Traumatic Brain Injury (TBI) is a leading public health issue that is a major cause of mortality and disability in the world affecting all age groups (GBD 2016 Traumatic Brain Injury and Spinal Cord Injury Collaborators, 2019). Among the many consequences of TBIs are neurocognitive impairment, functional disability, psychological distress, and other psychosocial issues such as delayed return to employment and poor quality of life (Cassidy et al., 2014; Colantonio & Biscardi, 2018; Kahan et al., 2018; Landre et al., 2006; Lin et al., 2010; McInnes et al., 2017). Global epidemiological trends as described in this chapter reveal the increasing burden of TBIs, the rising rates in attributable mortality, and the associated economic costs for many countries. This chapter additionally highlights the complexities within the current definitions and classifications of TBI. The chapter also describes the general coding systems used in trauma care, with explanations of how injuries including orthopaedic injuries used in this study, are coded. Given that enhancing measurement precision is an objective of this thesis, it is hoped that in this chapter the reader will gain an understanding of the difficulties inherent in capturing accurate estimates of injury outcomes, and the issues posed by problematic definitions and classification systems at the outset of diagnosis. The subsequent chapter will indicate that inaccuracy in these estimates is further compounded by the lack of robust data on the psychometric properties of outcome measurements.

Global incidence and prevalence rates of TBI

Current global estimates of TBI published in the latest Global Burden of Disease 2016 study reveal that there are 27.08 million (95% uncertainty interval [UI] 24.30–30.30 million) incident cases or new cases of TBI annually GBD 2016 Traumatic Brain Injury and Spinal Cord Injury Collaborators (2019). When these rates are standardised for age (to adjust for different cross-country age distributions), it emerges that every year 369 people per 100,000 population will have experienced a TBI. These estimates coincide with an apparent increase in rates of 3.6% between 1990 and 2016. The age-standardised rates in this global analysis were highest in central and eastern Europe, and central Asia, with central Europe having a rate of 857 (95% UI 750–988) per 100,000. By country, Syria had the highest age-standardised incidence rate worldwide with an

estimate of 1322 (95% UI 481–2779) cases per 100,000. In the Australasian region, age-standardised rates were estimated at 276 (UI 230–327) TBI cases per 100,000. with an apparent reduction by 12.1% between 1996 and 2016. For New Zealand (NZ) the figure in 2016 was placed slightly higher at 279 (UI 236–330) cases per 100,000 which also declined by 17.1% over 1996 and 2016. The rising number of falls and traffic-related injuries in most regions have been identified as the leading causes of TBIs (GBD 2016 Traumatic Brain Injury and Spinal Cord Injury Collaborators, 2019).

Some researchers have observed wide disparities in the reporting of incidence rates which are largely based on hospital discharge records or mortality records and that are prone to diagnostic and selection biases. The stark differences in estimates across studies have been attributed to the existence of various case definitions and case ascertainment methods e.g. hospital records versus population sampling (Maas et al., 2017; Ribbers, 2007). In contrast, population-based incidence studies, where a defined population is selected for assessment, tend to reveal higher rates than hospital-based studies (Feigin, 2013). Where hospital-based incidence rates in the USA were reported by Maas et al. (2017) to range between 69.7 to 103 per 100,000 per year, population-based estimates suggested that this figure was likely closer to 823.7 per 100,000 per year (Centers for Disease Control and Prevention, 2015; Fu et al., 2016). Within NZ, although hospital-based figures estimate the rate at 369 per 100,000 (GBD 2016 Traumatic Brain Injury and Spinal Cord Injury Collaborators, 2019), a population-based study by Feigin et al. (2013) indicated that the 'true' incidence rate of TBI was 790 per 100,000 per year. In this study, the incidence per 100,000 per year of mild TBI was estimated to be at 749 (709–790), compared to that for moderate or severe cases which was estimated at 41 (31–51). Most TBIs occurred as a result of falls (38%), mechanical forces (21%), transport accidents (20%) or assaults (17%). Feigin et al. also noted that TBI cases disproportionately affected children (0–14 years) and young adolescents (15–34 years), while males had a 77% increased risk of injury (rate ratio 1.77, 95% CI 1.58–1.97). By ethnicity, Māori had a higher risk for TBI (rate ratio 1.23, 95% CI 1.08–1.39) than the NZ European group.

Given that over 90% of all incidence cases are likely to be of mild severity, estimates reported across many studies are likely to be an underestimation of the true incidence of TBI, as it does not account for those cases that are mild to moderate that are typically not admitted to hospital (Maas et al., 2017). Additionally, the availability of robust data is limited to high income countries, with a notable gap in knowledge on estimates for

low- and middle-income countries. While much of the literature has focussed on incident rates of TBI within the general population or in specific groups (e.g. military personnel, athletes and prisoners), prevalence studies that aim to capture the total number of TBI cases alive across a period of time are sparse. A large meta-analysis conducted by James et al. (2019) showed that between 1990 and 2016 the number of prevalent cases globally was estimated to be 55.50 million (UI 53.40–57.62 million), with an age-standardised prevalence of 759 (95% UI 731–788) per 100,000 that had increased by 8.4% over this timeframe. An earlier meta-analysis by Frost et al. (2013) revealed that, from a pooled sample of 25,134 adults from 15 prevalence studies, 12% had experienced a TBI with loss of consciousness over their lifetime. Sub-group analyses also showed that males were twice as likely to experience a TBI than females (odds ratio: 2.22, 95% confidence interval [CI] 2.00–2.47). In a NZ birth cohort study of 0–25 years, 30% had indicated having experienced at least one TBI in their lifetime, with 90% of cases being mild TBI (McKinlay et al., 2008). As with incidence studies, available data on prevalence studies is limited to high income countries.

Mortality attributed to TBI

Mortality from TBI can be attributed to the direct impact of injury to the brain itself, or to complications arising from the injury. According to Mass et al. (2017), it is estimated that TBIs are responsible for approximately one million deaths worldwide, every year. Estimates for mortality vary internationally, from 0.95 per 100,000 per year in Spain to 27.20 per 100,000 per year in the USA. In the USA, TBIs contribute to 30.5% of all injury-related deaths, and have been found to reduce life-expectancy by about six years (Faul et al., 2010; Ventura et al., 2010). Within the European region, Majdan et al. (2016) reported a pooled age-adjusted mortality rate of 11.7 per 100,000 in 2012 across 25 European countries, with a wide range from 3.6 per 100,000 in Turkey to 21.8 per 100,000 in Switzerland. A NZ study has estimated the mean TBI mortality between 1999 and 2008 to be at 10.8 per 100,000 people (Kool et al., 2013).There was an apparent 32% increase in the annual rate in this period, suggesting that the fatalities arising from TBIs are of increasing importance to New Zealand. Changing epidemiologic patterns over the decades suggest that traffic-related TBI deaths are declining, but falls-related deaths are increasing worldwide, coinciding with ageing populations (Maas et al., 2017). Consequently, the highest mortality rates have been found to be concentrated in the age group of 60 years and over (Steudel et al., 2005). Similar to incidence rates described earlier, large disparities in rates across studies and

countries have been attributed to differences in diagnostic criteria and case ascertainment methods (Maas et al., 2017). There are also specific challenges in determining cause-specific deaths from mortality records such as whether deaths were directly attributed to the TBI or occurred as a result of concomitant complications.

Economic costs of TBI

TBIs are burdensome in terms of the economic costs incurred for both the individual and society. Costs can be disaggregated in the form of direct costs (resources consumed in healthcare as a result of the injury), indirect costs (resources foregone as a result of the injury such as productivity loss), and lifetime costs (ongoing costs of medical care and community services) (Te Ao et al., 2014). In Europe, it is estimated that in 2010 TBIs contributed to €33 billion in costs, with 41% accounting for direct costs to the individual, and 59% accounting for costs to society (Gustavsson et al., 2011; Olesen et al., 2012). In comparison, economic costs of TBIs are higher in the USA, likely due to the largely private-insurance based system, where indirect costs ranged from US$60.4 billion in 2000 (equivalent to about US$85.6 billion in 2017) to US$221 billion in 2009 (approximating to US$252.2 billion in 2017) (Finkelstein et al., 2006; Langlois et al., 2011). The economic burden of injuries in the USA highlight that 15% of all costs were attributed to lifetime medical costs, 31–85% to lifetime productivity loss and 62% resulting in intangible costs (e.g. loss of quality of life) (Langlois et al., 2011). In NZ the total costs incurred in the first 12 months for all new TBI cases identified in 2010 was estimated at US$47.9 million, whereas the total costs for prevalent cases (all cases) were approximated at US$101.4 million (Te Ao et al., 2014). The average costs per new TBI case in the first 12 months over a lifetime was estimated to be US$5,922 overall, for mild cases at US$4,636, and US$36,648 for moderate and severe cases. Total lifetime costs for all TBI survivors was estimated at US$146.5 million in 2010 and the authors projected this cost would increase to US$177.1 million by the year 2020 (Te Ao et al., 2014). Based on these projected trends healthcare costs due to TBI are therefore likely to experience further increases, where health systems worldwide may find cost of treatment becoming unmanageable over the next decade.

The section above highlights the increasing burden of TBIs globally and in NZ, that results in mortality and major economic costs for both the individual and society. Within NZ, there is limited robust data on national incidence and mortality rates of TBIs, concealing their true impact within the population. Furthermore, as the following sections of the chapter will show, current definitions and classification systems have

limitations in their application for accurate diagnosis of TBI, which could lead to underestimation of true cases.

1.2 Defining traumatic brain injury

There are many challenges in deriving a complete definition of traumatic brain injury, one being the difficulty in differentiating between the terms *head trauma*, *head injury*, and *brain injury*, which are often used interchangeably across research and health sectors to refer to the same type of injury. Head injuries as a collective term can encompass all injuries sustained to the brain, the skull and surrounding facial tissue, which can include brain injuries, skull fractures, and facial lacerations. *Acquired brain injury* (ABI) is typically used as an umbrella term for all brain injuries that result in post-natal cerebral damage, rather than as part of a hereditary, congenital, degenerative disorder or an injury induced by birth trauma (Brain Injury Association of America, 2020). Careful distinction needs to be made to delineate between the different subtypes of acquired brain injuries, such as between non-traumatic and traumatic brain injuries. In *non-traumatic brain injuries* damage to the cerebrum occurs as a result of internal factors such as due to a stroke, aneurysm, tumour, meningitis, lack of oxygen to the brain due to a heart attack, or a near-drowning incident (Kwan et al., 2019). *Traumatic brain injuries*, which are the focus of this research, refer to traumatically-induced injuries to the cerebral matter, including the brain stem and includes concussions, epidural and subdural haematomas, and penetrating injuries (Corrigan et al., 2019). Furthermore, the term *traumatic inertial injury* is a specific entity regarded as separate to a TBI but is also contained within the category of an ABI. These types of injuries often accompany severe TBIs, and are considered to be non-contact injuries occurring as a result of accelerating-decelerating forces within the skull (Brain Injury Association of America, 2020). Similarly, it is also worth commenting on *diffuse axonal injuries* (DAI), which are regarded as a more severe type of TBI, but which carries a separate clinical diagnosis. A DAI primarily affects axons that are sheared due to the acceleration-deceleration movements of the brain within the skull, more commonly seen in severe traffic-related injuries. These types of injuries are a major cause of coma, persistent vegetative state and death (Adams et al., 1989). Lastly, a TBI should be anatomically distinguished from a traumatic *spinal cord injury*, which can co-occur among TBI patients but which accompanies a different treatment regimen. In fact, Macciocchi et al. (2008) found that greater than 50% of spinal cord injury patients were at risk of also sustaining a TBI. In contrast to a TBI, a traumatic spinal cord injury is

categorised as an injury to any of the surrounding bones, tissue, blood vessels or neural pathways within the spinal canal, caused by an external force, and which may result in temporary or permanent sensory or motor deficits or dysfunction of the autonomic nervous system (World Health Organization Safety Promotion and Injury Control & Centre for Disease Control and Prevention, 1995).
In line with recommendations proposed by Maas et al. (2017), the term 'traumatic brain injury' or the abbreviation "TBI" will henceforth be used to refer to a brain injuries occurring as a result of external forces, for consistency throughout this thesis.

The World Health Organization (WHO), and the NZ TBI guidelines broadly define a TBI as an alteration in brain function caused by any of the following: an external force due to the head striking or being struck by an object; acceleration-deceleration movement of the brain without direct external impact to the head, due to blast forces or other undefined mechanical force (New Zealand Guidelines Group, 2006; World Health Organization Safety Promotion and Injury Control & Centre for Disease Control and Prevention, 1995). TBIs resulting from any other external causes of injury such as hanging, drowning, suffocation (anoxia), suicide, thermal mechanism (e.g. burns, hypothermia, frostbite), illicit drugs, medical or surgical intervention, or exposure to chemical/toxic poisoning are excluded from the WHO TBI case definition criteria (World Health Organization Safety Promotion and Injury Control & Centre for Disease Control and Prevention, 1995).

There are wide variations in the clinical manifestations of TBI. These are attributed to the structural complexities of the brain, and to the pattern and extent of damage, which depend on the type, intensity, direction and duration of the external force of impact (Maas et al., 2017). Although there is no gold standard for the diagnosis of TBI, many definitions still require evidence of some neurological symptoms attributed to the brain injury such as decreased level of or loss of consciousness; alteration in mental state at the time of injury (e.g. confusion, disorientation, slowed thinking, etc.); loss of memory of events immediately before or after the injury (post-traumatic amnesia); or neurological/neuropsychological changes (e.g. loss of balance, change in vision, slurring of speech, etc.) (Corrigan et al., 2019). Typically, these symptoms are confirmed by laboratory, radiological, neurological or neuropsychological examination where possible. It should be noted, however, that some forms of radiological imaging are not sensitive nor specific to TBI, and furthermore any absence of any clinical signs does not by definition rule out a TBI. There also may be instances where an individual

does not present with a loss of consciousness or a normal Glasgow Coma Scale score (GCS) but still shows evidence of injury to the brain such as a contusion on magnetic resonance imaging (MRI) scan (New Zealand Guidelines Group, 2006).

Nosology of TBI

Different classification systems exist for TBI, which include classification by severity using clinical indices (e.g. Glasgow Coma Scale), by pathoanatomic type (e.g. diffuse axonal injury, haematoma and haemorrhages, by outcome (e.g. the Glasgow Outcome Scale), or by prognosis (e.g. length of post-traumatic amnesia or loss of consciousness) (Saatman et al., 2008). Table 1 outlines the clinical criteria for the grading of TBI severity.

Table 1. Classification of traumatic brain injury severity

Clinical criteria	Mild TBI	Moderate TBI	Severe TBI
Structural imaging	Normal	Normal or abnormal	Normal or abnormal
Loss of consciousness	0–30 minutes	>30 minutes to <24 hours	>24 hours
Alteration of mental state*	A moment up to 24 hours	>24 hours	Severity based on other criteria
Post-traumatic amnesia	< 1 day	>1 day and <7 days	>7 days
Glasgow Coma Scale score†	13–15	9–12	3–8
Abbreviated Injury Scale score: Head	1–2	3	4–6

*Alteration of mental status must be immediately related to trauma to the head. Typical symptoms would include feeling dazed and uncertain of what is happening, confusion, difficulty thinking clearly or responding appropriately, being unable to describe events immediately before or after the trauma event.
†Best available score in 24 hours.
Source: Adapted from Corrigan et al. (2019)

Post-traumatic amnesia (PTA) is defined by the time interval between injury and the time until the patient is oriented and can form or recall new memories (Hawryluk & Manley, 2015). Duration of PTA is often used alongside the Glasgow Coma Scale (GCS) and length of loss of consciousness (LOC) to strengthen evidence of TBI severity. As PTA is assessed retrospectively, it can be confounded by the patient's initial confusion at time of injury. In addition, a patient's recollection of events can be influenced by what they have been told by another person, rather than what they actually recall (Bodin et al., 2012). LOC is not commonly used in isolation, but in addition to either GCS and/or PTA, as it has been found not to correlate well with

outcomes (Cantu, 2006). Lastly, the use of the Abbreviated Injury Scale which is a six-point anatomical scoring system based on mortality risk is also used to classify TBI severity, particularly in research studies. Further details of this scale are provided later in the chapter.

The Glasgow Coma Scale

Since its inception in 1974 by Teasdale and Jennett, the Glasgow Coma Scale has become ubiquitous in the neurologic assessment of injury severity, due to its high inter-rater reliability (Intraclass coefficient [ICC]=.8–1.0), simplicity, and objectivity in assessing loss of consciousness in trauma patients with TBI (Teasdale & Jennett, 1976). It is the most widely used tool for the clinical assessment of level of consciousness within 24 hours after TBI (Fischer & Mathieson, 2001). GCS scores form the basis of many important clinical decisions involving the need for use of computed tomography (CT) scans, surgical procedures and drug therapy. TBI research frequently utilises the GCS as within a set of other injury severity variables (including PTA) as a significant predictor of early and late outcome after TBI, and has shown to have moderate correlations with functional and cognitive status (Balestreri et al., 2004; Bishara et al., 1992; Zafonte et al., 1996).

Within the first 24 hours of sustaining a TBI, patients are assessed by a clinician and assigned scores for eye opening (1=no response to 4=spontaneous), verbal (1=no response to 5=appropriate/oriented conversation) and motor responses (1=no movement to 6=obeys commands). The relationship of the GCS and outcome is affected by the time of assessment where the strongest correlation is observed if assessment is conducted after initial stabilisation of *secondary brain injuries*, which then provides a more reliable indication of TBI severity than scores obtained at prehospital care or ED admission (Lesko et al., 2013; Teasdale et al., 2014). Secondary brain injuries or insults occur from cellular processes resulting from initial insult and commonly include hypoxia (lack of cerebral oxygen), hypovolaemia (severe loss of blood volume to the brain) and hypoglycaemia (lack of glucose to neurons) (Smith, 2011). Management guidelines suggest that assessment should be applied between 4 and 8 hours post-injury, and repeated measurements ideally every 30 minutes as the GCS can vary widely over this timeframe particularly if alcohol is present in the system (Jagger et al., 1983). Repeated measures of GCS scores can however inadvertently lead to difficulties in determining which score to document as evidence of severity (Yeates, 2010).

A total summed GCS score is often used to classify patients and can range from 3 to 15, with a lower score correlating with a more severe TBI. A distinction needs to be made between the Glasgow Coma Scale and the Glasgow Coma Score, which share the same acronym, and when used incorrectly can cause confusion and misleading results. The Glasgow Coma Scale refers to the subscales or three separate components of the scale: Eye-Verbal-Motor (EVM) (see Table 2), whereas the Glasgow Coma Score refers to the total summed score of the three components. According to Teasdale et al. (2014), the scale or separate components are most relevant for assessment of individual patients, whereas the GCS score is best used to distinguish across severity of groups of patients, whether it is used for auditing or research purposes. Often in clinical practice, the total score is used to categorise patients into three broad groups of TBI severity, where a GCS score of 3–8 categorises *severe* TBI, scores between 9 and 12 refer to *moderate* TBI, and 13–15 classifies *mild* TBI. However, the validity of the cut-off thresholds, which are more ad-hoc than evidence-based, have been criticised. The application of the GCS is especially problematic for the grouping of mild TBI, which assumes homogeneity across patients who may present with possible early complications or those with risks of adverse late outcomes (Servadei et al., 2001). Furthermore, not all injuries fall neatly within these thresholds, as for instance an injury can be classified as a GCS level 6 (severe TBI) but may only result in a LOC of only a few hours. This according to the clinical criteria in Table 1, indicates that this may likely be a moderate TBI.

Table 2. The Glasgow Scale components

Eye opening (E)	Verbal response (V)	Best motor response (M)
1 None	1 None	1 None
2 To pressure	2 Sounds	2 Extension
3 To speech	3 Words	3 Abnormal flexion
4 Spontaneous	4 Confused	4 Normal flexion (withdrawal)
	5 Orientated	5 Localising
		6 Obeying commands

Scores for eye (1 to 4), verbal (1 to 5) and motor responses (1 to 6). Total scores range from 3–15.

GCS and mild TBI

The heterogeneity of terms and criteria used for mild TBI patients has spurred ongoing debate about the nosological issues around brain injuries in this population, despite comprising approximately 90% of all TBI cases (Feigin et al., 2013). Classifying mild TBI is challenging due to the heterogeneity in case definitions, and the wide range of

conditions that are considered to comprise this category (Carroll et al., 2004). The Mild Traumatic Brain Injury Committee of the American Congress of Rehabilitation Medicine developed an operational definition for clinical identification of mild TBI as:

> "A traumatically induced disruption of brain function, as manifested by at least one of the following: any LOC, any loss of memory for events immediately before or after the accident, any alteration in mental state at the time of the accident, and focal neurological deficit(s) that may or not be transient"

The advisory committee also state that the severity of the injury cannot exceed a LOC of 30 minutes, PTA cannot be greater than 24 hours, and after 30 minutes of injury an initial GCS score is to be within 13 to 15 (Mild Traumatic Brain Injury Committee et al., 1993, p. 86). Since then, different adaptations of the definition above have been developed by the U.S. Centers for Disease Control and Prevention's MTBI Working Group (2003, p. 16), and the WHO Task Force on Mild Traumatic Brain Injury (2004, p. 115) that contain details on the extended time interval for recording of GCS, mechanism of injury, and mental states which are accepted as neurological deficits. Currently however, there is no consensus on the criteria for the diagnosis of mild TBI (Kristman et al., 2014). For mild TBI this can be problematic because a GCS score is often not recorded nor available immediately after injury (Dematteo et al., 2010). Furthermore, there are various case definitions for classifying mild TBI where some studies have used GCS from 13–15, some have considered only 14 and 15, and some only consider a GCS score of 15 to constitute mild TBI (Cassidy et al., 2004).

Furthermore, traditional imaging techniques such as CT and magnetic resonance imaging (MRI) are not sensitive enough to detect structural lesions in mild TBI, although more advanced neuroimaging scanning (such as functional MRI) has been used to document 'complicated' mild injuries that are pathoanatomically similar to moderate TBI (Matz, 2003). The use of the term *complicated mild TBI* further adds to the melange of terminology, which identifies mild TBI with positive neuroimaging findings. There is some evidence to suggest that complicated mild TBIs are more similar to moderate TBIs regarding neurobehavioural and neuropsychological outcomes (Levin et al., 2008). Much controversy also exists in the distinction between *concussion* and mild TBI and whether a concussion is simply a variant of mild TBI, or if it in fact represents different conditions (Maas et al., 2017). There remains no current consensus on guidelines for classifying concussions or mild TBI in the paediatric population, as current grading systems are based on the adolescent or adult brain injuries (Bodin et al.,

2012). There are additional limitations on the use of the GCS which clinicians and researchers need to acknowledge when assessing and interpreting scores. These are discussed in the next section.

Limitations of the GCS

GCS and untestable components

The use of the GCS can be challenging when assessing patients who present to the emergency department with a myriad of conditions. For example, a patient could be admitted to the emergency department having already received paralytic, anxiolytic, or analgesic drugs administered by prehospital providers (e.g. paramedics). The effects of these medications will likely confound neurologic signs (Fischer & Mathieson, 2001). In addition to the above factors, clinicians must be aware of co-occurring injuries with TBI, such as spinal cord injuries, that can potentially conflate GCS scores. In such a scenario, a patient will typically be intubated (thereby affecting verbal response), be unable to move his/her extremities but may still be able to open their eyes. For such cases, the GCS score is notably misleading and does not accurately depict the presence nor the severity of the brain injury. Teasdale et al. (2014) have in fact cautioned against combining the components where there are untestable components as it skews the GCS score, thus rendering it clinically meaningless. Other confounding factors have been noted to render GCS components untestable such as the presence of cranial nerve injuries, intoxication by drugs or alcohol, hearing impairments, dysphasia, dementia, pre-existing psychiatric disorders, ocular trauma, and even language and culture (Middleton, 2012; Zuercher et al., 2009).

The GCS is also limited in its applicability to the paediatric patient under three years of age, in that it does not incorporate the developmental differences of the infant brain in its scoring system. This is because the scoring is based on an adult patient's understanding of verbal commands which is not directly transferrable to paediatric patients (Ghaffarpasand et al., 2013). Another challenge in the paediatric context is the occurrence of hypoxic-ischemic type secondary insults that can confound GCS scores and inaccurately predict outcome in this population. To overcome these ambiguities, some have suggested that lowering the critical threshold for neurologic impairment in the severe category from 8 to 5, increases the predictive validity of GCS scores and outcome in the management of paediatric TBI (Chung et al., 2006).

To sum or not to sum?

Although the use of the total score of the GCS is common in practice and research, its usefulness has been criticised by a number of researchers, including the original authors of the scale. Teasdale and Jennett emphasised caution when utilising the summary score for convenience in lieu of separate components, as the latter entails more detailed information about a patient's clinical status (Teasdale et al., 1983). Mathematically, Bhatty (1993) critiqued that the summing of component scores results in a great loss of clinical information given that out of the 120 permutations of the total score, only 15 are clinically valid and useful for assessing loss of consciousness. Furthermore, there is a notable skewing towards the motor response component which carries more weight in the total score, and therefore the most predictive power (Bhatty & Kapoor, 1993; Vernberg et al., 1983). Research on the predictive ability of the GCS and the individual components has found that the motor component predicted outcome in severe TBI patients with the same levels of accuracy as the total GCS score (motor score sensitivity 91%, specificity 85%; total GCS score sensitivity 92%, specificity 85%) (Ross et al., 1998). Further comparisons using Receiver Operating Characteristic (ROC) curves including in mild TBI patients demonstrated that the motor component occupied similar areas under the curve (ROC=.87 to .89) as the total GCS score (ROC=.89 to .91) (Gill et al., 2005; Healey et al., 2003). Other studies have supported these findings in which the motor score was deemed equally effective if not better than the total GCS score in its ability to predict mortality in the most severely impaired group, whereas the eye and verbal components had better predictive ability of good recovery in less severe TBI groups (McNett, 2007). Others however have argued that the predictive validity of the GCS (either alone or combined with other variables such as age and brainstem reflexes such as pupillary response) does not appear to be high enough to have any usefulness in routine clinical practice (Prasad, 1996).

Reliability of the GCS

Despite being widely used as a standardised objective measurement of consciousness in TBI, no initial validation research was conducted to test for the reliability or the validity of the GCS in accurately assessing TBI severity or level of consciousness. When it was first published, Teasdale and Jennett (1976) did not provide any empirical evidence on the scale's validity, but later did publish evidence on the association of the GCS with 3-month mortality (Teasdale et al., 1978). Given that a gold standard for the evaluation of loss of consciousness does not exist, it was recommended by the original authors that the GCS not be used in isolation, but in conjunction with other important indicators

such as duration of brainstem reflexes, post-traumatic amnesia, intracranial pressure, structural damage evidenced on CT and MRI, or blood biomarkers (Teasdale et al., 1983; Teasdale et al., 2014).

In terms of reliability, some have reported on the observer variability in GCS scoring due to user experience. In a study, Rowley and Feilding (1991), observed discrepancies in the accuracy of ratings between experienced or trained users versus inexperienced users. They found that agreement level varied across segments of the scale, where agreement tended to be high for the lower (GCS 3–6) and upper (14–15) bound ranges (proportion agreement, 89.4%), but was markedly lower for the middle-range scores (proportion agreement, 30.2%). Starmark et al. (1988) found that the presence of environmental stimuli that either increased (arousal) or decreased (fatigue or habituation) responses on the scale components, consequently affected the total score. Others have also examined more closely the effect of different stimulation techniques (such as earlobe, sternal rub, supraorbital, nailbed, retromandibular, and trapezial grip) to elicit pain responsiveness, noting differences by method which consequently led to varied motor component scores (Starmark & Heath, 1988).

Section summary

This section highlighted the discrepancies among the various definitions and classification systems for the diagnosis of TBI, and the lack of consensus on the classification guidelines for mild TBI and paediatric TBI. Several authors, including the originators of the scale recommend that the commonly used Glasgow Coma Scale, be analysed as separate eye, verbal and motor components to assess TBI severity to produce more accurate information on a patient's status. When used as a total score, researchers frequently suggest that the GCS should be combined with other important predictor variables, (such as age and brainstem reflexes) to increase its predictive power on outcomes. Some limitations of the scale were highlighted, such as observer variability by experience level, low inter-rater reliability in middle range scores (GCS scores 7–13), and the effect of different stimulation techniques resulting in varied patient responses on components. Caution also needs to be exercised where components are untestable, or where clinical manifestations may be different such as for mild TBI and paediatric patients. Although findings appear to suggest that the use of motor components in place of total GCS scores yield higher predictive values in prognostic models, the evidence on the predictive ability of scores across the wider TBI spectrum (including paediatric cases) need further development. Until a sound base of guidelines

supported by robust psychometric and empirical evidence has achieved consensus amongst experts, researchers have collectively argued against the reliance on a single classification system for TBI. Rather, as asserted by Teasdale and Jennett, it is more appropriate to use a combination of measures to capture a more accurate diagnosis of TBI.

1.3 Injury coding in trauma registries

The previous section addressed the current limitations in the diagnostic criteria pertaining to the classification and grading of brain injuries. While the overarching goal of this PhD study is on understanding factors contributing to poor long-term outcomes in TBI, it is also important to understand TBI as a subset of other traumatic injuries in the trauma setting. Therefore this PhD incorporated a non-TBI sample, namely an orthopaedic injury control group in the comparison of outcomes, with the aim to make clinically relevant comparisons between the outcomes of two injury groups. In doing so, it allows one to understand the difficulties associated with the general experience of injuries, but to also identify factors that are uniquely attributable to the experience of a TBI. This section of the chapter briefly describes the general classification systems for injury coding in trauma registries, that are not specific to TBI. These systems are used to identify various injuries in the trauma setting including orthopaedic injuries, TBI and polytrauma injuries. Operational definitions for orthopaedic and polytrauma injuries used in this PhD are provided below.

Operational definition for orthopaedic and polytrauma injuries

Orthopaedic injuries are typically sub-grouped into three types: acute, chronic recurring, and chronic overuse. Chronic overuse injuries are caused by low-intensity forces of long duration such as tendinitis or bursitis, whereas chronic recurring injuries (e.g., chronic sprained ankle) are repeatedly occurring acute injuries (Knight, 2008). This PhD study included only acute orthopaedic injuries, which can be defined as acute injuries to the bones, joints, ligaments, tendons and muscles, and the skin surrounding these structures (Clay et al., 2010). Acute injuries such as fractures, sprains, strains, and contusions, are caused by sudden, high-intensity forces of short duration and often require hospital treatment (Knight, 2008). Polytrauma injuries refer to the existence of multiple systemic injuries in a patient, and can in many cases include the occurrence of a TBI (Butcher & Balogh, 2009).

International Classification of Disease

In many trauma care settings, injury diagnoses require standardised classification systems to enable standardised treatment, and to facilitate clinical auditing and health insurance reimbursements. One of the most commonly used classification systems is the International Classification of Diseases (ICD), which is the standard diagnostic tool used in epidemiology, health management, and clinical care (World Health Organization, 2016). In trauma care, ICD codes are also used for classifying mechanism of injury (e.g. vehicular crash, falls, penetrating vs blunt-type injuries). The ICD is currently in its 11th iteration and is regularly used for administrative purposes such as in hospital patient databases, and medical insurance reimbursements. However, one of the main limitations of the system is its limited ability to describe disease or injury severity. Owing to its unidimensional coding system, only one code is assigned for the description of multiple injuries, which therefore results in a loss of information. For example, where multiple injuries occur in a patient, often only the primary diagnosis is included, or a broad classification of 'multiple injuries' may be given (Aharonson-Daniel et al., 2005; Goldacre et al., 2003).

Despite definitions of TBI provided by advisory panels, there appears to be a lack of consensus on the most appropriate ICD codes for identification of brain injuries. It is therefore imperative that codes are selected for their comprehensiveness and for their ability to permit differential diagnosis. Having a standard defined set of codes also allows for comparability across countries. However, while using a broad set of codes may allow for more inclusion of TBI cases, it can also result in more false-positive cases and overinflated incidence of TBI rates, whereas a conservative definition results in some cases being missed (Chen & Colantonio, 2011). A review of the use of ICD-10 codes for neurotrauma surveillance by Barker-Collo and colleagues (2016) revealed a wide variation in the different codes used for defining TBI, with only half of individuals with potential TBIs being identified. Of concern was the finding that only 25% of hospitalised TBI patients were likely to receive an ICD-10 coding for a brain injury, reflecting the poor implementation of codes by medical personnel in the hospital setting, despite sufficient information being available in patient medical records.

Abbreviated Injury Scale and Injury Severity Scale

In contrast to the ICD, the Abbreviated Injury Scale (AIS) utilises a multidimensional coding system to assign a code and severity to each injury, and is widely used in trauma registries. Often, both the ICD and AIS classifications are simultaneously used in

patient systems, which can sometimes lead to duplicate coding or ambiguous cross-conversions (Nakahara et al., 2014).

The AIS was originally devised in 1971 by the Committee on Medical Aspects of Automotive Safety as a standardised system to categorise vehicular crash injuries by type and severity, and it is typically used in trauma care to code location and severity of all injuries (Huelke, 1975). The AIS coding structure consists of a seven-digit numeric code comprising of the *pre-dot code* for the first 6 digits and followed by a *post-dot* code as the last digit after the dot. The pre-dot code represents the body area of injury, anatomical structure(s) involved, and the level of injury. The post-dot digit denotes the severity of the injury to nine body regions, on a 6-point ordinal scale as follows: 1=minor; 2=moderate; 3=serious; 4=severe; 5=critical; 6=maximum (currently untreatable) and 9=unknown severity. The AIS Dictionary (Gennarelli & Wodzin, 2008) has 6 separate categories of code groups used for reporting and corresponds to injury types as defined below:

- AIS region 1 = Head/Neck
- AIS region 2 = Face
- AIS region 3 = Chest/Thorax
- AIS region 4 = Abdomen-Lumbar Spine
- AIS region 5 = Extremities, Shoulder and Pelvic girdle
- AIS region 6 = External including burns., hypothermia, asphyxiation, drowning, electrocution, and full body explosion.

To illustrate, an example of a femoral shaft fracture will have an accompanying AIS code of *851814.3* and can be explained as follows:

8= Body Region: *Lower extremity*
5 = Type of Anatomic Structure: *Skeletal*
18 = Specific Anatomic Structure: *Femur*
14 = Level of Injury: *Shaft*
.3 = AIS: *Severity Score*

The AIS demonstrates a non-linear relationship with survival (and mortality), where non-linearity at the lower severity levels indicates that mortality is not as important as for higher severity levels (Gennarelli & Wodzin, 2006). The most recent update, the AIS-2005, improved from the previous version AIS 1998 to be able to capture more

detailed information on TBIs, particularly hypoxic brain injuries and concussive TBI, and to better reflect clinical severity (Carroll et al., 2010). At the outset, the committee recognised that the AIS was limited by its ability to only describe the severity of individual injuries. A simple mathematical addition of all AIS scores across different systems to produce an average score was not possible as the quantitative relationship of AIS scores was not known (States et al., 1971). This limitation subsequently led to the development of the Injury Severity Score (ISS), which aimed to give a numerical rating across patients with multiple injuries, and which enables a total injury severity score to be derived (Baker & O'Neill, 1976).

Injury Severity Score

The ISS is the most commonly used measure of injury severity in hospital trauma care and is primarily used for the assessment of severity of multiple injuries across different injury groups. The ISS is defined as "the sum of the squares of the highest AIS grade in each of the three most severely injured areas" and provides a single measure of overall injury severity of an individual (Baker et al., 1974, p. 190). Scores can range from to 0 to 75, with higher scores denoting higher injury severity. Accordingly, minor and major injuries are categorised as ISS<16, and ISS 16–75, respectively. Injuries scored as AIS-6 (unsurvivable injury) are automatically assigned the highest ISS score of 75. An example of a score calculation for a fictitious polytrauma case is provided in Table 3.

Table 3. Calculation of the Injury Severity Score using an example from a fictitious participant

Body region	Injury description	AIS	Square of highest three AIS scores
1 Head & Neck	Cerebral contusion	3	**9**
2 Face	No injury	0	
3 Chest	Flail chest	4	**16**
4 Abdomen	Minor contusion of liver	2	
	Complex rupture of spleen	5	**25**
5 Extremity	Fractured femur	3	
6 External	No injury	0	
		Total ISS	**50**

Possible ranges 0 to 75; ISS<16=minor trauma; ISS> 16=major trauma
Source: The TraumaBank Information Repository http://www.trauma.org/archive/scores/iss.html

The ISS was originally intended to predict mortality risk of different severity groups but has also been correlated with outcomes such as length of hospital stay and cost (States et al., 1971). However, several studies have found that the ISS does not portray a linear relationship with mortality, and its relationships with other health outcomes is not known (Bellamy & Vayer, 1988; Beverland & Rutherford, 1983; Bull, 1978; Linn, 1995). One criticism of the ISS has been its inability to account for multiple injuries in the same body region, as it only captures the most severe injury in each region, whereas the less severe injury in the same region is not considered in the score (Poole et al., 1996). Multiple injuries in the same region is possible for instance in penetrating injuries (e.g., gunshot or stab wounds) or in lower extremity injuries. The cumulative effect of multiple injuries in each region carries important implications for a patient's recovery but is excluded from the ISS algorithm (Linn, 1995). Baker et al. (1974) also noted that the ISS is a better predictor of outcome for blunt injuries compared with penetrating injuries. As the ISS was designed to give equal importance to each body region it can overlook the severity of specific injuries. Compared to the AIS, the ISS attempts to summarise injuries in six categories of body regions, with only one category grouping all extremity injuries, and therefore does not account for the cumulative impact of extremity injuries.

The psychometric properties of the AIS and ISS are limited, with only scattered evidence available across a few studies. With regards to inter-rater reliability of the AIS 1980 version, Mackenzie, Shapiro and Eastham (1985) observed that physicians and nurses demonstrated higher reliability in ratings (ICC=.83 and .80, respectively) than emergency medical technicians (ICC=.76) or nonclinical technicians (ICC=.66), reflecting the years of clinical experience received despite having the same training prior to the assessment. Like its predecessor, the ISS has undergone changes over the decades and given birth to other trauma scoring systems such as the New Injury Severity which has shown to be a better predictor of survival with improved statistical performance (Osler et al., 1997).

1.4 Chapter summary

Chapter 1 introduced the epidemiological trends underlying the increase in TBI rates and associated mortality and economic costs. This chapter has also shown that there is more than one way to define and classify injuries such as with the Glasgow Coma Scale, International Classification of Disease, Abbreviated Injury Scale and Injury Severity Score, and it is important to bear in mind the limitations with each method. In light of these challenges, trauma registries often employ more than one scoring system in the coding of injuries. However, the lack of rigour in consistency in recording and lack of agreement on the correct use of codes leads to problematic representation of injuries, with a notable underreporting of TBIs in hospital data. It is recognised that there is no simple solution to the categorisation of injuries, yet further gains need to be made to arrive at an agreed set of guidelines and a standardised classification system. The chapter that follows is a literature review that describes some of the gaps in current literature, particularly concerning the impact of comorbidities on outcomes after TBI.

Chapter 2 The impact of comorbidities on outcomes after TBI: A focussed literature review

Chapter 1 navigated through the many and often complex classification systems involved in trauma care and the diagnosis of TBI. The chapter also illustrated the growing burden of TBIs highlighting some of the resulting effects including mortality and socioeconomic costs. The consequences of TBIs are numerous and include ongoing symptom experience and detrimental effects on quality of life. While it is recognised by some that the effect of a person's health bears significance on a variety of outcomes and prognosis (Librero et al., 1999), this relationship remains poorly measured and understood especially in the TBI literature. This review therefore aims to portray the current burden of health conditions or comorbidities in the TBI population, and to understand based on available evidence the potential impacts of comorbidities on injury outcomes such as postconcussion symptoms and quality of life.

2.1 Comorbidity definition and importance on outcome after TBI

Comorbidity is an important concept to measure as it has an important role in the treatment, prognosis and consequently health outcomes for an individual. According to Feinstein comorbidity can be defined as "any distinct additional entity that has existed or that may occur during the clinical course of a patient who has the index disease under study" (Feinstein, 1970, pp. 456-457). Similarly, the term *multimorbidity* can be broadly defined as the presence of multiple diseases or medical conditions in an individual (van den Akker et al., 1996).

Comorbidity is a difficult construct to measure due to the complexity of the construct itself, as well as limitations of data, and hence there is little consensus in how best to define and measure it. Sarfati (2012) highlights some key points that need to be considered when defining and measuring comorbidity. Defining what constitutes a comorbid condition can be difficult and gives rise to ambiguity. For example, conditions can be defined as specific problems e.g. angina, peripheral vascular disease or previous myocardial infarction or more broadly referred to as a group of related conditions called 'cardiovascular disease'. The definition depends on several factors such as the severity and nature of the primary condition, as well as disease aetiology and the outcome being investigated (Valderas et al., 2009). The importance of comorbidities also depends on the primary disease of interest. For instance, the impact and importance of any co-existing conditions on outcomes for a patient with breast

cancer would likely be different to that for a patient with congestive heart failure, and likewise more different for an individual suffering from psychological difficulties. Hence, some researchers have suggested that disease-specific measures may be more appropriate to use than general ones (van de Groot et al., 2003; van den Akker et al., 2001). It is also often difficult to understand and discern between the combined effects of comorbidities as conditions may or not have a synergistic effect on each other, and where an effect does exist, it may be additive or multiplicative (Sarfati, 2012). Furthermore, time is an important consideration for assessing outcome. A study by Preen and colleagues found that comorbidities present upon admission or the previous year were best predictive of mortality, whereas longer lookback periods (i.e. five years prior) were better able to predict hospital readmission rates (Preen et al., 2006).

Clinical profile of pre-existing comorbidities among TBI patients

TBI patients often present with pre-existing illnesses that can impact on their recovery from their injury. Previous research has found that between 10 and 55% of all TBI diagnoses are likely to present with baseline comorbidities (Myburgh et al., 2008; Yue et al., 2019), with older female TBI patients more likely to have a significantly higher proportion of comorbid disease upon admission to inpatient rehabilitation, than males (p<.001) (Chan et al., 2017). Although pre-injury health conditions are routinely collected during patient admission and documented in medical records, this information rarely receives attention in research as a potential prognostic indicator of recovery (Yue et al., 2019). The presence of these conditions has implications for the management of TBI patients, yet data on the prevalence of pre-existing illness prior to TBI is limited and variable. Evidence from international studies supports the common occurrence of pre-existing conditions in the TBI population which have been summarised in Table 4.

Comorbidities by age and sex

Chan et al. (2017) looked at the detailed clinical profile of TBI patients segregated by age and gender at acute inpatient rehabilitation. They found that a higher percentage of females than males experienced conditions of the endocrine, nutrition, metabolism and immune systems, as well as problems related to the circulatory and musculoskeletal systems (p<.001). Stratified by age, the proportions revealed that the most common comorbidities in younger patients (< 65 years) at rehabilitation in both sexes were related to mental health (34.1% males, 28.6% females) and the nervous system (29.0% male, 33.1% females). Among older patients aged 65 years and above, problems concerning the circulatory system were the most common health condition in both

sexes. Among older men, conditions specifically relating to the endocrine, nutrition, metabolism and immune systems (37.6%) and the nervous system (32.0%) were frequently reported, whereas older female TBI patients had significantly higher proportion of conditions relating to the musculoskeletal system (45.9%) than men (p<.001). Older men also commonly reported problems of the endocrine, nutrition, metabolism and immune systems (43.7%).

Although this retrospective study remains to date the only source of comprehensive information regarding the comorbidity burden in the TBI population, there are a number of limitations that affect the generalisability of findings to the wider spectrum of TBIs. One limitation is that comorbidities were only ascertained during admission at acute inpatient rehabilitation through medical record review and therefore it is unclear whether some conditions (such as musculoskeletal problems, nervous system disorders or psychological disturbances) were present prior to the injury or arose as a complication or consequence of the trauma itself. Another limitation is that acute inpatient rehabilitation facilities are more likely to be the discharge destination recommended for the rehabilitation of moderate to severe TBI patients, while those with less severe brain injuries are more likely to be discharged home (Zarshenas et al., 2019). Therefore, the clinical profile of patients illustrated in the study may not represent the majority of TBI patients in the general population, who are likely to have a mild TBI (Feigin et al., 2013). Lastly, the authors only carried out a cross-sectional analysis of comorbidities, without further investigating whether the presence of comorbidities predicted poor recovery.

Other studies have commented on various pre-existing conditions in the TBI population. Findings on the most commonly reported types of pre-existing conditions from other studies are summarised in the following sub-sections.

Table 4: Pre-existing disease in studies of TBI patients

ICD-10 Disease Groups	Prevalence (%)	Characteristics of sample	First Author (year)
Cardiovascular disease	18.7	All adult TBIs	Myburgh (2008)
	20.4	Blunt mild TBI	Yue (2019)
	79.6	All TBIs, mean age 71.7 years	Lustenberger (2013)
	20–80	All TBIs in acute inpatient rehabilitation	Chan (2017)
Hypertension	0.6	TBI vs TBI and other injuries	Rincon (2012)
	10.0	Moderate to severe TBI	Labi (2003)
	23.8	Blunt mild TBI	Yue (2019)
	29.0	ISS >9, polytrauma	Sellmann (2012)
	41.0	All adult TBIs	Gardizi (2014)
	41.4	>55 years, all blunt TBI	Thompson (2012)
	44.0	All TBIs	Lew (2002
	52.6	>50 years, moderate to severe TBI	Kumar (2018)
	56.2	TBI with/without renal failure	Liao (2014)
Cardiac arrhythmias	11.1	>55 years, all blunt TBI	Thompson (2012)
Coronary artery disease	9.9	>55 years, all blunt TBI	Thompson (2012)
Congestive heart failure	5.3	TBI vs TBI and other injuries	Rincon (2012)
	5.1	TBI with/without renal failure	Liao (2014)
	11.0	All TBIs	Lew (2002)
Myocardial infarction	2.8	TBI with/without renal failure	Liao (2014)
	7.4	>55 years, all blunt TBI	Thompson (2012)
Neurological problems	6.2	>55 years, all blunt TBI	Thompson (2012)
	22.0	All adult TBIs	Myburgh (2008)
	22.2	All TBIs, mean age 71.7 years	Lustenberger (2013)
	30–40	All TBIs in acute inpatient rehabilitation	Chan (2017)
Speech and swallowing difficulties	10–20	All TBIs in acute inpatient rehabilitation	Chan (2017)
History of TBI	2.0	Severe TBI	Baguley (2012)
History of seizures	8.5	Blunt mild TBI	Yue (2019)
	22.0	All TBIs	Lew (2002)

ICD-10 Disease Groups	Prevalence (%)	Characteristics of sample	First Author (year)
Headache/migraine history	11.5	Blunt mild TBI	Yue (2019)
Epilepsy	3.0	Severe TBI	Baguley (2012)
Parkinsonism	11.0	All TBIs	Lew (2002)
Stroke	65.5	TBI with/without renal failure	Liao (2014)
Psychiatric/behavioural disorders	4.3	All TBIs, population-based cohort	Cameron (2008)
	15–85	Severe TBI	Baguley (2012)
	30.0	Blunt mild TBI	Yue (2019)
	38.0	All TBIs in acute inpatient rehabilitation	Chan (2017)
Substance abuse	21.9	All adult TBIs	Myburgh (2008)
	29–71	Severe TBI	Baguley (2012)
Illicit drug use	10.0	Mild TBI	Robertson (1994)
	28.0	Severe TBI	Novack (2001)
	21–53	Review of studies	Taylor (2003)
Alcohol abuse	20.0	Mild TBI	Robertson (1994)
	25.3	>55 years, all blunt TBI	Thompson (2012)
	29.9	Severe TBI	Novack (2001)
	42–58.7	Review of studies	Taylor (2003)
Respiratory disease	13.1	All TBI	Myburgh (2008)
	18–20	All TBIs in acute inpatient rehabilitation	Chan (2017)
	51.8	>50 years, moderate to severe TBI	Kumar (2018)
Chronic pulmonary disease	4.8	TBI vs TBI and other injuries	Rincon (2012)
	8.6	>55 years, all blunt TBI	Thompson (2012)
	11.2	All TBIs, mean age 71.7 years	Lustenberger (2013)
	15.0	Blunt mild TBI	Yue (2019)
Metabolic/endocrine disorders	10–42	All TBIs in acute inpatient rehabilitation	Chan (2017)
Type 2 Diabetes Mellitus	8.1	Blunt mild TBI	Yue (2019)
	9.3	>55 years, all blunt TBI	Thompson (2012)
	10.8	TBI vs TBI and other injuries	Rincon (2012)
	27.0	TBI with/without renal failure	Liao (2014)

ICD-10 Disease Groups	Prevalence (%)	Characteristics of sample	First Author (year)
Renal	5.8	Blunt mild TBI	Yue (2019)
Chronic kidney failure	2.9	TBI vs. TBI and extracranial injuries	Rincon (2012)
Thyroid	5.0	Blunt mild TBI	Yue (2019)
Fluid imbalances	43.7	>50 years, moderate to severe TBI	Kumar (2018)
Skin/Musculoskeletal conditions	4.9	All TBIs, population-based cohort	Cameron (2008)
	23.0	All adult TBIs	Gardizi (2014)
	23–50	All TBIs in acute inpatient rehabilitation	Chan (2017)
Chronic back pain	11.0	All TBIs	Lew (2002)
Rheumatoid arthritis	7.4	>55 years, all blunt TBI	Thompson (2012)
Skin and subcutaneous tissue	2–5	All TBIs in acute inpatient rehabilitation	Chan (2017)
Others			
EENT problems	8–30	All TBIs in acute inpatient rehabilitation	Chan (2017)
	47.0	All adult TBIs	Gardizi (2014)
Gastrointestinal	15.8	Blunt mild TBI	Yue (2019)
	17–20	All TBIs in acute inpatient rehabilitation	Chan (2017)
Genitourinary	18–25	All TBIs in acute inpatient rehabilitation	Chan (2017)
Haematologic	5.0	Blunt mild TBI	Yue (2019)
	2–10	All TBIs in acute inpatient rehabilitation	Chan (2017)
Anaemia	5.6	>55 years, all blunt TBI	Thompson (2012)
Hepatic	7.7	Blunt mild TBI	Yue (2019)
Liver cirrhosis	0.2	TBI vs TBI and other injuries	Rincon (2012)
	0.7	All TBIs, mean age 71.7 years	Lustenberger (2013)
Neoplasms	0.1	TBI vs TBI and other injuries	Rincon (2012)
	2–17	All TBIs in acute inpatient rehabilitation	Chan (2017)
Infectious/parasitic	8–10	All TBIs in acute inpatient rehabilitation	Chan (2017)

EENT=problems relating to the eyes, ears, nose, throat

Cardiovascular disease

As shown in Table 4, pre-existing cardiovascular diseases are one of the most commonly reported groups of diseases in TBI literature, ranging from 18.7 to 80% across different reports (Chan et al., 2017; Lustenberger et al., 2013; Myburgh et al., 2008; Yue et al., 2019). The prevalence has been found to be as high as 80% among TBI patients as reported in a large elderly trauma sample of 35,005 patients from the US National Trauma Data Bank, with 90% aged >55 years (Lustenberger et al., 2013). Another study found that among TBI patients diseases of the circulatory system were more prevalent among females (50.4%) than males (34.5%) (Chan et al., 2017). Within the group of cardiovascular disease conditions such as congestive heart failure, coronary artery disease, arrythmias and myocardial infarction have frequencies around or less than 10%, with marginally higher figures reported in elderly samples.

Hypertension

Pre-existing hypertension as a risk factor for cardiovascular disease is another frequently reported condition, with prevalence ranging from 0.6% and 41% across different TBI studies (Gardizi et al., 2014; Labi et al., 2003; Rincon et al., 2012; Sellmann et al., 2012; Thompson et al., 2012). The large variation among these studies can be explained by heterogenous samples, such as in the study by Thompson et al. (2012), which noted a high prevalence of 41% among elderly patients. In other studies by Sellmann (2012) and Rincon (2012) where samples consisted of polytrauma TBI patients, it is unclear whether recorded high blood pressure occurred as a result of complications due to the presence of extracranial injuries, or whether hypertension was a pre-existing condition.

Psychiatric and behavioural disorders

Pre-injury psychiatric and behavioural problems have a wide variation in prevalence owing to the different sample compositions (mild versus moderate/severe TBI) and different methods of information retrieval (e.g. medical records review versus self-report). Up to 30% of participants with mild TBI reported having prior psychological difficulties (Yue et al., 2019), with some prevalence figures ranging from 15% to 85% among severe TBI patients as reviewed by Baguley et al. (2012). Chan et al., (2017) found that previous injury and trauma was the most common pre-injury comorbidity among younger TBI patients (prevalence approximately 45%). This was followed by previous mental health problems, as the second most common comorbidity that affected between 28% of females and 35% of males in their sample. In contrast, population-

based studies such as by Cameron et al.(2008) revealed much lower estimates at 4.3% for psychiatric history. However in this study pre-existing psychological problems were determined only from health service utilisation, which only captures a small proportion of patients who are affected. Among psychological disorders, prior history of substance abuse is commonly reported among TBI patients with figures ranging from 10–22%, (Myburgh et al., 2008; Robertson Jr. et al., 1994), while among severe TBI patients reported figures range from 21.9% to as high as 71% (Baguley et al., 2012). Alcohol dependence (20–58.7%) is more commonly reported than for drug use (10–53%) (Baguley et al., 2012; Castaño-Monsalve et al., 2013; Robertson Jr. et al., 1994; Thompson et al., 2012). Baguley et al. (2012) noted large discrepancies between figures when alcohol/drug use history was verified through medical records (29%) versus history ascertained through self-report (71%). The authors also found that for 85% of participants, psychological history was not reported in medical records.

Neurological problems

The existence of prior neurological problems such as history of post-traumatic seizures (22%) and stroke (65.5%) appear to be common neurological problems affecting predominantly elderly patients (Liao et al., 2014). Some studies have noted that among severe TBI samples, there is a small proportion that have prior history of TBI (2%) and epilepsy (3%) which correlates with previous evidence that links these conditions as risk factors for TBI (Feigin et al., 2010). Yue et al. (2019) noted that even among mild TBI patients a small proportion (8.5%) reported having a past history of TBI and/or seizures.

Other conditions

Across the literature there is scattered evidence on the prevalence of other pre-existing medical comorbidities that include respiratory problems ranging from 4.8–13.1%. Among older patients (>50 years) with moderate or severe TBI, prevalence of respiratory problems was 51.8% (Kumar et al., 2018). In addition, the prevalence of musculoskeletal conditions (23–50%), particularly chronic back pain and rheumatoid arthritis appear to be the most common pre-injury complaints among elderly patients, and those presenting to acute rehabilitation care (Chan et al., 2017; Gardizi et al., 2014). Pre-existing diabetes is also a common condition in this cohort ranging from 9.3% to 27% (Lew et al., 2002; Rincon et al., 2012; Thompson et al., 2012).

Section summary

Whilst there is inconsistent evidence regarding the nature of pre-existing illness among TBI patients, the wide variation in prevalence of certain conditions such as cardiovascular and neurological problems is a reflection of the age composition and other clinical differences of the cohorts studied. There is a tendency for more severely injured TBI patients to report higher prevalence of prior psychiatric or behavioural problems (such as alcohol and drug use) and neurological conditions (e.g. past TBI or seizures). Different sample compositions (by injury severity and age-group) and recruitment methods employed across studies may also in part explain the high variability in prevalence rates obtained. The heterogeneity in study samples therefore greatly limits the ability to pool data on pre-injury comorbidities, and to extrapolate findings to the wider spectrum of the TBI population. When ascertaining prevalence of psychological disorders researchers also need to be keenly aware of methods of data collection. As noted by Baguley (2012) there are marked differences in prevalence figures between self-report measures and medical record reviews, the former perhaps enabling more accurate measures of psychological problems.

2.2 Outcomes after TBI and the role of comorbidities

There is an abundance of evidence highlighting the association of comorbidity with a range of negative health outcomes, such as increased length of hospital stay, disability, quality of life, complications and mortality (Fortin et al., 2005; Gijsen et al., 2001; Satariano & Silliman, 2003). Comorbidities carry important clinical implications as TBIs may exacerbate pre-existing conditions or contribute to the development of new conditions following injury, such as the onset of neurological disorders and neurodegenerative diseases (Crane et al., 2016; Pavlovic et al., 2019). Additionally, comorbidities in injury patients also affect the treatment course that patients receive in both acute and rehabilitation settings, and can affect prognosis and injury outcomes (Mollayeva et al., 2017). Many acute care studies have focussed on the effect of comorbidity on mortality, and have identified patients with prior cardiovascular problems, stroke and diabetes mellitus as being particularly susceptible to a fatal outcome after TBI. Thompson et al. (2012) found that having a prior history of heart attack raised a patient's risk of in-hospital death by about 14 times (relative risk 14.3, 95% CI 2.1–97.1). Risk of mortality is also especially high for those with severe TBI and epilepsy, resulting in a doubling of risk of mortality (standardized mortality ratio of 2.11, 95% CI 1.35–3.30). From a health economics perspective, TBI patients with pre-

existing comorbidities also have higher health resources consumption and as a result incur higher hospital and medical costs (Te Ao et al., 2014). This is especially true for older patients with pre-existing comorbidities who have increasing healthcare needs, and for others who are unable to care for themselves following a TBI (Colantonio et al., 2011). There is a lack of research addressing how patients living with multiple conditions view their illness, and how the effects of illness impact on their day-to-day life.

Findings from these hospital-based studies clearly depict a strong association with prior comorbidities and mortality; however, the majority of the studies are composed of samples with moderate or severe TBIs. Therefore, caution must be exercised when extrapolating these findings to those who have experienced a mild TBI, as it is unclear whether the same conditions are associated with similar risks in adverse outcomes, or if other comorbidities not yet investigated should be considered as important prognostic indicators of outcomes. As many of these studies are conducted in the trauma setting, outcomes of interest are usually concerning clinical prognosis within the acute care setting, such as on risk of complications, length of days in the ICU/ventilator, discharge status, or mortality risk. Furthermore, the majority of these studies are focussed on the elderly population, for whom comorbidity burden is high, and it is unclear what comorbidity profiles are associated with younger TBI patients. Greater emphasis needs to be placed on long-term outcomes that extend beyond the hospital setting, and to determine whether the effects of comorbidity and TBI are inextricably linked with worse outcomes many years after injuries.

The sections that follow will discuss two commonly investigated outcomes for assessing recovery after TBI, namely the onset of postconcussion symptoms and effects of the injury on quality of life. The literature will also be reviewed regarding the effects of comorbidities and TBI exerted on these two outcomes.

Postconcussion syndrome and current debates in its classification and aetiology

One of the most commonly discussed outcomes in the area of mild TBI research is the onset of what is referred to as *postconcussion syndrome (PCS) symptoms* that occur after TBI. The existence of PCS symptoms or *postconcussion symptoms* is a heavily debated topic in TBI research, and despite decades of research into understanding this entity, its aetiology and validity of diagnosis remain controversial. PCS symptoms refer

to a constellation of symptoms commonly reported following concussion or mild TBI and can include headaches, fatigue, vertigo/dizziness, irritability, emotional lability, cognitive difficulty (e.g. memory or concentration), sleep disturbance, depression and/or anxiety (Broshek et al., 2015). It is estimated that 10–20% of patients who sustain a mild TBI will likely go on to experience PCS symptoms, which are known to last more than five years and even up to 10 years after TBI (Ashman et al., 2006; O'Connor et al., 2005). Although few studies exist, these symptoms have been found to affect those with moderate to severe TBI as well, but to a lesser extent (O'Connor et al., 2005). In one study, 40% of mild TBI, 30% of moderate TBI and 15% of severe TBI patients were diagnosed with PCS symptoms at three months after injury (Sigurdardottir, Andelic, Roe, & Schanke, 2009). While the prevalence of symptoms subsided for the mild group to 27% at 12 months post-injury, proportions remained relatively unchanged for the moderate (27%) and severe TBI groups (18%). Among those with extracranial injuries, estimates can vary anywhere from 7% to 40%, depending on the diagnostic criteria used (Boake et al., 2005). As expected, the prevalence of postconcussive symptoms in the TBI population subsides across the recovery trajectory with more frequent and severe symptoms being reported in the initial stages of injury (King et al., 1995). More than 50% of patients report experiencing at least one symptom immediately after TBI, commonly symptoms of fatigue, headaches, taking longer to think, forgetfulness, and dizziness (Barker-Collo et al., 2018). At six months post-injury less than half of patients report at least one symptom, and by 12 months more than 30% still experience ongoing symptoms of fatigue, taking longer to think and forgetfulness. Symptoms of visual disturbance (e.g. double vision) and nausea/vomiting are the least frequently reported (less than 10% of participants) (Barker-Collo et al., 2018; King et al., 1995). While symptoms generally dissipate over time, the small proportion of people who experience prolonged symptoms is sometimes referred to as the “miserable minority” (Ruff et al., 1996).

PCS symptoms as a condition can be diagnosed clinically using the criteria in the Diagnostic and Statistical Manual of Mental Disorders (DSM) (American Psychiatric Association, 1994) or the ICD-10 (World Health Organization, 1993). One notable difference between the two criteria is that according to the DSM-IV, the onset of symptoms must be immediate, and be persistent for at least three months, whereas this is not an explicit criterion stated in the ICD-10. The ICD-10 requires only that at least three symptoms are present for a definite diagnosis (World Health Organization, 1993).

The current version of the manual, the DSM-V omits postconcussion syndrome as a separate condition, but is instead simply referred to as “mild neurocognitive disorder due to TBI” which does not necessitate formal evidence of cognitive deficits for a diagnosis (Polinder et al., 2018). The criteria in the previous version of the manual, the DSM-IV, were viewed as a more stringent diagnostic tool than the ICD-10. In a cohort study of mild TBI patients comparisons between the two classification systems revealed that 64% in the sample were diagnosed as having PCS symptoms using the ICD-10 criteria, in comparison to only 11% who met the criteria according to the DSM-IV (Boake et al., 2005). The lack of specificity in the symptom cluster attributed to mild TBI and variability in diagnostic criteria make accurate case ascertainment for clinicians quite problematic, and have thus led to variable estimates across the literature (Mayer et al., 2017).

Further adding to the controversy around PCS is the non-specificity of the condition, where some researchers have argued that PCS symptoms is an entity not specific to the occurrence of a brain injury given that almost identical symptoms can manifest in other groups (Iverson & Gaetz, 2004; Meares et al., 2008; 2011). These assertions are supported by the mounting evidence for the presence of symptoms among depressed, chronic pain, spinal cord injury, and orthopaedic samples, but increasingly also among healthy populations (Chan, 2001; Gasquoine, 2000; Iverson, 2006; Iverson & Lange, 2003; Masson et al., 1996; Meares et al., 2011; Mickevičiene et al., 2004; O'Connor et al., 2005; Sawchyn et al., 2000; Smith-Seemiller et al., 2003; Snell et al., 2018; Theadom et al., 2018; Wang, Chan, et al., 2006). In fact, in a sample of healthy participants with no prior history of TBI or neurologic/psychiatric illness, Chan (2001) found unprecedented levels of symptoms reported by participants, where 66% reported taking longer time to think, 59% experienced forgetfulness and poor concentration, while 50–54% reported fatigue and sleep disturbance. Although the sample size was small (n=85) and was mostly composed of females (74%), the proportions allude to the normalcy of such symptoms even amongst healthy individuals.

Lishman first began postulating the differences in symptomatology in a review of PCS in 1988, where he distinguished between *physiogenesis* and *psychogenesis* in symptom presentation, noting that the interplay between organic and non-organic contributions was time-dependent (Lishman, 1988). He categorised the presentation of acute symptoms as those attributed to neurobiological mechanisms of a cerebral injury, as *physiogenic factors*. As physiogenic factors resolve over time he hypothesised that other

circumstantial factors related to the experience of an injury or trauma, termed *psychogenic factors* take precedence and contribute to the persistence of symptoms. In fact, in a later review, Silverberg and Iverson (2011) re-evaluated the literature and concluded that both neurobiological and psychological factors play an important part in the presentation of symptoms in the early stages of recovery. Regarding psychological factors, they asserted that these not only contribute to symptoms in the early stages of recovery, but also explain the persistence of lingering symptoms of PCS in the later phases of recovery. Further adding to the debate is Rees' (2003) proposition that the pathophysiological triggers of PCS symptoms in the hyperarousal limbic system are virtually the same as in posttraumatic syndrome (including posttraumatic stress disorder), and therefore the two are biologically inseparable. As such as he argues against the existence of PCS as a distinguishable entity.

Another highly debated topic in PCS literature is the misattribution and expectancy effects of symptoms on the experience of a TBI (Snell et al., 2013). The *expectation as aetiology* was a term coined by Mittenberg et al., which explains the phenomenon of attributing current albeit common symptoms to the previous experience of a TBI (Mittenberg et al., 1992). To demonstrate this, the team conducted a pseudo-experimental study, where a sample of 100 TBI participants were asked to indicate current symptoms, and any past symptoms previous to the mild TBI from a checklist of cognitive, affective and somatic symptoms. Similarly, a sample of 223 health community controls were asked to endorse any current symptoms, and also any symptoms they might expect to experience if they had sustained a brain injury in a simulated scenario. Whilst individuals who had a TBI endorsed 60% fewer symptoms pre-injury relative to the base rate for healthy controls, both groups appeared to report a higher number of symptoms currently experienced or imagined (for the controls). As such it was gathered from these results that there was a tendency for an expectation bias of symptoms to occur following a TBI, wherein individuals misattribute common symptoms and ailments (e.g. fatigue, depressed feelings) to the experience of a brain injury. In a similar vein, Snell et al. (2013), explored the effects on injury beliefs on outcome after mild TBI using Leventhal's Common Sense Model of illness perception (Leventhal et al., 1998). In their study it was found that participants who endorsed stronger injury identity beliefs (i.e. stronger symptom endorsement related to their injury) and expected longer lasting severe consequences from their injury, had a tendency to report greater odds of poor outcome at six months. Further examination of

injury beliefs, expectations of outcome and coping styles is needed to understand to what extent they contribute to the persistence and perception of symptoms compared with biomechanical factors (i.e. symptoms relating to the physical injury itself), and whether these factors remain significantly associated with TBI outcome over time.

Factors contributing to the development or persistence of postconcussion symptoms

There are many factors that contribute to the development or persistence of PCS symptoms. Some of the main characteristics commonly studied in literature are depicted in Figure 1, which shows a multidimensional approach to understanding PCS symptoms, as posited by Polinder et al. (2018). According to this model pre-injury health conditions and demographic factors play an important role from the outset of injuries. Findings from past studies indicate that typically those who are of older age (above 40 years), female, have lower socioeconomic status or low education level are at higher risk of persistent PCS symptoms (Iverson et al., 2017; King, 2014a, 2014b; Polinder et al., 2018; Tator et al., 2016). Polinder et al., highlight other relevant predictors that include biomechanical factors of the injury such as complicated versus uncomplicated TBI, neuro-inflammation and injury type that directly relate to the onset of symptoms (Reuben et al., 2014; Silverberg & Iverson, 2011). Some studies have observed an increased risk of symptoms if there is amnesia or loss of consciousness at the time of injury, where GCS scores are less than 15 and correlated with brain scan abnormalities, and where the patient presents with concurrent injuries (Silverberg et al., 2015; Tator et al., 2016). Nevertheless the relationship between injury severity and PCS symptoms, has been suggested to be weak, particularly among longitudinal studies (Barlow, 2016; Cassidy et al., 2014). Barlow et al. (2016) and Meares et al. (2011) note that the relative contribution of injury severity to persistence of symptoms diminishes over time, and instead premorbid factors such as history of migraines or headaches, and psychological disorders play a more prominent role. Polinder et al. (2018) also depict the overlapping symptoms shared between PCS symptoms and general psychological disturbances arising as a response to an injury, as well as potential mediators that may inhibit or exacerbate the severity of symptoms. These include, availability of social support networks (Stålnacke, 2007), coping strategies (Hou et al., 2012; Snell et al., 2011), participant beliefs about their injury, including maladaptive beliefs such as low resilience (Snell et al., 2013; Sullivan et al., 2016) and certain personality traits such as high anxiety sensitivity and alexithymia (difficulty in comprehending emotions of the self) (Wood et al., 2014). PCS symptoms have also been correlated with other outcomes

such as lower levels of life satisfaction (Stålnacke, 2007), and delayed return to work (Chu et al., 2017).

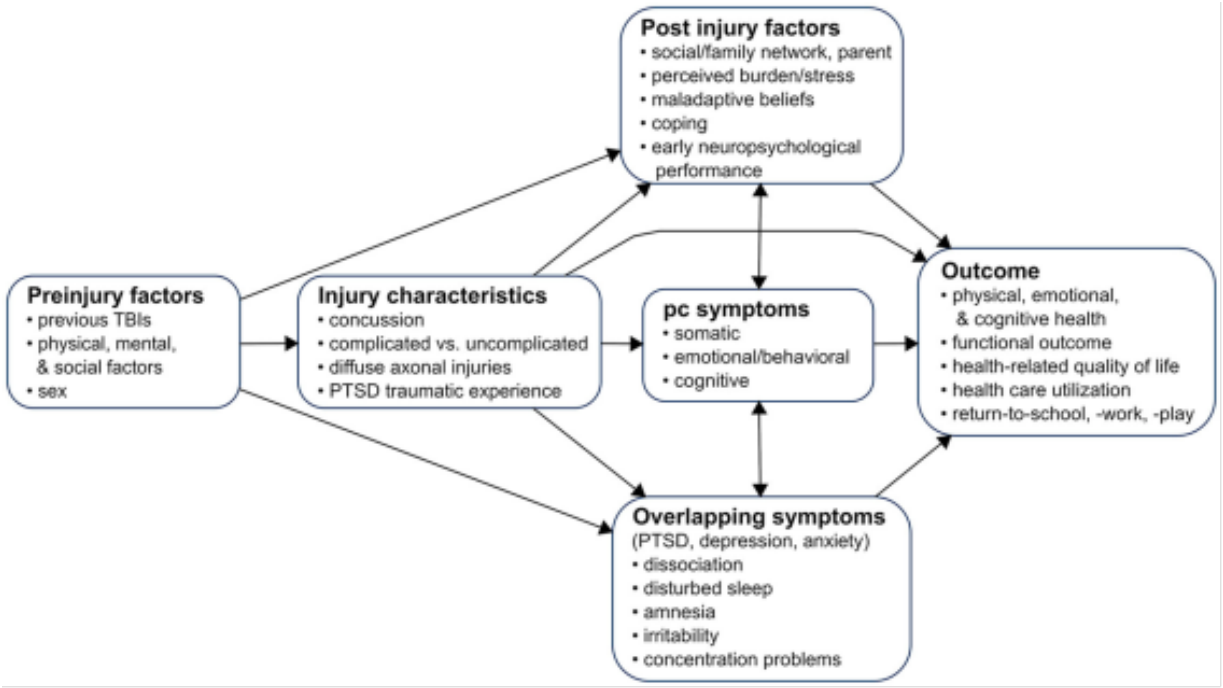


Figure 1. Factors associated with PCS symptoms
Reprinted with permission from Polinder et al., (2018).

History of psychological and neurological disorders and risk of prolonged PCS symptoms after TBI

Increasingly, there is agreement that attention needs to be paid to the burden of premorbid conditions on the persistence of PCS symptoms, given the increasing burden of chronic conditions in the general population. Stulemeijer et al. (2008) reported that individuals with no prior physical comorbidities are three and half times less likely to have persistent PCS symptoms six months after hospitalisation. Approximately 50% of patients with lingering symptoms suffer from pre-injury mental health issues, most commonly being anxiety and depression (Bryant et al., 2010; Reuben et al., 2014). Those with high disease burden (greater than six comorbidities) have been shown to experience more depression after TBI than those with low comorbidity levels (Guetta et al., 2016). Considerable attention has been paid to pre-injury mental and behavioural disorders among TBI patients which have collectively indicated an increased predisposition to psychosomatic problems, including prolonged postconcussion symptoms in both adults and paediatric populations (Barlow, 2016; Reuben et al., 2014; Silverberg et al., 2015; Silverberg & Iverson, 2011; Theadom et al., 2018; Yue et al., 2019). Meares et al. (2011), concluded that whilst mild TBI did not predict PCS

symptoms in their study, pre-injury depressive and anxiety disorders were early markers of symptoms regardless of whether TBI had occurred or not. However, the question of causality remains to be answered as mental health problems can increase the risk of reporting of symptoms (Polinder et al., 2018). It is hypothesised that other psychological difficulties such as behavioural problems like ADHD and learning disabilities among children may be linked to persistent PCS symptoms, with Miller et al. (2016) demonstrating that a history of ADHD presented a fourfold increased risk of prolonged symptom experience after 28 days. But according to Iverson et al. (2017), it is argued that such individuals may have different baselines scores on symptoms, and the presence of such conditions does not necessarily imply greater risk of prolonged symptoms.

There is a solid base of evidence that suggests that past history of successive TBI events leads to cumulative effects and delayed symptom resolution, particularly among high-school athletes (Tator et al., 2016; Theadom et al., 2018). However underlying pathophysiological mechanisms are currently not definitive. Based on evidence from rat models, Fehily and Fitzgerald (2017) postulated that the long-term sequalae of repeated mild TBI mirror those of moderate to severe brain injuries, and the similarities in underlying cellular and metabolic events may partly explain why symptoms are more pronounced and enduring in individuals with recurrent TBIs.

A handful of studies have found that other pre-existing neurological disturbances, such as prior history of migraines and headaches can contribute to ongoing PCS symptoms (Meehan et al., 2014; Mickevičiene et al., 2004; Register-Mihalik et al., 2018). This was recently confirmed by Yue et al. (2019) who found that in addition to history of psychiatric disorders, prior history of migraines and headaches predicted functional impairment and the presence of PCS symptoms at three months after mild TBI, with continued difficulties persisting at six months post-injury. However, after assessing the collective evidence in a systematic review Iverson et al. (2017), argued against there being a consistent relationship between neurological history and symptoms of PCS, given the difficulty adolescents and young adults have in differentiating between “headaches” and “migraine”. It is also important to note that a quarter of PCS symptoms such as headaches, dizziness, memory and concentration difficulties have neurologic aetiology and therefore more research is needed to establish a direct association between headache/migraine history and PCS symptoms. Among the elderly, interesting findings have been noted by some researchers, such as the common co-occurrence of heart

failure and cognitive difficulties (also symptoms of PCS), but the underlying mechanisms have remained elusive thus far (Angermann et al., 2012).

Section summary

Postconcussion symptoms as a diagnosable condition remains a heavily debated topic in TBI research, given the lack of consensus among experts regarding its diagnosis, causes and pathopsychological mechanisms. Furthermore, the evidence on the prevalence of PCS-like symptoms in non-TBI populations spurs the ongoing debate about the non-specificity of symptom clusters, and that its existence is not uniquely attributable to the experience of a brain injury. There is burgeoning evidence identifying history of mental health and behavioural difficulties, and neurological history as risk factors for PCS symptoms, but other physical illnesses have not been explored thus far. The literature largely ignores the influence of other chronic conditions which may also have overlapping symptoms with PCS. For instance conditions such as cardiovascular problems, endocrine-metabolic disorders (e.g. diabetes mellitus or hyperthyroidism) or chronic musculoskeletal difficulties can result in symptoms of fatigue, depression and visual disturbances (Bunevicius & Prange, 2006; Denollet, 1993), that are similar to those attributed to PCS, and which can be further compounded by the use of medication.

TBI and impact on quality of life

Among the many difficulties experienced by those who have suffered a TBI is the impact of the injury on their quality of life. *Quality of life* (QoL) although a broad concept is of special interest to researchers as it illustrates a patient's subjective view of their condition, treatment and how it impacts on their day-to-day life (Nichol et al., 2011). QoL encompasses a broad range of dimensions that individuals subjectively perceive as important or not important to daily life, including aspects related to physical, psychological, social and environmental components. Although in the literature *health-related quality of life* (HRQoL) and QoL are often used interchangeably, many researchers do not sufficiently discriminate between the use of the two terms. Given the varying approaches in defining HRQoL and QoL, and the considerable overlap between the two concepts, the distinctions between the two terms are often unclear (Moons et al., 2006). Karimi and Brazier (2016) suggest that HRQoL measures such as the Short Form 36 (SF-36) or the EQ-5D are more appropriately named measures of self-perceived health status as they evaluate a person's functionality (ability to carry out pre-defined activities) in everyday life, and how they perceive their

wellbeing regarding their physical, mental and social domains of health. In comparison, others have distinguished QoL measures such as the World Health Organization QoL (WHOQoL) instrument as those that capture subjective judgments of individuals' position in life in relation to their culture, value systems, goals and concerns (Division of Mental Health and Prevention of Substance Abuse, 1995). Some of the common aspects related to QoL in TBI research include resumption of work, access to resources, social relationships, physical functioning and mental health, among others (Dijkers, 2004).

Research suggests that quality of life does not follow a linear trajectory after TBI and that patients experience varying longitudinal changes across different domains. This was confirmed by Lin et al. (2010) who found that participants had the lowest quality of life scores across all domains at discharge, which continued to improve at 12 months post-injury. The largest decline in WHOQoL-BREF scores were observed between pre-injury and discharge, with the physical domain experiencing the largest change (-23.0 mean score change, SD 23.20, $p<.01$), and was the only domain where scores did not return to pre-injury levels after 12 months. Within the domains of social relationships and the environment, score changes between pre-injury and discharge were statistically significantly different, but this was no longer the case between 6 and 12 months, suggesting a plateauing effect. The study also found that a patient's disability level (on the Glasgow Outcome Scale) significantly influenced longitudinal changes over 12 months for the psychological and social domains, after adjusting for baseline factors preinjury QoL, marital status, alcohol consumption at injury, cognition, social support and depressive status. Changes in the physical and environmental domains were not associated with any factors in the study.

After more than one year, and compared to those without brain injuries, TBI patients have been shown to score lower in general physical and mental health dimensions of HRQoL, including physical, social and emotional functioning, vitality, and higher reports of ongoing pain (Colantonio et al., 1998; Findler et al., 2001; Hawthorne et al., 2009). According to Scholten et al. (2015), patients with mild, moderate and severe TBI appear to have different recovery trajectories. As expected in their study, HRQoL was reportedly lower amongst moderate and severe TBI patients than mild TBI patients in the first six months. Moderate TBI patients experienced the greatest improvement in recovery over 12 months, and mild TBI patients reached outcomes on par with population norms. Female gender, older age, comorbidity and high ISS were the

strongest independent predictors of decreased HRQoL at 6 and 12 months after TBI (Polinder, Haagsma, Belt, et al., 2010; Scholten et al., 2015). Surprisingly, in two studies by Findler et al. (2001) and Colantonio et al. (2011) it was found that mild TBI patients fared worse in QoL domains than the moderate to severe TBI groups, after controlling for age, income and gender. These observations were explained by the higher prevalence of depression among the mild TBI participants. In this group, physical aspects of HRQoL on the SF-36 (General Health, Physical Functioning, Physical Role, Bodily Pain, Vitality) were strongly correlated with physical symptoms, whereas psychological factors (cognitive and affective/behavioural) were strongly related to emotional functioning and mental health components (Findler et al., 2001). A meta-analysis by Polinder et al. (2015) showed that after the first year of TBI participants tend to score worse on the mental component summary scores than for the physical component summary scores of the SF-36. In the long-term, patients still showed deficits in recovery particularly on the physical role limitations and emotional components of quality of life, compared with population norms. Even after 22 years post-injury physical and mental health-related quality of life for TBI patients remain below general population norms after controlling for age, sex and education (Nestvold & Stavem, 2009).

Few studies have investigated the links between PCS symptoms and QoL, but collectively do indicate that those with symptoms have poorer quality of life not just on both functional and mental health components, as well as on sexual quality of life (Emanuelson et al., 2003; Moreno et al., 2015; Voormolen, Polinder, et al., 2018). Voormolen et al. (2018) recently investigated the link between PCS and quality of life in the first six months after TBI, and found that patients who had been diagnosed with PCS symptoms were more likely to score lower in all aspects of quality of life, including those related to physical and mental health. Fatigue as a factor consistently predicted lowest scores across all domains of quality of life on the SF-36, with the strongest negative correlations existing between fatigue and physical vitality. Among war veterans who had sustained a mild TBI, poor quality of life was associated mainly with affective symptoms, with moderate to strong correlations with symptoms of fatigue and depression (Schiehser et al., 2015). Researchers concur that further research is needed to delineate the specific effects between persistent symptoms and health-related quality of life (Levin & Diaz-Arrastia, 2015; Polinder et al., 2018), particularly to understand if the relationship is affected by the existence of health problems. As current

studies have focused on symptom duration only in the first 12 months, it is yet unknown to what extent symptoms affect quality of life in the longer-term.

Comorbidities and other factors affecting QoL after TBI

Factors such as being female, older age, living alone, pre-injury unemployment, comorbidity and high injury severity have been identified as independent predictors of decreased HRQoL after TBI (Azouvi et al., 2016; Forslund et al., 2013; Polinder, Haagsma, Belt, et al., 2010; Scholten et al., 2015; Theadom et al., 2016). In addition, other factors such as community integration and availability of family support have been identified as important determinants of quality of life after TBI (Forslund et al., 2013; Webb et al., 1995). Support from family in particular is vital in increasing functional independence and thereby improving quality of life (Webb et al., 1995). Webb et al. also found that those who are unable to pay for healthcare demonstrated slower improvement in functional independence, which indirectly and negatively impacted on quality of life.

In general, the presence of comorbidities either prior or post-injury has been shown to negatively impact on HRQoL after TBI (Gardizi et al., 2014; Theadom et al., 2016). Haagsma et al.(2011) concluded that the number of comorbid diseases and pre-existing osteoarthritis increased the disability weight on physical HRQoL post-injury, while Davis et al. (2012) noted that pre-injury psychiatric problems and substance abuse disorders predicted lower satisfaction with life after one year. Nestvold and Stavem (2009) are among the few researchers to have explored these links from a long-term perspective, and found that participants with a history of psychiatric disease have lower scores on mental components of quality of life even after two decades since the injury. Among prospective studies that have assessed long-term HRQoL, it is apparent that depression plays a major role in predicting poor quality of life many years after the injury. Andelic (2009) noted in a study that patients with moderate or severe disability were more likely to report higher depressive symptoms, and subsequently also reported significantly worse HRQoL at 10 years post-injury. Through structural equation modelling analyses, Williamson (2013) showed that HRQoL was directly affected by depression as well as by functional impairment, pain, and satisfaction with social support. Importantly they and others found that depression mediated the effects of pain and functional impairment on quality of life, and in particular, predicted scores on the mental health and social components of quality of life (Forslund et al., 2013; Lin et al., 2010; Williamson et al., 2013).

Regarding the physical dimension of HRQoL, persistent severe headaches at six-months post-injury as well as musculoskeletal discomfort and heart disease have been found to be important long-term determinants (Nestvold & Stavem, 2009). Posttraumatic headaches are a common complaint among TBI patients which have been associated with higher symptoms of depression and anxiety, posttraumatic stress disorder and lower long-term quality of life (Martins et al., 2012; Sawyer et al., 2015). Having at least one severe headache per month at three months post-injury has been shown to predict lower mental component scores relating to HRQoL at 22 years post-injury (Nestvold & Stavem, 2009). Symptoms of headaches and migraines may also overlap with postconcussion symptoms (Bigler, 2008), which as described earlier is a predictor of poor quality of life in TBI patients (Emanuelson et al., 2003; Voormolen, Polinder, et al., 2018).

One of the more interesting pieces of evidence scattered in the literature is the finding that hyperlipidaemia (elevated cholesterol) increases the risk of developing anxiety disorders after TBI. Ho et al. (2014) found that individuals with pre-existing hyperlipidaemia especially in females aged 35–65 years had a 60% increased risk of developing new onset anxiety disorders after TBI, after controlling for risk factors type 2 diabetes, hypertension and cardiovascular disease. This relationship has not been thoroughly investigated before, but it is hypothesised that there are correlations between hyperlipidaemia and markers of systemic inflammation. It is postulated by the authors that the exacerbation of neuroinflammation after TBI may be responsible for the onset of anxiety disorders. Further research is needed to investigate whether individuals with TBI who have co-existing hyperlipidaemia and anxiety also subsequently experience worse PCS symptoms and diminished quality of life.

2.3 Chapter summary

Chapter 2 placed emphasis on the importance of investigating comorbidity in TBI recovery. While many studies have outlined the detrimental effects of comorbidities on increased risk of mortality and complications during acute care, the evidence is largely concentrated within the geriatric demographic, with minimal evidence on younger age-groups. To date it is unclear to what extent comorbidities impact on long-term outcomes beyond the acute hospitalisation or rehabilitation stage, including how the cumulative effects of pre-existing conditions and factors relating to the trauma (including the severity of TBI and the presence of extracranial injuries) are likely to impact on outcomes over the course of recovery. One reason for the lack of knowledge around

comorbidity effects is that previous longitudinal studies in particular excluded patients with prior comorbidities in order to reduce outcome variability and to make it easier to isolate risk factors (Isokuortti et al., 2016). This chapter also highlighted a notable gap in studies investigating the impact of health conditions on the onset of PCS symptoms and subsequent effects on quality of life following TBI. The few studies attempting to isolate comorbidities as predictors of HRQoL tend to assume a biomedical and binary view of HRQoL dimensions, focussing on either the functional aspects or mental health aspects as defined in the SF-36. Arguably the SF-36 may be more appropriately seen as a measure of disability or health status rather than a reflection of patient values (Guyatt, 1997). While the components defined in the SF-36 are clearly useful markers of quality of life for clinical decision-making, there is an apparent oversight on other patient-centric dimensions that encompass quality of life, such as quality of social support, or quality of the environment which may impose further barriers to full recovery, but which are poorly understood. Furthermore, in many of the studies outlined earlier comorbidity is measured simply as a dichotomous 'Yes/No' variable without taking into account the severity of these conditions. Information regarding comorbidities is typically ascertained from medical record review and rarely is measured using an appropriate comorbidity measure that also accounts for severity of conditions. This is problematic as researchers and clinicians run the risk of assuming that all health conditions are equally weighted and carry the same consequences after an injury.

There is a pressing need for a more detailed understanding of the severity of health conditions and their consequences on long-term recovery after TBI given the global rise in both chronic conditions and TBIs. Prospective studies are therefore needed to investigate the potential risks associated with pre-existing illness in long-term recovery, particularly after the post-hospitalisation period. The importance of understanding these relationships may help clinicians and researchers to identify patients at higher risk of unfavourable recovery, improve early risk stratification and resource allocation, and ultimately tailor treatment regimens for TBI patients with specific medical conditions (Yue et al., 2019).

Chapter 3 Measurement of comorbidity, postconcussion symptoms and quality of life after TBI

Chapter 2 depicted the wide-ranging consequences arising from TBI with a focus on the experience of PCS symptoms and the detrimental effects of the injury on quality of life. While it is recognised that the effect of a person's health bears significance on a variety of outcomes and prognosis (Librero et al., 1999), this relationship has remained poorly measured and understood in the injury literature. The understanding of the effects of TBI on individuals' health and quality of life is driven by the development and validation of health measurement scales, which are required to have a sound scientific basis in order to produce accurate results, and which hold external validity to permit generalisations to wider populations (Lam, 2010). As discussed further in Chapter 4, instrument validation is an important preliminary step to undertake to ensure that measures are not only functioning as intended, but also have sound a psychometric basis for use in a particular population. Consequently, this short chapter aims to critically appraise three commonly used measurement instruments that are intended to measure comorbidity, postconcussion symptoms and quality of life that were addressed in the previous chapter. These are the Cumulative Illness Rating Scale, Rivermead Postconcussion Questionnaire and the World Health Organisation Quality of Life-BREF. Using evidence from literature these scales will be evaluated for their feasibility and applicability for use in the injury and TBI population.

3.1 Cumulative Illness Rating Scale

In the previous chapter, comorbidity was described as a difficult construct to measure and is dependent on several factors, two of which include the primary disease of interest and outcome being investigated (Sarfati, 2012). In general, there are four broad approaches to measuring comorbidity, which include individual conditions or counts on conditions e.g. Elixhauser Index (Elixhauser et al., 1998), organ-based systems e.g. Cumulative Illness Rating Scale (Linn et al., 1968), weighted indices e.g. the Charlson Comorbidity Index (Charlson et al., 1987) and various other approaches such as case-mix groups which allocate patient groups according to level of health care need. It is important to note that there is no single optimal or gold standard measure of comorbidity, as the choice depends heavily on the research question, population of interest and the data available (and limitations inherent within the data) (Sarfati, 2012). Furthermore, for many of the summary measures one runs the risk of simplifying

assumptions of individuals' health and disease aetiology, resulting in a loss of detail in information, and inadvertently leading to homogeneous 'disease' groups.

Some of the more common measures of comorbidity which have been designed for specific populations to investigate specific outcomes include the Charlson Index (Charlson et al., 1987), which is primarily used for clinical prognosis in acute care as it has been found to be a good predictor of mortality, disability, and hospital readmissions (Cleves et al., 1997; Librero et al., 1999; Rochon et al., 1996). Others such as the Cumulative Illness Rating Scale were developed for use in elderly patients but has been validated as a measure of comorbidity in various contexts, as discussed in the following section.

The Cumulative Illness Rating Scale (CIRS) is a brief questionnaire that assesses the prevalence of medical comorbidities and severity of conditions. The earliest version was developed by Linn, et al. in 1968 as a means of having a rapid assessment of organ impairment across 13 different systems (Linn et al., 1968). This scale was subsequently expanded by Miller and Towers (1991) to include hypertension as a separate category, to give 14 CIRS items instead of 13. The current adaptation of the CIRS (or CIRS-G) by Salvi et al. (2008) further improved on Miller and Towers' version, presenting modified guidelines that were clinically suitable for measuring comorbidity among elderly hospital patients, although it has since then also been used in other samples.

The CIRS consists of 14 items to measure severity of conditions across 12 different organ systems, namely cardiac, vascular, respiratory, eye-ear-nose-throat (EENT), upper gastro-intestinal, lower gastro-intestinal, hepatic, renal, other gastro-uterine, musculoskeletal/integumentary, neurological, endocrine-metabolic conditions. The scale also includes one risk factor of hypertension as the 13th item, and a separate distinct category for psychiatric/behavioural disturbances as the 14th item. The severity of each condition is assessed on a scale from 0 (no impairment) to 4 (indicating a life-threatening impairment requiring immediate treatment or hospitalisation) to produce a cumulative total score between 0 and 56, with higher values indicating higher comorbidity levels. An advantage of the layout of the CIRS, is that the five-number scoring (from 0–4) for each organ-specific category allows the assessor to see at a glance whether the total score reflects a combination of mild or moderate health problems, or a potentially severe or life-threatening health problem. Other scores can be derived from the CIRS, such as the Severity Index (mean of the 13 CIRS items,

excluding the psychiatric/behavioural category) (Salvi et al., 2008), and the number of organ-specific categories at level 3 and level 4 severity, which indicate if the patient is suffering from severe or extremely severe health problems (1992).

Rating guidelines of the CIRS

Miller et al. (1991) provide general principles to guide severity rating of comorbidities. Ideally, judgments of degree of impairment should be based on an adequate and complete medical examination and health history. The modified guidelines by Salvi et al. (2008) give specific criteria for different organ systems as summarised below, as well as a separate grading system for rating of malignancies.

0 – No problem affecting that system or past problem without clinical relevance
1 – Current mild problem or past significant problem
2 – Moderate disability or morbidity and/or requires first line therapy
3 – Severe problem and/or constant and significant disability and/or hard to control chronic problems (complex therapeutic regimen)
4 – Extremely severe problem and/or immediate treatment required and/or organ failure and/or severe functional impairment

- **Level 0** is rated where there is no medical problem; for healed minor injuries; past childhood illnesses (e.g. chicken pox); minor surgery (e.g. carpal tunnel syndrome completely healed, caesarean); uncomplicated healed fractures; or other past problems that have healed without sequel, residuals or complications (e.g. pneumonia).
- **Level 1** ratings are given for any current medical problem that causes mild discomfort or disability, or has occasional exacerbations, but have only a minor impact on morbidity (e.g. asthma controlled with medications on an as-needed basis, or occasional heartburn needing relief from antacids). This category also includes medical conditions that are not currently active but were significant problems in the past or required major surgery at the time and healed without sequel (e.g. kidney stone removal, hysterectomy, appendectomy).
- **Level 2** ratings are given for medical conditions that require daily treatment or first line therapy (e.g. asthma controlled by inhaled steroids, gastro-oesophageal reflux treated by daily medication, or osteoarthritis needing daily non-steroidal anti-inflammatory drugs); and/or those that have moderate disability or morbidity.

- **Level 3** category refers to chronic conditions that are not controlled with first line medication and/or result in constant significant disability, but not severe disability. Conditions such as asthma requiring continuous steroid medication, or symptomatic angina despite medical therapy, heart failure with symptoms or uncontrolled hypertension despite complex medical regimen may fall into this category.
- **Level 4** classification applies to any acute condition that requires immediate treatment or hospitalisation (e.g. unstable angina, acute myocardial infarction, stroke); and/or extremely severe problems including severe functional/sensory impairment, organ failure; or severely affected quality of life. For example, individuals with end-stage renal disease requiring dialysis, or terminal heart failure, or have almost or complete blindness or deafness, or are wheelchair-bound would be classed under this category.

For the scoring of psychiatric and behavioural conditions that include both dementia and behavioural disorders, the rater is expected to be familiar with at least the Diagnostic and Statistical Manual-IV (DSM-IV) (American Psychiatric Association, 1994), and for grading of dementia, the Mini-Mental State Examination (MMSE) (Folstein et al., 1975). It is also recommended that other assessments are used in conjunction with the CIRS to evaluate a patient's mental status, and where necessary the input from a psychiatric consult.

Grading of severity (e.g. for dementia, depression, anxiety, psychosis, substance abuse etc.) depends on the level of functional impairment or disability caused by the mental health issue. For example, a grading of 0 "no problem" is given for an individual with no history or current psychiatric problem. A grade of 1 "current mild problems" is given where a patient has a history of or current minor psychiatric condition; or previous psychiatric treatment without hospitalization; or major depressive event or use of antidepressants greater than 10 years prior; or presence of mild cognitive impairment. A grade 2 "moderate problem" is given for someone with mild dementia; or has a history of major depression within the last 10 years; or history of substance abuse (more than 10 years ago); or has had previous psychiatric hospitalization. A grade 3 which is classified as severe, categorises a patient with current major depression (according to DSM-IV criteria); or who has had episodes of depression in the past 10 years; has current use of daily anxiety/antipsychotic medication; or moderate dementia; or current/ past history of alcohol/substance abuse (using DSM-IV criteria); or previous suicidal

attempts. Lastly, a grade 4 of “extremely severe” is scored for a patient with current mental illness that requires hospitalization/institutionalization; has severe depression with suicidal purpose; acute psychosis; severe substance abuse; or severe dementia.

The CIRS has also a specified rating for various malignancies, where ratings are placed in the appropriate organ category affected, in which a Level 0 indicates no problem. Level 1 applies to any cancer diagnosed in the remote past without evidence of recurrence or sequel in the past 10 years; or skin cancer excised in the past without major sequel (other than melanoma). A level 2 rating indicates that there is no evidence of recurrence or sequel in the past five years. A level 3 rating applies for a malignancy that required major therapeutic intervention in the past five years e.g. (chemotherapy, radiation, hormonal therapy or surgical procedure). Level 4 is given where a patient has a recurrent malignancy or metastasis (other than to lymph glands), or is in the palliative treatment stage.

Some of the limitations in the CIRS should be noted here. According to the scoring system guidelines by Salvi et al. (2008), when multiple conditions exist in a particular organ system, only the most severe rating is given. For instance, in a patient suffering from angina controlled with daily medication (rated 2) as well as terminal heart failure (rated 4), only the highest rating would be given under the cardiac system category (hence rating 4). Similarly, for musculoskeletal issues, where several conditions can commonly co-exist with each other, only the worst rating is noted under this category. As an example, a patient with minor back pain (rated 1) who also suffers from osteoarthritis in their joints which require daily anti-inflammatory drugs (rated 2) would thus be given an overall rating of 2 in the musculoskeletal category. A limitation in prioritising rating for the most severe health condition is that it fails to acknowledge the potential cumulative effects of multiple problems existing within the same organ system. This is especially applicable to the musculoskeletal system where numerous problems can often co-exist and which can have a multiplier effect on functional outcome (Haagsma et al., 2011). Salvi et al. (2008) do also acknowledge that the complexity of rating malignancies quickly exceeds the ease of use or simplicity of the tool, given that each malignancy has its own rating system and prognostic indicators. The category of psychiatric and behavioural diseases is more challenging to grade given the wide-ranging psychological conditions (such as dementia, anxiety, depression, psychosis, drug/substance abuse) that the scale attempts to capture in a single category.

In doing so the scale in effect homogenises an array of psychological disorders, which thus limits its use.

Psychometric properties of the CIRS and association with outcomes

The CIRS is one of the few measures available to measure comorbidity in populations and has previously been used in primary care settings, (Miller & Towers, 1991), cancer patients (Wedding et al., 2007) and residential populations (Parmelee et al., 1995), but has also shown to be a valid indicator of health status in neurological and orthopaedic patients (Giaquinto et al., 2001; Holcomb et al., 2012).

Empirical evidence on the psychometric performance of the CIRS in the literature is limited to few studies, generally based on geriatric populations for whom the scale was initially developed. Across these studies the CIRS has demonstrated good face validity, intra-rater reliability [Intra Class Coefficient (ICC)=.83, 95% Confidence Interval (CI) 50.76 to .88] and interrater reliability (ICC between .76 and .88), and excellent test-retest reliability (ICC p=.05, 95% lower bound interval .91) (Extermann et al., 1998; Miller et al., 1992; Rochon et al., 1996; Salvi et al., 2008). The CIRS has been found to have high criterion validity when comorbidity ratings are based upon autopsy examinations (the gold standard in objective health assessment) rather than health histories or chart reviews, accounting for 75% of the variance (R^2=.74 p<.001) in CIRS scores (Conwell et al., 1993). Given that the observations by Conwell et al. (1993) were based on a sample of 98 suicide victims (with completed psychological autopsies), results from this study are limited in their generalisability to population groups with somatic conditions. Regarding convergent validity, the CIRS has also shown a fair degree of correlation with other comorbidity measures such as the Charlson Index (r=.39, 95% CI .26–.50), and good concurrent validity with outcomes such as mortality, rehospitalisation, length of stay and medication use, as well as cognitive impairment, depression and functional outcome among elderly patients (Extermann et al., 1998; Gardizi et al., 2014; Giaquinto et al., 2001; Parmelee et al., 1995; Salvi et al., 2008; Waldman & Potter, 1992). In one of the few studies to have demonstrated the use of the CIRS in the injury setting, Rochon et al. (1996) compared the predictive validity of three comorbidity indices the CIRS, the Charlson Index and ICD-9-CM medical diagnoses in the spinal cord injury population. Their analyses showed that the CIRS fared well in predicting mortality, even when comorbidity scores were adjusted for age (F=13.1; p<.001). The authors concluded that compared with the other two comorbidity indices, the use of the CIRS in addition to patient age adds meaningful information for

prognostic modelling of length of hospitalisation, contributing approximately 4.5% of variance explained. The authors in this study however administered the earlier 13 item CIRS version developed by Linn et al. in 1968, which did not contain hypertension as a separate category.

The use of the CIRS in the TBI context to date has been limited with no evidence on the clinimetric properties for use in this population. Holcomb, Millis & Hanks (2012) used the CIRS to assess and compare the long-term comorbidity burden experienced by TBI patients with a neurological sample consisting of stroke patients and a trauma sample of orthopaedic patients. Across different cross-sectional timepoints at 1, 5, 10 and 15 years post-injury, EENT problems, psychiatric/behavioural problems, musculoskeletal problems and hypertension appeared to be the most consistently prevalent medical conditions reported by TBI patients across this period. A few researchers have found the CIRS to be a useful indicator of functional outcome in neurological and orthopaedic populations. Gardizi et al.(2014), found that TBI patients of government-funded and private insurance with self-reported comorbidities (as measured by the CIRS) were more likely to also report higher levels of disability at one year than those without pre-existing conditions. In the assessment of comorbidity burden in neurological and injury populations, Giaquinto et al. (2001) observed an inverse relationship between functional independence and overall illness severity (excluding psychiatric and behavioural disorders) among stroke (r=-.35, p<.001), and orthopaedic patients (r=-.28, p<.001). Significant correlations also were found between the Functional Independence Measure (FIM) scores and comorbidities with moderate or severe impairment in both groups (r=-.33, p<.001 in stroke; r=-.21, p<.01, in orthopaedic). These findings were supported by Libero et al. (2001) who found that higher severity of comorbidities measured by the CIRS was negatively correlated with the FIM in stroke (r=-.43, p<.001) and hip fracture patients (r=-.57, p<.001). Only one study detailed observations on the CIRS and associations with quality of life. In a sample of 238 adult primary care patients, Fortin et al. (2005) compared the clinimetric properties of the CIRS, the Functional Comorbidity Index and the Charlson Index in relation to health-related quality of life using the Short Form 36 and found that among the comorbidity scales, the CIRS had a stronger association with quality of life. Specifically, there was a negative correlation between the CIRS and all components of the SF-36 except for the Mental Component Summary indicating that higher morbidity was significantly associated with lower quality of life (r =-.55 to -.18, p<.01). Furthermore, the CIRS explained the highest variation in all scores

of the SF-36 among the three comorbidity measures (R^2=.54, p<.01), with the exception of the Mental Component Summary where the variation explained was non-significant. The authors thus concluded that the CIRS is a better measure of multiple comorbidities than other similar measures such as Functional Comorbidity Index and Charlson Index, when health-related quality of life is the outcome of interest.

Section summary

This section introduced the Cumulative Illness Rating Scale as a feasible measure of comorbidity that can be applied in different contexts. The evidence from studies that have utilised the CIRS suggest that this measure has good psychometric properties, and has been correlated with long-term mortality, hospitalisation and length of stay, and functional impairment. Fortin et al. (2005) reported that the CIRS was the better measure to use when health-related quality of life was the outcome of interest, in comparison with other commonly used tools such as the Charlson Index or the Functional Comorbidity Index. However, it is important to bear in mind that much of this evidence is derived from geriatric samples, and there remains a dearth of literature on the psychometric properties in other samples, particularly in the injury population. There is also a lack of empirical evidence on the structural validity and overall reliability of the instrument. This limitation therefore greatly reduces the generalisability of the findings to the TBI or other injury populations, and the lack of validation of the scale in these samples needs to be addressed.

3.2 Rivermead Postconcussion Questionnaire

Postconcussion symptoms are one of the most common health problems experienced by those who have experienced a mild TBI and as discussed in Chapter 2 there is much debate on the accuracy of its diagnosis and causal mechanisms in different populations. A number of scales exist for measuring PCS symptoms which were initially developed for use in the TBI population, such as the Postconcussion Symptom Scale (Lovell et al., 2006), Postconcussion Syndrome Checklist (Gouvier et al., 1992), and the British Columbia Postconcussion Symptom Inventory (Iverson & Lange, 2003). The most frequently used among these is the Rivermead Post-Concussion Questionnaire.

The Rivermead Post-Concussion Questionnaire (RPQ) is a commonly used self-report measure specifically designed to assess the frequency and severity of post-concussion symptoms following TBI and is widely used in research (Eyres et al., 2005). The RPQ, originally developed by King et al. (1995) consists of 16 items that aim to measure an

array of physical symptoms (headaches, dizziness, nausea/vomiting, sleep disturbance, noise sensitivity, visual disturbances), cognitive symptoms (memory and concentration problems), and behavioural symptoms (fatigue, irritability, tearfulness/depression, impatience, restlessness) following the experience of a TBI. Participants are asked to compare themselves with before and after their injury and to rate the severity of symptoms in the last 24 hours. Items follow a 5-point ordinal structure with the following response categories: 0 (never experienced at all), 1 (no more a problem), 2 (a mild problem), 3 (a moderate problem), and 4 (a severe problem).

Psychometric properties of the RPQ

Key psychometric properties for the RPQ have been published using methods based on classical test theory (described in Chapter 4), illustrating good test-retest reliability in the TBI population (r=.72–.90), good inter-rater reliability among clinicians, (r=.87, p<.001), high overall internal consistency (Cronbach's alpha=.92 and person reliability .71–.81) and split-half reliability (r=.85) (Eyres et al., 2005; King et al., 1995; Lannsjö et al., 2011; Sullivan & Garden, 2011). Additionally, the measure has demonstrated good convergent validity with the Post-Concussion Symptom Checklist (r=.59), and acceptable concurrent validity with measures of anxiety/depression such as the Hospital Anxiety and Depression Scale (HADS), for HADS Anxiety (r=.45) and HADS Depression (r=.32), as well as the Beck Depression Inventory-II (r =.66) (Eyres et al., 2005; King et al., 1995; Sullivan & Garden, 2011). RPQ scores at 7–10 days post-injury have been found to be predictive of persisting symptoms (r=.37), and the presence of anxiety and depression at six months post-injury (HADS Anxiety r=.61, HADS Depression, r=.61) (King et al., 1999).

More robust statistical techniques such as Rasch analysis (detailed in Chapter 4) have been applied to validate the RPQ by Eyres et al. (2005) and Lannsjo et al. (2011). Both studies commented on the measure's poor internal construct validity citing poor fit to the Rasch unidimensional model. Although in both analyses RPQ items functioned invariantly by age and gender, in Eyres' analysis half of the items also demonstrated disordered thresholds particularly for the 'no' to 'mild' symptoms level response options (0–2). This indicated that the 0–4 response order did not function as expected according to the Rasch model. Furthermore, both studies commented on the poor targeting of the measure, with about 34% of floor effects and 1.8% of ceiling effects as reported by Eyres et al. This suggests that individuals experiencing the least extent of symptoms were likely to not be captured within the scale.

Although the RPQ was designed to measure postconcussive symptoms in the TBI population, this scale has been previously administered to capture symptoms in chronic pain patients (Smith-Seemiller et al., 2003; Snell et al., 2018), orthopaedic injury patients (Mickevičiene et al., 2004) and the healthy population (Chan, 2001; Sullivan & Garden, 2011; Wang, Chan, et al., 2006), including within a case-control design study using matched mild TBI and healthy samples (Theadom et al., 2018). Despite its frequent use in both TBI and non-TBI populations, the psychometric properties of the RPQ have not yet been evaluated beyond the TBI sample and it is currently unclear whether the measure functions as a robust measure in non-TBI samples. Furthermore, as highlighted by the next section the ambiguity in the dimensionality of the RPQ in the TBI population has caused confusion in the interpretability of scores and therefore limits the extent to which findings can be applied in research and clinical settings.

Debates about the dimensionality of the RPQ

The dimensionality of the RPQ has been the subject of ongoing debate given the varied results obtained from validation studies, and there is a lack of consensus on the most appropriate factor structure for clinical utility. Various factor structures have been proposed for the RPQ in the assessment of symptoms in TBI patients, but broadly seem to suggest that PCS symptoms as a construct is best represented by a 3-factor solution consisting of cognitive, affective and somatic dimensions (Barker-Collo et al., 2018; Lannsjö et al., 2011; Potter et al., 2006; Smith-Seemiller et al., 2003). Other factor structures utilising both classical test methods and Rasch analysis have also been proposed that suggest that the RPQ can exist as two factors (Eyres et al., 2005; Lannsjö et al., 2011; Potter et al., 2006), and possibly as a 4-factor construct (Lannsjö et al., 2009). As discussed below, cluster compositions and factor solutions within studies vary with sample composition, and between different statistical techniques applied, such as with classical test techniques, e.g. exploratory factor analysis (EFA) or confirmatory factor analysis (CFA), which are more commonly used, or whether more modern approaches, e.g. Rasch analysis, are employed.

In a sample of 168 TBI patients six months post-injury, Potter et al. (2005) using CFA confirmed the viability of the 3-factor solution as proposed previously by Smith-Seemiller (2003) and colleagues. Their results revealed a high degree of covariance existing between the ‘Somatic’ and ‘Emotional’ latent variables (covariance=1.02) which suggested a conjoining of the somatic and emotional factors as a single ‘Emotional-Somatic’ factor. The model fit of the two-factor solution comprising of

'Cognitive' and 'Emotional-Somatic' clusters was supported by structural equation modelling analysis and showed similar goodness of fit to the data as the three-factor model (Bollen-Stine p=.419). In a different study, Herrmann et al. (2009) found that among mild and moderate TBI depressed and non-depressed subjects, the three factors identified using CFA presented a mixture of symptoms consisting of 'Mood/Cognition', 'General Somatic', and 'Visual Somatic' factors. Comparisons between the depressed and non-depressed TBI groups also showed that the depressed group had higher weighted factor scores on all three PCS factors (Bonferroni-corrected p=.017).

An exploratory analysis within an Australian sample composed of mild (77%), moderate and severe TBI patients instead revealed a 4-factor solution, underpinned by 'Mood/Somatic' (47% variance), 'Cognitive' (9%), 'Vertigo' (6%) and 'Vision' (5%) clusters (Thomas et al., 2018). This factor solution best fitted scores obtained at 1-month (Comparative Fit Index=.95, Root Mean Square Error of Approximation=.060 95% CI .049–.071), but fit indices showed that the solution was equally appropriate for cluster presentation at 3-, 6- and 12-months timepoints. In a NZ study Barker-Collo et al. (2018) explored the factor structure of the RPQ in a longitudinal analysis of mild TBI participants (95% of sample) at 2 weeks, and 1-, 6- and 12-months post-injury. At two weeks after TBI, EFA revealed that the three factors extracted accounted for 64% of total variance in RPQ scores, where Factor 1 (49% variance) broadly comprised of a cognitive-physical cluster, Factor 2 (9% variance) included emotional and physical items, and Factor 3 (7% variance) consisted of only physical items. At one month, the 3-factor solution explained 63% of the variance, however considerable overlap was beginning to show amongst emotional items between Factors 1 and 2. At 6- to 12-months the factor structure appeared to be more stable, with the presentation of two factors explaining for 64% and 63% of variance, respectively. Factor 1 contained mostly mood and cognitive and some emotional symptoms, whereas Factor 2 was comprised of physical symptoms. The authors concluded that there was a relative stability in the factor structure after six months, distinguishing between dynamic or early symptoms present in the first three months and more stable symptoms thereafter. The concept of transient versus stable dimensions of PCS was explored further by Medvedev et al. (2018) using more sophisticated techniques such as the Generalisability theory. Their analysis using a NZ sample found that the RPQ was reliable in assessing enduring symptoms at 6-12 months, but insufficient in being able to assess dynamic symptoms that fluctuate across the initial days and weeks after TBI. Barker-Collo and colleagues'

(2019) recent re-analysis of their study sample at four years after injury within an embedded case-control design, however seemed to contradict their previous conclusions of a stable 2-factor structure appearing at 6 and 12 months. Instead, it was found that in both healthy controls and mild TBI patients at four years post-injury, a 3-factor model was the most appropriate structure for categorising symptoms, with 58% and 56% variance explained, respectively. Factor 1 included all RPQ items for both samples and Factor 2 contained mostly physical symptoms with only minor variations between mild TBI and control participants. Differences were mostly observed within samples for the third factor which consisted of a mixture of physical, vision and cognitive symptoms for the mild TBI group, while for the controls the factor was restricted to only vision symptoms. However, as the first factor containing all RPQ items explained for a considerable portion of variance in RPQ scores (43% variance among TBI, and 41% variance among controls) the results did allude to the possibility of a unidimensional construct, although this 1-factor model was not specifically tested for in their analysis.

In attempts to clarify on the ambiguity in factor structure of the RPQ, Eyres et al. (2005) and Lannsjo et al. (2011) applied more psychometrically robust techniques of Rasch analysis and further explored the dimensionality of the instrument. In Eyres' study, Rasch analysis of 369 TBI patients at six months post-injury lent support to a two-dimensional model consisting of a physical symptoms cluster (headaches, nausea/vomiting and dizziness symptoms) and a mixture of affective, cognitive and vision symptoms. The hypothesis that the RPQ is underpinned by a unidimensional construct was not supported as there was significant item-trait interaction, suggesting that the scale structure varies across different levels of the construct. The authors found that when the RPQ was disaggregated as RPQ-13 (items 4–16), and a subsidiary scale of RPQ-3 (items 1–3 on headaches, dizziness, and nausea/vomiting), it supported unidimensionality and permitted the calculation of two sets of total scores, although this may only have minimal clinical utility. Similar conclusions were derived from Lannsjo's Rasch evaluation of the RPQ of 2,523 mild TBI patients assessed at three months, which presents the largest Rasch analysis of the measure to date. Rasch analysis revealed that the Rasch factor (containing items 4–16) only explained 47.7% of variance in RPQ scores, and items 1–3 formed a separate scale similar to Eyres' study. Further evaluation of the Rasch dimension suggested that it was in fact comprised of at least three other dimensions, which therefore argues against the summation of a total score.

The differences in these two Rasch studies may be attributed to sample differences, in which Eyres' study recruited a more heterogenous TBI sample consisting of cases across the spectrum, while Lannsjo's sample was purposefully confined to studying a mild TBI cohort. Another difference is that in Lannsjo's study a third of participants were aged 6–15 years, whereas in Eyres' study the participants were adults aged 18 years and above. Children and adolescents may experience and report symptoms differently to adults, and one study showed that while the cognitive and somatic factors are similar between child-reported symptoms and parent ratings of PCS symptoms, emotional and behavioural dimensions were less consistent between the two groups (Ayr et al., 2009). Therefore, the differences in age composition between the samples may have contributed to different results in these two studies. Furthermore, one can postulate whether the differences in results may also be attributed to timing of assessment where Lannsjo's assessment of symptoms at three months revealed a 4-dimension solution, while Eyres' assessment which was conducted at six months post-injury produced two distinct symptom components. This hypothesis is also supported by the findings from Barker-Collo et al. (2018) who remarked that symptom dimensions are likely to amalgamate as the time elapsed since injury increases.

Section summary

The Rivermead Postconcussion Questionnaire is a widely used measure of PCS symptoms that has shown good psychometric properties in validation studies with TBI samples. However, available research has also consistently highlighted the unsuitability of the RPQ as measuring a single construct of PCS symptomology, but instead comprising of several different factor solutions. Despite validation efforts, there is no consensus as to the best structure for clinical utility. Sample differences relating to the inclusion of types of TBI (e.g. all TBIs or only mild TBI) and age-groups (i.e. children versus adults), as well as different methods of factor extraction (i.e. EFA, CFA, or Rasch analysis) may be contributing to differential results across studies. Furthermore, the timing of assessment e.g. 3 months to 12 months post-TBI appears to some extent explain the differences in the factor structures put forward by researchers. The evidence on factor structure on long-term PCS symptoms is insufficient to enable researchers to draw any definitive conclusions. One major limitation in the current research is that despite there being ample evidence on the existence of PCS-like symptoms in various populations, there is to date no empirical evidence on the validity of the RPQ as a suitable measure of PCS-like symptoms in non-TBI populations.

3.3 The World Health Organization Quality of Life (WHOQoL-BREF)

Quality of life (QoL) is a commonly measured outcome in research and broadly encompasses aspects of physical, social, psychological and daily life domains. QoL outcome measures have been used in the field of medicine for over 30 years, however these measures have only been widely used with TBI patients for the last 10 years. (Nichol, 2011). One of the difficulties with collecting quality of life information from neurological patients is the presence of potential cognitive deficits that may limit the individual's ability to understand questions and communicate effectively. This difficulty is commonly encountered when conducting assessments on moderate and severe TBI patients. At times, it may be necessary to use proxy respondents such as caregivers or family members, however these responses greatly limit understanding of a patient's own view of their condition or recovery. A number of generic QoL measures have been developed for use across diverse populations and include the commonly used Short Form (SF)-36, the WHOQoL-BREF, the Sickness Impact Profile (SIP) and the EQ-5D, which have been successfully applied in the TBI context (Lin et al., 2010; Pagulayan et al., 2006; Polinder, Haagsma, Belt, et al., 2010; Polinder, Haagsma, Bonsel, et al., 2010; Scholten et al., 2015). Only a few TBI-specific instruments have been developed recently such as the European Brain Injury Questionnaire (EBIQ) (Deloche et al., 2000) and the Quality of Life in Brain Injury (QOLIBRI) (von Steinbüchel et al., 2010). However, these TBI-specific scales have not been used frequently beyond initial validation studies, while some have questioned their construct validity (using Rasch analysis) and responsiveness over time (Bateman et al., 2009). The advantage of using generic QoL measures such as the widely used WHOQoL-BREF is that it allows comparability across diverse population groups. A review of the literature by Polinder et al. (2015) concluded that different domains are assessed by different outcome measures that make the pooling of estimates quite difficult. There is also a lack of consensus around the best QoL instruments to be used, given the wide variety of instruments available with varied psychometric strengths. Below, the WHOQoL-BREF is described, along with its psychometric properties and suitability as a measure of QoL in the TBI population.

The WHOQoL-BREF-26 is a shortened version of the original WHOQOL-100 that was designed to measure quality of life in the general population. This abbreviated version was developed for use in time-restricted settings, large epidemiological studies, and

with the aim to minimise respondent burden (Skevington et al., 2004). The WHOQoL-BREF was developed using data collected from 15 centres worldwide which were used for the WHOQOL-100 field trials. Items for the shorter version were selected for their ability to explain a large variance of their parent facet and domain, their relationship to the overall WHOQOL model, and for their discriminant validity (WHOQoL Group, 1998). The WHOQoL-BREF measure consists of 26 items; the first two items (Q1–Q2) relate to the overall quality of life and general health facet, and the remaining 24 items (Q3–Q26) are health-related facets categorised broadly into four domains of physical health (7 items), psychological health (6 items), social relationships (3 items) and the environment (8 items) (WHOQoL Group, 1998). A facet is defined as a behaviour (e.g. walking), a state of being (e.g. vitality), a capacity or potential (e.g. the ability to move around), or a subjective perception or experience (e.g. pain). Each item is a self-report score on a Likert scale of 1 to 5, which inquires 'how much', 'how completely', 'how often', 'how good' or 'how satisfied' an individual felt about certain facets in the last two weeks, with higher scores indicating higher quality of life (Szabo et al., 1997). Domain scores range from 4 to 20 and are calculated by multiplying the mean of all items within the domain by 4 (for e.g. social relationships domain score = (Q20 + Q21 + Q22)/3 * 4).

Psychometric properties of the WHOQoL-BREF

The WHOQoL-BREF has been translated and validated in different language versions across different samples in many countries (Cheung et al., 2017; Nedjat et al., 2006; Yao et al., 2002). One of the earliest validation studies of the WHOQoL-BREF using cross-country data found that the tool has good to excellent reliability and validity that is maintained across-cultural comparisons (Skevington et al., 2004). Skevington and colleagues reported that the measure demonstrated good psychometric properties overall (Cronbach's $\alpha > .7$), and very good internal consistency for the domain on physical health ($\alpha = .82$), psychological health ($\alpha = .81$) and the environment ($\alpha = .80$). The social relationships domain, however, was found to have a below-satisfactory level of internal consistency ($\alpha = .68$). The earlier version of the WHOQoL represented quality of life as a 6 domain construct, whereas the shortened WHOQoL-BREF revealed a 4-factor structure underpinning quality of life (Skevington et al., 2004). Since its development the WHOQoL-BREF has been validated and shown to be a suitable quality of life measure that can be applied across various populations including the general population, depressed primary care patients, cancer survivors, asthma patients, older

rural community dwellers, and the trauma population (Aggarwal et al., 2014; Krägeloh et al., 2013; Kruithof et al., 2018; Liang et al., 2009; Lin et al., 2019; Rocha et al., 2012a).

Estimates from these samples using both confirmatory factor analyses and Rasch methods show that the WHOQoL-BREF is a well-targeted measure that generally captures construct levels at opposite ends of the spectrum (Liang et al., 2009; Rocha & Fleck, 2009). The WHOQoL-BREF has been found to exhibit acceptable to very good internal consistency across the domains for physical health (α=.75 to .83), psychological health (α=.68 to .83), the environment (α=.70 to .80), with the exception of the social domain which generally shows unsatisfactory reliability (α=.49 to .68) owing to its poor psychometric properties (Chiu et al., 2006; Krägeloh et al., 2013; Kruithof et al., 2018; Liang et al., 2009; Rocha et al., 2012a; Wang, Yao, et al., 2006; Yao et al., 2002). Rasch analyses have also determined that the scale's items function invariantly by age, gender, education and marital status (Krägeloh et al., 2013; Liang et al., 2009). Few studies have assessed item performance on the basis of cultural differences and different medical conditions. Lin et al. (2019) are among the few to have conducted differential item functioning analyses by disease groups and found that items performed consistently across head/neck, colorectal, lung and gynaecological cancer survivors. Cross-national comparisons by Rocha et al. (2012a) noted that several items regarding medication, positive feelings, thinking, body image, and activity function inconsistently across depressed samples recruited from Spain, Israel, Australia, Brazil, USA and Russia. The authors did not expound on the differences further but attributed these findings to the method used for assessing differential item function, which involved conducting one-way analysis of variance for person-item deviation of residuals and person characteristics.

The validity of the WHOQoL-BREF has been ascertained in trauma populations including general trauma and spinal cord injury patients, indicating low floor and ceiling effects, good internal consistency across most domains (with the exception of the social domain), and adequate discriminant validity between diseased and non-diseased groups (Jang et al., 2004; Kruithof et al., 2018; Lin et al., 2010). The WHOQoL-BREF domains have also demonstrated good convergent validity with the EQ-5D measure (physical domain r=.66; psychological r=.44; social r=.21; environmental r=.46), as well as strong concurrent validity with the HADS Anxiety (physical r=.46; psychological r=.64; social r=.28; environmental r=.52), and HADS

Depression measures (physical *r*=.65; psychological *r*=.66; social *r*=.35; environmental *r*=.52) (Kruithof et al., 2018). To date, only one study by Chiu et al. (2006) has validated the WHOQoL-BREF in the TBI population, which used the 28-item Taiwanese translated version (internal consistency α=.70–.77; test-retest reliability= .76–.80) (Yao et al., 2002). This version includes two national items that are culturally-specific questions relating to quality of life. Within the TBI population, Chiu et al. (2006) confirmed through factor analysis the suitability of the WHOQoL-BREF at one-year post-injury (*n*=199) with nearly symmetrical distributions across the four domains, low floor and ceiling effects (0–3%), very good test-retest reliability (ICC=.74–.95), good to excellent internal consistency across domains (α=.75–.89), and known-groups validity (for employment status, effect size=-.53, *p*<.001). The WHOQoL-BREF also showed adequate concurrent validity between the physical domain and functional ability on the Glasgow Outcome Scale (*r*=.53) and Barthel Index (*r*=.31), between the psychological domain and the Center for Epidemiologic Studies Depression scale (*r*= -.64) and the Social Support Survey (*r*=.52), and between the social relationships domain and the Social Support Survey (*r*=.37). Discriminant validity effect sizes for all domains were >.20, and most were >.50 (*p*<.001). The study was however not able to find significant differences in quality of life scores (overall or across domains) across mild, moderate and severe TBI groups, possibly due to the small sample size (*n*=199).

Although the WHOQoL-BREF has been validated cross-culturally as a suitable measure of HRQoL in diverse populations, demonstrating good face and construct validity, the review of the literature indicates a lack of empirical evidence in the injury and TBI populations. Currently, psychometric evidence for use of the tool among TBI patients is restricted to just one study that was conducted using classical test approaches on the culturally-modified Taiwanese version of the WHOQoL-BREF which therefore limits the generalisability of these findings to the wider TBI population. Based on the review of the literature it can be concluded that more research is required on validation of the standard WHOQoL-BREF in TBI and injury groups to determine if this an appropriate measure of quality of life for these populations.

3.4 Chapter summary

Within this chapter three outcome measures were explored in-depth, namely the Cumulative Illness Rating Scale as a proxy measure of comorbidity, the Rivermead Postconcussion Questionnaire which is a self-report measure of postconcussive symptoms after TBI and lastly the WHOQoL-BREF, which is a widely used quality of

life questionnaire. These measures will form the main outcomes of interest for this PhD study, and will be tested on two injury samples comprising of TBI and orthopaedic participants, as is detailed in the chapter that follows. The latter half of this chapter also reviewed relevant psychometric properties of these three scales, however it was shown that validation of these measures using robust psychometric techniques in the injury population is either non-existent or limited at best. Validation of measures in a sample is a fundamental step particularly in the discipline of psychology, as it provides assurance that the selected measure is not only reliable and precise but that it also provides accurate results for use in a particular population.

Chapter 4 Methods and data analysis

So far, the previous chapters detailed the epidemiological burden of TBI worldwide and its long-term consequences on post-concussive symptoms and quality of life. The literature review in Chapter 2 also highlighted a dearth in knowledge regarding the impact of pre-existing illnesses on recovering from a TBI. Chapter 3 focussed on the psychometric properties of three commonly used instruments for assessing comorbidity, postconcussive symptoms and quality of life in diverse populations, and highlighted the limited psychometric evidence within the injury population.

The present chapter sets out the specific aims and objectives of this PhD which aims to bridge these gaps in knowledge and evidence addressed above. One of the primary aims of this research is to therefore validate and enhance instrument precision applying modern psychometric techniques of Rasch analysis, which forms an important contribution to the accurate assessment of injury outcomes. Consequently, Study 1 of this thesis is comprised of three sub-studies that aim to evaluate the psychometric properties, and to improve the precision of the three instruments described in the previous chapter. These are the Cumulative Illness Rating Scale, Rivermead Postconcussion Questionnaire, and the WHO Quality of Life-BREF. The second component of this thesis, Study 2, aims to explore the complex relationships existing between pre-injury, peri-injury and post-injury factors, and to test an empirically-derived model that can be used to identify the most important contributors to long-term outcomes after injuries. This will be accomplished through a series of multivariate linear regression and structural equation modelling techniques.

Chapter 4 begins by presenting the overarching goals and specific aims of this thesis and is followed by a description of the study's sample characteristics, data collection and data analytical steps. The second part of the chapter provides details explanations on the methodological framework and procedures underlying the process of Rasch analysis which will be applied for Study 1. Finally, the last part of this chapter explains the fundamental steps of structural equation modelling that is used for Study 2.

4.1 Thesis objectives

Study 1 is comprised of three sub-studies, each with specific aims:

1. To describe the comorbidity profiles of TBI and orthopaedic participants, and to evaluate the properties of the Cumulative Illness Rating Scale using Rasch analysis,
2. To assess the psychometric properties of the Rivermead Postconcussion Questionnaire as a suitable measure of postconcussive symptoms among TBI and orthopaedic populations using Rasch analysis, and
3. To validate the WHOQoL-BREF and existing shorter versions with Rasch methods in the TBI, orthopaedic and a comparison general population sample.

Study 2 employs methods of multivariate linear regression and structural equation modelling with the aim to:

1. Examine the relationships between pre-existing factors (e.g., baseline health, demographic factors), peri-injury factors (e.g., injury characteristics) and post-injury outcomes (e.g., post-injury comorbidities, postconcussive symptoms and quality of life),
2. Develop and test a conceptual framework of predictors of long-term outcome, with a particular focus on the relationship between post-injury onset of comorbidities, postconcussive symptoms and quality of life, and to make comparisons between TBI and orthopaedic injuries, and
3. Compare the effect of the use of ordinal and interval scales on strengths of relationships between factors in the proposed model.

The section below describes the data collection procedures involved in conducting this research, including the recruitment strategy implemented to enrol participants and the interview process in the gathering of primary data.

4.2 Recruitment procedures, data collection and sample characteristics

Catchment population

The catchment area for this study was the Greater Waikato region, which is the fourth largest in geographical size out of 16 regions in New Zealand, and accounts for 9.5% (*n*=403, 638) of the country's total population (Statistics New Zealand, 2013). This region was selected as the catchment region for study recruitment as its social and demographic characteristics are reflective of the general population, which thus allows extrapolation of study findings to the wider NZ context (Theadom et al., 2012).

The Midland Trauma Registry was used as the sampling frame, and at the time of designing the study it was the only existing research-based trauma registry available in NZ that captures clinical patient data for all trauma hospitalisations in the greater Waikato region (Midland Regional Trauma System, 2013). The registry contains trauma-related event data for the five Midland District Health Boards in this locality, namely Waikato, Bay of Plenty, Lakes, Taranaki and Hauora Tairāwhiti. Inclusion of events in the registry requires patients to have been admitted to an in-hospital bed in this region, within seven days of the injury. Fatality events recorded in the registry included all in-hospital deaths following the injury as well as deaths that occurred in the emergency department. Trauma patients seen and discharged alive from the emergency department, or patients who were admitted primarily for pre-existing medical conditions and not directly for their injuries were excluded in the trauma registry (Midland Regional Trauma System, 2013).

For this research, eligible cases were ascertained retrospectively by identifying all TBI and orthopaedic injuries recorded in the registry for the Waikato hospital between 2012 and 2016. Waikato hospital as the largest hospital in the greater Waikato region treats approximately 42% of all trauma events (Midland Regional Trauma System, 2013), and was selected due to the accuracy and completeness of data for hospitalisations at the time of recruitment. The eligibility criteria of cases and controls are defined on page 63.

Case-control study design

An important rationale often cited for using an orthopaedic control over a community control is that comparisons with a group that has experienced the psychological effects associated with injuries allow for more clinically relevant findings (Mathias et al., 2013). Despite this, less than 15% of studies in the TBI literature use orthopaedic controls due to the difficulty of case identification and the time and costs involved (Frencham et al., 2005). Against this background, it was therefore decided that adopting a cross-sectional case-control design to compare outcomes between TBI cases and age- and sex-matched orthopaedic controls best suited the purposes and aims of this research. Although samples were not strictly matched for injury severity, all efforts were made to ensure samples were of similar injury severity. Employing a TBI-orthopaedic injury case-control sample is argued by some to result in more precise findings as it maintains comparability between groups by controlling for important known confounders of disease outcome such as age and sex (Lewallen & Courtright, 1998). Perhaps more relevant to injury studies, Mathias et al. (2013) comment that having a matched TBI and

orthopaedic case-control design allows researchers to identify uniquely TBI-related sequelae, by comparing brain versus general-injury effects and related experiences (e.g. injury-related pain and stress). Furthermore, utilising a case-control sample enables concurrent validation of measures across different disease groups and which aligns with the overall aims of Study 1.

As highlighted in the preceding chapter, psychometric validation of outcome measures as evidenced in studies has typically focussed on a specific sample. Extended investigations into scales' applicability to other groups, particularly in the injury population are limited. This is exemplified by the Rivermead Postconcussion Questionnaire which was originally intended and validated for use in the TBI population (King et al., 1995). Despite recent studies remarking on the non-specificity of the RPQ and its potential applicability in non-TBI populations such as orthopaedic patients (Mickevičiene et al., 2004), there remains a lack of empirical evidence on the psychometric and clinical utility of this scale in non-TBI populations. A similar argument is offered for the widely used WHOQoL-BREF which has also previously demonstrated sound reliability and validity in diverse populations (Skevington et al., 2004). However, the evidence regarding its applicability in the wider injury population remains inconclusive. A case-control feature therefore adds a significant strength to this study that allows critical evaluation of the applicability of these scales across the wider injury population.

A priori power calculations indicated that between 106 and 141 participants on each case and control arms were needed to detect medium to small effect sizes of .40 to .20 respectively, at statistical power ß=.80, and significance α=.05.

Inclusion and exclusion criteria

All injuries were identified using either relevant AIS codes according to the AIS 2005-08 version (Gennarelli & Wodzin, 2006) or ICD-10 codes (World Health Organization, 1993). For explanations of code classifications, please refer to Chapter 1. A TBI was defined in accordance with the World Health Organization guidelines as an acute brain injury directly resulting from external physical forces, and not due to drugs, alcohol, medications, other injuries or treatment for other injuries (e.g., systemic injuries, facial injuries or intubation), or caused by other problems (e.g., psychological trauma, language barrier or coexisting medical conditions) (World Health Organization Safety Promotion and Injury Control & Centre for Disease Control and Prevention, 1995). Any

of the following indicators were taken as evidence of a confirmed TBI diagnosis by a trauma specialist: cerebellum injury, haematoma, contusion, diffuse axonal injury, brain swelling, or any loss of consciousness, alteration of mental state or presence of post-traumatic amnesia. TBI cases included all severity types (i.e. mild, moderate, severe), and were either first incidence (first ever) or recurrent (repeated) cases. Both isolated TBI (i.e., excluding other systemic injuries), and TBI cases who sustained additional injuries who are classified as "polytrauma" patients were eligible for inclusion. Orthopaedic injuries (first incidence or recurrent cases) included joint injuries relating to fractures, dislocations or sprains to the pelvic region as well as the upper and lower extremities. Injuries due to so-called insufficiency fractures (i.e., those resulting from physiologic stress on weakened bone), peri-prosthetic fractures, exertion injuries with no external force, hanging, drowning, asphyxiation, poisoning without evidence of external force, ingestion of foreign bodies or injuries as a result of a pre-existing medical condition (e.g., epilepsy, Parkinson's etc.) were excluded. Participants who were unable to give consent or did not speak English, or experienced traumatic severe injuries (such as amputations, crushes, severe fractures) were excluded due to the likely presence of significant psychological trauma. Table 5 presents the inclusion/exclusion criteria for recruitment of TBI and orthopaedic participants.

Recruitment procedures

Follow up of TBI and orthopaedic patients identified from the registry was conducted using similar recruitment procedures but over different recruitment periods. Due to the small number of incident cases of TBI per year in the catchment population, a four-year timeframe was applied to allow for a sufficient number of eligible cases to be identified for recruitment, provided that they met the inclusion criteria. In contrast, given the high number of orthopaedic admissions per year, a one-year recruitment timeframe was deemed appropriate for this group. Figure 2 illustrates the recruitment pathways for both groups.

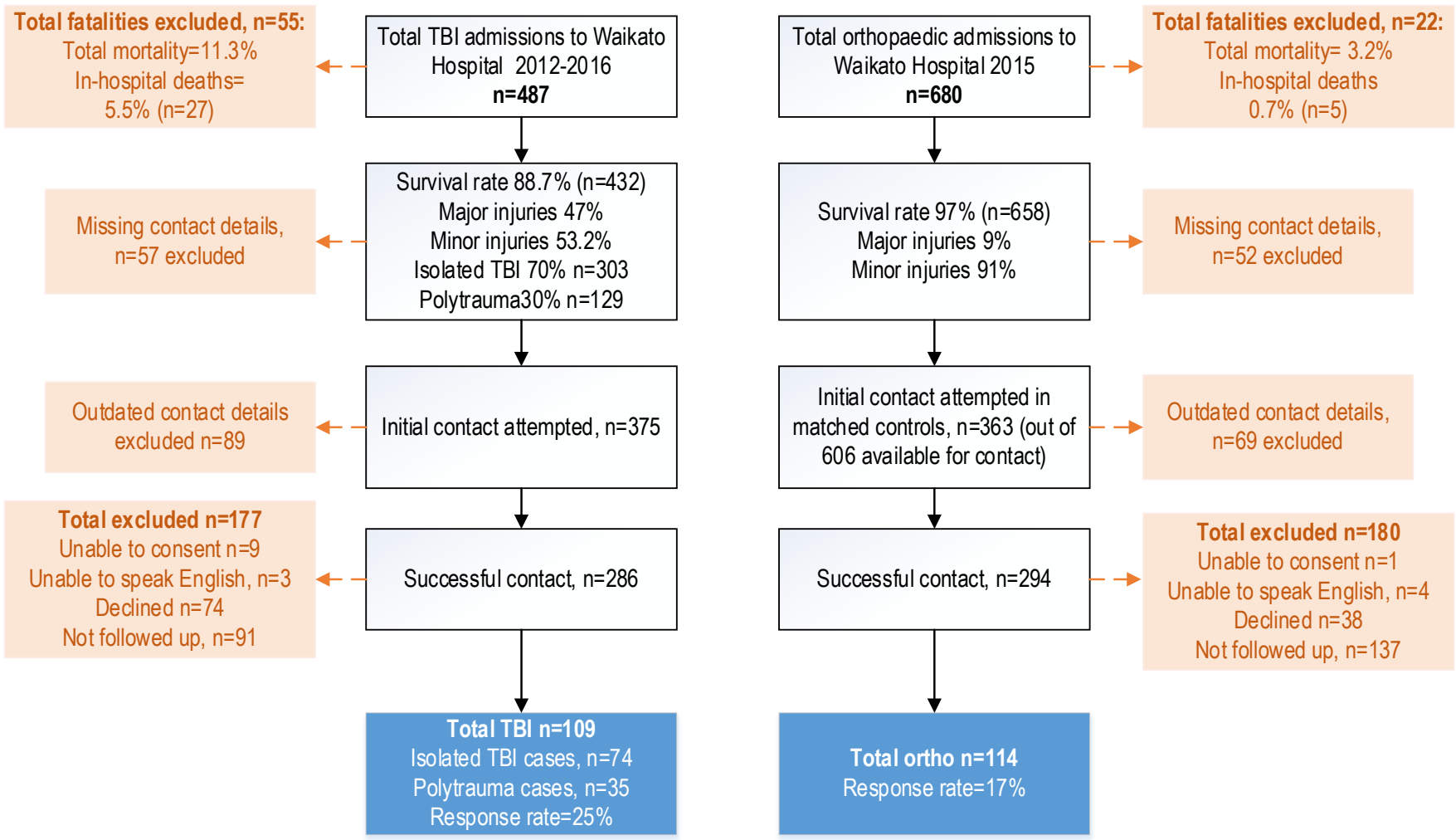


Figure 2. Recruitment pathway for TBI and orthopaedic participants

Between 1st of January 2012 and 31st of December 2016, a total of 487 TBI admissions (inclusive of mild, moderate and severe TBI) were recorded in the Waikato Trauma Registry, and a total of 680 orthopaedic admissions were recorded in the registry between the 1st of January 2015 and the 31st of December 2015. Following the exclusion of fatalities in the sample, a resulting 432 total TBI cases and 658 orthopaedic controls who met the inclusion criteria were eligible for initial contact regarding interest in participation. The proportion of incomplete contact details was found to be high in the registry, particularly for the TBI sample which had approximately 30% of missing or incomplete contact information, compared with only 18% for the orthopaedic sample. Orthopaedic patients were matched to TBI patients by age (within five-year age bands) and sex to ensure groups were as similar as possible.

Table 5. Eligibility criteria for TBI cases and orthopaedic controls

Inclusion	Exclusion
TBI cases	
• TBI admissions (first incidence, recurrent cases, isolated injury, and those with concomitant injuries) of all severity discharged alive between 1st of January 2012 and 31st of December 2016 at Waikato Hospital, NZ • TBI cases meeting WHO criteria • Relevant AIS or ICD-10 codes • ≥ 16 years of age at time of admission • Diagnostic verification by trauma specialist	• Patients who died prior to discharge • Unable to give consent • Non-English-speaking participants
Orthopaedic controls	
• Acute orthopaedic admissions (first incidence and recurrent cases) discharged alive between 1st of January 2015 and 31st of December 2015 at Waikato Hospital, NZ • Injuries caused by external consequences only • Relevant AIS or ICD-10 codes • ≥ 16 years of age at time of admission • Diagnostic verification by trauma specialist	• Patients who died prior to discharge • 'Insufficiency fractures' • Unable to give consent • Non-English-speaking participants • Severe injuries (e.g., amputations, crushes, severe fractures) resulting in significant psychological trauma

*AIS=Abbreviated Injury Scale; †ICD-10=International Classification of Disease

Excluding those with missing contact information, contact was attempted with a total of 375 TBI and 363 matched control orthopaedic patients and approximately 20% and 10% declined to participate, respectively. Some of the reasons for declining in the TBI group were related to the psychological distress associated with revisiting their injuries, particularly if it was a result of a motor vehicle crash or if it resulted in significant ongoing disability. Those with insufficient proficiency in spoken English or who were not able to consent due to cognitive or hearing difficulties were also excluded (*n*=17). The final response rates with completed interviews resulted in 38% for TBI and 39% for orthopaedic groups, yielding 109 and 114 participants in the respective sample sizes for analysis.

Data collection process

Ethical approval was sought and granted by the national (Health and Disability Ethics Committee 15/NTA/173), institutional (Auckland University of Technology Ethics Committee (15/454), hospital ethics committees (Waikato District Health Board RD015127) for access to patient data and overall conduct of the study (Appendices 1-5).

The procedures of informed consent involved initial contact of eligible participants by the principal investigator in order to explain the study and to determine their interest in the study. This was conducted either verbally on the phone and/or with a mailed information sheet and a copy of the consent form (Appendix 6 and Appendix 7) where a postal address was available. Participants were subsequently re-contacted after 1–2 weeks to enquire about their interest in taking part in the study and to set up a phone appointment. Verbal informed consent was recorded via audio tape, unless an in-person assessment was conducted (*n*=1) in which case written consent was obtained. For this study, telephone interview was deemed the most efficient method of gathering data on patients' self-reported health, given the wide geographical distribution of participants in the Greater Waikato region. Where participants requested an in-person assessment, every measure was taken to fulfil this request, although this was sometimes not possible. Given that Māori (indigenous) participants were included in recruitment, appropriate cultural protocols were required to be followed. These included conducting formal consultation with Māori health researchers and offering if requested a *mihi mihi* (formal introduction) or *karakia* (prayer) in accordance with the guidelines for conducting research in Māori populations (Pūtaiora Writing Group, 2010). Participants were also allowed to have a support person from their *whānau* (extended family) during

the interview if they wished. All interviews were conducted by the primary investigator. Each phone interview lasted approximately 30–45 minutes and followed a structured format consisting of questions about demographic details, self-reported pre-injury and post-injury health conditions (using the Cumulative Illness Rating Scale administered twice to ascertain pre-injury and post-injury health conditions), current post-concussive symptoms (Rivermead Post-Concussion Questionnaire) and quality of life (WHOQoL-BREF) at time of assessment (Appendix 8). In addition to primary data collection, the following clinical and injury details were obtained from the registry: date and location of event, injury mechanism, type of injury (TBI or orthopaedic), days in intensive care, days in hospital, Glasgow Coma Scale (GCS) score/length of Post-Traumatic Amnesia, Injury Severity Score, Abbreviated Injury Score codes, specific details on injuries (e.g. type of brain injury and types of concomitant injuries), and surgical/treatment procedures.

Sample characteristics

Power calculations indicated that the sample size of n=223 was powered at .8 beta to detect moderate effect sizes between d=.30 and .40, at .05 significance level. Additionally, the sample size for the Rasch analyses was deemed to be sufficiently powered to estimate person measures to ± .50 logits within 99% confidence levels (Linacre, 1994). The demographics for the total study sample (n=223) and non-respondents are presented in Table 6. There were no notable differences between the two samples, with the exception of ethnic minority representation, which was considerably lower in the study sample, as well as injury intent and post-discharge destination. Overall, the recruited cohort captured a reasonably representative sample of injury hospitalisations within the Waikato region.

Table 7 presents the demographic and clinical characteristics of the final sample, with comparisons between the TBI (n=109) and orthopaedic groups (n=114). Within the TBI sample, polytrauma patients (TBI plus extracranial injuries) constituted 32.1% (n=35) and showed no differences with isolated TBI patients with respect to demographic characteristics. The two groups only differed according to injury severity whereby polytrauma patients presented with more severe injuries (median ISS 17.0 vs. 10.0 for isolated TBI, U=901.5, p=.01). When compared with isolated TBI patients, those with polytrauma injuries were also more likely to have sustained transport-related accidents with 77.1% of cases attributed to transport accidents, and only 17.1% falls-related

injuries (χ^2 (4) =18.52, p<.01). Due to small sample sizes, isolated TBI and polytrauma cases were combined to constitute a single TBI group (n=109).

In the study sample TBI and orthopaedic groups did not have significant differences in demographic characteristics other than having a high representation of NZ European participants (60.6% and 72.8%, respectively). Other ethnic groups represented in the total sample were Māori (20.2%), Asian (3.1%), Pacific (2.2%) and Other ethnicities (7.6%). Both injury groups were mostly comprised of unintentional, blunt-type injuries that were classified as minor trauma (ISS <16). The groups differed across some key clinical characteristics. TBI patients were more likely than orthopaedic participants to have had transport-related injuries and experienced significantly more severe injuries (ISS p<.001). Available GCS scores indicated that although TBI patients sustained mostly mild brain injuries (GCS of 14), these were marginally more severe (p<.05*)* than suspected brain injuries for the orthopaedic group (GCS of 15). GCS scores for this sample however should be interpreted with caution, as scores were only recorded for 42% of the total sample, and only 69% specifically for the TBI group. Additionally, approximately 80% in the TBI group presented with blood alcohol concentration readings less than 2mg/dL when measurement was taken within a 24-hour period after the accident, and about 20% at levels exceeding 20mg/dL. However, blood alcohol was not well recorded in the sample, especially in the orthopaedic group, in which the completion rate was merely 35%. Days in the intensive care unit (ICU) after injury were significantly longer for the TBI group, although the median values were the same as for the orthopaedic sample (median ICU days =0 for TBI and 0 for orthopaedic, p<.001). Most orthopaedic injuries were either transport-related (36.8%) or occurred as a result of a fall (37.7%), and overall resulted in longer days in hospital than for TBI patients (median 12 days vs. 8 days, p<.05). The most common destination post-discharge among orthopaedic patients was to their own residence (89.5%) rather than to rehabilitation (5.3%) or acute care centres (5.3%). This pattern was significantly different for TBI patients, for whom the most frequent discharge destination was home (62.4%), while a third of the sample were discharged to receive further rehabilitation support following hospitalisation.

Mortality from injuries

While the focus of this PhD study is to investigate outcomes among those who have survived an injury, it is also noteworthy to describe in brief some of the mortality patterns observed from the regional trauma registry over the period 2012–2016. Among

all fatalities recorded in this period, the survival rate for TBI cases was marginally lower than for orthopaedic cases (88.7% vs. 97%). An 11% total mortality rate was observed for the TBI sample, with approximately 6% of fatalities occurring during hospitalisation. As expected, the fatality rate was much lower in the orthopaedic sample with a crude mortality rate of only 3.2%, however these differences were not significantly different (Bonferroni-adjusted $p>.05$). Some mortality cases noted post-discharge were verified with the Ministry of Health deaths records, however, cause of death information was not available for review due to ethics limitations to this study. An additional three cases of death in the orthopaedic group were recorded upon follow-up.

The distribution of major (ISS >12) and minor (ISS $\leq$12) injuries was relatively equal for TBI mortality cases, whereas in the orthopaedic sample 90% of fatalities constituted minor injuries. A point-biserial correlation test determined the existence of a weak but significant correlation between mortality and injury severity by ISS [*rho* (1620) =-0.14, $p<.001$], where mortality cases presented with a higher ISS (M=14.61, SD=13.97) than non-fatal cases (M=9.82, SD=9.62). Injury fatalities varied across age-groups, $\chi^2(2) =36.96$, $p<.001$, with deaths being overrepresented in older patients (60+years) mostly among orthopaedic controls (86%), than among TBI cases (50%). TBI fatalities disproportionately affected males (77%) than females (53%), $\chi^2(2) =36.96$, $p<.001$, while 73% of deaths occurred among those with severe TBI and who also had a recorded ISS >12. Among TBI fatality cases, 55% had a recorded GCS of 9–12 in the moderate TBI category.

A Mann-Whitney test conducted to look at differences between the two subgroups of TBI revealed that when compared with isolated TBI deaths, those with polytrauma presented with higher overall injury severity (median ISS 20.0 vs. median ISS 10.0, U=230.5, $p<.001$), more days spent in ICU (median days 8.00 vs. 3.00, U=164.0, $p<.01$), and overall longer hospitalisation (median length of days 8.00 vs. 4.00, U=464.0, $p<.05$). As expected, polytrauma patients who had died had a severe TBI (median GCS of 4.50) but differences in GCS scores were not significant (U=393.5, p=.138*)* when compared with isolated TBI fatal cases (median GCS of 8.50). Within the orthopaedic group, the 60+ years age group had significantly more fatalities overall (Bonferroni adjusted $p<.05$), and 86% of fatalities resulted from minor injuries (ISS <16). Cause of death was not detailed in the information.

Overall, the patterns suggest that survival rates between TBI and orthopaedic groups in this dataset were high and close to 90%, with the TBI group having a marginally higher mortality rate. Fatal outcomes were disproportionate among elderly especially in the orthopaedic groups, as well as among males. There was a minor but significant positive association between mortality and overall injury severity. Compared with isolated TBI fatal cases, those with polytrauma were more likely to have presented with higher overall injury severity and to have spent more days in hospital and in intensive care. The finding that TBI severity was relatively similar in these two groups suggests that higher fatality rate among polytrauma TBI cases may likely be attributed to the severity of extracranial injuries involved.

Table 6. Comparisons of study sample (*n*=223) and non-respondents (*n*=1,168).

	Characteristics	Study sample, *n* (%)	Non-respondents, *n* (%)	Sig.†
Mean age (SD)		45.21 (19.54)	44.26 (19.9)	.523
Sex	Male	142 (63.6)	736 (63.0)	.851
	Female	81 (36.3)	432 (37.0)	
Ethnicity	European	177 (79.3)	800 (68.5)	**.001***
	Māori/Pacific/Other	46 (20.6)	368 (31.5)	
Employment status	Employed	137 (61.4)	615 (52.7)	.055
	Unemployed	55 (24.7)	353 (30.2)	
	Retired	31 (13.9)	200 (17.1)	
Trauma type	Minor	172 (77.1)	857 (73.4)	.527
	Major	51 (22.9)	311 (26.6)	
Injury type	Blunt	223 (100)	1157 (99.0)	.229‡
	Penetrating	0	10 (0.8)	
	Burn	0	1 (0.2)	
Injury group	TBI	74 (33.2)	338 (28.9)	.058
	Polytrauma	35 (15.7)	137 (11.7)	
	Orthopaedic	114 (51.1)	693 (59.3)	
Median ISS		17.00	17.00	.399§
Median GCS		14.00	14.00	.303§
Discharge destination	Home	170 (76.2)	834 (71.4)	**.004***
	Rehabilitation	38 (17.0)	159 (13.6)	
	Acute Care/Hospital/ Other	15 (6.7)	172 (14.7)	

*Denotes statistical significance at $p<.05$; †χ^2 test; ‡Exact test; §Mann-Whitney test

Table 7. Characteristics of the study sample for the TBI (*n*=109) and the orthopaedic injury groups (*n*=114).

Characteristic		TBI, *n* (%)	Ortho, *n* (%)	Sig.[†]
Mean time since injury, years (SD)		2.51 (1.36)	2.66 (0.38)	.289[‡]
Mean age, years (SD)		48.78 (19.69)	47.96 (19.68)	.756[‡]
Age range, years		17–86	18–85	
Sex	Male	69 (63.3)	74 (64.9)	.802
	Female	40 (36.7)	40 (35.1)	
Ethnicity	NZ European	66 (60.6)	83 (72.8)	.052
	Māori/Pacific/Asian/Other	43 (39.4)	31 (27.2)	
Education	Primary/High School	59 (54.1)	50 (43.9)	.125
	Polytechnic/University	50 (45.9)	64 (56.1)	
Marital status	Single	50 (46.3)	46 (40.7)	.402
	Living as married	58 (53.7)	67 (59.3)	
Employment	Employed	65 (63.1)	72 (64.9)	.789
	Unemployed	38 (36.9)	39 (35.1)	
Injury mechanism	Transport	61 (56.0)	42 (36.8)	**.015***
	Falls	27 (24.8)	43 (37.7)	
	Other	21 (19.3)	29 (25.4)	
Trauma type	Minor	67 (61.5)	105 (92.1)	**.000***
	Major	42 (38.5)	9 (7.9)	
Injury intent	Unintentional	102 (94.4)	114 (100)	**.011***
	Intentional	6 (5.6)	0 (0)	
Injury type	Blunt	109 (100)	114 (100)	-
	Penetrating	0 (0)	0 (0)	
Median AIS	Head	1.00	1.00	.629[§]
	Face	1.50	1.00	.673[§]
	Neck	N/A	N/A	-
	Spine	2.00	1.50	.917[§]
	Thorax	2.00	1.00	.230[§]
	Abdomen/Pelvis	1.00	2.00	.069[§]
	Lower extremity	2.00	1.00	.231[§]
	Upper extremity	1.00	1.00	.121[§]
	External	1.00	N/A	-
Median ISS		11.00	4.00	**.000***[§]
ISS range		1–42	4–36	
Blood ETOH	<2mg/dL	47 (81.0)	18 (94.7)	.274
	>20mg/dL	11 (19.1)	1 (5.3)	
Median GCS[ǀ]		14.00	15.00	**.029***[§]

GCS‖ range		3–15	11–15	
Median ICU days		0	0	**.000***§
Median hospital days		8.00	12.00	**.036***§
Discharge	Home	62.4 (68)	89.5 (102)	**.000***
	Rehabilitation	29.4 (32)	5.3 (6)	
	Acute Care/Hospital	8.3 (9)	5.3 (6)	

Bonferroni-adjusted significance at $p<.05$; Ortho=orthopaedic; N/A=not available; AIS = Abbreviated Injury Scale; Blood ETOH refers to blood alcohol concentration in mg/dL; ICU=internsive care unit; †$\chi 2$ /exact tests; ‡ *t*-test; § Mann-Whitney; ‖GCS scores only available for 42% of total sample, and 69% recorded for TBI admissions in the dataset.

4.3 Application of Item Response Theory to enhance measurement properties of scales

Measurement theories

This section of the chapter describes the measurement theories often used in the psychological sciences, which includes methods or analyses based on *Classical Test Theory* and more modern frameworks that are based on *Item Response Theory*, such as *Rasch analysis*. Rasch methods are becoming increasingly popular in the psychometric assessment of measurement instruments, and its underlying framework and procedures will inform the first component of this PhD. This component, referred to as Study 1, aims to evaluate the psychometric properties and improve the precision of patient-reported outcomes utilising Rasch procedures and are detailed in the next few sections. Following this the conceptual framework underlying *Structural Equation Modelling*, or SEM will be explained, which will serve as the foundation for the analyses undertaken in Study 2. To achieve the aims of Study 2, SEM procedures were used to identify and test a model illustrating the relationships between comorbidities and outcomes after injury.

Classical Test Theory

Classical Test Theory (CTT) also referred to as the *true score model* underpins many psychometric approaches for the development of measurement tools in health. Essentially, CTT postulates a set of criteria to determine how effective proxy indicators (e.g., self-report questionnaires) are in estimating a variable of interest that cannot be directly observed (e.g., patient satisfaction). In as early as 1904, Charles Spearman recognised that making inferences about phenomena that are not directly observable was prone to some degree of error (Spearman, 1904). Spearman subsequently devised a method to correct a correlation coefficient for attenuation due to measurement error, and

to adjust for this correction using an index of reliability. These initial contributions to experimental methodology are regarded by some as pivotal in laying the theoretical groundwork for future development and refinement of the framework for CTT over the next quarter of the century (Traub, 1997). Lord and Novick's seminal work published in *Statistical Theories of Mental Test Scores* in 1968 culminated in the foundations of the model for CTT, with explanations of the true score and error score (Lord et al., 1968). They theorised that any observed score (*X*), is comprised of a true score (*T*) and errors associated with the observation (*E*), which can be represented by the following formula (Lord et al., 1968):

$$X = T + E$$

In other words, an observed score is determined by the actual state of an unobservable variable of interest (termed the hypothetical true score), plus all other influences (or random error) associated with this variable. Using pain as an example, which is an unobservable variable (X); it can be determined how an individual rates their subjective pain experience on a series of items in a questionnaire based on Likert-scale scoring (e.g., from 0 to 5, where 0=no pain, and 5=extreme pain). Each individual item is associated with sources of random error that could arise due to differences in the questionnaire used, method of administration (e.g., face-to-face interview, online questionnaire) or a person's mood/emotions at the time of the assessment. In CTT, measurement errors are assumed to be homogenous and are therefore represented as a single variable. These errors are also assumed to be independent and randomly distributed around a mean of zero. Hence, as more items are included in a scale, the greater the attenuation of errors, and therefore the less likely that errors will influence mean scores (Streiner et al., 2015).

Key statistical concepts associated with CTT include correlation, item difficulty (i.e., the proportion of people answering an item correctly), reliability and validity. *Reliability* refers to the strength of correlation between each item's score with the total (true) score and assesses how well an item serves as a proxy for the true score of the variable of interest. *Scale validity* refers to the ability of the tool to measure the phenomenon it purports to measure (e.g., whether a pain questionnaire accurately captures the construct of pain). Procedures such as *exploratory* and *confirmatory factor analysis* examine the correlations between a scale's items and are frequently used to explore dimensionality of a construct (*construct validity*). *Exploratory factor analysis*

(EFA) is used if factors are untested previously in literature, whereas *confirmatory factor analysis* (CFA) aims to confirm the presence of factors previously reported in the literature (Nunnally & Bernstein, 1994).

CTT has remained popular due to the simplicity in its concepts, and its wide-scale use in the development of many measurement scales. Many of the major statistical software packages such as SPSS incorporate components for scale development using CTT. Another main advantage is the non-specificity of the underlying model which allows it to fit most instruments well. The individual items do not all need to be optimal, and items with only modest associations with the underlying variable can be offset by combining multiple items in a scale. This can however result in scales with an unnecessarily large number of items with only superficial similarities between items (e.g., grammatical structure), instead of characteristics that are pertinent to the construct of interest (DeVellis, 2006). One of the shortcomings of CTT methods is the underlying assumption that all items in a scale contribute equally to the measurement of the construct. As a result, a CTT-based scale may demonstrate non-uniform sensitivity across the score range such that it may be more likely to distinguish between latent traits in the middle level than the upper and lower ends of the spectrum (Streiner et al., 2015). This psychometric approach has also been criticised for its lack of precision in measurement error, particularly for its assumption on the linearity between the observed and true score (Streiner et al., 2015). Proponents of alternative methods such as *Generalisability Theory* argue that CTT methods fail to address the different sources that lead to variability in errors in estimating instrument reliability (Bloch & Norman, 2012). Furthermore, as parameter estimates (e.g., item/scale reliability, discrimination) under CTT are only applicable to the sample it is tested on, results are limited in their transferability across samples. One of the fundamental limitations of CTT is that owing to the ordinal structure of scales, it violates the assumptions underpinning parametric statistics. This means that ordinal scales do not permit the calculation of means and standard deviations as they do not enable arithmetic operations such as addition, subtraction, multiplication and division. In obeying the rules of fundamental measurement, it also means that total scores from ordinal scales cannot theoretically-speaking be derived unless they have been transformed into linear scores. Nevertheless, the practice of reporting total scores from ordinal measures is one that is commonly but erroneously conducted across research.

Item Response Theory

In order to address the shortcomings of classical test theory, modern techniques such as *Item Response Theory* (IRT) were developed, the roots of which can be traced as far back as Thurstone's 1925 paper on latent trait theory entitled "*A Method of Scaling Psychological and Educational Tests*" (Thurstone, 1925). IRT allows a more precise way of evaluating the performance of scales in the measurement of latent traits. Where CTT looks at item-to-total correlations, the IRT model attempts to derive a precise mathematical relationship between each item and the variable of interest. Thus, this frequently results in shorter, more reliable scales producing interval-level scores (Bond & Fox, 2015). In principle, the IRT model assumes a nonlinear regression of a person's responses, whereby the probability of a response on an item is dependent on an individual's ability on a latent trait. This relationship can be represented graphically with an item characteristic curve (ICC), where the *x*-axis represents the location of an item or person on a latent variable, and the *y*-axis shows the expected value of a person with a specific amount of ability. The Rasch model discussed below can be considered a one-parameter variant of the IRT model given the mathematical similarities it shares with its parent model. However, the two approaches have a distinct difference in that IRT aims to find the optimal model that best fits the data, whereas in the Rasch model the data are required to meet the requirements of the model (Andrich, 2004). Detailed explanations of the Rasch model and its requirements are presented in the following section.

The Rasch unidimensional model

The Rasch model, first developed by Georg Rasch in 1960 (Rasch, 1960), overcame many of the limitations that were problematic with ordinal data. Its foundations are grounded in the concept of expected response probability, which addresses the probability of answering a question correctly (or successfully) as contingent on the ability of the person and difficulty of the item. The term probability is used as there is a chance that a person may pass or endorse an item when it was not expected (e.g., depending on their mood on a given day). There are a number of criteria that are required to be met for the model, and unlike in CTT which only provides statistical descriptions of responses, Rasch analysis tests whether data from a measurement scale fit with the model. The advantages of Rasch analysis include the ability to obtain detailed information about the performance of individual items, and the ability to evaluate to what extent an item measures the latent trait for individuals of the same

ability, but of a separate subgroup of (e.g. males versus females). Arguably the most important advantage offered by Rasch analysis is that when a scale has achieved the core criteria of the Rasch model, an ordinal scale can be transformed to an interval-level measure that permits the use of parametric statistics, which would normally be violating statistical assumptions if ordinal scores are used (Bond & Fox, 2015). When data are transformed into a linear measurement with Rasch analysis, total scores using ordinal-interval conversion tables can also be generated which provides a reflection of a person's latent trait level (e.g., how much pain, 'how much' quality of life).

The Rasch model is underpinned by a set of assumptions, where:

- Each item in a scale has an *item parameter*, which refers to each item's level of difficulty on an underlying latent trait or construct. For example, it might refer to the level of ease or difficulty in achieving a task (such as walking unaided) or how easy/difficult it is to agree with or endorse a statement (such as satisfaction with quality of life). Therefore, a scale will be comprised of items that are less difficult and more difficult to endorse, which can be represented along an interval logarithmic scale according to their level of difficulty.
- Every individual has a certain amount of the latent trait or construct, which is termed the *person parameter* or person ability (e.g., level of satisfaction with sleep or amount of pain). Similar to item parameters, it is possible to place individuals along a logarithmic scale according to person ability, using the total score derived for each person.
- A fundamental principle underlying the Rasch model is that comparisons of persons is unrelated to any two items within the set of total items in a scale and conversely, the comparison of items is independent of item responses.

Therefore, according to Rasch model assumptions, it follows that the likelihood that the individual will pass or endorse an item is dependent on how much of the trait or construct is held by a person and an item's level of difficulty. The Rasch model is illustrated by a hypothetical item characteristic curve, typically following an S-curve as there is non-linearity between the expected and real scores. The curve is monotonic, meaning that the likelihood of obtaining a higher raw score increases as the underlying trait or construct increases.

Figure 3 gives an example of an item characteristic curve for item 1 ("How would you rate your quality of life") on the WHOQoL-BREF used in this study. In factor analysis,

the approach is to explore which model can be derived from the data (i.e. the underlying factors of a construct emerging from the data), whereas Rasch analysis examines if data produced from a measurement scale fit the Rasch model. If a scale meets the above expectations of the Rasch model (model fitting), the summation of the raw ordinal scores can be transformed into an interval scale resulting in increased precision of the instrument (Andrich, 1985).

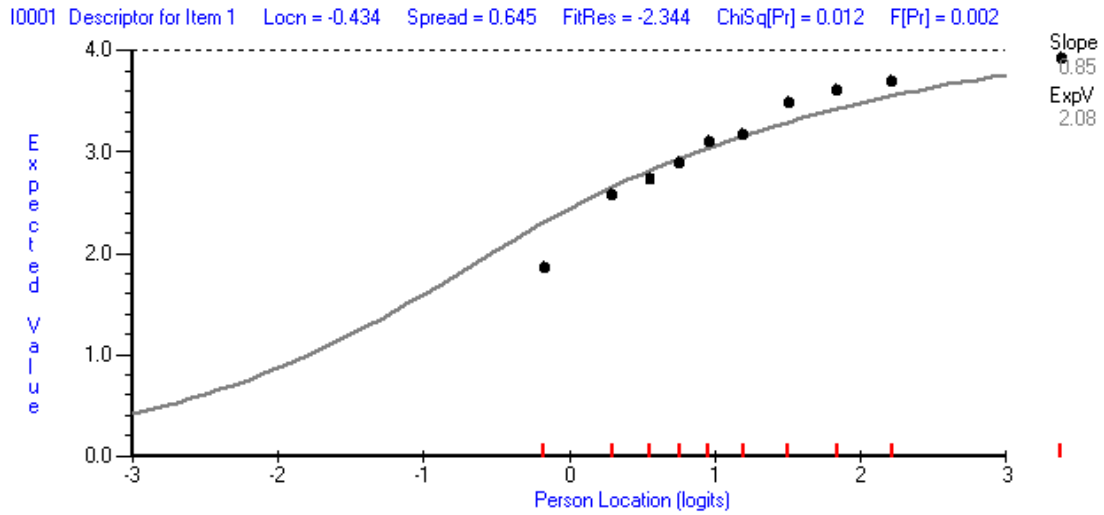


Figure 3. Item response curve for item 1 "How would you rate your quality of life" on the WHOQoL-BREF obtained from this thesis' data.

Note. The *x*-axis refers to the person parameter estimated from the Rasch analysis, and here signifies the level of quality of life, with lower values denoting lower quality of life. The *y*-axis displays expected scores on the item. The dots represent participants grouped by similar levels of the latent construct as defined by all items in the scale, and shows that those with higher quality of life are likely to score higher on this item. If the majority of dots are lying close to the line, it indicates that the item fits with the Rasch model. This item has a location of -0.43, which indicates its level of difficulty, relative to all other items in the scale (represented by a value of 0). Higher values indicate greater item difficulty.

The Partial Credit Model vs. Rasch Rating Scale Model

Two approaches exist within Rasch model theory and are commonly applied in instrument validation. These are the *Rasch Rating Scale Model* developed by D. Andrich (1978) and the *Partial Credit Model* by G. Masters (1982). The Rasch Rating Scale Model (RSM) is used when a set of items share the same rating scale structure and the distances between response thresholds are uniform across all items. In comparison, the Partial Credit Model (PCM) specifies that each item has its own rating scale structure owing to the variations in threshold distances across items. A likelihood ratio-test can be conducted prior to analysis to compare threshold distances between individual items. Where distances are significantly different (Bonferroni-adjusted $p<.05$) it dictates the appropriate use of the PCM over the RSM (Tennant & Conaghan, 2007).

Key considerations for evaluating model fit during Rasch analysis

When examining the fit of the data to the Rasch model there are several key points that need to be considered as discussed below. The steps involved in Rasch analysis are an iterative process, and were adopted from similar procedures described by Krägeloh et al. (2013); Lundgren Nilsson and Tennant (2011); Medvedev, Turner-Stokes, et al. (2018) and Siegert et al. (2010). Table 8 summarises the procedures that were followed in the conduct of Rasch analysis in Study 1.

1. Test of fit to the Rasch model

In order to assess whether the data fit the expectations of the Rasch model, three overall fit statistics are typically considered. Firstly, item and person fit residuals values should ideally be centred around a mean value of 0.00, with a standard deviation of 1.00 to indicate excellent fit of the data to the model (Krägeloh et al., 2013). Secondly, the *item-trait interaction* statistic is reported using a chi-square test, which measures the difference between the observed response and the expected scores by the model. Depending on the software package that is used, different fit statistics will entail slightly different information. For instance in the WINSTEPS program, INFIT and OUTFIT statistics are typically reported, whereas in the RUMM2030 package the residuals statistic is indicated by the use of chi-square, where observed values are compared against expected values across groups with different construct levels (called class intervals) (Tennant & Conaghan, 2007). Any significant deviation between these two scores where Bonferroni-corrected $p<.05$, indicates the presence of item-trait interaction, and reflects that the hierarchical ordering of items varies across the trait being measured. As well as overall model fit, individual item fit is also considered, where fit residuals falling within the range of -2.50 and +2.50 are deemed to have acceptable model fit. Items that are misfitting to the model, can be partly explained by disordered thresholds, differential item functioning, multidimensionality, or the presence of trait or local dependence (Tennant & Conaghan, 2007), as explained further in the following sections.

2. Order of item-response thresholds of polytomous data

Where items consist of polytomous options (i.e., items with more than two response categories), Rasch analysis creates log-transformed item scores from participants' responses to item response options, which theoretically should reflect increasing or decreasing levels of the construct. Following this assumption, it means that a person with very low 'ability' or location on the trait (as represented by the *x*-axis) will have a

higher probability of choosing a low response (e.g., low satisfaction), and consequently a lower probability of scoring on the higher response options (e.g., high level of satisfaction). Conversely, a participant with a high location on the trait, will be more likely to score higher on the item. This can be illustrated by a graph of probability curves (Figure 4), which shows the probability of an response option being chosen (*y*-axis) based on person location (ability) as denoted by the *x*-axis. Thresholds are the points where probability curves intersect, and indicate the equal probability of scoring either option 0 or 1, and 1 or 2 etc. It therefore follows that, for an item with ordered response thresholds the threshold points between 0 and 1 and between 1 and 2 etc., will increase from left to right along the *x*-axis as the overall latent trait increases. In some circumstances, thresholds are disordered and probability curves for response options do not work as theoretically expected as shown in Figure 5. Where there is significant threshold disorder, researchers may sometimes rescore items by collapsing response categories. The advantage of conducting this type of item inspection during Rasch analysis is that it allows researchers during the development phases to change items (either the phrasing of the question or response categories) where necessary. In traditional methods such as CTT, it is simply assumed that response categories will function as expected and as such is not explored further.

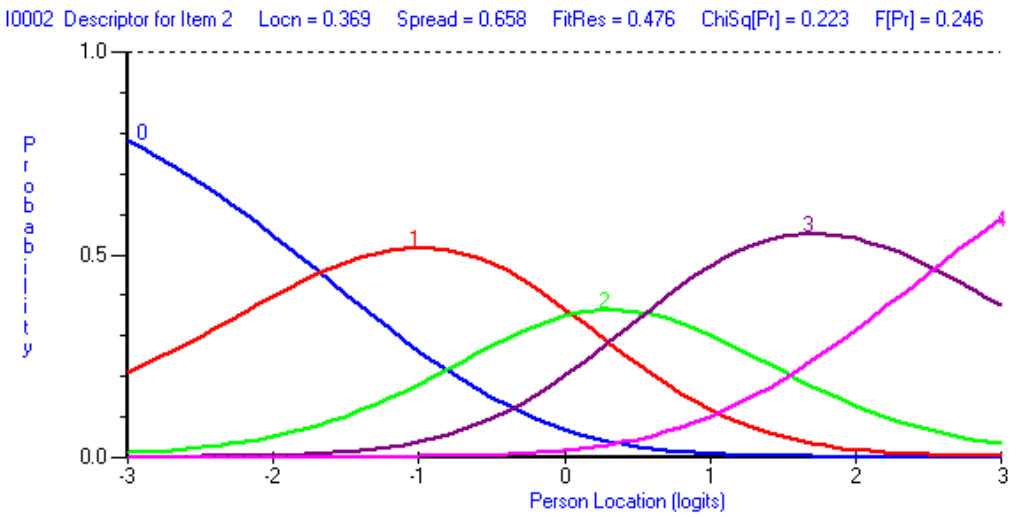


Figure 4. Item category probability curves illustrating ordered response thresholds item 2 (“How satisfied are you with your health”) on the WHOQoL-BREF instrument using data from this thesis.

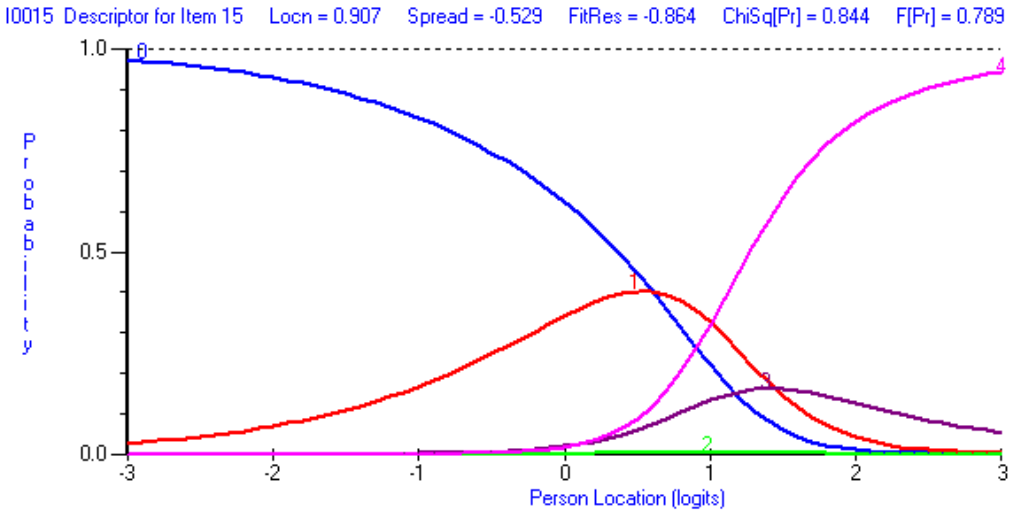


Figure 5. Item category probability curves illustrating disordered response thresholds for item 15 ("double vision") on the Rivermead Postconcussion Questionnaire using data from this thesis.

3. Item bias – Differential Item Functioning

One of the expectations of the Rasch model is that each item on a scale operates consistently across key demographic characteristics (e.g. gender or age). If a bias is detected, the item is said to have *Differential Item Functioning* (DIF). DIF can be uniform, where the bias is present at all levels of the trait, for example if scoring on an item is consistently lower amongst males at all levels of quality of life compared with females. Uniform DIF can be examined graphically using item characteristic curves and statistical analysis (analysis of variance). Employing DIF analysis is particularly useful during questionnaire development, where item bias can be addressed by removal of items (Tennant & Conaghan, 2007). In non-uniform or artificial DIF, bias is not present consistently across the trait and occurs spuriously as an artefact of the method for detecting DIF (Andrich & Hagquist, 2014). A post-hoc sign test of significance (Siegel & Castellan, 1988) as proposed by Krägeloh et al. (2019) gives indication of the presence of artificial (non-uniform) DIF.

4. Local dependency

Another key principle of the Rasch model is that items are only correlated through the measured trait or construct, which is referred to as *local independence*. There are circumstances when this assumption is violated, for instance where instruments contain item bundles that each measure a different component of the construct. In this situation, the primary higher-order component (or Rasch factor) alone does not explain the correlations between items in the same bundle, and points to the existence of multiple

factors or multidimensionality. This is sometimes also referred to as *local trait dependency* and can be investigated empirically in Rasch analysis by specifically testing for scale unidimensionality as described in the next section. A second way in which local independence is violated occurs when there are remaining correlations between residuals, once the Rasch component has been extracted. Evidence of residual correlations indicates that item responses depend not only on the latent trait but also on responses on other individual items on the scale and may occur due to similarities in item content or in response format (Olsbjerg & Christensen, 2015). The latter is known as *local item dependency* and results in the overestimation of reliability of the measure. Whilst there is no consensus on absolute cut-off values for the detection of local item dependency, some authors in this field have suggested examining values exceeding 0.20 of the mean of residual correlations as a guideline (Christensen et al., 2017; Marais & Andrich, 2008).

5. Unidimensionality

Unidimensionality refers to a scale that measures only a single construct or latent trait. In Rasch analysis any patterns emerging from the residuals are examined using principal components analysis to test for local independence of items. The test proposed by Smith (2002) inspects for any correlations evident between items and the first residual factor. An independent *t*-test is therefore conducted to look at differences between two subtests of positively and negatively correlated items for each person in the sample. The percentage of these differences exceeding the margin of -1.96 to +1.96 CI should not exceed 5% for the assumption of unidimensionality to be upheld (Tennant & Conaghan, 2007).

6. Reliability—Person Separation Index

It is important that a scale demonstrates the ability to clearly distinguish people with varying amounts of the construct. This can be measured by the *Person Separation Index* (PSI), which provides information on how individuals are spread out over the measurement construct. Values can range from 0 to 1 (Fisher, 1992; Wright & Stone, 1999), and values greater than .70 indicate the minimum threshold that allows for group comparisons. Tennant and Conaghan (2007) recommend using the more stringent PSI threshold of .85 for individual assessment.

7. Person—Item Threshold Distribution

A measurement scale should have a spread of items at varying levels of difficulty, with ideal values ranging from -3.00 to +3.00 SDs from the mean (Kersten & Kayes, 2011). For a well-targeted measure, where there is an equal proportion of easy and difficult items, the mean person-location should be ideally close to a value of zero. Positive values indicate that the sample is located at a higher level of the construct relative to the mean location of items, whilst a negative value suggests the opposite. Additionally, item coverage can be visually inspected to determine if the instrument has good coverage of the sample being tested. A scale that has many items clustered around the lower end of the scale (i.e., lower difficulty) and few at the upper end is indicative of *ceiling effects* (Figure 6), and suggests that the scale does not adequately measure higher levels of the construct. Conversely, *floor effects* (Figure 7) suggest that a measure does not effectively capture people on lower levels of the construct.

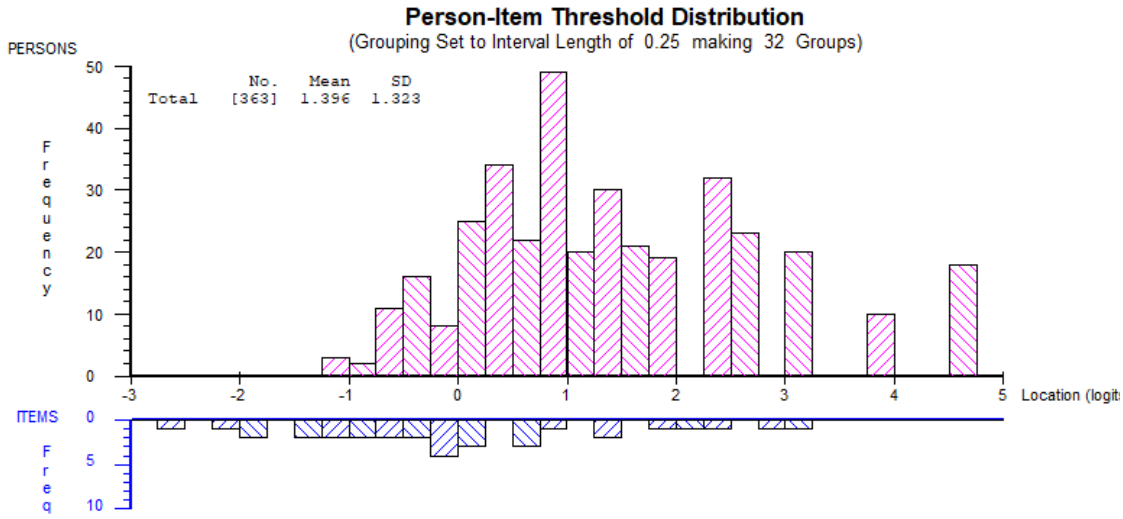


Figure 6. Person-item threshold plot indicating the presence of ceiling effects for the measure of quality of life using the EUROHIS-QOL-8 with data obtained from this thesis.

Note: The person location value of 1.396 as indicated in the plot suggests that respondents have higher quality of life relative to the mean item location.

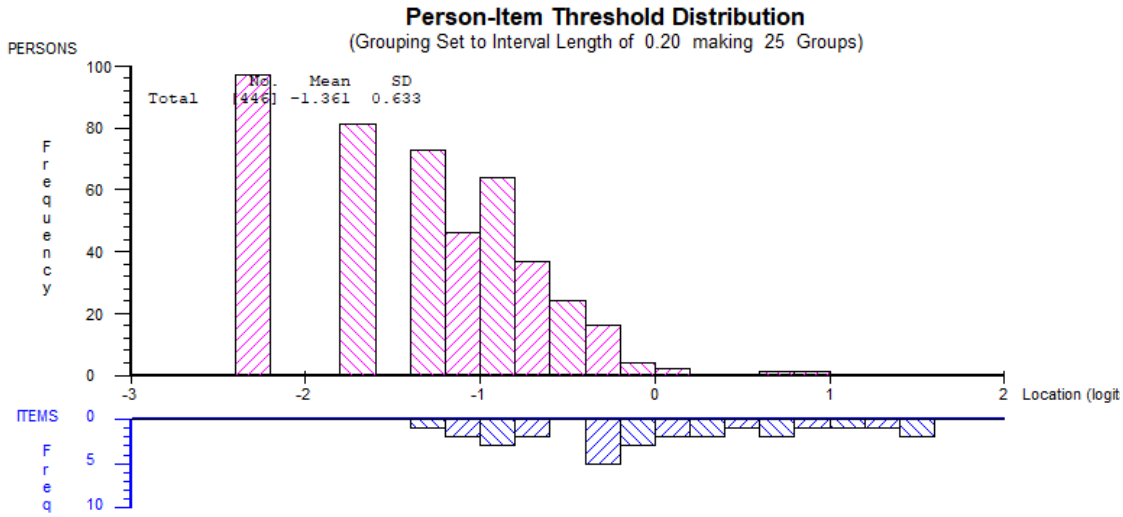


Figure 7. Person-item threshold plot depicting floor effects for the measure of comorbidity using the Cumulative Illness Rating Scale using data from this thesis.

Note: A person location value of -1.361 indicates that the sample in general has lower comorbidity levels, relative to the mean item location.

8. Creation of super-items

When deviations of the Rasch model are encountered (such as due to the presence of multidimensionality, DIF, local response dependency, threshold disorder) the conventional approach has been to rescore items by combining response categories, or to simply delete items that are affected. Many studies have employed this strategy albeit at the expense of shortening and modifying the scale. Recent changes in the approaches used in Rasch analysis by Lundgren Nilsson and Tennant (2011) suggest to use the method of '*super-items'*(also referred to as *subtests* and *testlets*) to overcome these deviations, whereby related items are paired according to their item correlations. In doing so, any common variance shared between items are effectively cancelled out and makes results easier to interpret. This method is superior to previous techniques as it maintains the clinical integrity and clinimetric properties of the scale, while at the same time satisfying modern psychometric standards without needing to delete items, which should only be conducted as a last-resort strategy.

9. Ordinal-to-interval score conversions

Lastly, in line with current guidelines for Rasch analyses Leung et al. (2014), recommend presenting ordinal-to-interval conversion tables where an instrument is found to have met the above requirements of the Rasch model. By employing these transformations from ordinal to interval scores, it allows the scale to have equal interval-level scaling. In doing so, it increases precision of estimates that accurately

informs magnitude of change and detects responsiveness (changes in scores) in measures.

Section summary

The first half of this chapter gave a brief account of the evolution of measurement theory, starting with classical test theory as the foundation of early psychometric measurement. The limitations of CTT methods were recognised by scholars and have subsequently led to the development and increasing use of more robust methods such as Rasch analysis, which is based on the framework of Item Response Theory. Rasch analysis offers an alternative approach to improve precision of instruments and is governed by certain assumptions that the data are required to meet, which were also explained in this section. The methods outlined in Rasch analysis detailed below and summarised in Table 8 were used to validate the outcomes as a collective aim of Study 1 of this thesis. The remainder of this chapter is dedicated to the theoretical framework and methods underlying structural equation modelling that informed Study 2 of this thesis.

Data analytical procedures for Study 1

Prior to conducting Rasch analysis, descriptive statistics are such as chi-square, t-tests were conducted IBM SPSS v. 25 statistical software (IBM Corp., 2017). Statistical significance was set at p=.05, two-tailed test. From continuous age data (in years), age groups were created as a categorical variable to assess DIF, and reflected equal proportions of participants in the sample. For the Rasch analyses of the CIRS and RPQ which utilised only the TBI and orthopaedic groups, the following age categories were used for DIF assessment: 17.0–30.5 years (28.7%), 30.5–60.3 years (35.9%), 60.6–86.0 years (35.4%). As the Rasch analysis for the WHOQoL-BREF and its shorter versions was supplemented with a third group of general population respondents, details of the sample's demographic features are described in its relevant chapter in Chapter 7. Where missing data was greater than 10%, listwise deletion of cases, or removal of variables was considered as appropriate.

The procedure for conducting the Rasch analysis using RUMM2030 software (Andrich et al., 2010), consisted of firstly determining the appropriateness of the use of the polytomous Partial Credit Model over the Rasch Rating Scale Model using a likelihood ratio test where p<.05, indicates the appropriateness of the Partial Credit Model. Subsequent steps of the Rasch analysis entailed evaluation of overall Rasch model fit, scale reliability, unidimensionality and person-item targeting, as well as detailed item analysis including item fit, threshold ordering, and differential item functioning. Issues relating to the presence of DIF, local dependency, threshold disorder were addressed using the *super-item* approach, where items were paired according to their cross-item correlations. Detailed steps and criteria used for the Rasch analysis are provided in Table 8. Where the data has met the assumptions of the Rasch model, conversions from raw total ordinal to total interval scores were generated using algorithms in SPSS.

Table 8. Procedures and criteria for assessing fit to the Rasch model.

Concept examined	Description of procedure
Rasch model fit	Overall fit to the Rasch model was evaluated by observing chi-square (χ^2) statistics for item-trait interaction, item and person fit residuals. Under ideal fit conditions, item-trait interaction is not significant (Bonferroni-adjusted $p>.05$) and means and standard deviations for overall item and person fit residuals are close to 1.00 and 0.00, respectively (Krägeloh et al., 2013). Where the χ^2 is significant it reflects that the hierarchical ordering of items (item difficulty) varies across the trait or construct. Individual items were also scrutinised for performance, with fit residuals falling within the range of -2.50 to +2.50 indicating acceptable fit to the Rasch model (Medvedev, Turner-Stokes, et al., 2018).
Unidimensionality	Unidimensionality was tested for by way of principal component analysis of residuals excluding the latent trait component (Rasch factor) to detect if there are any further remaining associations between items (Tennant & Conaghan, 2007) . An independent *t*-test where the percentage of significant *t*-tests beyond $\pm$1.96 confidence intervals is <5% and/or if the lower bound confidence interval of significant tests overlaps the 5% mark, gives supporting evidence that the scale is unidimensional.
Reliability	The Person Separation Index (PSI), equivalent to Cronbach's alpha, gives an indication of scale reliability, with ideal values >.70 that allow for group comparisons, and values >.85 that allow for individual assessment (Tennant & Conaghan, 2007).
Targeting of persons and items	For a scale to demonstrate good coverage, items of varying difficulty should range between -3.00 and +3.00 SDs from the mean (Kersten & Kayes, 2011). Person-to-item targeting reflects how well targeted a measure is, and ideally the mean location should be centred around 0. Positive values suggest that the sample is located at a higher level of the construct, compared with the average of the scale, whilst the converse would be true for negative values.
Differential Item Functioning	Items were inspected for the presence of differential item functioning (DIF), which describes the effect that item performance is not invariant across demographic and diagnosis groups. The distinction was made between real DIF (uniform or significant DIF) and artificial DIF whereby the latter may occur spuriously as an artefact of the method for detecting DIF (Andrich & Hagquist, 2014). A post-hoc sign test of significance (Siegel & Castellan, 1988), where $p>.05$, was used as an indication of artificial DIF.
Ordering of response thresholds	The presence of significantly disordered response thresholds (which indicates that item response categories do not work as intended) was examined visually with category probability curves. Where necessary, threshold disordering may be overcome by collapsing response categories and rescoring items (Leung et al., 2014).
Local item dependency	Using guidelines by Andrich (1985); Christensen et al. (2017), the pattern of local item dependency (item responses influencing one another) were examined by looking at values exceeding the margin of $\pm$ 0.20 of mean residual correlations.
Merging of related items—'super-items'	Issues concerning DIF, local dependency and threshold disordering were addressed with the pairing of related items based on their residual correlations to create '*super-items*'(Siegert et al., 2010).

4.4 Structural Equation Modelling

Researchers are often interested in simplifying the understanding of social phenomena by analysing and delineating the complex interactions that can exist among variables. Some examples commonly explored in psychology are concepts of intelligence, personality, mindfulness and recovery, which can be explained using both manifest and latent variables. *Manifest* variables are observable and can be directly measured such as with the use of physiologic measures of blood pressure, heart rate or the brain's electrical activity. *Latent* variables on the other hand are not directly observed, and information is inferred from proxy measurement of observable variables. For instance, information about an individual's level of anxiety or depression can be inferred from administering a questionnaire (Kline, 2011).

Theoretical framework of structural equation modelling

Structural equation modelling (SEM) is a commonly used data analytic method that can be used to reduce a large number of latent and manifest variables into a more simplified model, by examining an array of correlations or relationships between observed variables. It was first used by geneticist Sewell Wright in 1918, to model simultaneous equations of genetic influences across generations and has since become a popular explanatory technique used in the psychological sciences. SEM is an extension of the multiple linear regression model and can be seen as a combination of confirmatory factor analysis (CFA) and multiple regression (Schreiber et al., 2006; Ullman & Bentler, 2012). Essentially, SEM attempts to extract factors out of a collection of variables in a dataset that are important in predicting the outcome variable, and determines how well these predictors explain the outcome (i.e., how much variance in the outcome is accounted for by each independent variable). It can be represented by the equation below, where y refers to the *observed* scores on the dependent variable, i is the constant of the y-intercept, X is a matrix of continuous or categorical (dummy-coded) independent variables, b represents the regression weights and e represents errors or residuals (i.e., leftover information unexplained by the model):

$$y = i + Xb + e$$

A main advantage of SEM is its ability to produce a graphical interface of complex relationships which encompass both direct and indirect relationships among variables in a theoretically grounded framework (Byrne, 2010). Another advantage of SEM lies in its ability to fit numerous linear models, including non-standard models, longitudinal

data, autocorrelated data (i.e. time series analysis) and variables with non-normal distribution (Maruyama, 1998). While alternative procedures such as multivariate linear regression might be used in place of SEM, these types of analyses would produce "mini-tests" of model components as they are limited in their mathematical capability to only run linear equations one at a time (Tomarken & Waller, 2005). In comparison, SEM provides measures of global fit indices to summarise even the most complex of models that contains a large number of linear equations. Additionally, the use of chi-square tests allows researchers to assess and compare the fit of alternative models that may differ in their composition. Owing to its broad analytical framework, recent developments to SEM methods have led to unique modelling capabilities such as the use of multi-level modelling for analysis of nested data structures, and latent growth modelling to analyse repeated measures (Tarka, 2018).

SEM nomenclature

SEM encompasses two types, namely the *measurement model* – i.e. the CFA component, which has the main purpose of confirming the theoretical relationships between observed and unobserved variables. The second component, the *structural model*, looks at relationships between *exogenous* and *endogenous* variables, and runs a succession of structural equations, which is equivalent to running a series of regression equations simultaneously (Byrne, 2010). The distinction between the two types of variables is that an *exogenous* variable is independent and exerts influence on other factors in the model, but is not itself influenced by these other factors. In comparison, an *endogenous* variable is an outcome and is affected by either exogenous variables or other endogenous variables. Exogenous and endogenous variables can be either latent or manifest depending on the model that is being tested.

Path diagram

A path diagram allows the structural relationships between exogenous and endogenous variables to be displayed pictorially. Figure 8 illustrates a regression model with six predictor variables (*X1* to *X6*) that are hypothesised to have an influence on the outcome variable, quality of life. It is important to note here that by convention, predictors that are manifest variables are illustrated by a box. For example, responses to a Likert-scaled item (e.g., from 1 to 5) would be signified by the use of a box. In contrast, latent variables (e.g., functional outcome and mental health status) are signified by the use of ovals. Here, the single-headed arrow from each predictor is pointed to the outcome with

the beta or regression coefficients denoted in the diagram as "*b*" representing the weights of the relationships. The residual "*e*" represents the unexplained information or variance, and the curved, double-headed dotted arrows between the predictor variables represent their intercorrelations, or covariance (a total of 15 in the diagram). If there was an absence of intercorrelations between predictors, then regression coefficients are interpreted in a simple way, by observing the bivariate weights. In circumstances where predictors are interrelated (as is often the case in actual empirical datasets) then variance must be partitioned (Kline, 2011). If interrelations among predictors are too large (referred to as *multicollinearity*), then the solution derived from the regression analyses may become too unstable, whereby individual coefficients fluctuate easily between strongly significant to nonsignificant status (Byrne, 2010). Multicollinearity in regression analyses is specifically examined with the *Variance Inflating Factor* which estimates the extent to which a regression coefficient is inflated due to the presence of intercorrelations between predictors. One approach to dealing with this problem in SEM is to conceptualise related variables as a single variable in analyses, instead of including them as two individual predictors. Alternatively variables might be dropped, such as with items that are seen to have low reliability in latent variables (Ullman & Bentler, 2012).

Direct and indirect effects

SEM uses directionality of relationships whereby *direct effects* represent the effect of an exogenous (independent) variable on an endogenous variable (dependent), such as the effect of experiencing a stroke on functional disability, or the effect of a person's mental health status on quality of life. An *indirect effect* represents the effect of an exogenous factor on an endogenous variable mediated by a separate third factor. In Figure 8, the impact of functional status (exogenous) on quality of life outcome (endogenous) is shown to be mediated by a person's mental health status (mediating factor). Therefore, the total effects on the outcome quality of life would be the sum of all the direct and indirect effects in the model.

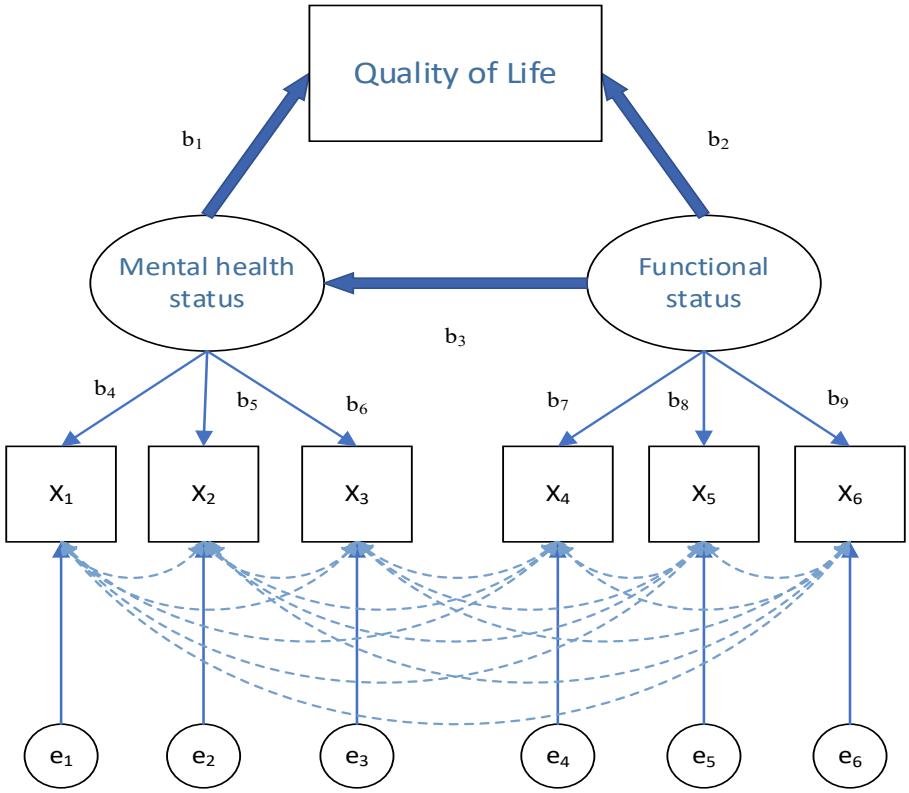


Figure 8. Example of a path diagram in SEM illustrating factors predicting quality of life.

Model identification

For SEM, the ability to derive solutions to regression equations is contingent on the number of known parameters versus unknown parameters in the model. This important preliminary step is known as *model identification*. The known parameters are the number of data points in the dataset, which is equal to the number of nonredundant sample variances and covariances. It can be expressed by the following equation, where "*p*" equals the number of measured variables (Ullman & Bentler, 2012):

$$Number\ of\ data\ points = \frac{p\ (p+1)}{2}$$

The number of parameters yet to be estimated (unknown parameters) in the model is equal to the total number of regression coefficients, variances and covariances that are to be calculated. In *just-identified models*, there are equal numbers of equations (known parameters) as there are unknown parameters. This means that there is just enough information to solve the simultaneous equations, and degrees of freedom are therefore zero. In *under-identified* models, there are more unknown parameters than known equations, and hence there would not be sufficient amount of information to solve the unknown parameters. In such situations, the number of unknown parameters need to be reduced by fixing, constraining or deleting. A parameter can be fixed by assigning a

specific value to the unknown parameter (e.g., 1), or constraining by making the parameter equal to another parameter. Conversely, models in which the known parameters exceed the number of unknown parameters referred to as *over-identified* models, result in more than one way of uniquely solving the equations (Maruyama, 1998). Although both just-identified and over-identified models can produce regression, over-identified models generally yield the best solutions (Schreiber et al., 2006).

Path analysis versus SEM

It is helpful to distinguish between the differences in path analysis and SEM, which are sometimes interchangeably and erroneously used to describe the same technique. In the correct definition of *path analysis*, hypothesised causality is only in a single direction (unidirectional), and therefore does not allow feedback loops among variables. This means that in path analysis variables cannot be cause and effect at the same time (Maruyama, 1998). Other assumptions of path analysis include the need for variables to be measured without error, which theoretically means that only observed variables can be used, and where latent variables are used any error terms stemming from model fit (residuals) should not be intercorrelated. These assumptions underlying path analysis, although desirable, rarely occur in real-world phenomena especially in psychology. Hence, one of the major limitations in path analysis is that it cannot determine direction of causality and is only applicable in a minority of cases where a relatively small number of hypotheses can be represented by a single path, such as in simple linear models. In comparison, SEM is less parsimonious in that it allows bidirectionality among variables (i.e., variables can be both cause and effect) and permits intercorrelations among residuals.

Parameters of SEM

The general guideline for SEM suggests the use of at least 10 participants per estimated parameter in the model (Schreiber et al., 2006). Pre-analytical stages include methods of handling missing data, which involve analysing response patterns to see if data are missing completely at random. This can be tested using Little's *Missing Completely At Random* (MCAR) test, where $p<.05$ indicates that missing data is not at random order (Little, 1988). The pre-analysis stage can also employ different techniques of estimating missing data such as using *Full Information Maximum Likelihood* (FIML) or *Expectation-Maximisation* (EM) where data are MCAR. In general, pairwise deletion is not recommended, and listwise deletion is cautioned against unless data are missing at

random (Allison, 2003). The post-analysis phase examines the model fit to determine if the hypothesised model is a good fit to the observed data. Depending on the software used, common goodness-of-fit indicators include the *Normed Fit Index* (NFI), *Non-Normed Fit Index* (NNFI also known as *Tucker Lewis Index* or TLI), *Incremental Fit Index* (IFI), *Comparative Fit Index* (CFI), and *Root Mean Square Error of Approximation* (RMSEA). For continuous data, suggested cut-off values for a good fit are RMSEA <.06, TLI >.95, CFI >.95 and *Standard Root Mean Square Residual* (SRMR) <.08 (Schreiber et al., 2006). These thresholds are applicable to categorical data as well, except for SRMR, which can be substituted with the *Weighted Root Mean Square Residual* (WRMR) with a cut-off at <.90 (Schreiber et al., 2006).

For one-off analyses, NNFI, CFI and RMSEA are generally used, but where modifications are made to the model following initial analysis, or where multiple models are iteratively tested, different indices are used. It is important to pay attention to individual structural paths, which often become secondary to the model fit. The significance of paths is determined by *t*- or *z*-values for structural coefficients. In this step, examination of residuals is also conducted, where the number of standard deviations of observed residuals transgressing from zero residuals indicates whether the model fits perfectly. A secondary method to analyse residuals is by inspection of the *Q*-plot, to determine if standard residuals deviate excessively from the *Q*-plot line (Ullman & Bentler, 2012).

Following initial examination of the fit indices, parameter estimates and residuals, post-hoc model modifications can be conducted to obtain a better fit than the original hypothesised model. A model that has been modified from the original is termed a *nested* or *hierarchical* model, and a chi-square test should indicate that the modified version is superior to the original model. Researchers, however, caution against applying modifications with the sole aim of merely improving fit, especially if the modifications do not hold sufficient theoretical justification (Byrne, 2010).

Section summary

The second half of the chapter summarised the applications of SEM in the social sciences, which can be a powerful statistical tool to empirically test a specified hypothetical model. This section also explained the assumptions and requisites of conducting an SEM analysis that involves steps of model identification, handling missing data, computing initial model fit, and applying model modifications. The next

section proceeds to the specific data analytical steps of the second study which aims to conceptualise and test a model to explain the relationships between pre-injury, peri-injury factors and outcomes.

Data analytical procedures for Study 2

Hypothesised framework for modelling outcome after injury

The main objective of Study 2 is to present an outcome model for the TBI and orthopaedic samples, and to enable an exploration into the factors that are unique to the outcomes for individuals with TBI in comparison with those who have experienced orthopaedic injuries.

Within the hypothesised framework, the aim is to present and test a theoretical model that encompasses demographic factors, injury and clinical characteristics and post-injury health conditions in predicting postconcussive symptoms, and consequently the impact on quality of life. Given the restrictions imposed by the small sample size (n=109 TBI and n=114 orthopaedic participants), relevant variables to be included in the models will be informed by significant predictors identified from the multiple linear regression models, that act as a preliminary step in model building. Thus, relevant demographic characteristics, injury and clinical variables, post-injury comorbid conditions as exogenous variables will be used to model predictive ability of RPQ and WHOQoL-BREF scores. A hypothesised model is presented in Figure 9, which outlines potential theoretical relationships between factors at different stages of the injury experience. Here, pre-injury factors include demographic factors such as age, sex, ethnicity, education, marital and employment status, as well as pre-existing health conditions assessed by the CIRS. Indicators of injury characteristics include overall injury severity score (ISS) and TBI severity (Glasgow Coma Scale). Lastly, factors occurring in the post-injury phases will incorporate the onset of comorbidities (post-injury scores on the CIRS), post-concussion symptoms (RPQ scores) and quality of life (WHOQoL-BREF) scores as outcomes. This hypothetical model was used as a guiding framework for the analyses of Study 2.

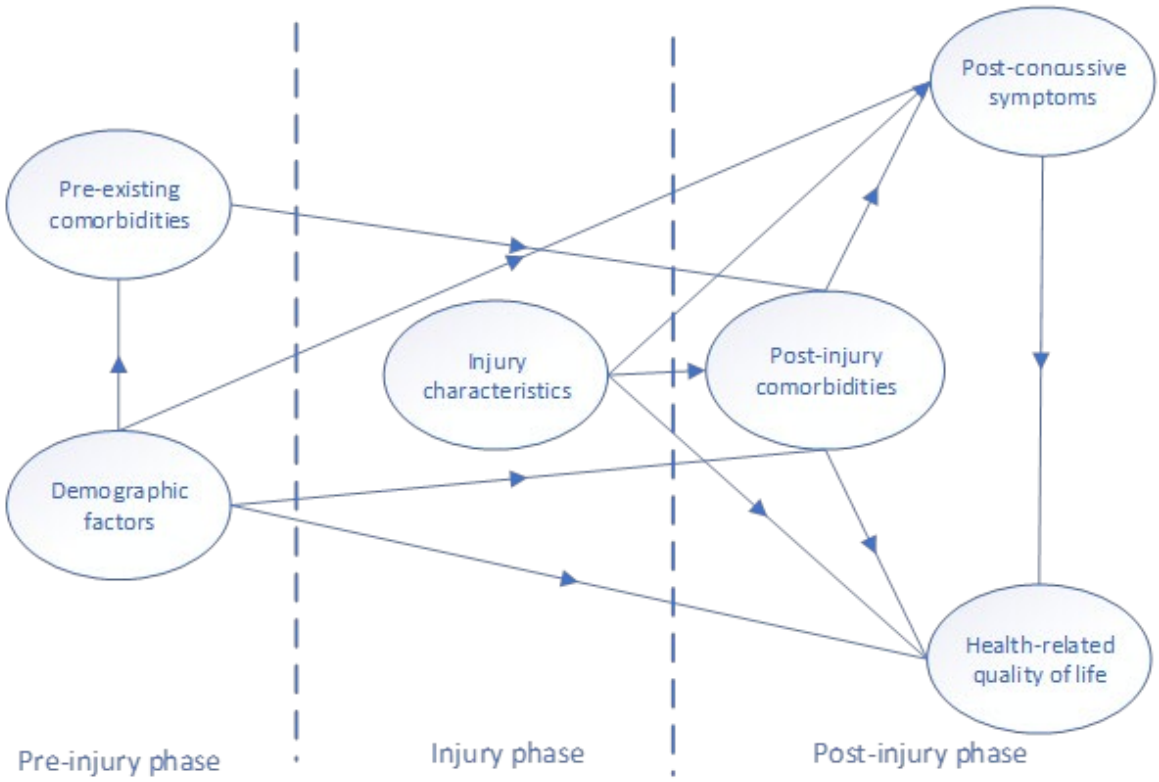


Figure 9. Conceptual model of recovery showing relationships between factors at different stages of injuries.

Multivariate linear regression procedures

Prior to conducting structural equation modelling, preliminary regression analyses using IBM SPSS v. 25 statistical software (IBM Corp., 2017) were used to identify the most relevant variables to include in the hypothesised model. The procedures for regression analysis including test assumptions are described briefly below. For the pre-analytic stages of multiple regression analysis, the following diagnostics were undertaken to ensure assumptions were met: linearity of dependent variables, outlier effects (Cook's Distance values <0.50), and normality of data (Kolmogorov-Smirnov test p>.05) (Belsley et al., 2005). In the overall sample (TBI + orthopaedic), all variables deviated from normality (p<.001) and some injury variables (LOS and GCS) and most comorbidity variables displayed excess kurtosis and skewness >|2.0| (Appendix 9). To correct for excessive skewness, comorbidity data were transformed using logarithmic base 10 function. In addition, the presence of multicollinearity was inspected by examining for Variance Inflation Factor values >10, in which case may necessitate removal of variables. Independence of residuals (homoscedasticity) was examined using residual plots. Statistical significance was tested at p=.05, two-tailed distribution.

For selection of variables into the hierarchical stepwise regression, demographic characteristics (age, sex, ethnicity, marital status, education level, and employment status), injury details (injury severity–ISS, and TBI severity–GCS), prior comorbidities, and post-injury comorbidities (measured by the CIRS) were entered using block-entry stepwise selection for predicting outcome measures RPQ and WHOQoL-BREF. In analyses with the WHOQoL-BREF as the dependent variable, RPQ scores were also included in the model using the forced entry method to determine the amount of additional variance that is explained by this variable, after controlling for the effects of demographic and injury characteristics, as well as prior and post-injury health problems. Statistical significance for inclusion in the stepwise selection was set at p=.05, with removal of variables at beta coefficients of <.10.

Separate hierarchical linear regression models were conducted for TBI and orthopaedic samples. The variable GCS was removed from the regression analyses due to 30% of missing data in the TBI sample. Lastly, moderation effects existing between demographic, pre-injury comorbidities and postconcussive symptoms were tested for in each model using multiplication terms.

SEM procedures

Using the statistical package AMOS v. 25 (Arbuckle, 2017) and informed by preliminary results produced by the regression analyses in the previous step, relevant demographic, injury and variables that were found to exert a statistically significant influence on outcome variables, were then modelled using the SEM methods described in section 4.4. Participants with non-random missing data (n=1) in the TBI sample were removed prior to analysis. In order to be able to discern between different outcome paths unique to each injury, SEM analyses were conducted firstly for the combined sample, and then separately for the TBI and orthopaedic groups. In addition, the use of ordinal versus ordinal-to-interval transformed scores (either through Rasch or logarithmic transformation) was compared in the models to determine the influence of ordinal and linear measures on model fit and beta coefficients. The procedures for SEM included evaluation of model fit using model chi-square, CFI and RMSEA, evaluation of individual paths and residuals, and regression weights to determine strength of relationships. Following transformation of measures using either Rasch analysis or log10 function, data showed normal distribution, and therefore the FIML parameter estimation method was selected. Post-hoc modifications to the model were carried out iteratively, by inspecting the statistical significance of relationships and modification

indices. Any non-significant relationships were removed from the model as they affected overall fit. All modification indices greater than 10 and which had theoretical basis were addressed by performing appropriate modifications in the model in a step-by-step process to yield the best model fit. Where indices were >15, modifications were addressed straight away in one step. All relationships between variables in the models are represented by standardised beta (β) coefficients and are significant at $p<.05$. Emboldened values and arrows indicate significance at $p<.001$, and "NS" indicates non-significance at $p<.05$.

Chapter summary

This chapter provided an in-depth discussion of the data analytical procedures involved in Study 1 and Study 2 of this PhD thesis, starting with an overview of the research objectives, participant recruitment process, and data collection procedures. This was followed by an introduction to the theoretical foundations of Item Response Theory and Rasch analysis, that inform the analyses for Study 1, which is focussed on enhancing instrument precision of outcome measurements. The section that followed described the framework of structural equation modelling for Study 2, that is used to model relationships between factors and outcomes in two injury samples. The next three chapters will be dedicated to discussing the results obtained from the Rasch analysis of the three measures used in this study: the CIRS (Chapter 5), the RPQ (Chapter 6) and the WHOQoL-BREF (Chapter 7). Chapter 8 presents and discusses the results for the SEM analysis. Chapter 9 integrates findings from both studies and discusses their implications to the wider research context.

Chapter 5 Study 1–Comorbidity profiles of TBI and orthopaedic participants and validation of the CIRS using Rasch analysis

Comorbidity profiles of injury patients are inconsistently reported in the injury literature, with many studies reporting only selected conditions with high prevalence in certain populations (van den Akker et al., 2001). One of the aims of this present chapter is to describe the pattern of pre-existing conditions and long-term post-injury comorbidities using the Cumulative Illness Rating Scale among participants who have experienced a TBI or an orthopaedic injury. The CIRS consists of 14 items assessing the severity of conditions across different organ systems, where ratings are given from 0–"no problem or past significant problem"; 1–"current mild problem"; 2–"moderate problem"; 3–"severe problem"; and 4–"extremely severe problem" (Salvi et al., 2008). As identified in the literature review in Chapter 2, validation of the CIRS is generally limited to the geriatric population (Miller et al., 1992; Parmelee et al., 1995), with no existing evidence for its utility in the injury population. Furthermore, in the existing literature no study to date has assessed the overall reliability and structural validity of the scale as a comorbidity measure. The aim of this chapter to therefore provide a descriptive analysis of the health profiles of TBI and orthopaedic participants at pre- and post-injury timepoints. Applying modern techniques of Rasch analysis described in Chapter 4, the psychometric properties of the CIRS are also evaluated. This seeks to determine whether the scale provides a reliable and unidimensional measure of overall comorbidity in the TBI and orthopaedic populations.

5.1 Data analysis

The sample consisted of both isolated cases of TBI and TBI cases with extracranial injuries grouped together (n=109), and orthopaedic participants (n=114) as presented in Table 7. Missing data were <1% and occurred at random order. Prior to conducting Rasch analysis, preliminary univariate statistics were conducted to explore some of the comorbidity differences on the CIRS ordinal measure between the TBI and orthopaedic samples, at the pre- and post-injury levels. One-way repeated measures multivariate analysis of variance (MANOVA) was used to determine if there were any differences across the 14 CIRS categories, between the pre- and post-injury timepoints. Where the Mauchly's test of sphericity indicates that the assumption of all variances between all possible pairs were not met, the non-parametric Friedman's test for correlated samples

(Friedman's Q) was applied. Differences in mean scores and mean Severity Index between TBI and orthopaedic groups (Table 9) and between TBI and polytrauma groups (Table 10) were evaluated using non-parametric Mann Whitney tests. Repeated measures were assessed separately for each injury group using Wilcoxon Signed Ranks tests and presented in the same tables.

The steps described in Chapter 4 and Table 8, were applied for Rasch analysis using the software RUMM2030, and included evaluation of model fit, scale reliability, item threshold ordering, differential item functioning, unidimensionality and person-item targeting. Deviations of the Rasch model such as the presence of DIF, local dependency and item threshold disorder were addressed using super-items. For Rasch analysis, only post-injury comorbidity scores were used for analysis, for the total sample of n=223. A likelihood ratio test did not support the use of the Rasch Rating Scale Model, $\chi^2(38)=268.20$, $p<.001$, and therefore the Partial Credit Model for polytomous items was applied for Rasch analysis, with results presented in Table 11.

5.2 Results

Descriptive profile of pre- and post-injury comorbidities in TBI and orthopaedic participants

Preliminary descriptive statistics revealed that the most common pre-existing conditions affecting TBI participants were psychiatric/behavioural problems such as anxiety and depression, which affected nearly a quarter of the sample. This was followed by hypertension controlled by medications (17%), musculoskeletal/skin problems (14%) and endocrine-metabolic disorders (14%). Pre-injury musculoskeletal problems reported by the TBI group were most commonly related to arthritis and past injuries that resulted in mild back or joint aches. Prior endocrine-metabolic disorders were mostly related to thyroid imbalances, elevated cholesterol or type 2 diabetes mellitus.

In comparison, in the orthopaedic sample, pre-existing musculoskeletal/skin problems affected about 40% of participants, which were most commonly arthritis-related and included mild chronic pain or discomfort of the back and joints (pelvis or extremities). Most pre-existing problems did not require the use of medication, and for some of these were due to experiences of past injuries. This category also included integumentary (skin) problems, where a small number of participants (n=5) reported having previous carcinoma or skin cancers that required surgical intervention. Endocrine-metabolic disorders such as elevated cholesterol and type 2 diabetes compensated by diet or

medication were reported by 25% of the group, while psychiatric problems such as anxiety and depression were reported by 25% of respondents in this sample.

Comorbidities affecting TBI participants at the post-injury phase included predominantly musculoskeletal problems (42%), of which many participants reported experiencing mild to moderate physical discomfort, as well as mild arthritis. Just over a third of the group reported neurological ailments with most complaints regarding frequent headaches or migraines, as well as chronic pain, and mild to moderate nerve damage. Within the neurological category, some reported having mild speech impediments, and noticeable changes in their olfactory and gustatory senses, and a further few reported additionally experiencing seizures, stroke or transient ischemic attacks since their injuries. Psychiatric disturbances (34%), notably anxiety and depression, were also commonly reported difficulties in this group.

In the orthopaedic group, the majority of participants (75%) reported experiencing post-injury musculoskeletal problems, with most somatic complaints regarding mild to moderate chronic pain and discomfort associated with the back, shoulder and extremity regions possibly relating to their injuries. For some, management of pain was required through occasional use of medications, and many also reported limitations in functional movement. Few expressed arthritis-related discomfort. Following musculoskeletal ailments, the second most frequently reported problem post-orthopaedic injury was related to psychological difficulties (35%) including feelings of anxiety, depression and in some cases experience of PTSD following injuries. This was followed by endocrine-metabolic disorders as the third most frequently reported comorbidity, notably elevated cholesterol and type 2 diabetes that were managed by medication. Neurological complications also affected almost a quarter of participants (23%), and these included most commonly numbness and nerve damage near the injury site, but also post-injury incidents of mild TBI, headaches. A small number also reported ischaemic events and slurred speech.

Univariate Statistics

A one-way repeated measures MANOVA was conducted to assess whether there were differences in scores across the 14 CIRS items at the two different timepoints. The violation of sphericity indicated by the Mauchly's tests [$\chi^2(0) = 1.00$, $p < .001$], required the appropriate use of the nonparametric Friedman's Q. Results of this test indicated that in the overall sample there was a statistically significant difference between pre-

injury and post-injury scores, $\chi^2(28) = 1706.07$, $p<.01$. Additional tests were conducted to explore this finding further by injury group as described below.

A Mann-Whitney test comparing overall comorbidity between TBI and orthopaedic participants did not indicate any group differences in terms of overall disease severity, Severity Index, or for severe (level 3) or extremely severe (level 4) conditions (Table 9). Upon closer examination at individual body systems, Mann-Whitney tests revealed significantly higher mean ranked scores among orthopaedic participants for pre-existing musculoskeletal/skin problems (mean rank 124.94 vs. 98.47, $p<.001$) and endocrine-metabolic conditions (mean rank 118.67 vs. 105.03, $p<.05$) when compared with the TBI group. With regards to comorbidities occurring post-injury, orthopaedic patients exhibited more musculoskeletal problems (mean rank 74.6 vs. 42.2, $p<.001$), whereas TBI patients reported more neurological-related health problems (mean rank 119.04 vs. 105.27, $p<.05$).

The right-hand side of Table 9 presents comparisons of repeated measures for the pre- and post-injury scores, separately for the TBI and orthopaedic group. In both groups, the total comorbidity scores ($p<.001$), comorbidities at level 3 category ($p<.05$) and Severity Index ($p<.001$), were significantly higher at the post-injury timepoint overall. Across specific categories, the TBI group demonstrated higher post-injury comorbidity scores for musculoskeletal ($p<.001$), neurological ($p<.001$), endocrine-metabolic ($p<.05$), and psychiatric/behavioural problems ($p=.001$). In the orthopaedic sample, post-injury comorbidity scores were higher in the EENT ($p<.05$), lower gastrointestinal ($p<.05$), musculoskeletal ($p<.001$), neurological ($p<.05$) and psychiatric/behavioural categories ($p<.001$).

Distinguishing between the isolated TBI ($n=74$) and the polytrauma ($n=35$) groups in Table 10, some minor differences were observed. Participants who had experienced polytrauma injuries reported significantly higher pre-injury comorbidity scores for renal (mean rank 59.81 vs. 52.72, $p<.01$), and neurological-related conditions (mean rank 59.94 vs. 52.66, $p<.05$) than isolated TBI cases. Following injuries, the polytrauma group reported significantly more problems in the respiratory (mean rank 60.46 vs. 52.42, $p<.05$), and also renal categories (mean rank 59.81 vs. 52.71, $p<.01$), but most notably in the musculoskeletal region (mean rank 64.74 vs. 50.39, $p<.05$).

Table 9. Comparisons of CIRS scores between TBI (*n*=109) and orthopaedic groups (*n*=114), and across pre- and post-injury repeated measures

	Pre-injury comorbidity‡					Post-injury comorbidity‡					Pre-post injury scores for TBI sample§		Pre-post injury scores for ortho sample§	
Disease category (CIRS item)	TBI *n* (%)	TBI mean rank score	Ortho *n* (%)	Ortho mean rank score	Exact Sig. (2-tailed)	TBI *n* (%)	TBI mean rank score	Ortho *n* (%)	Ortho mean rank score	Exact Sig. (2-tailed)	Z statistic	Exact Sig. (2-tailed)	Z statistic	Exact Sig. (2-tailed)
1. Cardiac	13 (11.9)	114.28	9 (7.9)	109.82	.332	17 (15.6)	114.85	12 (10.5)	109.27	.289	-1.983	.078	-1.841	.125
2. Hypertension	18 (16.5)	114.06	14 (12.3)	110.03	.449	19 (17.4)	112.48	18 (15.8)	111.54	.863	-1.043	.305	-2.060	.063
3. Vascular	7 (6.4)	111.08	9 (7.9)	112.88	.647	9 (8.3)	111.62	10 (8.8)	112.36	.858	-1.342	.500	-1.000	1.000
4. Respiratory	9 (8.3)	111.00	11 (9.7)	112.96	.648	11 (10.1)	111.03	13 (11.4)	112.93	.677	-1.000	.531	-2.000	.125
5. EENT	13 (11.9)	111.45	15 (13.2)	112.52	.835	26 (23.9)	113.47	25 (21.9)	110.60	.651	-2.905	**.004***	-2.352	**.027***
6. Upper gastrointestinal	10 (9.2)	113.27	8 (7.0)	110.79	.527	9 (8.3)	110.78	12 (10.5)	113.17	.621	-1.414	.500	-2.000	.125
7. Lower gastrointestinal	3 (2.8)	110.60	6 (5.3)	113.34	.491	5 (4.6)	108.63	12 (10.5)	115.22	.119	-1.414	.500	-2.271	**.031***
8. Hepatic	4 (3.7)	112.07	4 (3.5)	111.93	1.000	4 (3.7)	112.07	4 (3.5)	111.93	1.000	0.000	1.000	0.000	1.000
9. Renal	6 (5.5)	111.67	7 (6.1)	112.32	.958	6 (5.5)	111.18	8 (7.0)	112.79	.752	0.000	1.000	-1.000	1.000
10. Other genitourinary	13 (11.9)	112.73	12 (10.5)	111.30	.791	16 (14.7)	112.89	15 (13.2)	111.15	.762	-1.403	.266	-1.134	.500
11. Musculoskeletal/Skin	15 (13.8)	98.47	45 (39.5)	124.94	**.000***	46 (42.2)	98.62	85 (74.6)	124.79	**.001***	-5.221	**.000***	-6.488	**.000***
12. Neurological	12 (11.0)	110.82	15 (13.2)	113.13	.653	37 (33.9)	119.04	26 (22.8)	105.27	**.044***	-4.514	**.000***	-2.566	**.012***
13. Endocrine-Metabolic	15 (13.8)	105.03	30 (26.3)	118.67	**.025***	22 (20.2)	109.57	28 (24.6)	114.32	.456	-2.599	**.010***	-0.905	.563
14. Psychiatric/Behavioural	26 (23.9)	113.67	24 (21.1)	110.40	.607	37 (33.9)	111.32	40 (35.1)	112.65	.855	-3.097	**.001***	-4.011	**.000***
Comorbid disease frequency	70 (64.2)		84 (73.7)		.126†	92 (84.4)		103 (90.4)		.180†				
Severity Index		106.72		117.05	.217		110.59		113.35	.747	-6.545	**.000***	-7.193	**.000***
Level 3 category		116.81		107.40	.095		116.04		108.14	.205	-2.352	**.027***	-2.673	**.013***
Level 4 category		112.04		111.96	1.000		113.57		110.50	.401	-2.236	.063	-1.342	.500
Total score		108.85		115.01	.468		111.46		112.51	.903	-6.734	**.000***	-7.443	**.000***

* significance at $p<.05$; †χ^2 test; ‡ Mann-Whitney test; § Wilcoxon signed rank test; EENT=eyes, ears, nose, throat; comorbid disease frequency refers to total % of sample with any reported comorbidity; Severity Index = mean of 13 CIRS items excluding psychiatric/behavioural; levels 3 and 4 denote severe and extremely severe conditions, respectively; total score = sum of 14 CIRS items.

Table 10. Comparisons of CIRS scores for TBI (*n*=74) and polytrauma groups (*n*=35) at pre- and post-injury timepoints

	Pre-injury comorbidity†			Post-injury comorbidity†		
Disease category (CIRS item)	TBI mean rank score	Polytrauma mean rank score	Exact Sig. (2-tailed)	TBI mean rank score	Polytrauma mean rank score	Exact Sig. (2-tailed)
1. Cardiac	55.10	54.79	.946	55.32	54.33	.871
2. Hypertension	55.51	53.91	.738	55.07	54.84	.945
3. Vascular	54.36	56.34	.433	54.05	57.00	.270
4. Respiratory	54.92	55.17	1.000	52.42	60.46	**.028***
5. EENT	54.41	56.26	.684	55.00	55.00	1.000
6. Upper gastrointestinal	56.57	51.67	.163	56.34	52.16	.267
7. Lower gastrointestinal	54.99	55.03	1.000	55.46	54.03	.532
8. Hepatic	55.21	54.56	1.000	55.21	54.56	1.000
9. Renal	52.72	59.81	**.009***	52.72	59.81	**.009***
10. Other genitourinary	55.14	54.71	.867	55.89	53.13	.457
11. Musculoskeletal/Skin	54.13	56.84	.488	50.39	64.74	**.013***
12. Neurological	52.66	59.94	**.039***	53.49	58.20	.398
13. Endocrine-Metabolic	55.52	53.90	.744	54.95	55.11	.962
14. Psychiatric/Behavioural	55.63	53.67	.680	55.20	54.57	.911
Severity Index	55.91	53.09	.651	52.08	61.17	.158
Level 3 category	56.44	51.96	.397	55.47	54.01	.766
Level 4 category	53.50	58.17	.031	53.21	58.79	.108
Total score	55.78	53.34	.701	52.60	60.07	.248

* significance at $p<.05$; †Mann-Whitney test.

Rasch analysis of the CIRS

Table 11 presents the summary fit statistics for the Rasch model with corresponding Person Separation Index (PSI) and unidimensionality test statistics. Preliminary analyses for all 14-item pre-injury CIRS scores showed strict fit to the Rasch model [$\chi^2(56) = 64.05$, $p = .215$], evidence of unidimensionality but very low scale reliability (PSI=.26). Inspection of individual items in Figures 12–14, present item-person threshold distributions by diagnosis, age-group and ethnicity, respectively. Overall targeting of persons to scale items was not optimal given that the person mean was -2.56 (SD 0.66) and not close to the ideal value of 0. This suggests that the sample in general is located on the lower-most end of the comorbidity scale, with both TBI and orthopaedic participants showing similar levels of comorbidity (Figure 12). Item mean locations on the scale showed a range of spread across the construct, from -4 to 8 logits, while coverage of persons by items was very good, with no ceiling or floor effects. By age-group, older participants (60+ years) were placed higher in the comorbidity scale than younger age-groups [between-groups $F(220) = 16.43$, $p < .001$] (Figure 13). Results also showed significant group differences in item-person means by ethnic group (Figure 14). The NZ European group with a person-mean of -2.47 (SD 0.62) exhibited higher comorbidity levels than the Māori/Pacific/Asian/Other participants [person-mean of -2.75, SD 0.72; between-groups, $F(221) = 8.66$, $p < .01$].

Table 12 also showed no item misfit. Item-threshold plots show that thresholds were disordered for all items (example Figure 10) except for item 12 on neurological problems (Figure 11), as only a small proportion of individuals endorsed scores in the higher response categories. Figures 12–14, present item-person threshold distributions by diagnosis, age-group and ethnicity, respectively. Overall targeting of persons to scale items was not optimal given that the person mean was -2.56 (SD 0.66) and not close to the ideal value of 0. This suggests that the sample in general is located on the lower-most end of the comorbidity scale, with both TBI and orthopaedic participants showing similar levels of comorbidity (Figure 12). Item mean locations on the scale showed a range of spread across the construct, from -4 to 8 logits, while coverage of persons by items was very good, with no ceiling or floor effects. By age-group, older participants (60+ years) were placed higher in the comorbidity scale than younger age-groups [between-groups $F(220) = 16.43$, $p < .001$] (Figure 13). Results also showed significant group differences in item-person means by ethnic group (Figure 14). The NZ European group with a person-mean of -2.47 (SD 0.62) exhibited higher comorbidity levels than

the Māori/Pacific/Asian/Other participants [person-mean of -2.75, SD 0.72; between-groups, $F(221) = 8.66$, $p < .01$].

Table 12 also presents the response category distributions of the initial analysis, showing that endorsement of response categories for 3 or 4 (severe and extremely severe, respectively) across all 14 items were low, with the majority endorsing the 0 "no problem" response option. According to item fit locations, the comorbidity category on lower gastrointestinal problems (item 7) was the most difficult item for participants to endorse (fit location 1.65), whereas the category on musculoskeletal/skin conditions was the least difficult item to endorse (fit location -1.45). Examination of item bias revealed only non-significant DIF by age on items 2 (hypertension) and 14 (psychiatric/behavioural) using the post-hoc sign test, and some minor local dependency existing between items 1 (cardiac), 6 (upper gastrointestinal), 8 (hepatic), 10 (other genitourinary), and 14 (psychiatric/behavioural).

Table 11. Rasch model fit statistics for the CIRS (*n*=223)

Analyses	Item fit residual		Person fit residual		Goodness of fit		PSI	Significant *t*-tests Unidimensionality	
	Value	SD	Value	SD	χ^2 (df)	*p*-value		%	Lower bound
Initial (14 items)	-0.98	0.48	-0.38	0.57	64.05 (56)	.215	.26	0.45	-2.41 (YES)
Rescored (14)	-0.45	0.81	-0.31	0.78	55.35 (42)	.081	.33	4.04	1.18 (YES)
Final Super-items (7)	-0.13	0.64	-0.20	0.70	21.63 (21)	.421	.41	0.90	-1.96 (YES)

Note: Rescored—14 items rescored (0,1,1,1,1) denoting disease/no disease categories

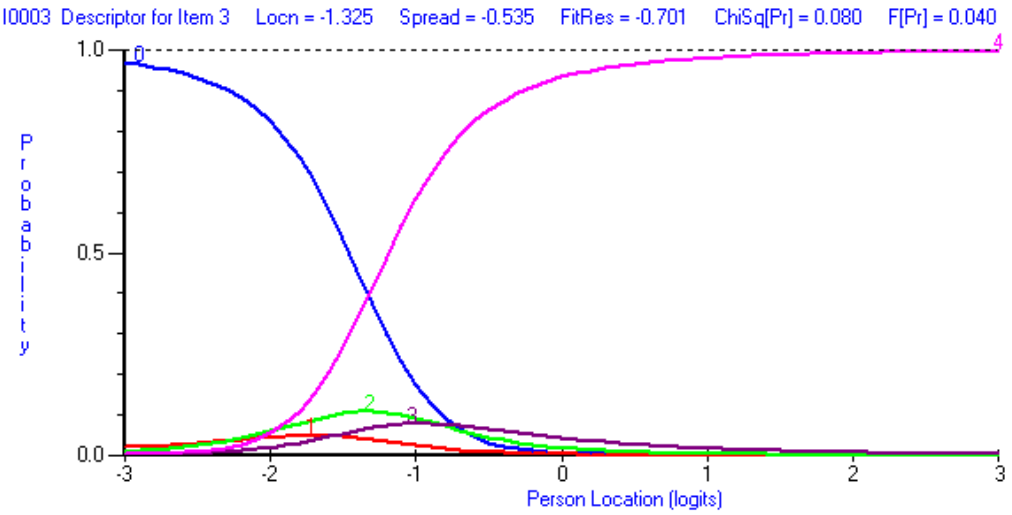


Figure 10. Item-threshold plot of CIRS item 3 (vascular conditions) showing disordered thresholds

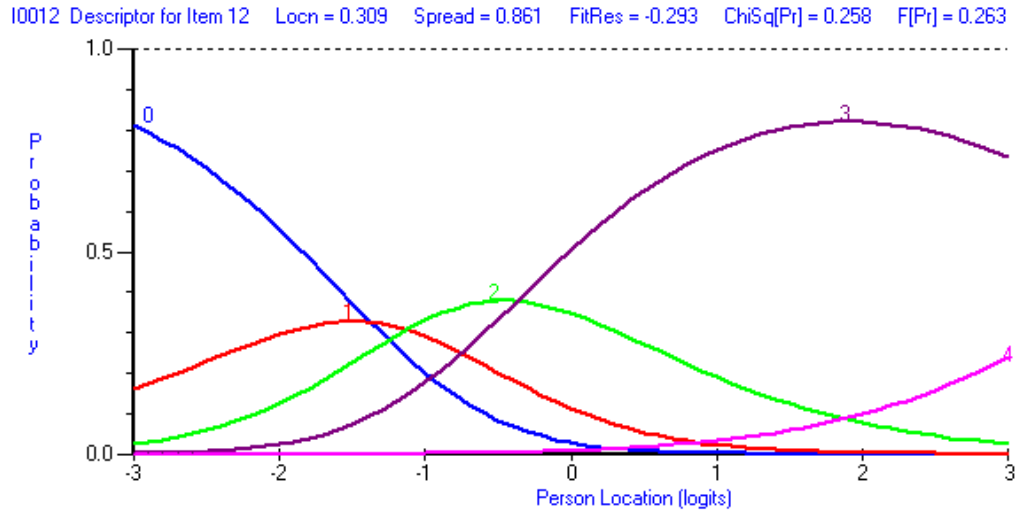


Figure 11. Item-threshold plot of CIRS item 12 (neurological conditions) showing marginally ordered thresholds

Figures 12–14, present item-person threshold distributions by diagnosis, age-group and ethnicity, respectively. Overall targeting of persons to scale items was not optimal given that the person mean was -2.56 (SD 0.66) and not close to the ideal value of 0. This suggests that the sample in general is located on the lower-most end of the comorbidity scale, with both TBI and orthopaedic participants showing similar levels of comorbidity (Figure 12). Item mean locations on the scale showed a range of spread across the construct, from -4 to 8 logits, while coverage of persons by items was very good, with no ceiling or floor effects. By age-group, older participants (60+ years) were placed higher in the comorbidity scale than younger age-groups [between-groups $F(220) = 16.43$, $p < .001$] (Figure 13). Results also showed significant group differences in item-person means by ethnic group (Figure 14). The NZ European group with a person-mean

of -2.47 (SD 0.62) exhibited higher comorbidity levels than the Māori/Pacific/Asian/Other participants [person-mean of -2.75, SD 0.72; between-groups, $F(221) = 8.66$, $p < .01$].

Table 12. Rasch model person fit statistics and response category distribution for initial analysis of the CIRS (n=223)

Disease category	Loca-tion	SE	Fit Resid	χ^2	Prob.	Response categories†				
						0	**1**	**2**	**3**	**4**
1. Cardiac	0.74	0.09	-1.97	8.66	.070	166	11	8	10	0
2. Hypertension	0.60	0.09	-1.28	2.91	.573	158	4	29	4	0
3. Vascular	-1.33	0.08	-0.70	8.33	.080	176	6	6	2	5
4. Respiratory	0.80	0.14	-0.35	4.91	.296	171	17	5	2	0
5. EENT	-0.88	0.09	-1.38	4.98	.290	144	33	11	6	1
6. Upper gastrointestinal	0.80	0.14	-0.82	2.99	.560	174	15	4	2	0
7. Lower gastrointestinal	1.65	0.17	-1.25	2.51	.643	178	11	6	0	0
8. Hepatic	-0.57	0.22	-0.93	1.95	.745	187	7	0	0	1
9. Renal	-0.84	0.15	-0.73	2.67	.615	181	11	1	0	2
10. Other genitourinary	0.73	0.12	-1.29	2.14	.710	164	21	6	4	0
11. Musculo-skeletal/Skin	-1.45	0.09	-0.97	0.74	.947	64	81	46	1	3
12. Neurological	0.31	0.11	-0.29	5.30	.258	132	45	15	3	0
13. Endocrine-Metabolic	0.49	0.09	-1.42	5.83	.212	145	15	28	7	0
14. Psychiatric/ Behavioural	-1.06	0.07	-0.41	10.15	.038	118	27	31	18	1

0— “no problem or past significant problem”; 1—“current mild problem”; 2—“moderate problem”; 3—“severe problem”; and 4—“extremely severe problem”; EENT=eyes, ears, nose, throat; *indicates misfitting items to the Rasch model, $p < .01$; †for post-injury CIRS.

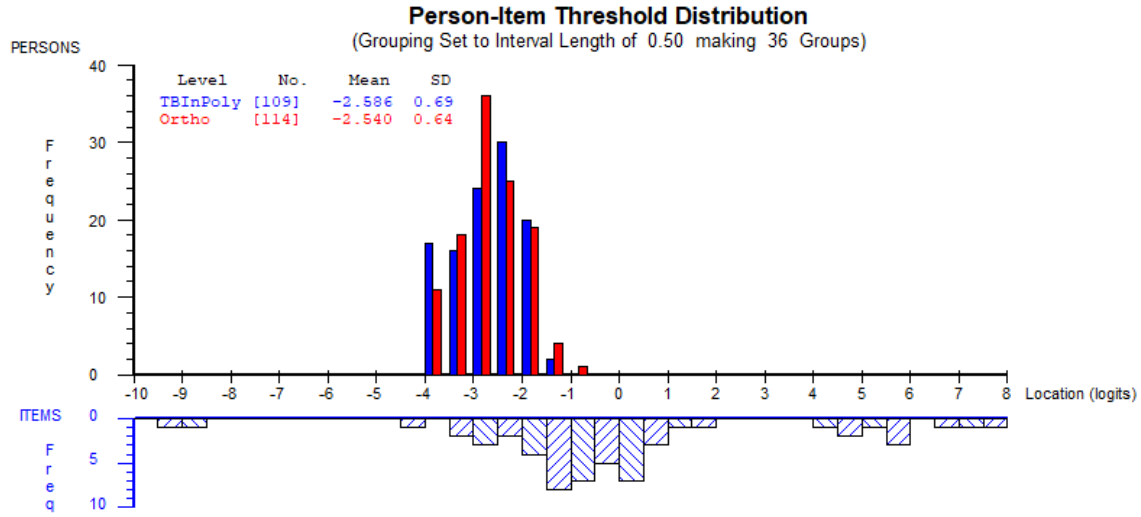


Figure 12. Person-item threshold distribution for the CIRS by diagnosis group: TBI and polytrauma (*n*=109) and orthopaedic injury (*n*=114)

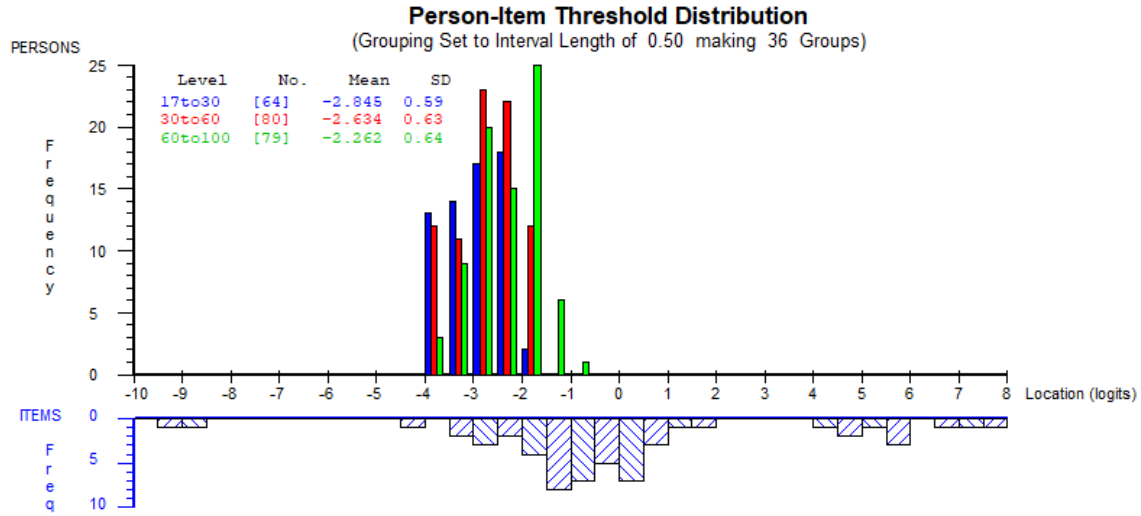


Figure 13. Person-item threshold distribution for the CIRS by age-groups: 17 to 30 years, 31 to 60 years and 60+ years (*n*=223)

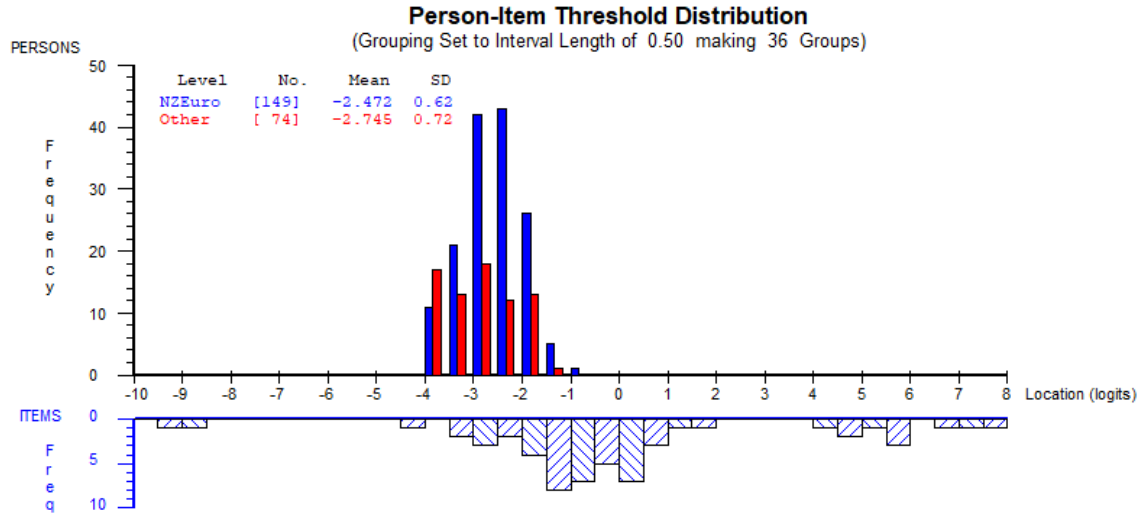


Figure 14. Person-item threshold distribution for the CIRS by ethnicity: NZ European and Others – Māori/Pacific/Asian/Others (*n*=223)

Following similar procedures conducted by Siegert et al. (2010), the original 14 items were rescored in an attempt to improve Rasch model fit parameters into dichotomous disease/no disease categories (0,1,1,1,1). As shown in analysis A1 in Table 11, rescoring of items retained strict Rasch model fit and unidimensionality, and corrected for disordered thresholds. This strategy resulted in a modest improvement in reliability, however the PSI remained unacceptably low at .33. The presence of artificial DIF by age-group was noted for item 2 on hypertension as shown in Figure 15, and the presence of minor local dependency was also observed for items 1, 2, 6, 8, 10 and 13. Employing the method of super-items with the pairing of the following items: 1+12, 2+11, 3+14, 4+13, 5+10, 6+8, 7+9, resulted in the creation of seven super-items in the final analysis as shown in Table 11. This approach enabled the correction of local dependency, and reliability to be improved to a PSI of .41 (corresponding to a Cronbach's α of .64), although overall scale reliability still remained below acceptable standards. Item bias was also evident by diagnosis group on the hypertension-musculoskeletal super-item [$F(1)=12.16$, $p<.001$], which is illustrated in Figure 16.

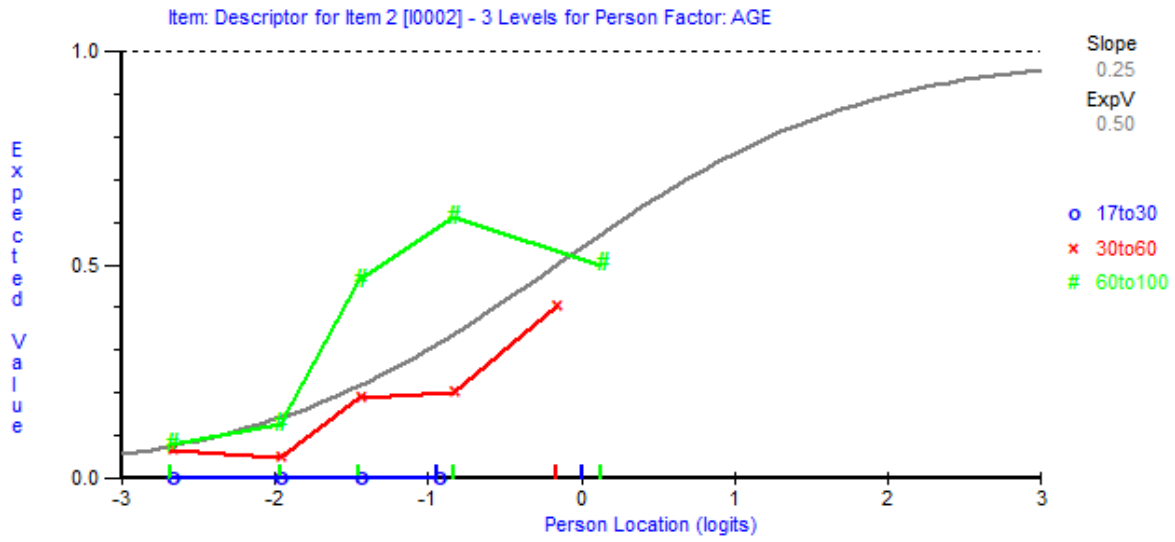


Figure 15. Item-characteristic curve for item 2 "hypertension", showing the presence of uniform DIF by age-group (17 to 30 years, 31 to 60 years, 60+ years)

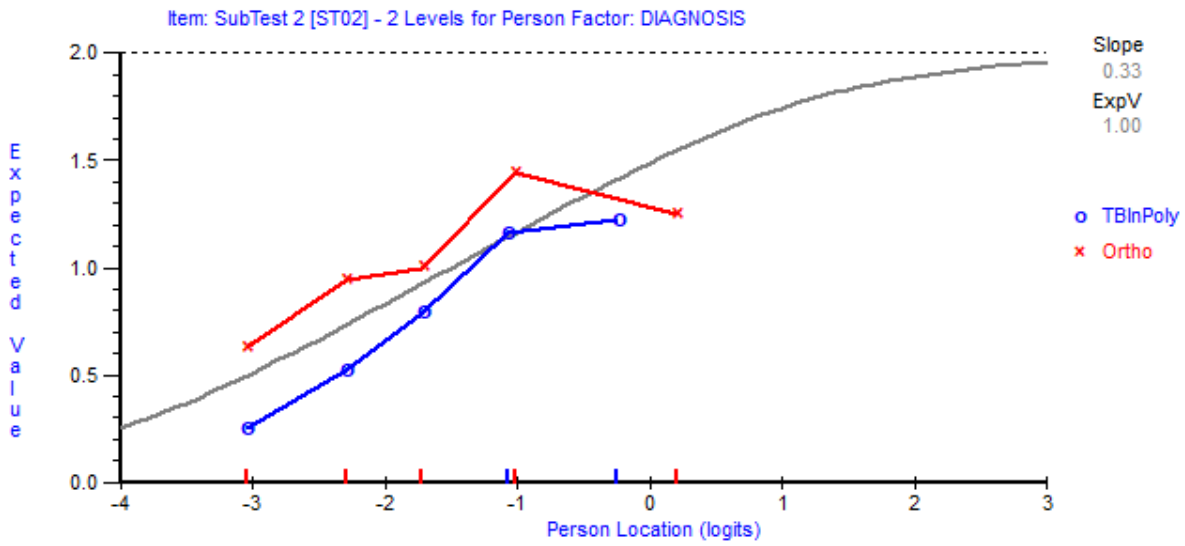


Figure 16. Item-characteristic curve for super-item "hypertension-musculoskeletal/skin" category, showing the presence of uniform DIF by diagnosis (TBI/polytrauma versus orthopaedic injuries)

5.3 Discussion

Preliminary statistics found that the most prevalent pre-existing conditions for TBI participants were psychiatric difficulties, with most participants reporting having a prior history of anxiety or depression. Additionally, pre-existing musculoskeletal injuries were also a common health problem in this group, with issues mostly relating to arthritis, and mild physical discomfort of the back, pelvis or joints. When the TBI group was sub-grouped by isolated and polytrauma groups, it was found that the latter reported marginally higher pre-existing renal and previous neurological problems (including past history of TBI). Among studies that have reported on pre-existing illness in TBI patients, the most frequently reported is history of psychological problems, and in line with the current study's observations (Myburgh et al., 2008; Novack et al., 2001; Robertson Jr. et al., 1994; Taylor et al., 2003). Others have also noted that individuals with prior psychological disorders have a higher predisposition to sustaining TBIs. One case-control study identified a 60% increased risk of TBI (adjusted relative risk of 1.6; 95% CI 1.4–1.9), for individuals with a prior psychiatric diagnosis compared with those without a history of psychiatric disorders (Fann et al., 2002).

Among orthopaedic participants, musculoskeletal problems were the most commonly reported pre-existing health condition, and similar to the TBI group, complaints were around mild pain and discomfort relating to arthritis or to previous injuries. The high proportion of pre-existing musculoskeletal problems is not an uncommon finding given

its increasing burden in the NZ population, which has been identified as the second most common cause of disability among 25–44 year olds (Ministry of Health, 2016), as well as being a common work-related problem (Lai et al., 2013). The higher pre-injury scores for musculoskeletal problems may also suggest an increased predisposition to sustaining an orthopaedic injury, and musculoskeletal deficits have been identified as a risk factor in falls-related injuries due to resulting unsteady gait and extremity weakness (Callis, 2016). In this sample orthopaedic participants were also more likely than the TBI group to report chronic conditions relating to the endocrine and metabolic disorders such as hyperlipidaemia (elevated cholesterol) and type 2 diabetes mellitus. Previous studies, which have typically used samples of older participants, have collectively found that the most prevalent pre-existing health problems were related to cardiovascular conditions, hypertension and diabetes mellitus (Bliemel et al., 2017; Lew et al., 2006).

Overall comorbidity severity, and total scores were significantly elevated at post-injury levels among both groups, particularly for musculoskeletal, neurological and psychiatric problems. Post-injury difficulties reported by the TBI group were most commonly musculoskeletal difficulties with participants more frequently reporting chronic pain, and mild to moderate discomfort in the back, shoulders and joints. For a small percentage, ongoing difficulties were related to extracranial injuries sustained to other regions of the body during the accident. Studies have shown that up to 80% of TBI patients commonly experience injuries to other parts of the body, which is linked to reduced physical functioning, chronic pain and lower quality of life (Gross et al., 2012; Lippert-Grüner et al., 2007; Stulemeijer et al., 2006). Within group analyses the TBI group only significantly differed from orthopaedic participants in the reporting of higher post-injury scores for neurologically-related issues. In line with the current literature (Masson et al., 1996), ongoing complaints were mostly related to frequent headaches and migraines, although Mickevičiene et al. (2004) found that symptom rates did not significantly differ between TBI and minor injury patients after one year. In the current study, a smaller percentage of TBI participants also reported experiencing mild speech impairments. Language and communication problems although more commonly seen moderate and severe TBI patients, have been found to affect those who have complicated mild TBI (Borgaro et al., 2003). Additionally, sub-group analyses for the TBI group revealed that polytrauma participants tend to report higher respiratory and musculoskeletal difficulties than the isolated TBI group, most likely resulting from the severity of additional injuries.

Orthopaedic participants portrayed significantly higher comorbidity scores in the musculoskeletal system following injuries, where 75% of the sample reported ongoing difficulties relating to mild to moderate chronic pain in the back, shoulders and extremity regions. In other studies, orthopaedic patients even with injuries in the mild spectrum often reported chronic pain as the most persisting difficulty following injuries, which is found to affect functionality and quality of life (Archer et al., 2016; Balogh et al., 2012; Ponsford et al., 2008). Interestingly, there were no significant differences in the reporting of psychological problems between the two groups, with approximately a third of both TBI and orthopaedic participants reporting ongoing problems with anxiety or depression and/or PTSD. In some recent studies researchers have found that psychological symptoms of anxiety and depression between injury groups are in fact similar (Archer et al., 2016; Stein et al., 2019).

In addition to providing a descriptive comorbidity profile of TBI and orthopaedic participants, one of the main objectives of this study is to psychometrically validate the CIRS measure using Rasch methods, to assess its reliability as a scale. When subjected to Rasch analysis, the CIRS measure achieved fit to the Rasch model, and also indicated that the scale is a unidimensional measure of comorbidity. However, results indicated that the scale overall has poor psychometric performance with very poor reliability (PSI .41) and therefore should be used with caution.

Closer examination of response distributions and item-threshold plots indicated major disordering and suggests that items are not functioning as intended, given that the majority of participants scored on the lower-most end of the comorbidity spectrum. As a result, item-person targeting for the CIRS was sub-optimal, although floor or ceiling effects were not evident in this analysis. The analysis also indicated the presence of item bias on the “hypertension-musculoskeletal” super-item between the TBI and orthopaedic injury groups. As the previous analyses did not indicate any item bias by diagnosis group in either the hypertension or musculoskeletal items, the reasons for the presence of DIF when the two items were paired, are unclear and require further exploration. Although the super-item approach resolved many of the issues of threshold disorder, DIF and minor local dependency, it achieved very little in improving person reliability of the measure.

Interestingly when scale reliability is compared between the PSI (.41) and Cronbach’s alpha value (.64), the pronounced differences entail different conclusions to be drawn

from the analysis. In reference to the PSI, the scale reliability suggests that the scale's scores should be used with great caution given the extremely low instrument stability. The Cronbach's α value on the other hand, suggests that although the overall scale reliability is marginally below the acceptable threshold of .70, it does maintain some clinimetric and psychometric utility. The differences in these values may be attributed to the way in which reliability estimates are derived. For example, in the calculation of person reliability, Rasch analysis uses non-linear transformed raw scores, and estimates for extreme persons in the RUMM 2030 software are by default excluded given that their standard errors are infinite (Clauser & Linacre, 1999). In the present analysis this meant that extreme persons who had a total comorbidity score of 0 and who accounted for about 10% of participants, were excluded from the sample. This subsequently reduced the available sample size to n=195, which is below the recommended number of 200 for use with the one-parameter Rasch model (Streiner et al., 2015; Wright & Tennant, 1996), and may have potentially affected results. In comparison, Cronbach's α is calculated with all raw scores including minimum and maximum scores, and thus scale reliability can be overinflated where there are outliers or skewed distributions (as was the case in this sample). Accordingly, when items and persons are misaligned, resulting in skewed distributions with extreme values, a difference emerges between α and the PSI, where the α remains more constant than the PSI. This means that, as scores become more extreme the error variance for persons increases, subsequently increasing error variance in the calculation of PSI. As such this will result in a lower person reliability for the PSI estimate, whilst such an effect is not seen in the calculation of the Cronbach's α (Linacre, 1997).

Previous studies that have validated the CIRS using classical test methods have reported on some psychometric properties such as good face validity, intra-rater and inter-rater reliability and test-retest reliability (Conwell et al., 1993; Extermann et al., 1998; Miller et al., 1992; Parmelee et al., 1995; Rochon et al., 1996; Salvi et al., 2008). The CIRS has also been demonstrated to have good concurrent validity with functional disability, but only adequate convergent validity with existing comorbidity measures such as the Charlson Comorbidity Index (r=.25 to .39) (Conwell et al., 1993; Extermann et al., 1998; Miller et al., 1992; Rochon et al., 1996; Salvi et al., 2008). There is, however, a notable lack of evidence regarding the internal consistency of the measure, which to date has only been assessed by the present study. From the findings of the present analysis it can therefore be concluded that the CIRS although a useful comorbidity

measure, nevertheless fails to meet modern psychometric standards required of scales. It is suggested that the scale's total scores, be interpreted with caution. Although as shown by the low scale reliability total scores on the CIRS present very limited accuracy, researchers might find instead greater informational value in analysing the comorbidity items individually, which did meet the requirements of the Rasch model in the present study.

Limitations

Given that this is the first analysis to have attempted to elaborate on the scale's internal consistency and construct validity the above findings should be treated with caution until further empirical evidence can be gathered to support or refute these results. In addition to the relatively small sample sizes (n=109 TBI cases and n=114 orthopaedic controls) it should be noted that this study was further limited by two generally healthy injury samples who presented with low comorbidity levels. Another limitation is that the pre- and post-injury CIRS scores were measured only at a single assessment timepoint, rather than at two timepoints. Given the wide timeframe of injuries (0.5 to 6 years post-injury) it is likely that self-reported pre-injury conditions were affected significantly by recall bias. Future studies may be able to undertake a validation of the CIRS in samples with higher comorbidity levels to assess if the psychometric properties in a more 'diseased' sample are likely to yield different results.

5.4 Chapter summary

The above findings suggest that TBI and orthopaedic groups have in general similar health profiles prior to their injuries with only minor differences, whereby the orthopaedic participants have a higher prevalence of pre-injury musculoskeletal problems, and endocrine-metabolic disorders than the TBI group. The present analysis also indicated that both injury groups have similar post-injury ailments, relating to musculoskeletal pain and discomfort, and psychological difficulties. The TBI group differed only with regards to having more neurologically related problems. Validation of the CIRS demonstrated in general good fit to the Rasch model, but also low instrument reliability. Further validation work on the CIRS is needed to ascertain its reliability as a health assessment tool, especially in samples who have higher levels of comorbidity.

Chapter 6 Study 1–Validation of the RPQ in a sample of TBI and orthopaedic participants using Rasch analyses

Chapter 2 described postconcussion syndrome as an array of symptoms commonly attributed to the experience of a mild TBI. Symptoms often include dizziness, headaches or migraines, fatigue, cognitive difficulty and feelings of depression and/or anxiety. The Rivermead Postconcussion Symptoms Questionnaire (RPQ) developed by King et al. (1995) is a 16-item self-report questionnaire that assesses the severity of 16 different postconcussion symptoms, and is typically administered to TBI patients following injury. In this questionnaire participants are asked to compare themselves with before and after their injury, and to rate the severity of symptoms experienced in the last 24 hours. Items employ a 5-point ordinal structure with the following response categories: 0 (never experienced at all), 1 (no more a problem), 2 (a mild problem), 3 (a moderate problem) and 4 (a severe problem). The instrument is one of the most widely used scales to assess PCS symptoms following TBI that has demonstrated good internal consistency, test-retest and inter-rater reliability (Eyres et al., 2005; King et al., 1995; Sullivan & Garden, 2011). As discussed in section 3.2, previous Rasch analyses of the RPQ in the TBI population in the first few months after injury yielded inconclusive evidence regarding the factor structure with Eyres et al. (2005) reporting two factors, whereas Lannsjo et al. (2011) reported the existence of three or more dimensions underpinning the construct. This ambiguity in factor structure can lead to difficulty in the interpretation of results, particularly regarding whether symptoms have to be analysed as separate clusters of symptoms, or if symptoms conform to a unidimensional measure of postconcussion syndrome to enable the calculation of a total score. While PCS symptoms scales have been used to show the existence of these symptoms among patients with chronic pain, psychological disorders, orthopaedic injuries and the healthy population (Chan, 2001; Dikmen et al., 2010; Iverson, 2006; Iverson et al., 2017; Smith-Seemiller et al., 2003; Theadom et al., 2018), there remains to date no psychometric evidence of these scales in non-TBI samples.

The present study aims to evaluate the psychometric properties of the RPQ with comparisons between TBI and orthopaedic participants who experienced injuries between six months to six years previously. This study attempts to assess whether the RPQ constitutes a reliable measure of PCS symptoms, that is useful for the assessment of long-term outcome after injuries, and to clarify on its factor structure.

6.1 Data analysis

The sample was comprised of 109 TBI (isolated TBI and polytrauma combined) cases and 114 orthopaedic cases. Table 7 presents the sample demographics and clinical characteristics. Missing data were approximately <1% and occurred at random order. The likelihood ratio test indicated the appropriate use of the Partial Credit Rasch model over the Rasch Rating Scale Model [χ^2 (44)=150.60, p<.001]. Evaluation of the RPQ as meeting the criteria of the Rasch model were followed according to the procedures in Table 8. Issues relating to the presence of DIF, local dependency, threshold disorder were addressed using the super-item approach, where items were paired according to their residual correlations. In line with current Rasch recommendations ordinal-to-interval conversion tables are presented in the Appendix 10, that can be used to improve precision of scoring, and to generate total interval scores.

6.2 Results from the Rasch analysis of the RPQ

In addition to summary fit statistics for item-person and Rasch model fit (Table 13), the percentage of symptom endorsement by injury group are presented alongside item fit statistics in Table 14. Distribution patterns of symptom endorsement were similar in both groups, with the majority of participants reporting that most symptoms were either not experienced post-injury or were not a current problem. TBI and orthopaedic groups differed across response categories on most items (p<.05) except on symptoms of sleep disturbance (item 5) and restlessness (item 16). TBI participants presented with significantly higher RPQ total ordinal scores than the orthopaedic sample (median score 15.00 vs. 4.00, Mann-Whitney U=2908.500, p<.001). Within the sample only 1.8% TBI participants and 14.5% orthopaedic participants had never experienced any symptoms after injuries. In comparison, 67.9% TBI and 2.6% orthopaedic participants endorsed experiencing at least one current PCS symptom. Approximately 47.7% of TBI and 17.5% of orthopaedic participants in the sample met the ICD-10 guidelines for a PCS diagnosis (World Health Organization, 2016). PCS symptoms were not correlated with length of time elapsed since injury (p =.106), or GCS scores (p =.229), but were correlated with injury severity (p<.05).

Table 13. Rasch model fit statistics for the RPQ (*n*=223)

Analyses	Item fit residual		Person fit residual		Goodness of fit		PSI	Significant *t*-tests Unidimensionality	
	Value	SD	Value	SD	χ^2 (df)	*p*-value		%	Lower bound
Initial (16 items)	-0.47	1.40	-0.30	0.95	111.37 80)	.010	.84	9.87	0.48 (NO)
Super-items (8)	-0.49	0.67	-0.37	1.02	63.77 (72)	.740	.87	3.59	0.73 (YES)
Final super-items (7)	-0.28	0.78	-0.38	1.06	41.24 (35)	.220	.87	4.04	1.18 (YES)

Preliminary Rasch analyses of the 16-item scale demonstrated high reliability (PSI=.84) and unidimensionality. However, the data did not meet the expectations of the Rasch model due to significant interactions existing between items and the trait [$\chi^2(80) =111.37$, p=.01], as shown in Table 13. Closer examination at the individual item level in Table 14 shows that item 5 (sleep disturbance), item 11 (poor concentration) and item 12 (longer to think) has significant misfit to the Rasch model exceeding the ± 2.50 acceptable threshold. In general, physical items with the highest item locations (e.g. dizziness, nausea, vision) were the most readily endorsed compared with affective or cognitive symptoms (e.g. sleep, fatigue frustration, memory) which displayed higher item difficulty. Items 3, 13, 14 and 15 illustrated some degree of minor, but non-significant threshold disordering (see Figure 17 and Figure 18). Artificial DIF by injury group was only present for items 5 (sleep disturbance) and 10 (forgetfulness). Figure 19 shows that orthopaedic participants reported more problems relating to sleep disturbance, whereas TBI participants reported more difficulties associated with forgetfulness as shown in Figure 20. A post-hoc sign test however, deemed both DIF effects to be non-significant.

Table 14. Item-level Rasch model fit statistics presented for the initial analysis of the 16-item RPQ with item locations, fit residuals, chi-square statistics, and % of participants endorsing symptoms by response category and injury group (TBI, *n*=109; Orthopaedic injuries, *n*=114)

	Rasch model person fit statistics					% Endorsing symptom category										
						TBI					Orthopaedic					Sig.
Item	Location	SE	Fit Resid	χ^2	Prob	0	1	2	3	4	0	1	2	3	4	
1. Headaches	-0.17	0.10	0.08	7.54	.581	37	47	9	4	4	72	20	4	4	0	.000*
2. Feelings of dizziness	0.65	0.12	-0.31	5.86	.754	36	50	11	3	0	76	21	1	2	0	.000*
3. Nausea and/or vomiting	1.54	0.15	1.03	5.49	.790	56	42	2	0	0	76	23	1	0	0	.009*
4. Noise sensitivity, easily upset by loud noise	0.16	0.10	-1.68	8.54	.480	48	34	10	6	2	86	10	3	2	0	.000*
5. Sleep disturbance	-0.44	0.08	**2.86**	27.43	.001	50	24	6	16	5	46	40	5	8	0	.571
6. Fatigue, tiring more easily	-0.87	0.09	-0.26	15.23	.085	21	40	14	22	3	40	38	11	8	3	.024*
7. Being irritable, easily angered	-0.52	0.09	-0.80	3.28	.952	37	36	8	14	6	59	28	9	3	2	.003*
8. Feeling depressed or tearful	-0.13	0.09	-0.40	5.24	.813	45	32	12	9	2	64	27	4	4	1	.006*
9. Feeling frustrated or impatient	-0.80	0.09	-1.33	8.72	.464	22	42	16	14	6	40	46	8	4	1	.001*
10. Forgetfulness, poor memory	-0.53	0.09	-0.77	7.33	.602	19	36	21	18	6	76	12	6	5	0	.000*
11. Poor concentration	-0.30	0.09	**-2.88**	14.85	.095	38	32	12	13	6	75	17	4	4	0	.000*
12. Taking longer to think	-0.52	0.08	**-2.80**	11.34	.253	28	31	18	16	6	72	19	4	4	1	.000*
13. Blurred vision	0.56	0.11	0.41	13.43	.144	71	19	5	5	1	85	11	3	1	0	.032*
14. Light sensitivity, easily upset by bright light	0.79	0.11	-0.32	8.15	.519	61	29	6	5	0	84	10	3	4	0	.001*
15. Double vision	0.91	0.18	-0.86	5.08	.828	81	17	0	1	1	96	4	0	0	0	.002*
16. Restlessness	-0.32	0.09	0.50	21.49	.011	48	30	12	6	5	60	32	6	2	1	.091

0—not experienced at all; 1—no more of a problem; 2—mild problem; 3—moderate problem; 4—severe problem; **Bold indicates significant misfit to the Rasch model**; *statistical significance at $p<.05$; † Mann-Whitney Test

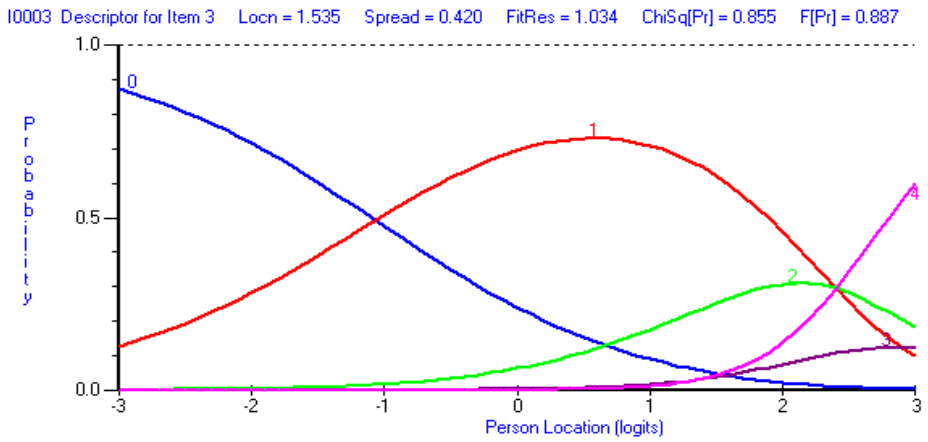


Figure 17. Disordered thresholds for item 3 "nausea/vomiting"

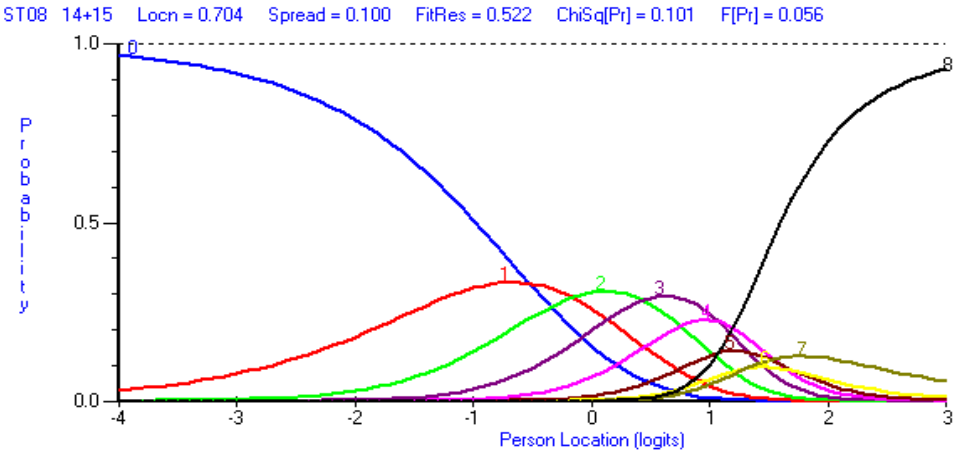


Figure 18. Disordered thresholds for super-item 8 "light-sensitivity-double vision"

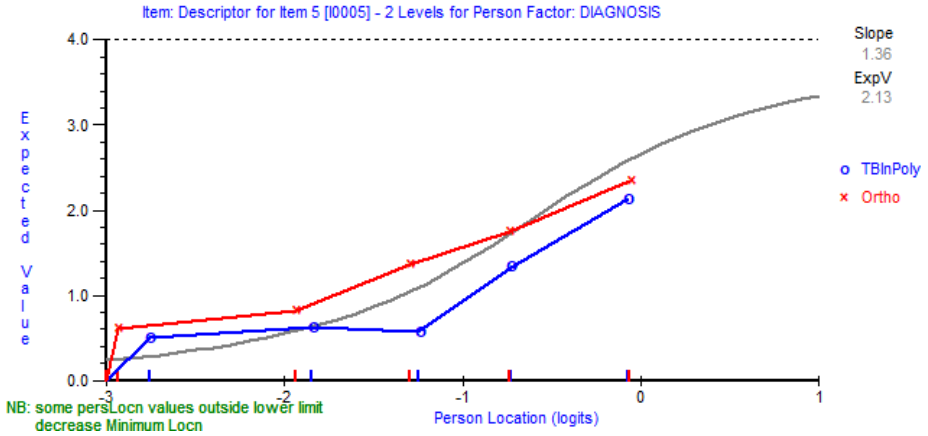


Figure 19. Item characteristic curve by diagnosis group showing non-significant DIF for item 5 "sleep disturbance"

Figure 20. Item characteristic curve by diagnosis group showing non-significant DIF for item 10 "forgetfulness"

Examination of the residual correlations indicated the presence of local dependency amongst several items (5, 7, 9, 10, 11, 12, 13, 14, 15), that suggests that items' responses may be influenced by one another. To reduce this measurement error affecting fit to the Rasch model, related items were subsequently paired to create eight super-items as follows: 1+9, 2+7, 3+12, 4+16, 5+10, 6+11, 8+13, 14+15. The eight super-items analysis showed a considerable improvement and yielded strong fit to the Rasch model [$\chi^2(72) = 63.77$, $p = .74$], unidimensionality and improved reliability (PSI=.87). There was some evidence of potential threshold disordering for three of the super-items, particularly for super-item 8 "light-sensitivity-double vision item", as well as evidence of local dependency between the super-items "depressed-blurred vision" and "light sensitivity-double vision".

To correct for the above deviations, these two super-items were thus condensed further to create a "super-super-item" hereby termed "depressed-vision" item. The final seven super-item analysis (inclusive of a single super-super-item) therefore retained strict unidimensionality and acceptable Rasch model fit, $\chi^2(35) = 41.24$, $p = .22$. Some minor but non-significant threshold disorder was still detected in the super-super item "depressed-vision", while there was also some residual evidence of local dependence between super-items "nausea-longer to think" and "fatigue-concentration". Further adjustment by way of merging these two items did not improve the Rasch model parameters.

As per Figure 21, targeting of the RPQ was not ideal for TBI participants (person mean -1.43, SD 1.56) who scored higher than the orthopaedic group (person mean -2.94, SD 1.59) and therefore portrayed higher severity of PCS symptoms. Overall targeting for the sample was sub-optimal and there was a considerable degree of floor effects (50%), mainly associated with the orthopaedic sample who generally displayed less severe symptoms. For the TBI group floor effects were acceptable at 12%, with individuals presenting with only minor symptoms of PCS not being well covered by items.

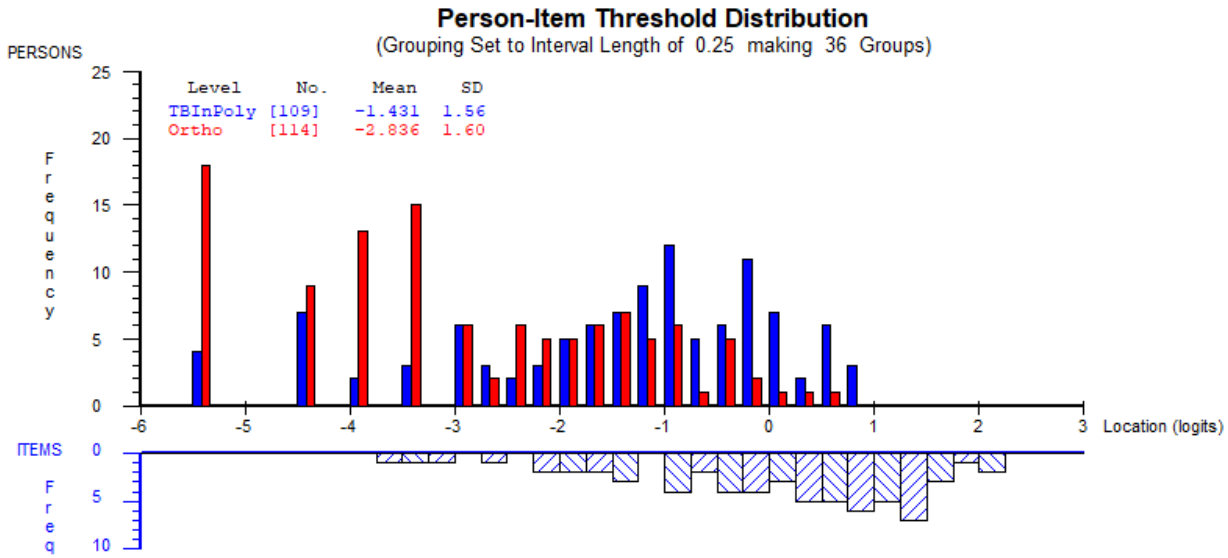


Figure 21. Person-item threshold distribution for the 16-item RPQ (*n*=223)

Transformation of ordinal to interval-level scores using the conversions presented in Appendix 10 produced a significant difference in scores [*t* (222)= -33.13, *p*<.001], as shown in Table 15. This means that for example, a participant with a total ordinal score of 1 on the scale Rasch transformation would actually shift this value to a 'true' interval-level score of 6.08 according to the conversions. Similarly, a raw ordinal total score of 2 means an individual's total score is 10.40 at the interval level. The Rasch converted scores to interval-level scores correlated with age for both injury groups, and ISS only for the orthopaedic group (*p*<.05), but not with GCS scores (Table 16). The RPQ interval scores also demonstrated good concurrent validity with comorbid illness on the CIRS, by comorbidity severity (SV), post-injury neurological comorbidity (*p*<.001), psychiatric comorbidity (*p*<.001), as well as with the WHOQoL-BREF Rasch converted total scores and domain scores (*p*<.001).

Table 15. Group comparisons using RPQ interval and ordinal-level scores, for TBI (*n*=109) and orthopaedic injury participants (*n*=114)

RPQ	Injury category	Mean (SD)	Median	Sig.
Interval scores	TBI	26.45 (10.77)		.000*†
	Orthopaedic	16.71 (11.02)		
Ordinal scores	TBI	15.16 (10.58)	13.00	.000*‡
	Orthopaedic	6.94 (7.36)	4.00	

Note: Mean ordinal scores were only calculated to support direct comparisons with mean interval scores; *denotes statistical significance at *p*<.05; †*t*-test; ‡ Mann-Whitney test was conducted on the median values of ordinal scores

Table 16. Bivariate zero-order correlations with comparisons across RPQ total (Rasch transformed) interval scores and RPQ total ordinal scores

Variables	TBI (*n*=109)				Orthopaedic (*n*=114)			
	Interval		Ordinal		Interval		Ordinal	
	r	Sig.	*rho*	Sig.	*r*	Sig.	*rho*	Sig.
Age	-.244	.011*	-.219	.022*	-.272	.003*	-.296	.001*
Follow-up (years)	.069	.479	.064	.508	-.126	.182	-.127	.179
LOS	.075	.441	.148	.124	.340	.000*	.400	.000*
ISS	-.014	.883	-.066	.494	.311	.001*	.390	.000*
GCS	-.143	.223	-.169	.147	-.220	.366	-.304	.206
CIRS SI post-injury	.193	.044*	.267	.005*	.219	.019*	.215	.021*
CIRS neurological post-injury score	.334	.000*	.327	.001*	.355	.000*	.336	.000*
CIRS psychiatric post-injury score	.375	.000*	.389	.000*	.375	.000*	.389	.000*
WHOQoL-BREF total interval scores†	-.612	.000*	-.675	.000*	-.481	.000*	-.466	.000*
Physical QoL domain interval scores†	-.523	.000*	-.575	.000*	-.467	.000*	-.470	.000*
Psychological QoL domain interval scores†	-.614	.000*	-.670	.000*	-.392	.000*	-.390	.000*
Social QoL domain interval scores†	-.297	.002*	-.323	.001*	-.326	.000*	-.290	.002*
Environmental QoL domain interval scores†	-.593	.000*	-.645	.000*	-.433	.000*	-.402	.000*

Note: Total ordinal scores were only calculated for the purposes of demonstrating correlations with variables; SI=Severity Index; LOS=length of stay; *significant at $p<.05$; † 24-item WHOQoL-BREF Rasch transformed scores (excluding anchor items 1 and 2) and its related domains: physical, psychological, social and environmental.

Table 16 also shows that when RPQ scores are transformed from ordinal into interval scores, the correlation coefficients between most variables only show a marginal reduction in strength, after adjusting for measurement error. In comparison for some variables, conversion from ordinal to interval resulted in minor improvements in strengths of correlations. This was particularly noticeable for age and RPQ for the TBI group, *r*=-.244 interval RPQ vs. *rho*=-.219 ordinal RPQ. For the orthopaedic group, this was evident between the WHOQoL-BREF social domain (Rasch transformed) interval scores and RPQ (*r*=-.326 interval vs. *rho*=-.290 ordinal), and between the WHOQoL-BREF environmental domain interval scores and RPQ (*r*=-.433 interval vs. *rho*=-.402 ordinal).

6.3 Discussion

The main objective of this study was to validate the RPQ in a sample of TBI and orthopaedic participants using Rasch analysis. This has not been conducted to date and the results from this analysis shows that the RPQ achieved good fit to the Rasch model, demonstrating strong reliability and unidimensionality. Items functioned invariantly across key demographic features (e.g. age, sex, ethnicity) and by injury group. A PSI value of .87 provides evidence for the measure's usefulness across group comparisons, as well as its clinical utility for the individual assessment of symptoms. Internal consistency is in accordance with estimates obtained from two other Rasch validation studies available on the RPQ (person reliability .71 to .95) as evidenced by Eyres et al. (2005); and Lannsjö et al. (2011). The RPQ in the present study additionally demonstrated good concurrent validity with neurological and psychiatric comorbidity scores on the Cumulative Illness Rating Scale and quality of life outcomes on the WHOQoL-BREF. While the RPQ demonstrated good coverage for the TBI sample, some minor floor effects that were detected (approximately 10%) suggested that the scale does not adequately capture those with low or no symptoms. These results are similar to those by Eyres et al. (2005) and Lannsjö et al. (2011), although Eyres et al. did note a marginally higher degree of floor effects (17.3%) in their sample. In the current study, coverage was also examined for the orthopaedic sample, and the considerable extent of floor effects (about 45%) suggests that the informational value provided by the RPQ for long-term PCS symptoms is limited, particularly if respondents present with no or only mild symptoms.

Using Rasch analysis, it was possible to confirm the structural construct validity of the RPQ as representing a unidimensional construct of PCS symptoms, which has not been achieved in past studies and therefore represents a unique finding from this study. In previous Rasch analyses Eyres et al. (2005) found support for a two-dimensional model consisting of a mixture of somatic (items 1 to 3), and psychosomatic symptoms (item 4 to 16). In comparison, Lannsjo's analysis (2011) revealed the existence of three or more dimensions underpinning PCS symptoms. Other studies using factor analysis methods have also lent support to multidimensionality proposing structures comprising of two to four factors (Barker-Collo et al., 2018; Herrmann et al., 2009; Lannsjö et al., 2009; Potter et al., 2006; Thomas et al., 2018). The lack of consensus amongst researchers as to a consistent factor structure of the RPQ has led to challenges in the calculation and interpretability of summary scores (Potter et al., 2006).

As these studies tend to be composed primarily of patients with mild TBI, discrepancies between study findings, may be explained by differences in timing of assessment of symptoms. Many of these studies tend to be focused on the first 12 months following injury and have collectively supported evidence for multidimensionality. In comparison, in the present study symptoms were assessed in the long-term phase following injuries (approximately 2.50 years). One may speculate whether in addition to the analytical approach (i.e. use of subtests or super-items), and sample differences (TBI and orthopaedic participants), the assessment of symptoms from a long-term timepoint may partly explain findings of unidimensionality that were observed in the current analysis. One may also gather from this finding that long-term enduring symptoms exist as a unitary construct for both TBI and orthopaedic injury patients, which is a novel finding in the PCS literature. Some researchers have also alluded to the possibility of symptom clusters amalgamating across the recovery path. A NZ study by Barker-Collo et al. (2018) supporting this hypothesis noted temporal changes to the factor structure, consisting of three factors at one month, and two factors at 6 and 12 months post-injury. The authors concluded a relative stability in factor structure after six months, distinguishing between dynamic or early symptoms present in the first three months and more stable symptoms thereafter. The concept of transient versus stable dimensions of PCS symptoms was further explored empirically by Medvedev et al. (2018) using the Generalisability theory. This study found that the RPQ was reliable in assessing enduring symptoms at 6–12 months, but insufficient in being able to assess dynamic symptoms that fluctuate across the initial days and weeks following TBI.

A more recent analysis by Barker-Collo et al. (2019) regarding the long-term structural validity of the RPQ at four years post-injury with comparisons to matched healthy controls, however, seemed to contradict their previous hypotheses of a stable factor structure appearing at 6–12 months. Instead, it was found that symptom composition was best explained by a 3-factor model for both long-term TBI patients (58% variance explained) and healthy controls (56% variance), with only minor variations in symptoms between the groups. Additionally, the authors did also note that among TBI patients, a 1-factor structure explained for 43% of variance in RPQ scores, suggesting it as an alternative model. Studies exploring the factor composition of long-term PCS symptoms are still in their infancy and require further development for conclusive statements to be drawn. Nevertheless, the present study helps to some extent to alleviate previous uncertainty of factor structure, by specifically testing for and confirming the

presence of unidimensionality within the measure when assessing symptoms from a long-term timeframe.

Within the Rasch analysis conducted in this study, detailed examination at the individual item level confirmed previous Rasch analysis work that RPQ items function invariantly by age and sex (Eyres et al., 2005; Lannsjö et al., 2011). However, unlike previous studies, the present study is the first to have evaluated DIF additionally by injury group. The lack of significant DIF by injury group across items suggested that items function invariantly by injury group and can be reliably administered to both TBI and orthopaedic patients as a measure of PCS symptoms.

From the above discussion, two notable findings have been produced by this study. The first is that, PCS symptoms exist as a unidimensional construct in both TBI and orthopaedic injury patients, and second, that the RPQ is a reliable measure that can capture long-term enduring symptoms in these two populations. This study also noted significant differences in the manifestation of enduring PCS symptoms, with TBI participants expectedly scoring much higher on the measure than orthopaedic participants. However there remains the question of whether the RPQ is actually measuring postconcussion symptoms as a unique sequel of TBI, or whether it is measuring a different construct, more common across the general population. The lack of specificity of the RPQ is corroborated by evidence from studies on the existence of PCS-like symptoms measured by the RPQ in various groups such as patients with chronic pain (Smith-Seemiller et al., 2003), depression (Chan, 2001), orthopaedic injuries (Mickevičiene et al., 2004), and even in healthy samples (Barker-Collo et al., 2019; Theadom et al., 2018). In light of this evidence, several researchers have questioned whether scales such as the RPQ are measuring PCS symptoms solely attributable to neurobiological mechanisms of a cerebral injury, referred to as *physiogenic factors*, or whether they are measuring symptoms that are circumstantial factors related to the experience of an injury, traumatic experience or simply daily stressors. The latter have been referred to as *psychogenic factors* (Meares et al., 2008; Williams et al., 2010). It is important to note that these two factors do not need to occur mutually exclusively, but can arise as a combination (Villemure et al., 2011).

The achievement of a unidimensional fit of the RPQ discussed earlier has several implications, the first being that it is a prerequisite for the calculation of a single total score (Reckase, 1979). The transformation of an ordinal scale to an interval

measurement using the conversions provided therefore allows for the summation of item scores to obtain a total score. From a clinical standpoint total scores are a useful indicator for clinicians to compare group and individual patients' change scores across repeated measures (Tennant et al., 2004). Secondly, from a statistical perspective, these conversions from ordinal to interval level also strengthen the precision of the scale by permitting the use of more precise parametrical testing methods that would otherwise violate the assumptions that are required to be met.

Comparisons between the ordinal scores and interval scores showed a considerable difference, where corresponding mean interval scores on the RPQ would result in an increase by about 10 points. As can be seen from the conversion table in Appendix 10, the magnitude of score differences is mostly concentrated in the lower-most end of the spectrum, amongst individuals who are seemingly asymptomatic but who may actually be experiencing some degree of PCS symptoms. Having demonstrated unidimensionality and conversion to interval total scores, this study may serve as a starting point for researchers to potentially develop thresholds for the RPQ to serve as a diagnostic tool for PCS symptoms. These future developments may help to determine to what degree collective symptoms indicate the presence of PCS symptoms in an individual (i.e. by establishing instrument sensitivity and specificity), and at what point clinical intervention may be necessary.

Limitations

Some limitations need to be acknowledged in this study. In addition to the small sample size, the assumption that most of the TBI participants were mild was based on the availability of GCS scores, which were only available for two thirds of the sample. Lack of complete data or inconsistent recording of GCS scores is not unique to this study, but is commonly reported in hospital registry data (Shivasabesan et al., 2018). As severe injuries were underrepresented in the sample, it does limit the generalisability of findings particularly to the severe TBI group who have also been found to experience PCS symptoms, but for whom the evidence is less well documented (Mittenberg & Strauman, 2000; Sigurdardottir, Andelic, Roe, Jerstad, et al., 2009). Another limitation is that isolated TBI cases and multiply injured TBI cases (i.e. TBI with extracranial injuries) were combined to achieve adequate statistical power. This may introduce some confounding to the results, making it difficult to differentiate between different injury groups within the TBI spectrum itself. Lastly, it should be acknowledged that different approaches have been undertaken to derive total scores. The original authors of the

RPQ measure King et al. (1995) excluded all responses of 1 “no more of a problem”, to detect change in symptoms since injury whereas other studies including for Rasch analysis have either combined response categories 0 “not experienced at all” and 1 (Eyres et al., 2005), or included all responses in the total score (Lannsjö et al., 2011; McMahon et al., 2014). The present analysis followed the convention used by Lannsjo et al., (2011) to include all scores in the calculation of the total score, provided that there was no threshold disordering, and the assumption of unidimensionality has been met. In the extant literature there remains no gold standard on how the RPQ should be scored (Voormolen, Cnossen, et al., 2018), and therefore care needs to be taken during interpretation of total scores particularly when comparing between individuals.

6.4 Chapter summary

The main findings confirm that when subjected to Rasch analyses the RPQ remains a reliable measure that can be used as a tool for individual assessment of PCS symptoms in both TBI and orthopaedic patients. Using the recommended approach of super-item analysis, it was possible to demonstrate the RPQ as a unidimensional construct of PCS symptoms , which helps elucidate on previous inconsistent findings on its structural validity. Employing new strategies of evaluating DIF by disease group, the results also demonstrated that the RPQ items function consistently irrespective of injury group, and therefore can be reliably administered to measure PCS and PCS-like symptoms in both TBI and orthopaedic patients. The conversion of scores provided in Appendix 10 allow for the calculation of summary scores that is useful for assessing responsiveness across the scale, possibly for the future development of cut-off total scores to establish clinical thresholds of PCS. Future studies may be able to include injury patients at different assessment intervals, with samples that are more representative of severe TBI, but also other non-TBI samples.

Chapter 7 Study 1–Rasch validation of the WHOQoL-BREF and shorter versions in traumatic brain injury and orthopaedic populations

The WHOQoL-BREF is a widely used quality of life questionnaire that has been shown to be a valid and reliable quality of life measure in the general population (WHOQoL Group, 1998), and in various clinical population such as cancer and psychological patients (Chang et al., 2014; Krägeloh et al., 2013; Liang et al., 2009; Lin et al., 2019; Rocha et al., 2012a; Skevington et al., 2004; Wang, Yao, et al., 2006). The instrument consists of 26 items which measure physical, psychological, social and environmental domains of quality of life. Items are rated on a 5-point Likert scale with higher scores denoting higher quality of life for most items except for items 3,4, and 26. Previous psychometric evaluation in trauma patients (Kruithof et al., 2018), including TBI and spinal cord injury patients (Chiu et al., 2006; Jang et al., 2004), has confirmed good internal consistency, test-retest reliability, discriminant and convergent validity of the measure. The dimensionality of the instrument however has not yet been evaluated in the TBI population. There exists shorter versions such as the EUROHIS-QOL-8 (Schmidt et al., 2005) and WHOQoL-5 (Geyh et al., 2010) which were developed as economic screening measures that can be useful in time-constrained settings and for addressing issues around respondent burden. Response burden refers to the (often mental) effort required by an individual to take part in lengthy questionnaires, and can be a challenge for researchers when conducting assessments with cognitive deficits such as in the neurological population. The use of these shorter versions has potential in reducing response burden, but their psychometric properties and their clinical utility for use in the injury population has not been assessed to date.

The purpose of the study was to analyse the psychometric properties of the WHOQoL-BREF, and its shorter versions the EUROHIS-QOL-8 and WHOQoL-5 using Rasch analysis within a TBI and orthopaedic population, and with a comparative general population sample. Rasch analysis was also used to develop a new 12-item WHOQoL as an alternative short-scale version. Results from this study have been published elsewhere by Balalla et al. (2019).

7.1 Data analysis

For the WHOQoL-BREF anchor items G1 and G2 on general quality of life and general health were excluded as they are typically not used in data analysis or total score calculation. Items 3, 4, and 26 were reverse coded prior to data analysis. The procedures described in Chapter 4 and Table 8 were adopted for Rasch analysis. Patterns of missing data were examined and were found to be approximately at 2% and occurring in random order. A likelihood ratio test did not support the use of a Rasch Rating Scale Model [$\chi^2(74)=298.67$, $p<.001$], and therefore the polytomous Partial Credit Rasch model was applied to examine: a) the WHOQoL-BREF items and domains, b) EUROHIS-QOL-8, and c) WHOQoL-5. Issues concerning DIF, local dependency and threshold disordering were addressed with the merging of items to create super-items. As per Krägeloh et al. (2013) *domain super-items* were also created by combining related items belonging to each of the domains: physical, psychological, social, and environmental.

Results from the Rasch analysis of the WHOQoL-BREF were also used to inform the development of the new modified 12-item WHOQoL. The aim of the proposed shortened scale was to have a psychometrically robust abbreviated scale with equal domain representation, that also allows for domain-level scores, in addition to the calculation of a total score. In the selection process, the three best-fitting items from each domain of the 24-item WHOQoL-BREF scale were selected for inclusion based on item fit residuals. Three items per domain are recommended as the minimum number of items to allow for sufficient reliability and for conducting factor analyses (Guilford, 1952). Decisions to discard items were also based on a combination of statistical properties and conceptual relevance to the construct. Conversions from ordinal-to-interval total scores for the WHOQoL-24 (excluding anchor items G1 and G2), and the EUROHIS-QOL-8 and WHOQoL-5 are presented in Appendix 12 and 13, respectively.

Sample characteristics

From the total sample, participants with confirmed isolated TBI (n=74) and orthopaedic injuries (n=114) were included in the final analysis. Polytrauma patients (TBI and extracranial injuries) were excluded due to the presence of confounding injury characteristics existing between the TBI and orthopaedic injuries.

In addition, a comparison group of general population residents was included in the final sample. This group consisted of a subset of participants (n=140) who were randomly selected from a sample obtained from a previous national validation study of

the WHOQoL-BREF conducted by Krägeloh et al. (2013). In this study, participants had been randomly sampled using the national electoral register and through purposive convenience sampling. Informed consent for the two clinical samples was obtained either written or audio-taped.

Table 17. Sample characteristics of TBI (*n*=74), orthopaedic injury (*n*=114), and general population samples (*n*=140).

Characteristic		TBI, *n* (%)	Ortho, *n* (%)	Healthy, *n* (%)	Sig.†
Sex	Male	45 (60.8)	74 (64.9)	64 (45.7)	.006*
	Female	29 (39.2)	40 (35.1)	76 (54.3)	
Age-group	18–37 years	24 (32.4)	41 (36.0)	43 (31.6)	.175
	38–60 years	21 (28.4)	35 (30.7)	57 (41.9)	
	>60 years	29 (39.2)	38 (33.3)	36 (26.5)	
Education	Primary/High School	38 (51.4)	50 (43.9)	73 (52.1)	.213
	Polytechnic/University	36 (48.6)	64 (56.1)	67 (47.9)	
Marital Status	Single	36 (49.3)	46 (40.7)	51 (37.0)	.221
	Living as married	37 (50.7)	67 (59.3)	87 (63.0)	
Health Status	Unwell	10 (13.5)	11 (9.7)	19 (13.7)	.596
	Well	64 (86.5)	102 (90.3)	120 (86.3)	
Mean time since injury, in years (SD)		2.26 (1.32)	2.66 (0.04)	-	.015*‡

*denotes statistical significance at $p<.05$; † χ^2 test for proportions; ‡ *t*-test—comparison between TBI and orthopaedic groups for time elapsed since injury; Health status refers to participant reporting whether feeling well or unwell at time of assessment.

7.2 Results of the Rasch analysis of the WHOQoL-BREF

Table 17 presents the demographic characteristics of the sample. There were no significant differences across the sample, with the exception of mean time since injury between TBI and orthopaedic groups (p=.015), and sex (p=.006), whereby males were overrepresented in both injury groups. Glasgow Coma Scale scores were only available in approximately 66% of TBI cases. TBI participants were predominantly in the mild category (median GCS=14.00) but had significantly higher injury severity (mean ISS=12.68, SD 10.0) than orthopaedic participants, mean ISS=6.26, SD 6.21, t (109.93) =4.95, p=.000.

Summary fit statistics for the overall Rasch model fit, PSI, and unidimensionality tests are presented in Table 18. Initial analysis that included all 26 items of the WHOQoL-BREF shows overall significant misfit to the Rasch model and lack of

unidimensionality (21.49% significant *t*-tests, lower bound CI 19.25), although scale reliability was already high (PSI=.92). Similarly, initial analysis with the 24 items (excluding anchor items 1 and 2), demonstrated a poor overall fit to the model, lack of unidimensionality, but also excellent reliability. Across domains, the reliability of the physical (PSI=.78), psychological (.77) and environmental (.75) dimensions were satisfactory, with the exception of the social domain (.57), which was below acceptable.

Table 19 presents the Rasch model statistics for the individual item fit of the initial 24-items analysis. Closer examination of individual items revealed that participants found items 16 (satisfaction with sleep) and 21 (satisfaction with sex life) to be the most difficult to score highly on, as shown by their corresponding fit locations (0.77 SE=0.06 and 0.77 SE=0.05, respectively). The easiest item to endorse was item 5 (enjoyment of life) with a location of -0.64, SE=0.08. Seven items (3, 4, 5, 17, 19, 21, and 24) showed significant misfit to the Rasch model, with item-fit residuals exceeding the acceptable threshold of ±2.50. Some artificial DIF effects by diagnosis and age were observed across several items. The presence of real DIF (item bias) was seen by age (item 21), sex (item 11), marital status (item 20) and well/unwell groups (item 17). Item responses between items 6, 12, 15, 16, and 21 were seen to be correlated and therefore indicated the presence of local dependency.

The creation of super-items for the four domains in the subsequent step to correct for item misfit, DIF and local dependency resulted in the best model fit [$\chi^2(36) = 35.15$, $p=0.51$], achieving strict unidimensionality and strong reliability (PSI=.84). According to item fit residuals in Table 19, the super-item representing the social domain was the most readily endorsed (item location -0.05, SE=0.03), and environment was the second easiest domain to endorse (-0.04, SE=0.02). The physical domain was the most difficult domain to score high on (0.10, SE 0.02), followed by the psychological domain (0.00, SE=0.02). Uniform DIF effects by diagnosis were observed for the physical [F (2, 361) =19.29, $p<.01$], and psychological [F (2, 361) =20.16, $p<.01$] domain super-items. DIF was also observed by age for the physical [F (2, 361) =15.25, $p<.01$], psychological [F (2, 361) =7.52, $p<.01$], and environmental [F (2,361) =25.20, $p<.01$] domain super-items.

Table 18. Summary of fit statistics for the Rasch analyses of existing versions of the 26-Item WHOQoL-BREF, 24-item WHOQoL-BREF (excluding anchor items 1 and 2), EUROHIS-QOL-8 and WHOQoL-5, and a proposed new 12-item WHOQoL version (*n*=363).

Analyses	Item fit residual		Person fit residual		Goodness of fit		PSI	Significant *t*-tests Unidimensionality	
	Value	SD	Value	SD	χ^2 (df)	*p*-value		%	Lower bound
WHOQoL-BREF									
Initial (26)	0.22	2.44	-0.20	1.61	449.19 (234)	.000	.92	21.49	19.25 (NO)
Initial (24)†	0.24	2.46	-0.20	1.58	446.95 (216)	.000	.91	16.25	14.01 (NO)
4 Domain Super-items	-0.12	2.05	-0.39	1.01	35.49 (36)	.510	.84	3.86	1.61 (YES)
Final 3 Domain Super-items	-0.42	2.52	-0.48	1.00	11.35 (27)	.990	.82	4.56	2.28 (YES)
EUROHIS-QOL-8									
Initial/ Final	0.03	1.76	-0.30	1.12	84.18 (72)	.150	.81	6.06	3.82 (YES)
WHOQoL-5									
Initial/ Final	-0.14	1.37	-0.34	0.98	54.66 (40)	.060	.68	2.76	0.25 (YES)
New proposed 12-item WHOQoL version									
Initial 12 items	0.17	1.52	-0.25	1.21	134.18 (84)	.000	.83	8.54	6.30 (NO)
4 Domain super-items	-0.08	1.41	-0.38	0.98	45.77 (36)	.130	.79	1.93	-0.31 (YES)
3 super-items	0.24	0.96	-0.39	0.91	35.21 (27)	.130	.82	4.14	1.90 (YES)

† Initial analysis excluding anchor items G1 and G2 of the WHOQoL-BREF

Table 19. Rasch model fit statistics with item locations, fit residuals and chi-square for the 24-item WHOQoL-BREF (excluding anchor items G1 and G2), and for the four domain super items (*n*=363).

WHOQoL-BREF item	Location	SE	Fit Resid	χ^2	Prob.
3. Extent physical pain prevents what you need to do	0.07	0.06	3.26*	33.20	.000
4. Medical treatment to function in daily life	0.20	0.06	7.25*	118.79	.000
5. How much do you enjoy life	-0.64	0.08	-2.59*	30.06	.000
6. Extent life is meaningful	-0.13	0.07	-1.21	8.96	.440
7. How well able to concentrate	0.11	0.07	-0.75	11.46	.250
8. Safety in daily life	-0.51	0.07	-0.81	15.39	.080
9. How healthy is physical environment	-0.60	0.08	-0.50	8.77	.460
10. Enough energy in everyday life	0.01	0.07	-1.21	10.40	.320
11. Able to accept bodily appearance	0.07	0.07	1.25	6.75	.660
12. Enough money to meet needs	0.42	0.06	1.30	4.13	.900
13. Information needed in daily life	-0.32	0.07	-1.93	12.52	.190
14. Opportunity for leisure activities	0.39	0.06	0.38	10.64	.300
15. Ability to get around	-0.63	0.07	0.38	5.61	.780
16. Satisfied with sleep	0.77	0.06	1.85	6.07	.730
17. Satisfied with ability to perform daily activities	-0.04	0.07	-3.04*	23.99	.000
18. Satisfied with capacity for work	0.28	0.06	-1.64	12.62	.180
19. Satisfied with yourself	0.30	0.07	-2.76*	34.55	.000
20. Satisfied with personal relationships	0.05	0.06	-0.77	5.16	.820
21. Satisfied with sex life	0.77	0.05	4.95*	43.58	.000
22. Satisfied with support from friends	-0.28	0.07	-1.10	9.78	.370
23. Satisfied with conditions of living place	-0.45	0.07	-0.86	8.13	.520
24. Satisfied with access to health services	0.21	0.06	2.64	5.71	.770
25. Satisfied with transport	-0.23	0.07	1.60	14.35	.110
26. How often have negative feelings	0.19	0.07	0.05	6.35	.700
Domain super-items					
Physical	0.10	0.02	1.81	10.20	.330
Psychological	0.00	0.02	-2.49	16.46	.060
Social	-0.05	0.03	1.36	4.96	.840
Environmental	-0.04	0.02	-1.17	3.53	.940

*denotes significant misfit to the Rasch model, $p<.01$

Upon inspection of the pattern of residual correlations, local dependency was found between the psychological and physical super-items. After these super-items were combined into a physical-psychological super-item, the data met the assumptions of the Rasch model and achieved strict unidimensionality [$\chi^2(27) = 11.35$, $p = .99$], with good reliability (PSI=.82), and no DIF by diagnosis. Whilst DIF effects by age still remained for the environmental domain super-item, a post-hoc sign test indicated that DIF between individual age groups was not significant ($p < .05$). The final analysis for the WHOQoL-BREF therefore showed no individual item bias (i.e. no DIF), and none of the individual super-items showed misfit to the Rasch model Table 18.

The item-person plot in Figure 22 shows scale coverage for over 95% of the sample with only minor ceiling effects, and acceptable item-person targeting (mean score of 0.70, SD 0.60). By sub-group, targeting was better for the general population (person-item mean 0.57, SD 0.45), followed by the TBI group (mean 0.75, SD 0.70) and slightly worse for the orthopaedic sample (mean 0.86, SD 0.68). Overall, this seems to suggest that the scale is perhaps not well suited to distinguish between sample respondents located within the uppermost levels of quality of life.

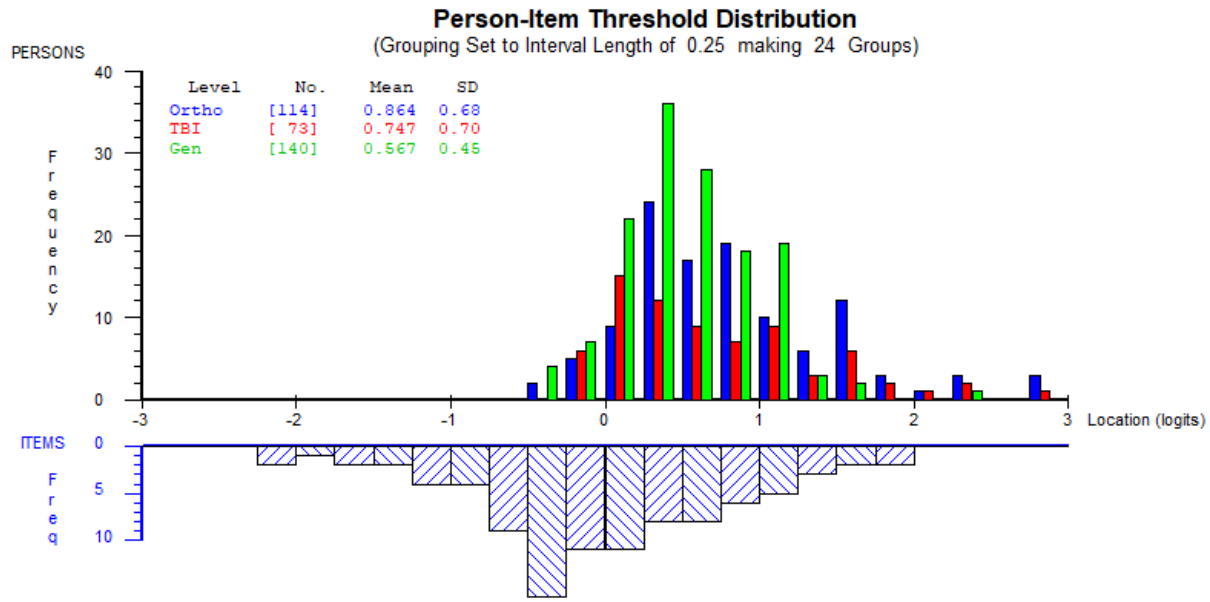


Figure 22. Person-item threshold plot for the WHOQoL-BREF three-domain super-items analysis disaggregated by diagnosis: TBI, orthopaedic, and general population groups (n=363)

7.3 Results of the Rasch analysis of EUROHIS-QOL-8 and WHOQoL-5

Supplementary analysis of the EUROHIS-QOL-8 as displayed in Table 18 indicated overall acceptable model fit [$\chi^2(72) = 84.11$, $p = .15$], and evidence of unidimensionality. A PSI of .81 showed good scale reliability of the measure that is suitable for group comparisons. Table 20 details the item fit statistics for the EUROHIS-QOL-8 and the WHOQoL-5. There was no item misfit or threshold disorder, and only artificial DIF was present by diagnosis group (item 1), age (item 23) and marital status (item 20), which post-hoc sign tests revealed to be non-significant. Person-item targeting for the scale was however sub-optimal with a person mean of 1.40 (SD 1.32). Minor ceiling effects were noticeable, with about 8% of the overall sample not covered by item thresholds (Figure 23).

Results from the WHOQoL-5 analysis also presented in Table 18, showed overall satisfactory fit to the Rasch model [$\chi^2(40) = 54.66$, $p = .06$], and confirmation of unidimensionality. Scale reliability (PSI=.68) for the initial analysis however was below acceptable thresholds to be useful for group comparisons. As illustrated in Figure 24, the sample was also not adequately covered by item-thresholds, with about 16% of the sample lying outside the scale range, and poor person-item targeting with a person-item mean of 1.49 (SD 1.31). Examination of individual items revealed no item misfit to the Rasch model, no threshold disorder, and only the presence of artificial DIF by age for item 23, and marital status for item 20. Some minor local item dependency was observed between items 2 and 20, but this was not large enough to necessitate a further super-item analysis.

Table 20. Rasch model fit statistics with item locations, fit residuals and chi-square for the EUROHIS-QOL-8 and WHOQoL-5 (n=363)

EUROHIS-QOL-8 item	Location	SE	Fit Resid	χ^2	Prob
1. Quality of life	-0.50	0.08	-1.62	13.83	.130
2. Satisfied with health	0.37	0.07	1.76	9.09	.430
10. Enough energy in everyday life	-0.04	0.08	0.39	5.42	.800
12. Enough money to meet needs	0.41	0.06	2.45	11.88	.220
17. Satisfied with ability to perform daily activities	-0.08	0.07	-2.12	14.92	.090
19. Satisfied with yourself	0.28	0.08	-1.89	14.19	.120
20. Satisfied with personal relationships	0.03	0.07	1.34	6.69	.670
23. Satisfied with conditions of living place	-0.48	0.07	-0.10	8.16	.520

WHOQoL-5 item	Location	SE	Fit Resid	χ^2	Prob
1. Quality of life	-0.37	0.08	-1.71	18.82	.020
2. Satisfied with health	0.51	0.07	1.30	7.31	.500
17. Satisfied with ability to perform daily activities	0.05	0.07	-1.39	12.63	.130
20. Satisfied with personal relationships	0.16	0.07	1.05	8.71	.370
23. Satisfied with conditions of living place	-0.36	0.07	0.05	7.20	.520

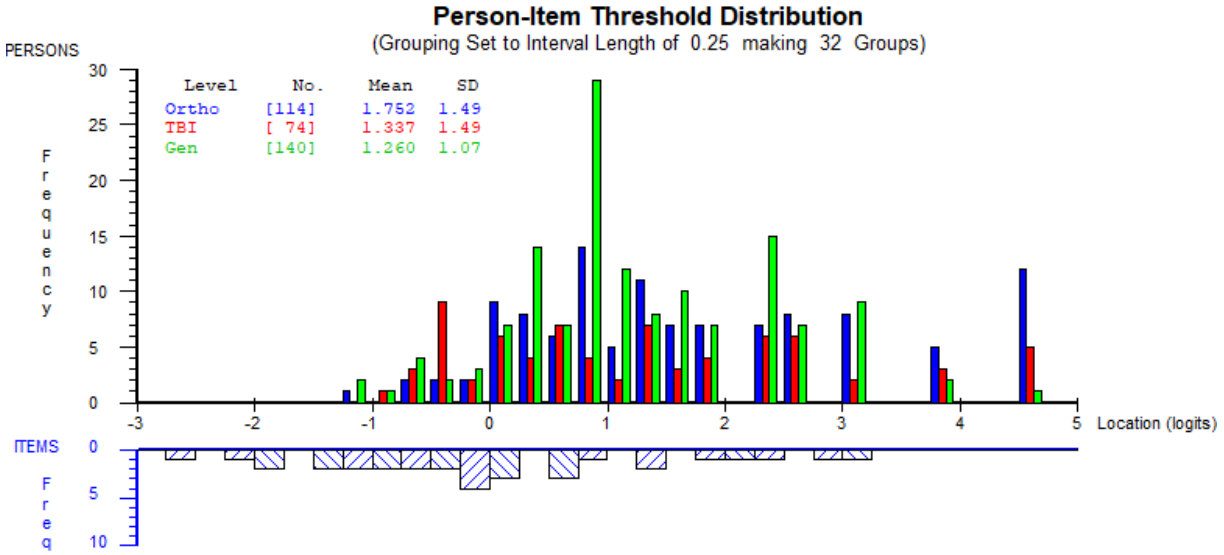


Figure 23. Person-item threshold plot for the EUROHIS-QOL-8 by diagnosis group TBI, orthopaedic and general population samples (*n*=363)

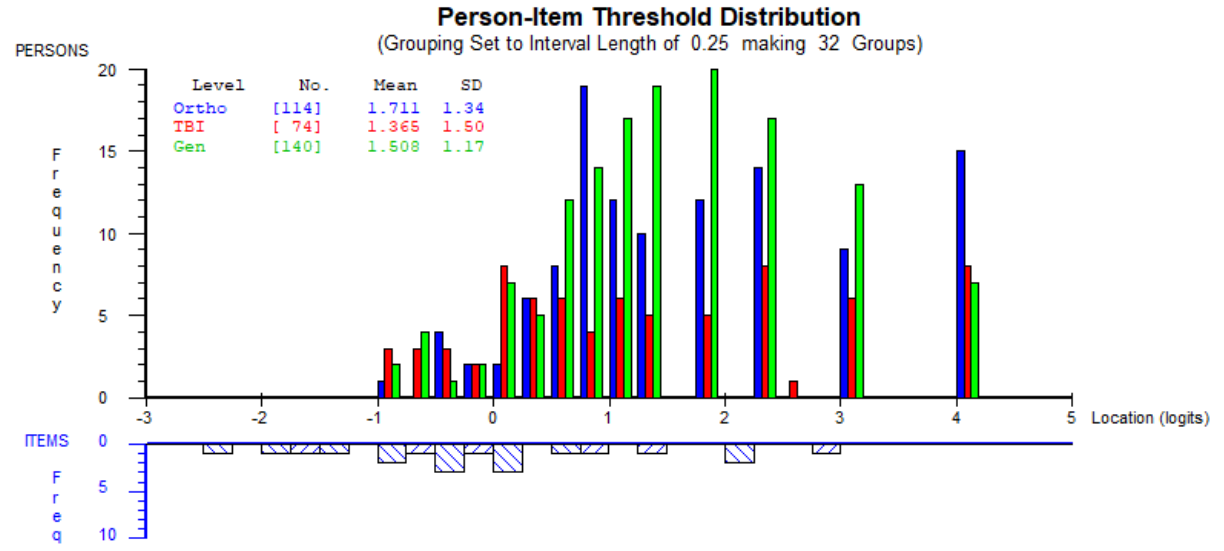


Figure 24. Person-item threshold plot for the WHOQoL-5 for the three super-items analysis by diagnosis group TBI, orthopaedic and general population samples (*n*=363)

7.4 Development of a new 12-item WHOQOL

The formation of the newly proposed 12-item WHOQoL was derived from items with the best fit residuals across each of the four domains, from the previous Rasch analysis of the 24-item WHOQoL-BREF. Items with poor fit to the Rasch model, and/or displaying DIF or local dependency were iteratively removed from each domain resulting in three items per domain for the 12-item version as described below.

In the physical domain of the WHOQoL-BREF, local dependency was detected between items 15 and 18, but as item 15 displayed better individual fit (fit residual 0.38), compared to item 18 (fit residual -1.64), it was retained in the new proposed 12-item model. Within the environmental domain, items 9, 23 and 25 displayed local dependency as evidenced by their residual correlations exceeding the margin of 0.20 of mean residual correlations. Looking closer at these items—item 9 relates to the perception of the health of the physical environment, item 23 asks about a person's satisfaction with the conditions of their living place, and item 25 measures satisfaction with transport. As local dependency between these items suggests that a person who scores high on item 23 is also likely to score high on items 9 and 25, it was therefore decided that the latter two items should be removed, and to retain instead the more generally-worded item 23. Similarly, evidence of local dependency was seen between items 12 and 13. Here, it was decided that item 13 (amount of information available in daily life) should be discarded as it is arguably less relevant in today's context, which has wide accessibility to internet, than for instance item 12, which enquires about body image and appearance. In addition, item 13 had also had a negative fit residual of higher magnitude (-1.93) compared to item 12 (1.30), and therefore the latter was retained in the modified environmental domain of the new 12-item WHOQoL. Item 14 (opportunity for leisure activities) was also deleted as it was deemed less relevant to environmental quality of life. Consequently, the following items were retained in the formation of the proposed 12-item WHOQoL which permits equal representation of the four domains: physical— items 10, 15, 16; psychological—items 6, 7, 26; social—items 20, 21, 22; and environmental—items 8, 12, 23. Table 21 presents the items contained in the proposed 12-item WHOQoL version, with their corresponding item-fit statistics.

Preliminary analyses for the proposed new 12-item version as shown in Table 18 failed to achieve a Rasch model fit and unidimensionality, but demonstrated good reliability (PSI=.83). Item fit statistics show that only item 21 *"*how satisfied are you with your sex life*"* deviated significantly from the Rasch model (Table 21). The subsequent

formation of domain super-items produced evidence of unidimensionality and fit to the Rasch model but resulted in a marginally diminished PSI of .79. Some minor artificial DIF was seen by diagnosis, age, and marital status. There was also some evidence of minor local dependency between the psychological and environmental super-items. A subsequent analysis containing three super-items (physical-social, psychological and environmental) yielded the best result with improved PSI to .82, strict Rasch model fit [χ^2 (27) =35.21, p=.13] and evidence of unidimensionality. Person-item targeting was acceptable but not ideal, with a person-item mean of 1.14 (SD 1.00), and coverage of the sample was more than 95% with less than 3% of ceiling effects (Figure 25).

Table 21. Rasch model fit statistics with item locations, fit residuals and chi-square for the new proposed 12-item WHOQoL, and four domains super-items (n=363)

Proposed 12-item WHOQoL version items	Location	SE	Fit Resid	χ^2	Prob
6. To what extent do you feel your life to be meaningful?	-0.15	0.07	-0.83	7.09	.420
7. How well are you able to concentrate?	0.08	0.07	-0.89	13.50	.060
8. How safe do you feel in your daily life?	-0.52	0.07	-0.64	12.67	.080
10. Do you have enough energy for everyday life?	0.006	0.07	-0.14	10.28	.170
12. Are you able to accept your bodily appearance?	0.39	0.06	1.73	5.55	.590
15. How well are you able to get around?	-0.65	0.07	1.65	9.11	.240
16. How satisfied are you with your sleep?	0.74	0.06	1.74	3.41	.840
20. How satisfied are you with your personal relationships?	0.005	0.07	-1.44	12.70	.080
21. How satisfied are you with your sex life?	0.75	0.05	3.26*	29.22	.000
22. How satisfied are you with the support you get from your friends	-0.32	0.07	-1.23	11.90	.100
23. How satisfied are you with the conditions of your living place?	-0.49	0.07	-0.86	6.32	.500
26. How often do you have negative feelings such as blue mood, despair, anxiety, depression?	0.15	0.07	-0.34	12.42	.090
Four domain super-items					
Physical	0.07	0.03	0.98	5.28	.810
Psychological	0.03	0.03	-1.67	12.00	.210
Social	0.04	0.03	1.23	9.09	.430
Environmental	-0.15	0.03	-0.85	19.41	.020

Note: * denotes significant misfit to the Rasch model, p<.01

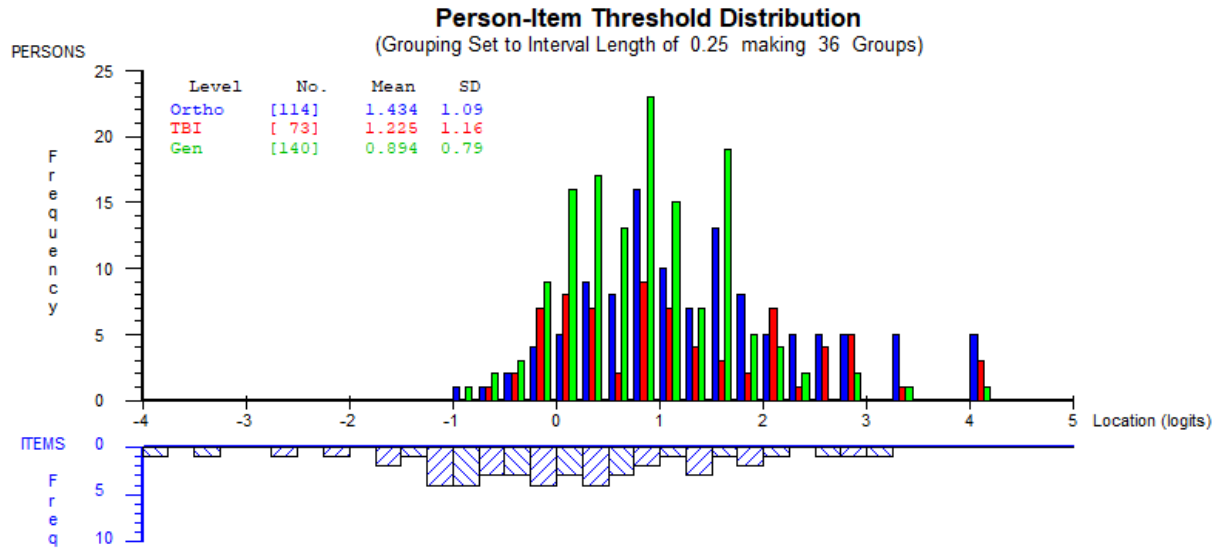


Figure 25. Person-item threshold plot for the proposed new 12-item WHOQoL version using three super-items analysis, separated by diagnosis group: TBI, orthopaedic and general population samples (*n*=363)

7.5 Discussion

The present study is the first to have evaluated the WHOQoL-BREF and shorter versions in a sample of TBI, orthopaedic participants, and a general population sample to assess its feasibility as a QoL measure in an injury population with Rasch methods. The creation of the three super-items physical-psychological, social, and environmental permitted the analyses of the WHOQoL-BREF to meet the expectations of the Rasch model, unidimensionality, good reliability, and 95% coverage of the sample. Whilst the super-item method does not necessarily challenge the validity of the standard practice of calculating separate ordinal-level scores for the physical, psychological, social, and environmental domains of the WHOQoL-BREF, the analyses did indicate the presence of a potential method effect between the physical and psychological items, as shown by the presence of local dependency between these domains. Significantly, these results compared and showed that the WHOQoL-BREF items perform well and invariably across injury groups as well as healthy populations, although person-item distribution by diagnosis group reflects that most participants had likely recovered from their injuries.

Evidence for the TBI and injury population from the literature is limited to three studies that used classical test-based methods, and two of which used the translated Taiwanese version with national items (Chiu et al., 2006; Jang et al., 2004; Kruithof et al., 2018). Comparable to the current study's findings, the authors found symmetrical distribution across most domains, low floor and ceiling effects (0–10.2%), and good internal

consistency (α .74 to .89). Estimates from other samples also indicate acceptable to good reliability across domains (α .70 to .89) (Krägeloh et al., 2013; Rocha et al., 2012a; Skevington et al., 2004; Wang, Yao, et al., 2006; Yao et al., 2002), with the exception of the social domain which generally shows unsatisfactory reliability (α .54 to .68) (Chiu et al., 2006; Kruithof et al., 2018; Rocha et al., 2012a; Skevington et al., 2004). The finding that the WHOQoL-BREF is underpinned by a unidimensional construct is similar to previous findings (Chang et al., 2014; Krägeloh et al., 2013; Liang et al., 2009; Lin et al., 2019; Rocha & Fleck, 2009; Wang, Yao, et al., 2006). Rocha et al., (2012a) found that the social domain failed to meet the Rasch unidimensional model due to its poor psychometric properties. The evidence obtained from previous studies is not confirmatory however, in that the authors did not specifically test for unidimensionality as in the current study. Also, unlike previous studies which traditionally dealt with the presence of DIF, local dependency or misfitting items by rescoring or deleting items, the present analysis overcame these deviations of the Rasch model by utilising the super-item approach to retain all items. This method follows best practice guidelines as recommended by Lundgren Nilsson and Tennant (2011), who argue that creation of super-items attenuates measurement error inherent within individual items without needing to re-order thresholds or delete items which should only be applied as a last-resort strategy.

The supplementary Rasch analysis of the EUROHIS-QOL-8 indicates that it retains the psychometric properties of its parent WHOQoL-BREF, with acceptable fit to the Rasch model, good reliability (PSI 0.81) and unidimensionality. However, poor person-item targeting and minor ceilings effects in the sample suggested that it was not able to discern between individuals who score on the lower-most end of the spectrum. Reliability of the EUROHIS-QOL-8 in this study is consistent with findings from four other studies which have reported reliability values between .72 and .86 (Pires et al., 2018; Rocha et al., 2012b; Schmidt et al., 2005; Snell et al., 2016). However, these studies have so far presented inconsistent evidence regarding the property of unidimensionality. In studies by Schmidt et al. (2005), Rocha et al. (2012b) and Pires et al. (2018) there was a lack of strong evidence of unidimensionality, which was not specifically tested for in their samples (and only implied within the use of the Rasch unidimensional model). Only one other study produced evidence of unidimensionality in a sample of largely geriatric patients undergoing joint replacement, in which the authors did also note some degree of multidimensionality (Snell et al., 2016). In

addition in two of the studies (Pires et al., 2018; Schmidt et al., 2005), Rasch model expectations were not met overall or for some items, whereas Rocha et al. (2012b) were only able to achieve Rasch model fit through the deletion of items. Person-item targeting of the EUROHIS-QOL in the current analysis appeared to be similar to that for Rocha, although there were discrepancies across the other two studies, in which the authors observed a large variation of floor and ceiling effects across items (1.37 to 27.46%) (Pires et al., 2018; Schmidt et al., 2005). Few validation studies are available for the EUROHIS-QOL-8 than for the WHOQoL-BREF, the latter which is more commonly utilised. The collective evidence from varied contexts such as large cross-national studies, depressed patients, minor surgical patients, and presently with the current study's evidence in injury and healthy participants, does nevertheless point to the clinical utility of this shortened scale across diverse groups.

Evaluation of the WHOQoL-5 in this study indicated that despite obtaining evidence of satisfactory model fit and unidimensionality, the 5-item scale has poor reliability, that does not enable comparisons between healthy and injury groups. Furthermore, poor targeting and ceiling effects across the sample indicated that the WHOQoL-5 is unable to measure higher levels of quality of life very well. The assumption of unidimensionality was implied (although not specifically tested for) in just one study available by Geyh et al. (2010), who conducted Rasch analysis on the WHOQoL-5 in a multicentre spinal cord injury sample (n=243), where respondents had experienced recent injuries (within the 14 days). This study was able to demonstrate much higher reliability (PSI=.76) than in the current sample of TBI and orthopaedic participants (PSI=.68), who were in the later stages of recovery, at approximately 2.50 years post-injury. The limited evidence might suggest that the WHOQoL-5 may be better at differentiating groups of people with similar levels of QoL when injuries are relatively new. Nevertheless, despite its appeal as a 5-item version that can be quickly administered as a quality of life measure, further validation studies of the WHOQoL-5 are needed to demonstrate its utility as a psychometrically robust measurement. Researchers therefore need to exercise caution when interpreting results from the WHOQoL-5.

Lastly, the rationale for developing a 12-item WHOQoL was to test for a psychometrically robust shortened scale that focused on having items equally representing each domain, but which maintained the psychometric properties of the parent WHOQoL-BREF. In comparison with other existing shorter versions such as the

EUROHIS-QOL-8 and the WHOQoL-5 discussed earlier, it could be argued that these scales do not sufficiently represent all four factors pertinent to quality of life. For example, in the 8-item EUROHIS-QOL-8, two anchor items are included which are generally not included in the original calculation of total and domain-level scores of its parent scale the WHOQoL-BREF. The remaining six items of the EUROHIS-QOL-8 are comprised of two physical items (items 10 and 17), one psychological item (item 19), one social item (item 20) and two environmental items (items 12 and 23). Similarly, in the much shorter 5-item WHOQoL-5, which also includes the two anchor items, only the physical (item 17), social (item 20) and environmental (item 23) domains are represented each by a single item. The psychological domain is notably absent in the WHOQoL-5, and is an important determinant of quality of life that needs to be represented particularly in the injury population (Lin et al., 2010).

The empirical findings of the analysis of the 12-item model demonstrated sound psychometric properties displaying acceptable fit to the Rasch model, unidimensionality and marginally better item and person-fit parameters than the existing WHOQoL-BREF. The PSI value of .82 indicates very good reliability on par with the WHOQoL-BREF and the EUROHIS-QOL-8, and demonstrates that the scale allows for group comparisons and can potentially be used for clinical assessment at the individual level. Person-item targeting was however worse for the new model when compared with the WHOQoL-BREF but represents an improvement on the EUROHIS-QOL-8, especially for the orthopaedic and general population groups. Additionally, coverage of the scale was improved in the new 12-item version with approximately 95% of the sample being covered by items. It was found that ceiling effects were less than 5% for the 12-item version, while it was slightly higher at 8% for the EUROHIS-QOL-8. In light of the necessity in reducing participant fatigue during assessment, the proposed 12-item model aims to not only minimise participant response burden especially in the neurological population, but to also permit the calculation of domain-level scores. Another advantage offered by the 12-item is that it permits factorial analysis to be conducted, given that it meets the minimum requirement of three items per domain to be represented on a measurement scale (Guilford, 1952).

Despite researchers having already developed the 8-item EUROHIS-QOL-8 which is a much-abbreviated version of the 24 item WHOQoL-BREF, a quick perusal of the literature shows that latter is more favoured by researchers and clinicians. One reason may be due to the limitations in the capacity of the EUROHIS-QOL-8 to assess

respondents' scores across domains, as well as the limited psychometric evidence available especially within the injury population. The proposed new 12-item WHOQoL may therefore offer an alternative condensed format, with the advantage of allowing one to analyse domain-specific scores, as well as marginal improvements to existing shorter scales, as noted earlier. These preliminary results are encouraging and have shown that it also maintains psychometric properties of its parent scale and is suitable to be administered across healthy and injured populations. These results should however be approached with cautious optimism as they are far from conclusive and need to be empirically tested in other contexts (e.g. cross-culturally, different groups) using larger samples. It would be useful to demonstrate evidence of convergent validity of the new WHOQoL-12 to established HRQoL scales such as the abbreviated Short Form-12, and Short-Form 8, which was not conducted in this study.

Limitations

A limitation of this study is that in addition to the small sample size and variable length of follow-up between TBI and orthopaedic participants (0.5–6 years), the injury sample consisted predominantly of mildly injured participants with an underrepresentation of severe injuries. The generalisation of these findings to all cases with TBI or orthopaedic injuries should be done with caution, as the QoL of people with severe injuries may have different recovery paths following an injury. Furthermore, the cross-sectional design of the study does not permit longitudinal analysis of quality of life across the recovery trajectory. Collection of quality of life information from the outset of injury and at different timepoints (e.g. 1, 6, 12, 24 months) would provide useful comparisons to explore if the scale is sufficiently sensitive to detect minimal changes in QoL across the recovery path.

7.6 Chapter summary

To the candidate's knowledge, this study is the first to have applied the robust methods of Rasch analysis to validate the WHOQoL-BREF and its existing derivatives, the EUROHIS-QOL-8 and WHOQoL-5 within injury and healthy populations. The results demonstrated that the WHOQoL-BREF and the EUROHIS-QOL-8 perform invariably and effectively across general and clinical populations and can serve as a sound measure of QoL across diverse populations. The shorter EUROHIS-QOL-8 is psychometrically robust for use in national surveys containing multiple measurements or time-constrained clinical settings. The WHOQoL-5 however did not meet modern psychometric standards demonstrating poor reliability. The provision of ordinal-to-interval conversion

tables (Appendix 12 and 13) for the WHOQoL-BREF, EUROHIS-QOL-8 as well as the WHOQoL-5 enables the interpretability of summary scores which will be useful in clinical practice. Finally, the development of a 12-item model of the WHOQoL showed good psychometric properties, with marginal improvements to the existing EUROHIS-QOL-8 and WHOQoL-5. The 12-item version also offers the advantage of calculating domain-level summary scores that are not possible with the current shorter versions. Future studies should attempt to ameliorate the above limitations in larger samples, with assessment across more severe injury groups, and evaluation of cross-cultural validity in representative samples internationally.

Chapter 8 Study 2–Modelling predictors of long-term outcome after injury: A comparison between TBI and orthopaedic samples

In Chapter 2 it was identified that there is currently a limited understanding on the potential effects of health conditions or comorbidities on outcomes after injuries. The purpose of the present study, Study 2, is to disentangle the complex relationships underlying outcomes after injury, with the overarching goal being to identify predictors of long-term outcomes unique to TBI individuals. Specifically, using multivariate regression and structural equation modelling techniques, a hypothesised model was tested with the aim to show the interplay between pre-injury factors including pre-existing comorbidities, injury characteristics, and post-injury comorbidities on long-term postconcussion symptoms and quality of life. Outcome pathways for the TBI and orthopaedic samples were also modelled separately to delineate the relationships between the two injury groups. As no studies have previously compared outcome pathways with a focus on the effect of pre-existing and post-injury comorbidities between different injury groups, this study therefore presents a novel investigation into the factors that are specific determinants of outcome after TBI, compared with the experience of an orthopaedic injury.

In Chapters 5, 6, and 7 that collectively formed Study 1, the psychometric properties of the CIRS, RPQ and WHOQoL-BREF were examined using Rasch analysis. In two out of the three scales which met the Rasch model criteria outlined in Chapter 4, the precision of the scales was improved with transformation from ordinal to interval-level scores. The conversions resulted in linear interval measures for the WHOQoL-BREF and RPQ, which can be used to strengthen the accuracy of multivariate statistical analyses of outcomes in Study 2. Therefore, as an additional aim for this study, comparisons between the use of ordinal and Rasch-transformed interval scores were conducted to identify if the use of interval measures resulted in differences in the strength of relationships in the SEM analyses.

8.1 Overview of data analysis

As presented in 4.4, under the data analytical steps for Study 2, the hypothesised model of outcome pathways is broadly represented in Figure 9, and provides a guiding framework for the SEM analyses. Multivariate linear regression analyses for the combined injury sample, and separately for the TBI and orthopaedic samples were

conducted as a preliminary step to help isolate relevant variables to be entered into the SEM analyses in the second phase. While the analyses were largely informed by this theoretical framework, practical challenges imposed by the small sample size and the large number of variables in the dataset required the exclusion of some variables, which was achieved by employing multivariate linear regression using stepwise (selection criteria set at $p<.05$) and/or forced entry methods. Importantly, the focus of these regression analyses was also to highlight the impact of pre-existing health conditions affecting the onset of PCS symptoms and quality of life following injuries. Rasch-transformed RPQ and WHOQoL-BREF interval scores were used as outcome variables for predicting PCS symptoms and quality of life, respectively. As the CIRS demonstrated low instrument reliability in Chapter 5, raw scores were not transformed to interval-level scores. Rather, to address issues of positive skewness as suggested by Harwell and Gatti (2001), logarithmic (base 10) transformation was applied to CIRS scores to yield normality in the data. Regression analyses are presented with unstandardised (B) estimates with their corresponding standard error (SE), as well as standardised (β) estimates, *p*-values, R square, and R square change values, at the statistical significance level of $p<.05$.

SEM analyses were subsequently performed with 108 TBI (with one participant excluded due to high missing responses) and 114 orthopaedic respondents' data, and path models are presented separately for each sample, including for domain-level analysis. Following the step-by-step process in 4.4, assessment of model fit was conducted using chi-square/df ratio, CFI and RMSEA, including examination of individual paths, residuals and regression weights (standardised). Post-hoc modifications to models were iteratively applied where it was deemed necessary. All models presented display only significant relationships (at $p<.05$) represented by standardised beta (β) coefficients to two decimal places to enhance the clarity of diagrams. Bold values indicate significance at $p<.001$, and "NS" indicates non-significance at $p<.05$. Covariances are represented by dashed curved arrows. Lastly, standardised regression coefficients are also presented for direct, indirect and total effects in corresponding tables.

To guide the reader, the section 8.2 that follows firstly describes results of the regression analyses, highlighting important determinants of postconcussive symptoms and quality of life for the combined injury sample (Table 23 and Table 24), and separately for TBI (Table 25 and Table 26), and orthopaedic groups (Table 27 and

Table 28). SEM analyses with path diagrams and model fit statistics of the relationships are then presented and described in section 8.3, for the combined sample in Figures 26–27, and Table 29. This is followed by separate analyses for the TBI sample (Figures 28–33, and Tables 30–31) and the orthopaedic sample (Figures 34–39, and Tables 32–33), including by domain level analyses for the WHOQoL-BREF dimensions. Within the results, comparisons are also made between the models that have used ordinal-level outcome measures and those that have utilised the Rasch-transformed RPQ and WHOQoL-BREF interval scales, and the log10-transformed CIRS scale. This helped to determine whether use of interval measures appears to have an effect on the strength of the associations between variables. The discussion section in 8.4 that follows explains the study's findings in relation to existing knowledge from literature.

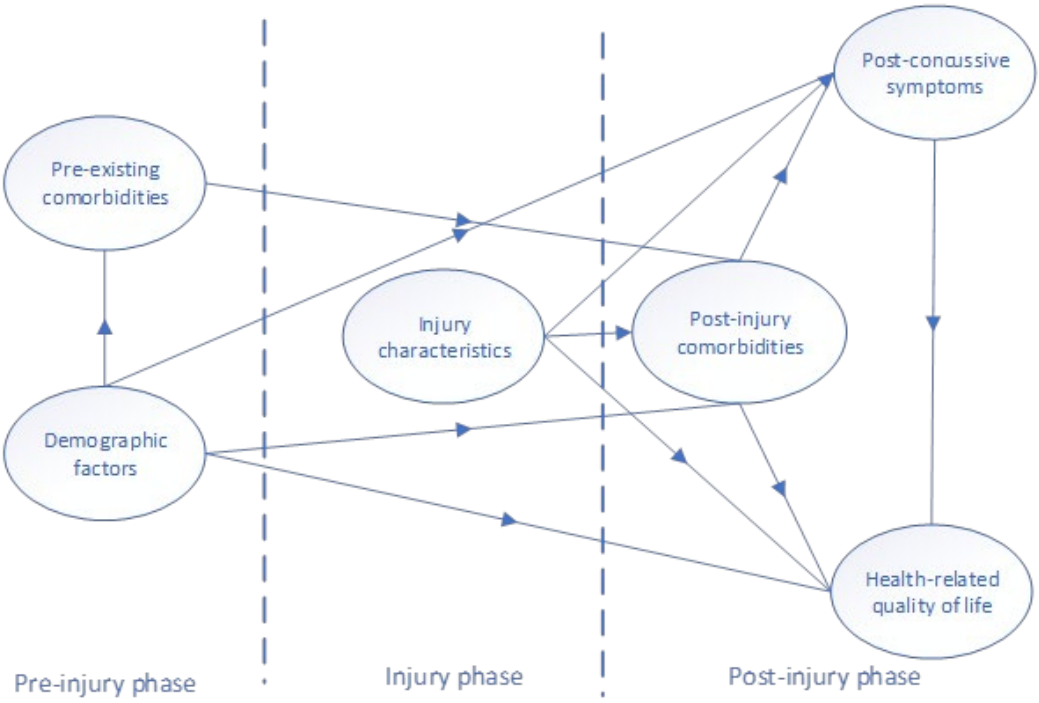


Figure 9. Hypothesised model of outcome pathways showing relationships between variables at different stages of injuries

Sample characteristics

Table 22 presents sample characteristics of the TBI and orthopaedic participants in the study, as well as scores on the CIRS, RPQ and WHOQoL-BREF measures. Participants with isolated TBI and polytrauma TBI were grouped together for the purposes of these analyses. TBI and orthopaedic participants were similar by demographic characteristics and only differed by overall injury severity and length of hospital stay. In terms of scores across the three outcome measures, TBI demonstrated significantly higher postconcussion symptoms on the RPQ (p<.001), and lower scores on quality of life for

the WHOQoL-BREF than the orthopaedic group (p<.05). Group differences for the total pre-existing and post-injury comorbidities on the CIRS measure were not evident. Appendix 14 presents the zero-order correlations of sample characteristics and outcome variables. Appendix 15 presents the partial correlations (adjusted by age) for log10 transformed pre-injury and post-injury CIRS disease categories, against the Rasch converted interval RPQ total score, and WHOQoL-BREF total and domain scores.

Table 22. Sample characteristics and scores across the CIRS, RPQ and WHOQoL-BREF measures, for the TBI, (n=109) and orthopaedic samples (n=114)

Variable		TBI, *n* (%)	Ortho, *n* (%)	*p*-value†
Mean age, years (SD)		48.78 (19.69)	47.96 (19.68)	.905
Mean time since injury, years (SD)		2.51 (0.13)	2.66 (0.04)	.289
Median LOS		6.00	4.00)	.036*‡
Median ISS		11.00	4.00	.000*§
Sex	Male	69 (63.3)	74 (64.9)	.802§
	Female	40 (36.7)	40 (35.1)	
Ethnic group	NZ European	66 (60.6)	83 (72.8)	.052§
	Māori/Pacific/Asian/ Other	43 (39.4)	31 (27.2)	
Education	Primary/High School	59 (54.1)	50 (43.9)	.125§
	Polytechnic/University	50 (45.9)	64 (56.1)	
Marital Status	Single	50 (46.3)	46 (40.7)	.402§
	Living as married	58 (53.7)	67 (59.3)	
Pre-injury total CIRS median score		0.30	0.30	.349
Post-injury CIRS median score		0.60	0.60	.585
RPQ mean score (SD)		26.45 (10.76)	16.70 (11.02)	.000*
WHOQoL-BREF mean score (SD)		81.86 (11.57)	85.21 (11.59)	.034*

ISS=Injury Severity Score; LOS=length of hospital stay; pre-injury and post-injury (log10 transformed) CIRS scores; Rasch transformed RPQ and WHOQoL-BREF scores; †independent samples *t*-test; ‡Mann-Whitney test; § χ^2 test; * denotes statistical significance at p<.05

8.2 Results of the multivariate linear regression analyses

Combined injury sample

Regression analyses conducted for the combined injury sample are presented in Table 23 and Table 24. Table 23 presents predictors of postconcussive syndrome symptoms (PCS), with a combination of stepwise (for demographic and injury variables) and forced entry methods (total comorbidity score) within the injury sample of n=222

participants. Variance in PCS symptoms explained by the model (R^2=.407) are mainly attributed to differences in age (p=.001), sex (p<.05), injury type (i.e. TBI or orthopaedic) and length of hospitalisation (both p<.001). Pre-injury total comorbidity explained an additional 2.3% of variance within the model, while post-injury total comorbidity explained a further 8.6%. The presence of moderation effects existing between age and pre- and post-injury total comorbidity were tested, and were found to be non-significant (p=.41and p=.99, respectively). Where total comorbidity scores were replaced by separate pre- and post-injury comorbidity categories in Model 2, results revealed that prior neurological, EENT, lower gastrointestinal and musculoskeletal were relevant predictors of PCS symptoms (p-values <.05), and altogether explained for 10.6% of total variance in the model. Post-injury existence of psychiatric/behavioural, EENT and neurological problems collectively explained a further 10% of variance. When compared with the model containing only total comorbidity scores where R^2=.405, the model containing specific comorbidity categories explained 10% more variance in RPQ scores in the combined injury sample (R^2=.499). No moderation effects between prior comorbidities (e.g. neurological, psychiatric and musculoskeletal), and age or injury group were seen to be significant (p>.05).

Significant predictors of score variance for the WHOQoL-BREF (Table 24) in Model 1 (R^2=.420), were marital status, length of hospitalisation, pre- and post-injury total comorbidities, and RPQ scores. RPQ scores contributed the most variance to WHOQoL-BREF total scores, with 17.3% (p<.001). When comorbidity categories were modelled separately through stepwise selection in Model 2, pre-injury psychiatric/behavioural (p<.001), followed by prior respiratory (p<.01), and to a lesser extent, prior neurological problems (p<.05) were deemed significant predictors of quality of life after injuries, and collectively explained just over 10% of score variance. The occurrence of psychiatric (p<.001), musculoskeletal (p=.001) and neurological difficulties (p<.05) after injuries were also significant, and together contributed a further 14% variance. After adjusting for demographic and injury characteristics, prior health conditions, and post-injury occurring problems, RPQ scores alone contributed 10.8% of variance to the full model, which overall accounted for 44.6% of score variance on the WHOQoL-BREF. As with the previous models, no significant moderation effects were detected.

Table 23. Predicting PCS symptoms (RPQ) in the combined injury (TBI+orthopaedic) sample (*n*=223)

RPQ	Predictor	B	SE B	β	*p*	R Square	R Square Change
Model 1							
Step 1	Age	-0.136	0.040	-.225	.001	.051	.051
	Sex	3.592	1.657	.144	.031	.072	.021
Step 2	TBI vs Ortho	-9.594	1.441	-.403	.000	.234	.162
	Length of stay	7.573	1.774	.252	.000	.296	.062
Step 3	Pre-Injury Total Comorbidity Score	6.123	2.331	.179	.009	.318	.023
Step 4	Post Injury Total Comorbidity Score	17.021	3.118	.473	.000	.405	.086
	Age X PreInjuryTotal Comorbidity	-0.084	0.100	-.172	.402	.407	.002
RPQ	**Predictor**	**B**	**SE B**	**β**	***p***	**R Square**	**R Square Change**
Model 2							
Step 1	Age	-0.136	0.040	-.225	.001	.051	.051
	Sex	3.592	1.657	.144	.031	.072	.021
Step 2	TBI vs Ortho	-9.594	1.441	-.403	.000	.234	.162
	Length of hospital stay	7.573	1.774	.252	.000	.296	.062
Step 3	Pre-Neurological	22.216	5.868	.217	.000	.341	.046
	Pre-EENT	-12.343	4.795	-.148	.011	.362	.021
	Pre-Lower Gastrointestinal	24.062	9.561	.145	.013	.381	.019
	Pre-Musculoskeletal	11.730	4.544	.153	.011	.401	.020
Step 4	Post Psychiatric	13.918	2.951	.258	.000	.460	.059
	Post EENT	15.827	5.179	.225	.003	.484	.024
	Post Neurological	10.703	4.275	.153	.013	.499	.016
Step 5	Age X PreNeuro	-0.260	0.318	-.153	.416	.501	.002
	Age X PreMusc	-0.023	0.227	-.018	.918	.499	.000
	PreEENT X PreNeuro	39.445	28.807	.096	.172	.504	.005
	PreNeuro X PrePsych	30.084	23.183	.091	.196	.503	.004
	PreMusc X PrePsych	-10.565	22.481	-.030	.639	.500	.001
	InjuryGrp X PrePsych	-4.701	3.033	-.116	.123	.505	.006
	InjuryGrp X PreMusc	12.655	8.032	.283	.117	.505	.006
	InjuryGrp X PreNeuro	-3.311	10.885	-.053	.761	.499	.000

Model 1 contains total comorbidity (CIRS) scores by forced entry method; Model 2 contains specific disease categories of the CIRS by stepwise selection method; Ortho=orthopaedic; EENT=eyes/ears/nose/throat; neuro=neurological; musc=musculoskeletal; psych=psychiatric/behavioural

Table 24. Predicting quality of life (WHOQoL-BREF) in the combined injury (TBI+orthopaedic) sample (*n*=223)

WHOQoL -BREF	Predictor	B	SE B	β	*p*	R Square	R Square Change
Model 1							
Step 1	Marital status	4.942	1.579	.211	.002	.044	.044
Step 2	Length of hospital stay	-5.804	1.949	-.197	.003	.083	.039
Step 3	Pre-Injury Total Comorbidity Score	-9.564	2.130	-.286	.000	.164	.081
Step 4	Post Injury Total Comorbidity Score	-16.416	3.412	-.466	.000	.247	.084
Step 5	RPQ	-0.453	0.058	-.463	.000	.420	.173
Step 6	Age X PreInjuryTotal Comorbidity	0.095	0.073	.200	.194	.425	.005
Model 2							
Step 1	Marital status	4.942	1.579	.211	.002	.044	.044
Step 2	Length of hospital stay	-5.804	1.949	-.197	.003	.083	.039
Step 3	Pre-Psychiatric	-16.699	3.979	-.267	.000	.154	.071
	Pre-Respiratory	-19.366	7.226	-.172	.008	.183	.028
	Pre-Neurological	-13.070	6.463	-.130	.044	.198	.016
Step 4	Post Psychiatric	-21.945	4.725	-.416	.000	.274	.076
	Post Musculoskeletal	-12.708	3.598	-.217	.001	.316	.042
	Post Neurological	-11.634	4.512	-.170	.011	.338	.022
Step 5	RPQ	-0.384	0.061	-.392	.000	.446	.108
Step 6	Age X PreMusc	-0.036	0.075	-.029	.637	.446	.001
	Age X PreNeuro	-0.101	0.309	-.061	.743	.446	.000
	Marital X PrePsych	2.443	6.694	.061	.716	.446	.000
	InjuryGrp X PrePsych	-6.662	6.022	-.168	.270	.449	.003
	InjuryGrp X PreMusc	0.166	2.625	.004	.950	.446	.000
	InjuryGrp X PreNeuro	17.852	10.272	.290	.084	.454	.008
	PreMusc X PrePsych	-25.343	21.595	-.074	.242	.449	.004
	PreMusc X PreNeuro	-21.982	29.983	-.058	.464	.447	.001

Model 1 contains total comorbidity (CIRS) scores by forced entry method. Model 2 contains specific disease categories of the CIRS by stepwise selection method; EENT=eyes/ears/nose/throat; neuro=neurological; musc=musculoskeletal; psych=psychiatric/behavioural

TBI sample

Separate regression analyses modelling RPQ and WHOQoL-BREF for the TBI group were conducted, and results are presented in Table 25 and Table 26, respectively. In the TBI sample, age was negatively correlated with RPQ scores (p=.01), while tertiary-level education and increased hospitalisation were positively linked to PCS symptoms (p<.05) (Table 25). Prior existence of neurological and EENT problems significantly predicted symptoms after injuries (p<.01), and together accounted for just over 13% of explained variance, although pre-injury EENT difficulties were found to be negatively correlated (β -.237) with PCS symptoms. Injury characteristics such as overall injury severity (measured by ISS), and TBI severity (GCS score), were not found to be predictive of RPQ scores in the model (p>.05). After adjusting for pre-injury problems, the onset of genitourinary (p<.001), psychiatric (p=.001), neurological (p<.01) and musculoskeletal problems (p<.05) following injury, were deemed significant predictors of PCS symptoms among those with TBI. Results also indicated that participants with genitourinary issues (commonly enlarged prostate or previous hysterectomy) were negatively correlated with PCS symptoms (β=-.326). Collectively, post-injury health conditions contributed to over 22% of explained variance in the model, which had an overall R^2 of .515. Potential interaction effects between age and previous health problems (e.g. musculoskeletal, genitourinary, neurological), and between previous history of psychiatric and neurological-related problems were tested in the model but yielded no statistical significance.

With regards to the WHOQoL-BREF scores in the TBI sample (Table 26), marital status (p<.01) was a significant predictor that explained 9% of total variance, while prior neurological problems (p<.001) explained a further 11% of variance in the model. Similar to PCS symptoms, overall injury severity and GCS scores were not significant predictors of quality of life among TBI participants. In the post-injury phase, musculoskeletal (p<.001), neurological (p<.01) and psychiatric/behavioural disorders (p<.01), were shown to be significant determinants of quality of life, altogether accounting an additional 23% of variance in the model. After controlling for demographic variables, hospitalisation, and pre- and post-injury health conditions, the remaining 13% of variance was explained by the presence of PCS symptoms (p<.001). Looking across the specific domains of the WHOQoL-BREF, prior and post-injury neurological and psychiatric difficulties were consistent significant predictors of physical, psychological and environmental domains. The experience of post-injury

musculoskeletal problems was also found to be a determinant of quality of life in the social and environmental domains, but particularly important in the physical domain, in which musculoskeletal problems alone explained for 23% of score variance. The presence of PCS symptoms was also a strong predictive factor across the physical, psychological and environmental domains, explaining approximately 15% of variance in WHOQoL-BREF scores, except for the social domain where PCS symptoms were non-significant (p=.131). Model fit statistics across most domains indicated acceptable fit of data to the overall model, with approximately 50% of score variances being explained by the variables, except for the social domain where only 28% variance was predicted by variables. Moderator variables were entered into each model but did not yield any predictive value (p>.05).

Table 25. Predicting PCS symptoms in the TBI sample (n=109)

RPQ	Predictor	B	SE B	β	*p*	R Square	R Square Change
Step 1	Age	-0.140	0.053	-.254	.010	.064	.064
	Education	4.676	2.081	.213	.027	.110	.045
Step 2	Length of hospital stay	5.270	2.543	.194	.041	.147	.037
Step 3	Pre-Neurological	28.101	8.855	.293	.002	.227	.080
	Pre EENT	-17.041	6.270	-.237	.008	.283	.055
Step 4	Post Psychological	13.859	4.234	.282	.001	.355	.073
	Post Musculoskeletal	11.239	4.346	.222	.011	.398	.043
	Post Genitourinary	-25.826	6.984	-.326	.000	.475	.077
	Post Neurological	13.096	4.787	.224	.007	.515	.039
Step 5	Age X PreMusc	0.006	0.114	.005	.958	.515	.000
	Age X PreGenitourinary	0.031	0.153	.026	.838	.515	.000
	Age X PreNeuro	0.781	0.887	.508	.381	.519	.004
	Age X PostMusc	0.297	0.209	.358	.159	.525	.011
	PrePsych X PostPsych	7.781	12.484	.073	.535	.517	.002
	PreNeuro X PostNeuro	31.691	38.645	.128	.414	.518	.004

EENT=eyes/ears/nose/throat; neuro=neurological; musc=musculoskeletal; psych=psychiatric/behavioural

Table 26. Predicting quality of life in the TBI sample (*n*=109), by total WHOQoL-BREF scores and by domain levels

WHOQoL-BREF	**Predictor**	**B**	**SE B**	**β**	***p***	**R Square**	**R Square Change**
Step1	Marital status	6.875	2.205	.298	.002	.089	.089
Step 3	Pre-Neurological	-33.542	9.130	-.332	.000	.198	.109
Step 4	Post Musculoskeletal	-20.296	4.601	-.380	.000	.331	.133
	Post Neurological	-16.214	5.351	-.263	.003	.389	.058
	Post Psychological	-11.819	4.215	-.228	.006	.435	.046
Step 5	RPQ	-0.440	0.082	-.417	.000	.566	.131
Step 6	Marital X PrePsych	-0.129	4.181	-.003	.975	.566	.000
Physical Domain	**Predictor**	**B**	**SE B**	**β**	***p***	**R Square**	**R Square Change**
Step 3	Pre-Neurological	-10.528	3.435	-.293	.003	.086	.086
Step 4	Post Musculoskeletal	-9.550	1.642	-.503	.000	.319	.233
Step 5	RPQ	-0.153	0.029	-.408	.000	.471	.152
Step 6	Age X PreMusc	-0.037	0.040	-.080	.359	.476	.005
Psychological Domain	**Predictor**	**B**	**SE B**	**β**	***p***	**R Square**	**R Square Change**
Step 1	Marital status	2.025	0.654	.296	.003	.088	.088
Step 3	Pre-Psychological	-5.065	1.618	-.287	.002	.170	.082
	Pre-Neurological	-7.706	2.671	-.258	.005	.235	.065
Step 4	Post Neurological	-5.963	1.666	-.326	.001	.324	.089
	Post Psychological	-6.55	1.983	-.427	.001	.393	.069
Step 5	RPQ	-0.133	0.025	-.427	.000	.533	.140
Step 6	Marital X PrePsych	-1.622	2.607	-.141	.535	.535	.002

Social Domain	Predictor	B	SE B	β	*p*	R Square	R Square Change
Step 1	Marital status	1.503	0.465	.308	.002	.095	.095
Step 2	Length of hospital stay	-1.297	0.566	-.214	.024	.140	.046
Step 3	Pre-Neurological	-4.316	1.973	-.202	.031	.180	.040
Step 4	Post Musculoskeletal	-2.538	1.051	-.225	.018	.227	.046
	Post Endocrine	2.544	1.166	.194	.032	.263	.037
Step 5	RPQ	-0.032	0.021	-.142	.131	.281	.018
Step 6	Marital X PrePsych	-0.606	0.736	-.074	.412	.286	.005
Environmental Domain	**Predictor**	**B**	**SE B**	**β**	***p***	**R Square**	**R Square Change**
Step 1	Marital status	1.800	0.678	.256	.009	.066	.066
Step 2	Length of hospital stay	-1.680	0.831	-.193	.046	.103	.037
Step 3	Pre-Neurological	-8.381	2.843	-.273	.004	.176	.073
	Pre-Respiratory	-10.098	3.668	-.246	.007	.236	.060
Step 4	Post Neurological	-5.541	1.744	-.295	.002	.308	.073
	Post Musculoskeletal	-3.973	1.405	-.245	.006	.362	.054
	Post Psychological	-2.846	1.381	-.181	.042	.390	.028
Step 5	RPQ	-0.149	0.026	-.467	.000	.547	.157
Step 6	Age X PreMusc	-0.026	0.033	-.065	.437	.550	.003
	Employment X PreResp	-1.945	5.934	-.073	.744	.547	.001

neuro=neurological; musc=musculoskeletal; psych=psychiatric/behavioural; resp=respiratory. For the WHOQoL-BREF model, step 2 is omitted in stepwise selection as there are no significant injury variables for inclusion at $p<.05$. Physical domain—steps 1 and 2 are omitted given that demographic and injury variables are non-significant. Psychological domain—step 2 is omitted as injury variables are non-significant.

Orthopaedic sample

Table 27 and Table 28 present the results from the regression models predicting RPQ and WHOQoL-BREF scores for the orthopaedic sample. For RPQ scores (Table 27), decreased age ($p<.01$), and increased hospitalisation ($p<.001$) were significant predictors, as were pre-existing lower gastrointestinal ($p=.001$), and musculoskeletal difficulties ($p=.001$). Post-injury psychological ($p=.001$), and neurological disturbances

(p=.001) significantly predicted PCS, and collectively explained for almost 10% of variance in the overall model (R^2 =.437).

Analysis of the WHOQoL-BREF (Table 28) did not reveal any demographic characteristics to be relevant predictors of quality of life among orthopaedic participants, although as with the TBI sample, increased hospitalisation predicted lower WHOQoL-BREF scores (p<.05). Prior health problems such as psychiatric/behavioural difficulties (p<.001), lower gastrointestinal (p<.05) and musculoskeletal issues (p<.05) predicted almost 20% of variance in the model, among which history of mental health issues alone explained for 12% of score variance. Among all post-injury health problems, only the occurrence of psychiatric difficulties was found to be predictive of quality of life scores, accounting for 8.5% of variance. After adjusting for length of hospitalisation, as well as previous and post-injury health problems, the remaining variance was accounted for by the presence of PCS symptoms (p<.05, R^2 change= .040). The full model however, inadequately fit the data and only explained a small proportion of variance in WHOQoL-BREF scores (R^2 =.362).

Table 27. Predicting PCS symptoms in the orthopaedic sample (n=113)

RPQ	Predictor	B	SE B	β	*p*	R Square	R Square Change
Step 1	Age	-0.137	0.051	-.248	.009	.061	.061
Step 2	Length of hospital stay	10.734	2.472	.374	.000	.201	.140
Step 3	Pre LowerGI	36.681	10.771	.283	.001	.279	.078
	Pre-Musculoskeletal	18.660	5.714	.271	.001	.345	.066
Step 4	Post-Psychological	14.107	4.053	.284	.001	.413	.068
	Post-Neurological	13.085	6.222	.180	.038	.437	.024
Step 5	Age X PreMusc	0.155	0.309	.136	.618	.438	.001
	Age X PreNeuro	0.006	0.148	.004	.969	.437	.000
	PreNeuro X PrePsych	28.793	23.679	.109	.227	.445	.008
	PreMusc X PrePsych	7.228	29.641	.024	.808	.437	.000

GI=gastrointestinal; neuro=neurological; musc=musculoskeletal; psych=psychiatric/behavioural

Separate analyses by domain-level of the WHOQoL-BREF indicated that for the orthopaedic sample, younger age ($p<.05$, R^2 change=.047), and living as married ($p<.05$, R^2 change=.044) predicted higher scores on the social domain, whereas older age predicted higher scores on the environmental domain ($p=.001$, R^2 change=.094). In terms of clinical characteristics, increased length of hospitalisation predicted lower scores only in the physical domain ($p<.05$, R^2 change=.047). With regards to pre-existing health, previous psychiatric and musculoskeletal problems were found to be consistent predictors across the different domains. For instance, prior history of psychiatric disturbances accounted for 10.3% of variance in the physical domain ($p<.001$), 7.9% in the psychological domain ($p<.01$), and 9.7% in the social domain ($p=.001$). Pre-injury musculoskeletal problems accounted for between 3.2 and 5.5% of variance in the physical ($p<.01$), psychological ($p<.05$), and environmental domains ($p<.05$). Other pre-injury conditions that were found to be predictive of quality of life were previous endocrine problems in the physical domain (R^2 change=.041, $p<.05$), and lower gastrointestinal issues in the environmental domain (R^2 change=.032, $p<.05$). With regards to post-injury health conditions, psychiatric difficulties appeared as a significant predictor in all QoL domains accounting for between 4.6 to 9.8% of all variance explained in the models. Additionally, post-injury musculoskeletal difficulties also predicted lower physical quality of life (R^2 change=.030, $p<.05$), while post-injury genitourinary problems predicted lower scores on social QoL (R^2 change=.038, $p<.05$). After controlling for baseline sample characteristics, and previous and post-injury health problems, PCS symptoms remained a significant determinant of quality of life for orthopaedic injury participants, but only for the physical (R^2 change=.065, $p=.001$), and psychological (R^2 change=.040, $p<.05$) domains. Overall, R^2 was sub-optimal for the different domains of the WHOQoL-BREF: physical $R^2=.387$, psychological $R^2=.251$, social $R^2=.287$ and environmental $R^2=.349$. Moderation effects existing between sample characteristics (e.g. age, marital and employment status), health problems and PCS symptoms did not yield statistical significance in any of the models.

Table 28. Predicting quality of life in the orthopaedic sample (*n*=113), by total WHOQoL-BREF scores and domain levels

WHOQoL BREF	**Predictor**	**B**	**SE B**	**β**	***p***	**R Square**	**R Square Change**
Step 2	Length of hospital stay	-6.122	2.841	-.202	.033	.041	.041
Step 3	Pre-Psychological	-22.097	5.631	-.347	.000	.161	.120
	Pre-LowerGI	-32.223	13.21	-.235	.016	.205	.044
	Pre-Musculoskeletal	-13.312	6.213	-.184	.034	.238	.033
Step 4	Post Psychological	-21.87	6.027	-.418	.000	.323	.085
Step 5	RPQ	-0.261	0.103	-.247	.013	.362	.040
Step 6	Age X PreMusc	0.087	0.288	.073	.763	.363	.001
	Age X PreNeuro	0.068	0.148	.041	.648	.364	.001
	Marital X PrePsych	4.775	9.257	.119	.607	.364	.002
	PreMusc X PrePsych	5.313	36.827	.017	.886	.362	.000
	PreMusc X PreNeuro	-15.053	35.317	-.038	.671	.363	.001
Physical Domain	**Predictor**	**B**	**SE B**	**β**	***p***	**R Square**	**R Square Change**
Step 2	Length of hospital stay	-2.327	1.014	-.215	.024	.046	.046
Step 3	Pre-Psychological	-7.328	2.030	-.321	.000	.149	.103
	Pre-Musculoskeletal	-6.118	2.241	-.236	.007	.204	.055
	Pre-Endocrine	-4.679	1.950	-.206	.018	.245	.041
Step 4	Post Psychological	-5.792	2.213	-.309	.010	.291	.046
	Post Musculoskeletal	-4.933	2.283	-.208	.033	.322	.030
Step 5	RPQ	-0.119	0.036	-.315	.001	.387	.065
Step 6	Age X PreMusc	0.068	0.108	.159	.528	.390	.002
	Age X PreNeuro	0.022	0.050	.037	.661	.388	.001

Psychological Domain	Predictor	B	SE B	β	*p*	R Square	R Square Change
Step 3	Pre-Psychological	-5.406	1.765	-.282	.003	.079	.079
	Pre-Musculoskeletal	-4.084	1.979	-.187	.041	.114	.035
Step 4	Post Psychological	-7.044	1.936	-.447	.000	.212	.098
Step 5	RPQ	-0.072	0.030	-.225	.020	.251	.040
Step 6	Age X PreMusc	0.027	0.093	.074	.774	.252	.001
	Age X PreNeuro	0.033	0.044	.067	.449	.255	.004
	Marital X PrePsych	-0.579	2.985	-.048	.847	.252	.000
Social Domain	**Predictor**	**B**	**SE B**	**β**	***p***	**R Square**	**R Square Change**
Step 1	Marital status	0.929	0.415	.210	.027	.044	.044
	Age	-0.026	0.011	-.238	.020	.091	.047
Step 3	Pre-Psychological	-3.776	1.057	-.312	.001	.188	.097
Step 4	Post Psychological	-3.600	1.225	-.362	.004	.249	.061
	Post Genitourinary	-3.494	1.474	-.211	.020	.287	.038
Step 5	RPQ	-0.034	0.019	-.171	.073	.309	.022
Step 6	Age X PreGenitourinary	0.014	0.041	.059	.726	.310	.001
	Marital X PrePsych	2.393	2.091	.314	.255	.318	.009
Environmental Domain	**Predictor**	**B**	**SE B**	**β**	***p***	**R Square**	**R Square Change**
Step 1	Age	0.056	0.017	.306	.001	.094	.094
Step 3	Pre-LowerGI	-15.625	3.651	-.366	.000	.225	.131
	Pre-Musculoskeletal	-4.277	1.988	-.189	.034	.257	.032
Step 4	Post Psychological	-4.713	1.411	-.289	.001	.328	.071
Step 5	RPQ	-0.057	0.031	-.173	.068	.349	.021
Step 6	Age X PreMusc	-0.005	0.106	-.014	.962	.349	.000
	Age X PreLowerGI	-0.365	0.255	-.539	.155	.361	.013

neuro=neurological; musc=musculoskeletal; psych=psychiatric/behavioural; GI=gastrointestinal. For the model predicting the WHOQoL-BREF total score and physical domain score, step 1 is omitted in stepwise selection as there are no significant demographic variables for inclusion at $p<.05$. For the psychological domain – steps 1 and 2 are omitted as both demographic and injury variables are non-significant. Social and environmental domains – step 2 is omitted as injury variables are non-significant.

Section summary

Whilst the overarching analyses in Study 2 are largely informed by the theoretical framework outlined in Figure 9 presented earlier, the practical challenges with dealing with a large number of variables with a relatively small sample size (*n*=108 TBI and *n*=114 orthopaedic) required a preliminary multivariate regression analysis with stepwise methods to be undertaken to exclude variables that were not predictive of PCS and QoL as the outcomes of interest. The regression analyses also aimed to highlight pre-injury comorbidities that were most predictive of the outcomes.

Based on preliminary findings from the regression models it was found that, among TBI and orthopaedic groups, higher PCS symptoms were predicted by younger age and increased hospitalisation. In the TBI group, who were more likely to score higher on the RPQ measure than orthopaedic participants, those with higher education levels were also more likely to report more PCS symptoms. Results also revealed that, prior neurological and EENT problems predicted higher RPQ scores for the TBI sample, whereas in the orthopaedic sample, those who had pre-existing lower gastrointestinal and musculoskeletal difficulties were likely to report more PCS symptoms. With regards to quality of life, being or living as married predicted higher WHOQoL-BREF scores, but only in the TBI sample. Among pre-existing conditions, prior neurological problems explained greater variance in the model and correlated with overall lower quality of life in the TBI group. Supplementary domain analyses revealed other conditions such as pre-injury psychiatric/behavioural and respiratory conditions should be taken into consideration when analysing physical, psychological, social and environmental quality of life in TBI participants. For the orthopaedic sample, prior psychiatric/behavioural, lower gastrointestinal and musculoskeletal problems were significant predictors of lower quality of life. Furthermore, in this sample prior psychological and musculoskeletal problems consistently affected scores across all QoL domains. The regression results demonstrated that the post-injury experience of PCS symptoms remained a significant predictor of poorer quality of life, irrespective of injury type, and after controlling for all other factors.

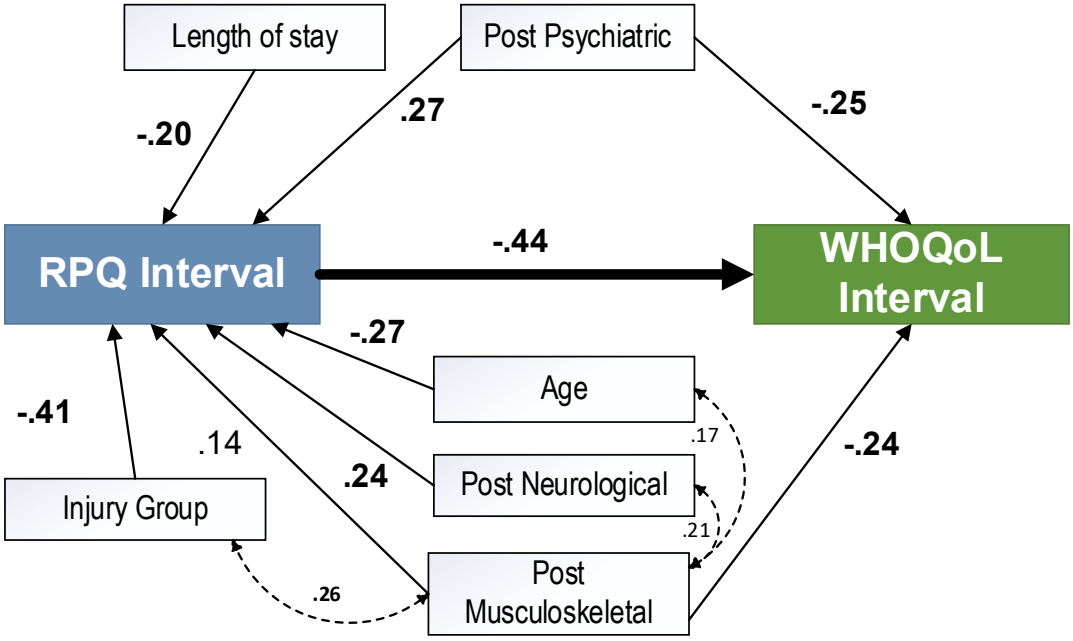
Having identified relevant predictors of outcomes in the preliminary analyses, the subsequent SEM analyses described next attempted to model determinants of outcomes, with a focus on highlighting relevant post-injury comorbidities that impact on PCS symptoms and quality of life between TBI and orthopaedic groups.

8.3 Results of the SEM analyses

Modelling PCS symptoms and quality of life in the overall injury sample

Guided by the results from the previous regression models, the relationships existing between demographic and injury characteristics, post-injury comorbidities, PCS, and QoL were analysed using SEM methods. Predictors of postconcussion symptoms (RPQ), and quality of life (WHOQoL-BREF) were modelled for the combined injury sample (*n*=222), using log10 transformed comorbidity scores and Rasch transformed RPQ and WHOQoL-BREF scores, and these are depicted in Figure 26. Corresponding effect sizes (beta coefficients) are additionally presented in Table 29. Of sample characteristics, age (β =-.206), length of hospitalisation (β =.197), and injury group (β =-.408) directly affected PCS symptoms (all *p*-values <.001), which acted as a mediating variable on quality of life. In terms of comorbidities, post-injury neurological problems affected only postconcussion symptoms, whereas the existence of post-injury psychiatric and musculoskeletal difficulties were common predictors of both PCS symptoms and QoL. The highest total effects, which are equal to the sum of direct effects and indirect effects on quality of life, were due to PCS symptoms (β =-.436), followed by post-injury psychiatric (β=-.365), and musculoskeletal difficulties (β=-.306), as shown in Table 29. Fit indices suggested that the model was a good fit to the data (CFI=.940; RMSEA=.070; CI .036–.104, χ^2/df=2.08, *p*=.007).

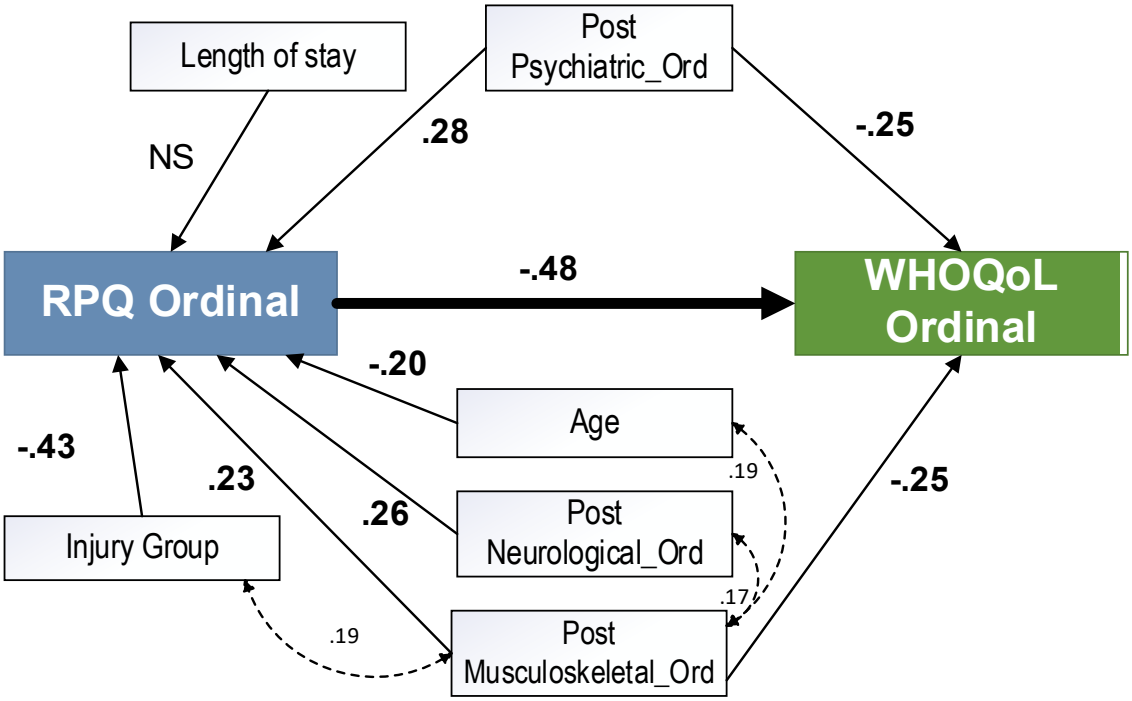
In Figure 27, where ordinal-structured comorbidity and outcome measures were used in lieu of transformed interval-level scores, overall standardised coefficients appear to be marginally higher. Two exceptions were noted, where the relationship between age and RPQ scores decreased in strength of association from β -.266 to -.201, and the relationship between post-injury psychiatric problems and quality of life remained unchanged. Another difference between the two models is that in Figure 26, log 10 transformed length of stay (LOS) variable was a significant predictor of RPQ scores, whereas in Figure 27, the untransformed variable is not seen to be significant (*p*>.05). Overall model fit between the two models is similar, where log10 transformed CIRS scores, as well as Rasch transformed RPQ and WHOQoL-BREF scores, were replaced with ordinal-level measures (Figure 27), resulted in only a diminutive increase in model fit indices (CFI from .940 in Figure 26, to .946 in Figure 27).



CFI=.940; RMSEA=.070, CI=.036–.104; χ^2/df=2.08, *p*=.007

Figure 26. Role of post-injury comorbidities influencing PCS symptoms and quality of life in the total injury sample (*n*=222), using log10 transformed comorbidity scores and Rasch-transformed interval outcomes (RPQ and WHOQoL-BREF total scores)

Note: Bold signifies statistical significance at *p*<.001; CFI=Comparative Fit Index; CI=Confidence Interval; RMSEA=Root Mean Square Error of Approximation



CFI=.946; RMSEA=.069, CI=.034–.102; χ^2/df=2.04, *p*=.008

Figure 27. Role of post-injury comorbidities influencing PCS symptoms and quality of life in the total injury sample (*n*=222), using ordinal comorbidity and outcome measures

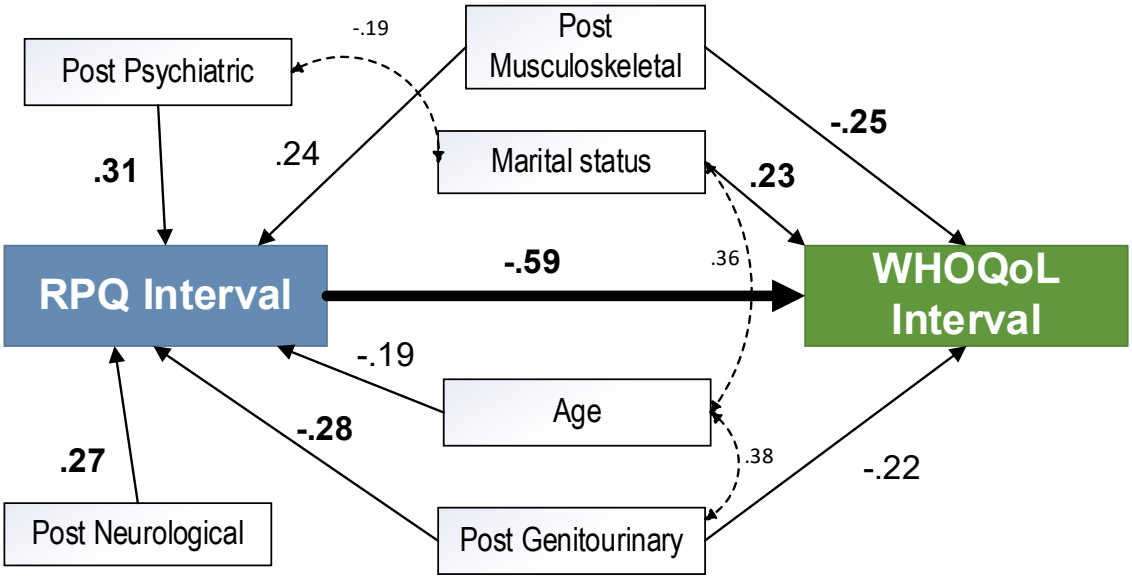
Table 29. Model fit statistics, effect sizes with standardised coefficients for modelling PCS symptoms and quality of life in the total injury sample (*n*=222), with comparisons between interval (top half), and ordinal-level (bottom half) outcomes

Log10 transformed comorbidity scores and Rasch-transformed interval measures of RPQ and WHOQoL-BREF total scores							
	Post-Musc	Post Neuro	LOS	Age	Post Psych	Injury Group	RPQ Interv
	ß	ß	ß	ß	ß	ß	ß
Direct effects							
RPQ Interv	.142	.236	.197	-.266	.266	-.408	0
WHOQoL Interv	-.244	0	0	0	-.248	0	-.436
Indirect effects							
RPQ Interv	0	0	0	0	0	0	0
WHOQoL Interv	-.062	-.103	-.086	.116	-.116	.178	0
Total effects							
RPQ Interv	.142	.236	.197	-.266	.266	-.408	0
WHOQoL Interv	-.306	-.103	-.086	.116	-.365	.178	-.436
Model fit: CFI=.940; RMSEA=.070, CI .036–.104; χ^2 =33.340, df=16, *p*=.007							
Ordinal-level comorbidity scores and ordinal RPQ and WHOQoL-BREF total scores							
	Post Musc Ord	Post Neuro Ord	LOS	Age	Post Psych Ord	Injury Group	RPQ Ord
	ß	ß	ß	ß	ß	ß	ß
Direct effects							
RPQ Ord	.230	.257	.071	-.201	.280	-.427	0
WHOQoL Ord	-.249	0	0	0	-.245	0	-.483
Indirect effects							
RPQOrd	0	0	0	0	0	0	0
WHOQoL Ord	-.111	-.124	-.034	.097	-.135	.206	0
Total effects							
RPQ Ord	.230	.257	.071	-.201	.280	-.427	0
WHOQoL Ord	-.360	-.124	-.034	.097	-.381	.206	-.483
Model fit: CFI=.946; RMSEA=.069, CI .034–102; χ^2 =32.636, df=16, *p*=.008							

neuro=neurological; musc=musculoskeletal; psych=psychiatric/behavioural; LOS=length of hospital stay; interv=interval scores; ord=ordinal scores; injury group: TBI (1) vs. orthopaedic (2)

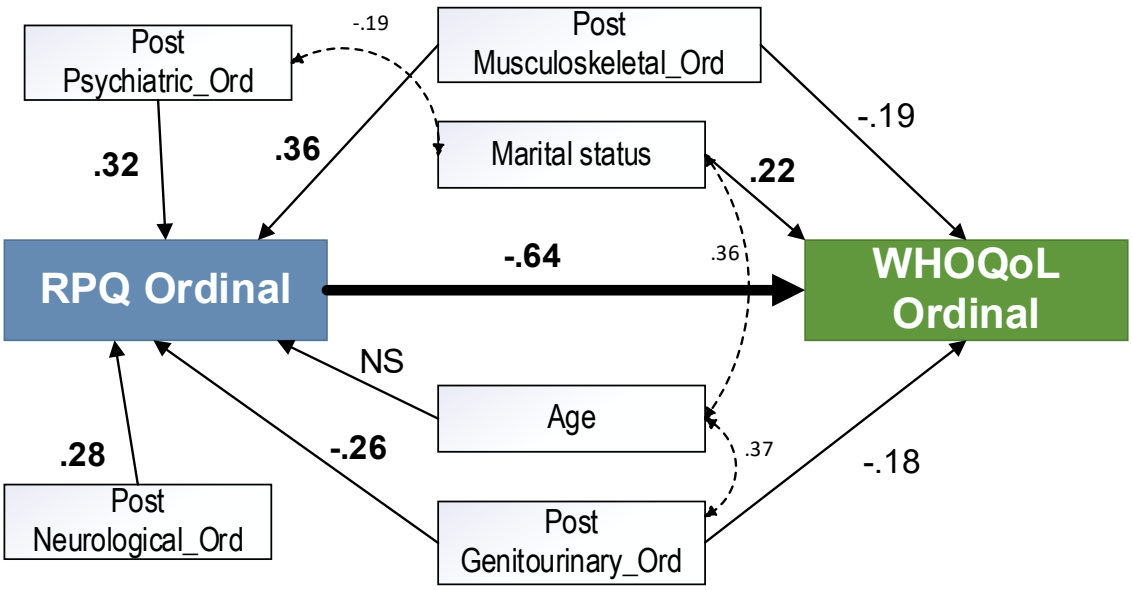
Modelling PCS symptoms and quality of life in the TBI sample

Separate SEM analyses with corresponding tables of effect sizes for the TBI sample were conducted with the use of interval-level (Figure 28, and Table 30), and ordinal-level measures (Figure 29, and Table 30). In Figure 28, in addition to age of TBI participants (β=-.187), the onset of psychiatric problems (β=.305), followed by neurological (β=.271) and musculoskeletal conditions (β=.243) after injuries, directly impacted on self-reported PCS symptoms, which also indirectly showed small effects on overall quality of life (β -.145 to -.182). Conversely, the onset of genitourinary problems was associated with reporting of lower PCS symptoms (β=-.280), and also lower quality of life (β=-.217). Post-injury musculoskeletal (β=-.249), and genitourinary problems (β=-.217) also had direct negative influence on quality of life, whilst being in a relationship was seen to be positively correlated with quality of life (β=.234). The strongest total effect on quality of life was exerted by PCS symptoms (β=-.595), followed by post-injury musculoskeletal problems (β=-.394). Comparisons between the path models for Figure 28 and Figure 29, and effect sizes in Table 30 show that overall, the use of interval measures compared with ordinal measures tend to reduce the strength of effects between relationships, but at the same time enhances other associations (such as between post-injury musculoskeletal and quality of life, and that between post-injury genitourinary problems, PCS and quality of life). In addition, in Figure 28 the use of Rasch-transformed RPQ scores results in a statistically significant relationship with age (β=-.187, p=.023) whereas the ordinal measure of this variable results in non-significance (p=.063). Comparisons of p-values of the direct relationships (not shown) also indicate that use of interval-level measures enhances p-values between WHOQoL-BREF and musculoskeletal and genitourinary variables. Lastly, overall model fit was marginally better when using interval and log10 transformed scales than ordinal measures (CFI=.940 vs. .919; RMSEA=.079 vs. .096; χ^2/df=1.66 vs 1.99).



CFI=.940; RMSEA=.079, CI .010–130; χ^2 /df=1.66, *p*=.047

Figure 28. Role of post-injury comorbidities influencing PCS symptoms and quality of life in the TBI sample (*n*=108), using log10 transformed comorbidity scores and Rasch-transformed interval outcomes



CFI=.919; RMSEA=.096, CI .046–145; χ^2 /df = 1.99, *p*=.010

Figure 29. Role of post-injury comorbidities influencing PCS symptoms and quality of life in the TBI sample (*n*=108), using ordinal comorbidity and outcome measures

Note: "NS" refers to non-significance at *p*<.05

Table 30. Model fit statistics, effect sizes with standardised coefficients for modelling PCS symptoms and quality of life in the TBI sample (*n*=108), with comparisons between interval (top half) and ordinal-level (bottom half) outcome measures

Log10 transformed comorbidity scores and Rasch-transformed interval measures of RPQ and WHOQoL-BREF total scores							
	Post GU	Post Neuro	Post Psych	Post Musc	Marital status	Age	RPQ Interv
	ß	ß	ß	ß	ß	ß	ß
Direct effects							
RPQ Interv	-.280	.271	.305	.243	0	-.187	0
WHOQoL Interv	-.217	0	0	-.249	.234	0	-.595
Indirect effects							
RPQ Interv	0	0	0	0	0	0	0
WHOQoL Interv	.166	-.161	-.182	-.145	0	.111	0
Total effects							
RPQ Interv	-.280	.271	.305	.243	0	-.187	0
WHOQoL Interv	-.051	-.161	-.182	-.394	.234	.111	-.595
Model fit: CFI=.940; RMSEA=.079, CI .010 –130; χ^2 =26.564, df=16, *p*=.047							
Ordinal-level comorbidity scores and ordinal RPQ and WHOQoL-BREF total scores							
	Post GU Ord	Post Neuro Ord	Post Psych Ord	Post Musc Ord	Marital status Ord	Age	RPQ Ord
	ß	ß	ß	ß	ß	ß	ß
Direct effects							
RPQ Ord	-.264	.283	.319	.364	0	-.145	0
WHOQoL Ord	-.176	0	0	-.187	.217	0	-.641
Indirect effects							
RPQOrd	0	0	0	0	0	0	0
WHOQoL Ord	.169	-.181	-.204	-.233	0	.093	0
Total effects							
RPQ Ord	-.264	.283	.319	.364	0	-.145	0
WHOQoL Ord	-.007	-.181	-.204	-.420	.217	.093	-.641
Model fit: CFI=.919; RMSEA=.096, CI .046–145; χ^2 =31.882, df=16, *p*=.010							

GU=genitourinary; neuro=neurological; psych=psychiatric; musc=musculoskeletal; marital status: single vs. living as married; interv=interval scores; ord=ordinal scores

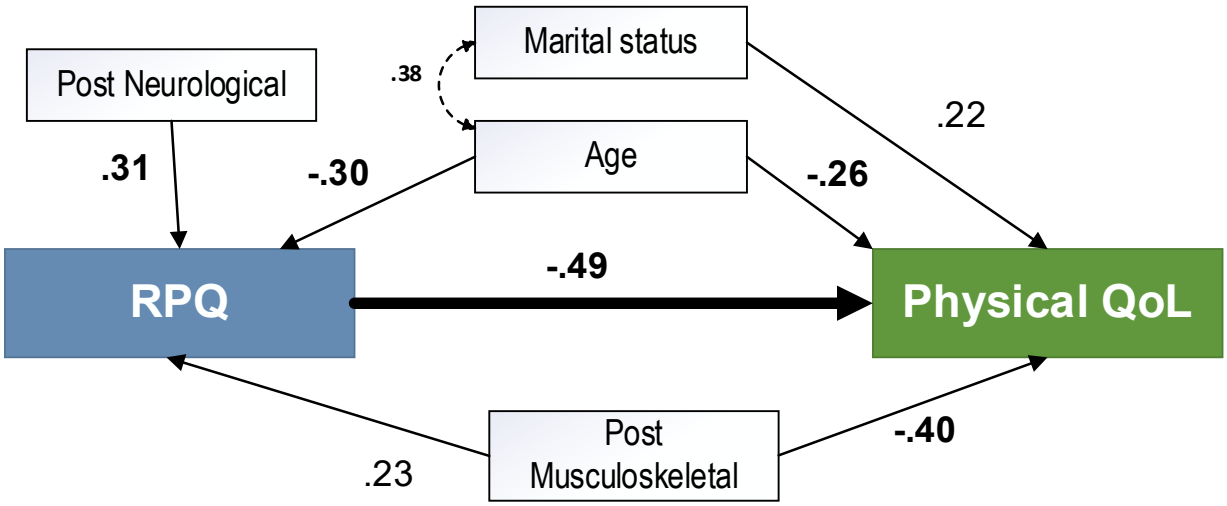
Supplementary analyses on the physical (Figure 30), psychological (Figure 31), social (Figure 32), and environmental (Figure 33) domains of the WHOQoL-BREF were also conducted, with domain-level effect estimates for each domain presented in Table 31. Across the different domains of the WHOQoL-BREF, baseline factors such as age portrayed direct relationships with both PCS and WHOQoL-BREF, while a person's marital status (being or living as married) was strongly associated with higher quality of life, especially in the social domain (β=.345). No injury-related factors such as overall injury severity, TBI severity or length of hospital stay were seen to be relevant to the predictive models at the domain-level. Similarly, comorbidities appear as consistent predictors across domains, notably post-injury difficulties associated with the musculoskeletal, psychological and neurological categories.

In the physical domain, neurological problems (β=.305) exerted the strongest effect directly on PCS symptoms. Musculoskeletal difficulties also directly influenced symptoms (β=-.230), which together exerted a strong negative impact on physical quality of life (β=-.511), as shown in Table 31. As in Figure 30, PCS symptoms demonstrated a strong relationship with the physical domain (β=-.488).

In the psychological domain (Figure 31), both post-injury neurological and psychiatric disturbances exhibited direct influences on postconcussive symptoms (β=.293 and .326, respectively) and the WHOQoL-BREF (β=-.176 and -.247, respectively). The total effects of neurological problems on PCS symptoms and psychological quality of life were, β=.293 and β=-.308, respectively, whereas the total effects of psychiatric difficulties on symptoms and psychological quality of life were, β=.326 and β=-.394, respectively (Table 31). In the model, PCS symptoms were seen to be the strongest predictor of psychological quality of life by regression weight (β=-.452).

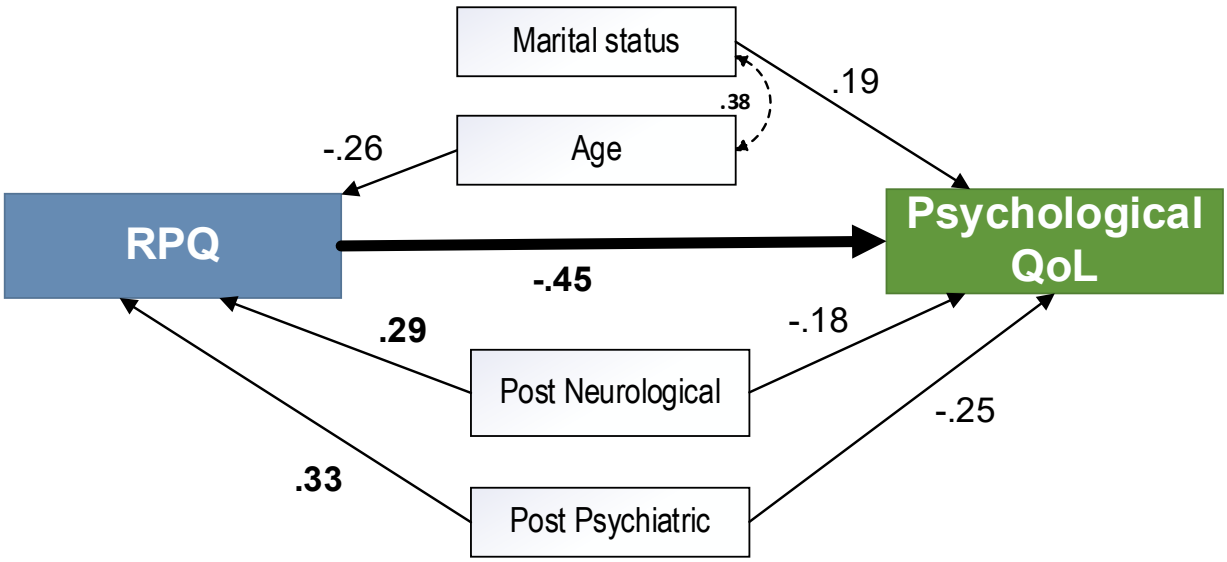
In addition to age (β=-.263) and marital status (β=.345), higher level of education (β=.217) also predicted higher scores on the social component of the WHOQoL-BREF, as shown in Figure 32. Post-injury psychiatric (β=.305), neurological (β=.271) and musculoskeletal problems were directly predictive only of postconcussive symptoms. Post-injury genitourinary conditions affected both PCS symptoms and QoL directly (β=-.280 and β=-.238), while endocrine-metabolic disorders were associated with higher quality of life scores on the social domain (β=.232). PCS symptoms exerted the strongest effects on social quality of life with a beta coefficient of -.399 (Table 31).

In the environmental domain (Figure 33), post-injury psychiatric (β=.305), genitourinary (β=-.280) and neurological conditions (β=.271) directly affected PCS symptoms, whereas post-injury musculoskeletal problems had similar direct effects on symptoms (β=.243), as well as on quality of life (β=-.240). These comorbidities only had minimal indirect effects on environmental quality of life through PCS symptoms as a mediator, with coefficients ranging from β=.096 to .144 as seen in Table 31. Total effects exerted on the environmental domain were highest for PCS symptoms (β=-.514), followed by musculoskeletal conditions (β=-.365). Although respiratory problems were found to be a predictor of environmental QoL in the regression analysis earlier, this variable was found to be non-significant in the SEM analysis, which resulted in lowering model fit, and therefore had to be removed from the model. Overall model fit indices for the physical (CFI=.987; RMSEA=.046, CI 0–133; χ^2/df=1.23), psychological (CFI=.983; RMSEA=.052, CI 0–.137; χ^2/df=1.29), social (CFI=.909; RMSEA=.064, CI 0–.103; χ^2/df=1.44), and environmental domains (CFI=.903; RMSEA=.092, CI .041 to .139; χ^2/df=1.90) indicated good to excellent fit of the data to the models.



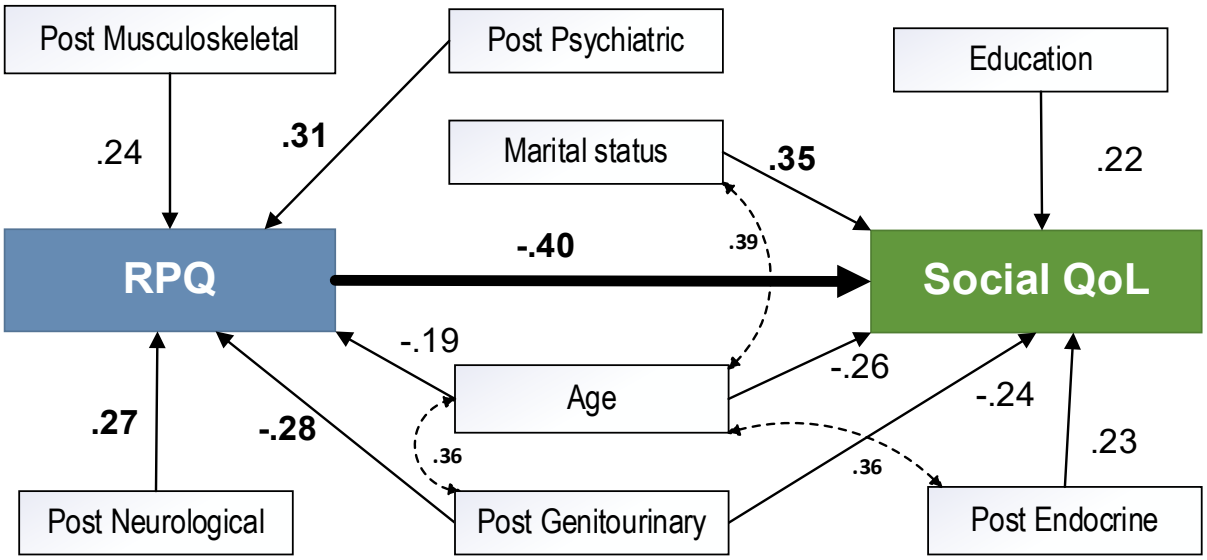
CFI=.987; RMSEA=.046, CI 0–.133; χ^2 /df =1.23, *p*=.281

Figure 30. Role of post-injury comorbidities influencing the physical domain of the WHOQoL-BREF in the TBI sample (*n*=108)



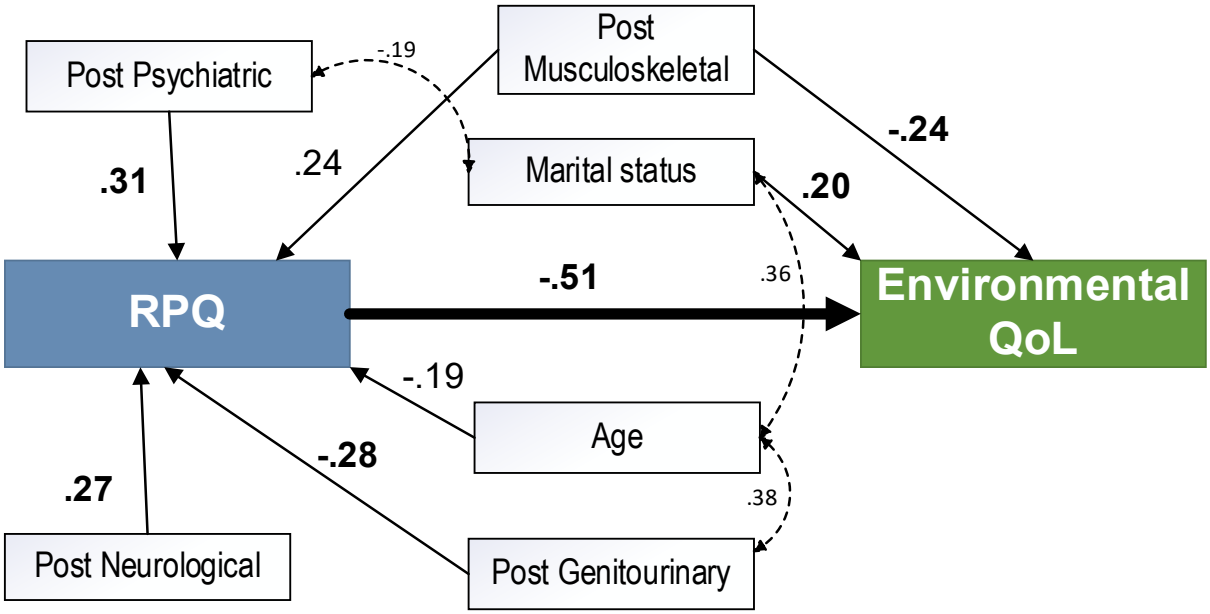
CFI=.983; RMSEA=.052, CI 0–.137; χ^2 /df =1.29, df=7, *p*=.250

Figure 31. Role of post-injury comorbidities influencing the psychological domain of the WHOQoL-BREF in the TBI sample (*n*=108)



CFI=.909; RMSEA=.064, CI 0–103; χ^2 /df =1.44, *p*=.053

Figure 32. Role of post-injury comorbidities influencing the social domain of the WHOQoL-BREF in the TBI sample (*n*=108)



CFI=.903; RMSEA=.092, CI .041–139; χ^2 /df =1.90, *p*=.014

Figure 33. Role of post-injury comorbidities influencing the environmental domain of the WHOQoL-BREF in the TBI sample (*n*=108)

Table 31. Model fit statistics, and standardised beta coefficients for direct, indirect, total effects of relationships modelled for PCS symptoms, and the physical, psychological, social and environmental QoL domains of the WHOQoL-BREF for the TBI sample (*n*=108)

Physical Domain	Post Neuro	Marital status	Age	Post Musc	RPQ
	ß	ß	ß	ß	ß
Direct effects					
RPQ	.305	0	-.301	.230	0
WHOQoL	0	.223	-.264	-.399	-.488
Indirect effects					
RPQ	0	0	0	0	0
WHOQoL	-.149	0	.147	-.112	0
Total effects					
RPQ	.305	0	-.301	.230	0
WHOQoL	-.149	.223	-.117	-.511	-.488
Model fit: CFI=.987; RMSEA=.046, CI 0–133; χ^2=8.619, df=7, *p*=.281					
Psychological Domain	Post Neuro	Marital status	Post Psych	Age	RPQ
	ß	ß	ß	ß	ß
Direct effects					
RPQ	.293	0	.326	-.256	0
WHOQoL	-.176	.186	-.247	0	-.452
Indirect effects					
RPQ	0	0	0	0	0
WHOQoL	-.133	0	-.147	.116	0
Total effects					
RPQ	.293	0	.326	-.256	0
WHOQoL	-.308	.186	-.394	.116	-.452
Model fit: CFI=.983; RMSEA=.052, CI 0–137; χ^2=9.037, df=7, *p*=.250					

Social Domain	Post Neuro	Post Psych	Educ	Post Endo	Post Musc	Post GU	Marital status	Age	RPQ
	ß	ß	ß	ß	ß	ß	ß	ß	ß
Direct effects									
RPQ	.271	.305	0	0	.243	-.280	0	-.188	0
WHOQoL	0	0	.217	.232	0	-.238	.345	-.263	-.399
Indirect effects									
RPQ	0	0	0	0	0	0	0	0	0
WHOQoL	-.108	-.122	0	0	-.097	.111	0	.075	0
Total effects									
RPQ	.271	.305	0	0	.243	-.280	0	-.188	0
WHOQoL	-.108	-.122	.217	.232	-.097	-.127	.345	-.188	-.399
Model fit: CFI=.909; RMSEA=.064, CI 0–103; χ^2 =44.662, df=31, *p*=.053									

Environmental Domain	Post Musc	Post GU	Post Neuro	Post Psych	Marital status	Age	RPQ
	ß	ß	ß	ß	ß	ß	ß
Direct effects							
RPQ	.243	-.280	.271	.305	0	-.187	0
WHOQoL	-.240	0	0	0	.201	0	-.514
Indirect effects							
RPQ	0	0	0	0	0	0	0
WHOQoL	-.125	.144	-.139	-.157	0	.096	0
Total effects							
RPQ	.243	-.280	.271	.305	0	-.187	0
WHOQoL	-.365	.144	-.139	-.157	.201	.096	-.514
Model fit: CFI=.903; RMSEA=.092, CI .041–139; χ^2 =32.279, df=17, *p*=.014							

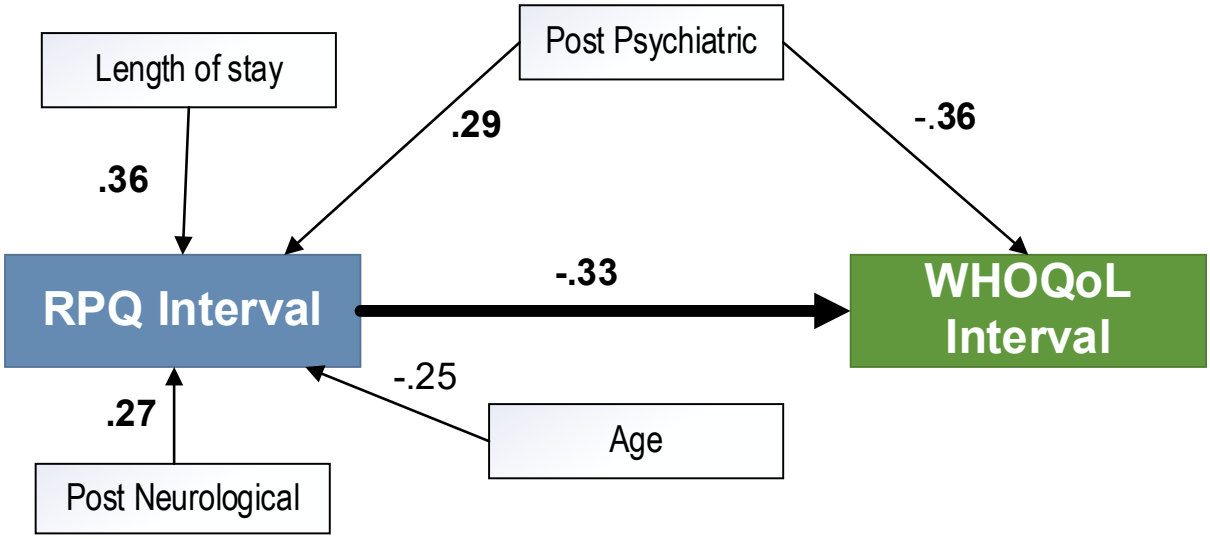
neuro=neurological; psych=psychiatric; endo=endocrine; musc=musculoskeletal; GU=genitourinary; education: primary/secondary vs. polytechnic/university; marital status: single vs. living as married; educ=education level: primary/high school vs. polytechnic/university; interv=interval scores; ord= ordinal scores

Modelling PCS symptoms and quality of life in the orthopaedic sample

Similar to the TBI group, SEM analyses were conducted to explore the role of post-injury comorbidities in the orthopaedic sample in predicting log10 transformed comorbidity scores and Rasch-transformed interval-level outcome measures for the RPQ (postconcussion symptoms) and WHOQoL-BREF (QoL) in Figure 34. Comparisons were also made to ordinal-level measures (Figure 35) with effect sizes for both provided in Table 32. Additional path models demonstrate the relationships for the interval-level RPQ and different domains of the WHOQoL-BREF, namely for the physical (Figure 36), psychological (Figure 37), social (Figure 38), and environmental aspects related to quality of life (Figure 39), with effect estimates detailed in Table 33.

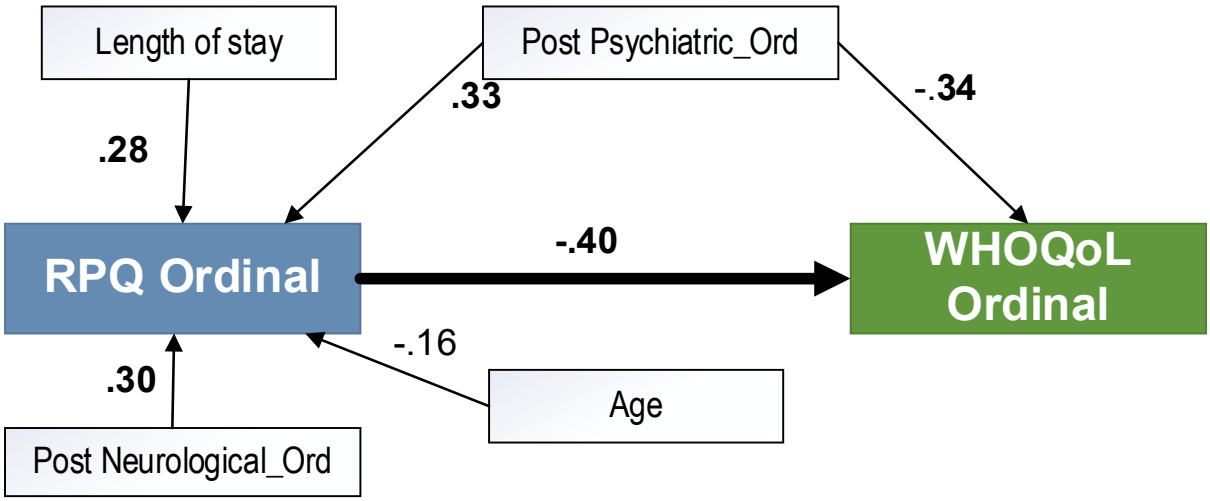
In general, all models illustrated a simplified model of outcome with close to excellent fit statistics (minimum CFI=.885, maximum RMSEA=.095). Among baseline factors, only age correlated with PCS as a negative gradient across all models (ß=-.242 to -286). Younger age was also positively associated with higher quality of life scores in the social domain, ß=-.205 (Figure 38), while in the environmental domain these participants were likely to score lower than older participants, ß=.267 (Figure 39). Marital status also appeared to have direct associations with quality of life, but only in the social domain (ß=.192). In addition, increased length of hospitalisation as a result of injuries directly affected PCS symptoms across all domains, which also indirectly affected quality of life scores, with ß coefficients ranging from .345 to .358.

Across models, the experience of psychiatric and neurological difficulties by orthopaedic participants appear as consistent predictors of PCS symptoms and quality of life, which are evident even at the domain-level. In the general model using interval-measures (Figure 34), it can be seen that there are moderate direct effects between PCS symptoms and overall quality of life (β=-.334). Post-injury neurological problems directly affected PCS symptoms (β=.271), while the experience of psychiatric difficulties also appeared to exacerbate symptoms (β=.294), and negatively impacted on overall quality of life (β=-.362). Psychiatric difficulties exerted moderately strong total effects on quality of life (β=-.460), followed by PCS symptoms (β=-.334) as shown in Table 32.



CFI=.986; RMSEA=.038, CI .000 –116; χ^2 /df =1.16, *p*=.315

Figure 34. Role of post-injury comorbidities influencing PCS symptoms and quality of life in the orthopaedic injury sample (*n*=114), using log10 transformed comorbidity scores and Rasch-transformed interval outcomes



CFI=.986; RMSEA=.037, CI 0–116; χ^2 /df =1.16, *p*=.319

Figure 35. Role of post-injury comorbidities influencing PCS symptoms and quality of life in the orthopaedic injury sample (*n*=114), using ordinal comorbidity and outcome measures

Table 32. Model fit statistics, effect sizes with standardised coefficients for modelling PCS symptoms and quality of life in the orthopaedic sample (*n*=114), with comparisons between interval (top half) and ordinal-level (bottom half) outcome measures

Log10 transformed comorbidity scores and Rasch-transformed interval measures of RPQ and WHOQoL-BREF total score					
	Post Neuro	Age	LOS	Post Psych	RPQ Interv
	ß	ß	ß	ß	ß
Direct effects					
RPQ Interv	.271	-.247	.358	.294	0
WHOQoL Interv	0	0	0	-.362	-.334
Indirect effects					
RPQ Interv	0	0	0	0	0
WHOQoL Interv	-.090	.082	-.120	-.098	0
Total effects					
RPQ Interv	.271	-.247	.358	.294	0
WHOQoL Interv	-.090	.082	-.120	-.460	-.334
Model fit: CFI=.986; RMSEA=.038, CI 0–116; χ^2 =10.452, df=9, *p*=.315					
Ordinal-level comorbidity scores and ordinal RPQ and WHOQoL-BREF total scores					
	Post Neuro Ord	Age	LOS	Post Psych Ord	RPQ Ord
	ß	ß	ß	ß	ß
Direct effects					
RPQ Ord	.298	-.163	.277	.327	0
WHOQoL Ord	0	0	0	-.339	-.401
Indirect effects					
RPQOrd	0	0	0	0	0
WHOQoL Ord	-.120	.065	-.111	-.131	0
Total effects					
RPQ Ord	.298	-.163	.277	.327	0
WHOQoL Ord	-.120	.065	-.111	-.471	-.401
Model fit: CFI=.986; RMSEA=.037, CI 0–116; χ^2 =10.397, df=9, *p*=.319					

neuro=neurological; psych=psychiatric; LOS=length of hospital stay; interv=interval scores; ord=ordinal scores

When ordinal-level measures are used in place of interval measures as in Figure 35, some coefficients decreased in strength (Table 32). This was seen between psychiatric conditions and total quality of life, (decrease from β=-.362 to -.339), and most notably between length of hospitalisation and PCS symptoms (β=.358 to .277), and between age and symptoms (β=-.247 to -.163). P-values did not change, except for the relationship between age and PCS symptoms, where the significance reduced from p=.001 at the interval-level to p=.038 at the ordinal-level. In comparison, the strength of association between PCS symptoms and quality of life increased when using ordinal measures (from β=-.334 to -.401). Similarly, the correlation between neurological conditions and PCS symptoms increased marginally from β=.271 to .298, when using ordinal scales in place of interval scales. Overall, both models using interval-level and ordinal-level data presented with almost identical fit statistics, indicating strong fit of the data to the models.

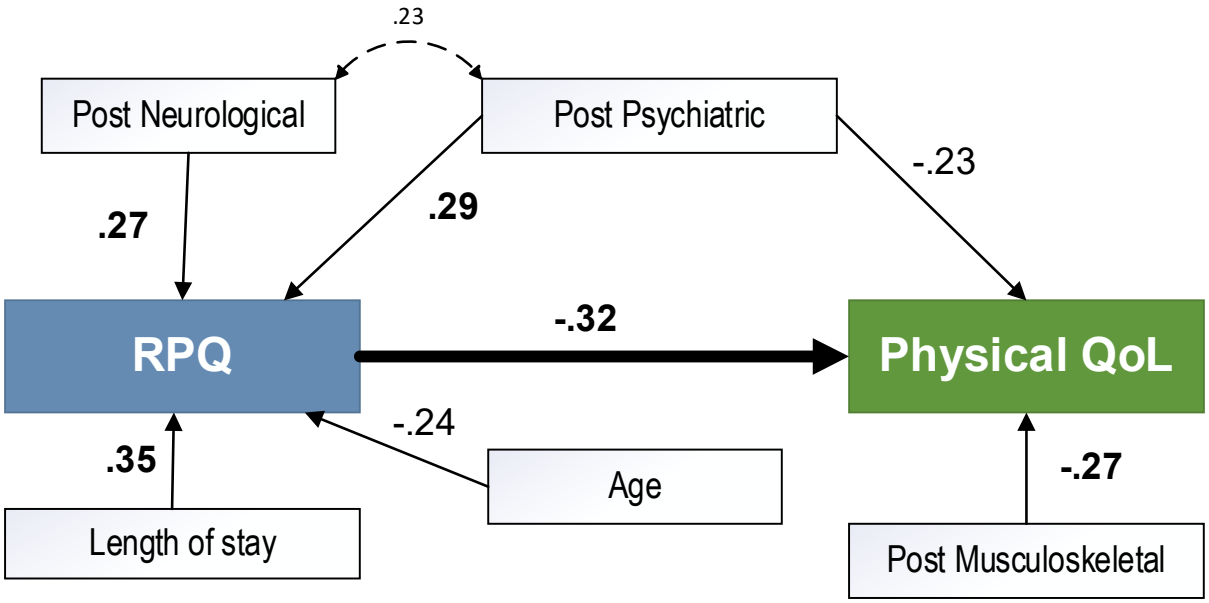
When the physical domain is specifically examined (Figure 36), post-injury experience of psychiatric difficulties exerted moderate effects on PCS symptoms and physical QoL, with total effects of β=.289 and β=-.324, respectively (Table 33). In the same model, neurological complications only demonstrated a small effect on symptoms directly (β=.266), while musculoskeletal conditions only directly influenced physical quality of life (β=-.273).

Similar to the physical domain, scores on the psychological component of the WHOQoL-BREF was predicted strongly by the presence of post-injury psychiatric difficulties (total effects β=-.411), which also directly predicted the presence of PCS symptoms among orthopaedic participants, β=.289 (Figure 37, and Table 33). The presence of post-injury neurological problems had a small direct effect on the persistence of PCS symptoms (β=.266), but did not predict quality of life scores on the psychological domain. The direct relationship between PCS symptoms and psychological quality of life was small, but remained statistically significant (β=-.257, p=.003).

Within the social domain in Figure 38, neurological (β=.271), and psychiatric difficulties (β=.294) had similar direct effects on postconcussion symptoms, whereas the impact of total effects of psychiatric difficulties on social quality of life was moderately high, β=-.369 (Table 33). Post-injury genitourinary problems reported by participants also appeared to directly affect scores on the social domain, but only to a

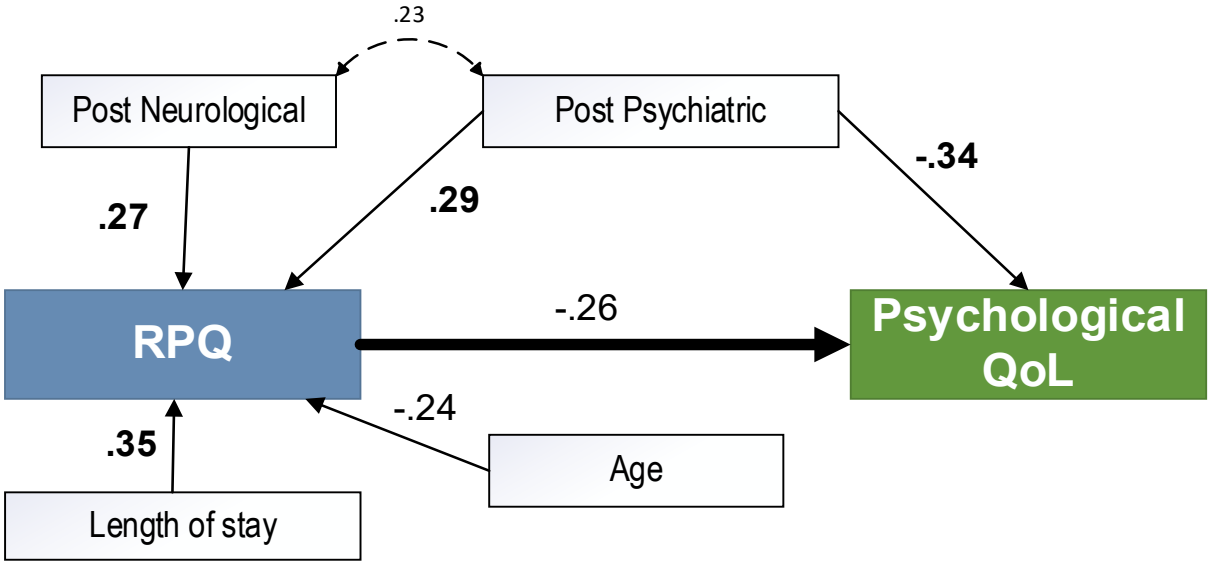
small extent (β=-.194). The relationship between PCS symptoms and social QoL although significant at $p<.05$, was relatively small (β=-201).

Lastly, in the environmental domain model, post-injury neurological complications were found to be negatively linked with the onset of PCS symptoms (β=.229), followed by psychiatric disturbances (total effects of β=.283), as depicted in Figure 39, and Table 33. Psychiatric difficulties also had a moderate effect on scores for the environmental domain, with total effects of β=-.385. Similar to the analysis in the TBI sample in Figure 33, and informed by the preliminary regression analyses, post-injury respiratory conditions were entered into the environmental model for the orthopaedic sample. Unlike for the TBI group, post-injury respiratory problems in the orthopaedic group appeared to demonstrate small but significant total effects on both PCS symptoms (β=.161), and environmental QoL (β=-.200). Similar to the social domain analysis above, the relationship between postconcussion symptoms and environmental QoL was shown to be statistically significant, albeit small (β=-.200).



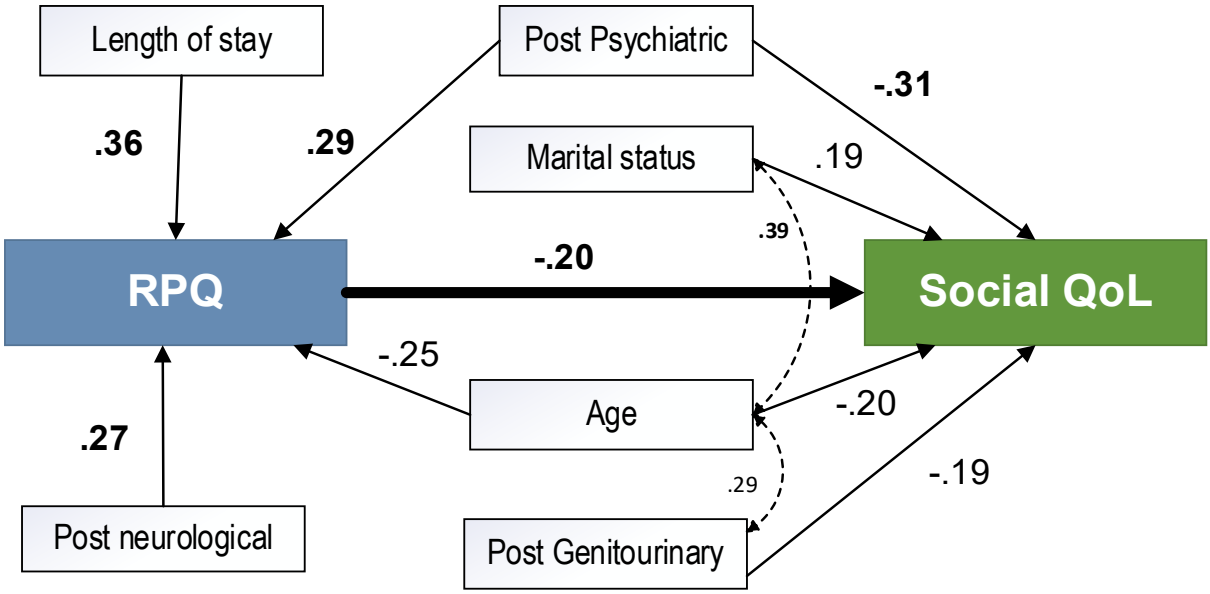
CFI=.885; RMSEA=.095, CI .040–.148; χ^2 /df =2.02, *p*=.015

Figure 36. Role of post-injury comorbidities influencing the physical domain of the WHOQoL-BREF in the orthopaedic sample (*n*=114)



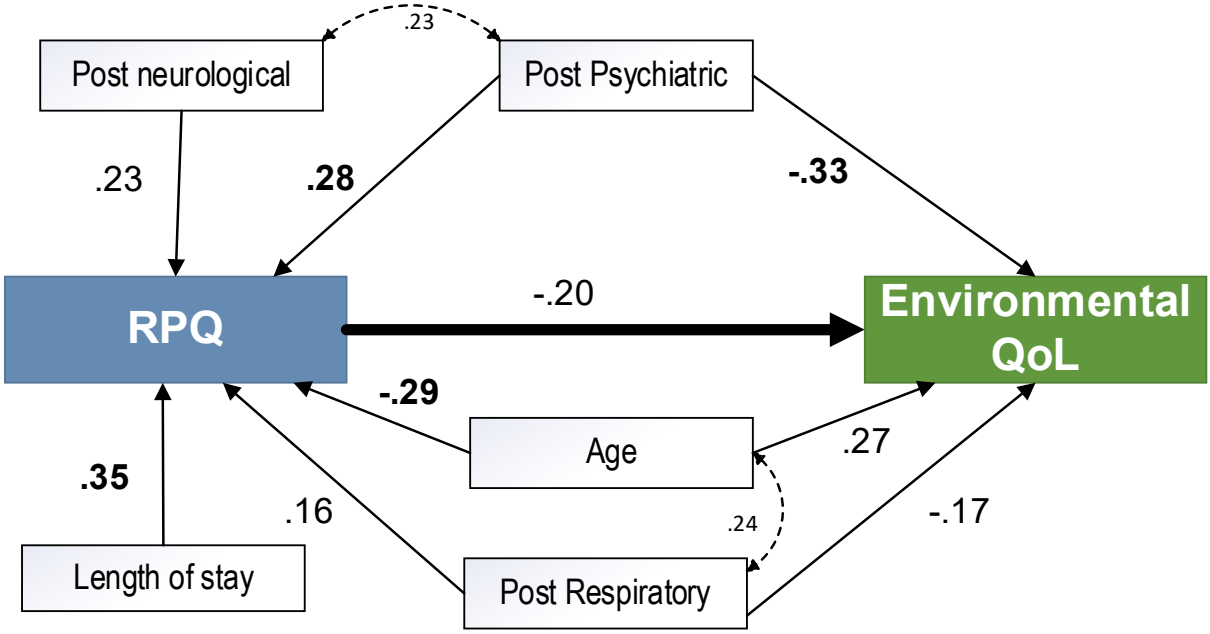
CFI=1.000; RMSEA=.000, CI 0–.084; χ^2 /df =0.68, *p*=.709

Figure 37. Role of post-injury comorbidities influencing the psychological domain of the WHOQoL-BREF in the orthopaedic sample (*n*=114)



CFI=.942; RMSEA=.062, CI=0–.113; χ^2 /df =1.43, *p*=.110

Figure 38. Role of post-injury comorbidities influencing the social domain of the WHOQoL-BREF in the orthopaedic sample (*n*=114)



CFI=.944; RMSEA=.076, CI 0–139; χ^2 /df =1.66, *p*=.084

Figure 39. Role of post-injury comorbidities influencing the environmental domain of the WHOQoL-BREF in the orthopaedic sample (*n*=114)

Table 33. Model fit statistics, and standardised beta coefficients for direct, indirect, total effects of relationships modelled for PCS symptoms, and the physical, psychological, social and environmental QoL domains of the WHOQoL-BREF for the orthopaedic sample (*n*=114)

Physical Domain	LOS	Post Musc	Post Neuro	Age	Post Psych	RPQ
	ß	ß	ß	ß	ß	ß
Direct effects						
RPQ	.352	0	.266	-.242	.289	0
WHOQoL	0	-.273	0	0	-.229	-.324
Indirect effects						
RPQ	0	0	0	0	0	0
WHOQoL	-.114	0	-.086	.079	-.094	0
Total effects						
RPQ	.352	0	.266	-.242	.289	0
WHOQoL	-.114	-.273	-.086	.079	-.323	-.324
Model fit: CFI=.885; RMSEA=.095, CI .040–.148; χ^2 =26.310, df=13, *p*=.015						

Psychological Domain	Post Psych	Post Neuro	Age	LOS	RPQ
	ß	ß	ß	ß	ß
Direct effects					
RPQ	.289	.266	-.242	.352	0
WHOQoL	-.337	0	0	0	-.257
Indirect effects					
RPQ	0	0	0	0	0
WHOQoL	-.074	-.068	.062	-.090	0
Total effects					
RPQ	.289	.266	-.242	.352	0
WHOQoL	-.411	-.068	.062	-.090	-.257
Model fit: CFI=1.000; RMSEA=.000, CI 0–.084; χ^2 =5.448, df=8, *p*=.709					

Social Domain	Post GU	Post Neuro	Marital status	Age	Post Psych	LOS	RPQ
	ß	ß	ß	ß	ß	ß	ß
Direct effects							
RPQ	0	.271	0	-.246	.294	.358	0
WHOQoL	-.194	0	.192	-.205	-.310	0	-.201
Indirect effects							
RPQ	0	0	0	0	0	0	0
WHOQoL	0	-.054	0	.049	-.059	-.072	0
Total effects							
RPQ	0	.271	0	-.246	.294	.358	0
WHOQoL	-.194	-.054	.192	-.156	-.369	-.072	-.201
Model fit: CFI=.942; RMSEA=.062, CI 0–113; χ^2=24.374, df=17, *p*=.110							

Environmental Domain	Post Resp	Post Psych	Age	Post Neuro	LOS	RPQ
	ß	ß	ß	ß	ß	ß
Direct effects						
RPQ	.161	.283	-.286	.229	.345	0
WHOQoL	-.168	-.328	.267	0	0	-.200
Indirect effects						
RPQ	0	0	0	0	0	0
WHOQoL	-.032	-.057	.057	-.046	-.069	0
Total effects						
RPQ	.161	.283	-.286	.229	.345	0
WHOQoL	-.200	-.385	.324	-.046	-.069	-.200
Model fit: CFI=.944; RMSEA=.076, CI 0–139; χ^2=16.585, df=10, *p*=.084						

GU=genitourinary; neuro=neurological; musc=musculoskeletal; resp=respiratory; psych=psychiatric; LOS=length of hospital stay; marital status: single vs. living as married; interv=interval scores; ord= ordinal scores

Section summary

The aim of the SEM analyses was to highlight post-injury comorbidities affecting PCS symptoms and quality of life distinctly among TBI (*n*=108) and orthopaedic participants (*n*=114). In general, there were consistent patterns emerging from all models across both TBI and orthopaedic samples. Among TBI participants in this study, aside from age and marital status, post-injury conditions such as neurological, psychiatric, musculoskeletal, and genitourinary problems, exhibited direct and indirect influences on postconcussion symptoms and quality of life overall, as well as across specific QoL domains. The relationship between PCS symptoms and QoL was particularly strong in this group.

In the orthopaedic sample, patterns were relatively similar across domains, with age, marital status, and length of hospitalisation after the injury consistently predicting outcomes. In terms of post-injury comorbidities, neurological conditions directly impacted on postconcussive symptoms, while psychiatric difficulties were shown to be common significant predictors of both PCS symptoms and QoL. In addition, the models revealed that musculoskeletal conditions affected physical QoL, and genitourinary conditions affected social QoL, whereas respiratory conditions were shown to have some effects on environmental QoL. Compared with the TBI sample, the relationship between PCS symptoms and QoL in the orthopaedic group was small, but remained statistically significant. Supplementary analyses in both samples also compared the use of log10 transformed comorbidity (CIRS) scores and interval-level measures of the RPQ and WHOQoL-BREF, with their equivalent ordinal level measures, and their effects on regression coefficients. Comparisons revealed marginal but inconsistent differences in effect estimates, where some relationships were enhanced as a result of using log10 or Rasch-transformed scores in place of ordinal measures, while other relationships experienced a reduction in strength.

The results from the previous multiple linear regression analyses that highlighted the impact of pre-injury comorbidities on PCS symptoms and quality of life, will be discussed in the next part of the chapter. Following this, the results from the SEM analyses modelling post-injury comorbidities on outcomes will also be discussed in relation to findings from current literature.

8.4 Discussion

What are the long-term predictors of postconcussive symptoms in injury populations?

Findings from the stepwise multiple linear regression model for the combined sample comprising of both TBI and orthopaedic injuries revealed that, younger age, experience of TBI, and longer stay at hospital, were all predictive of persistent symptoms of PCS (i.e. higher RPQ scores) at approximately 2.50 years post-injury. Prior comorbidity was a significant predictor of PCS, although in the analyses post-injury comorbidity explained more variance in PCS symptoms. This confirmed the findings of an early study by Bohnen et al. (1994), who found that total comorbidity remained a significant predictor of persistent postconcussion symptoms 1 to 5 years after mild TBI, compared with trauma controls. When individual comorbidity categories are investigated, results suggest that PCS symptoms within the general injury sample comprising both TBI and

orthopaedic participants, are affected by prior neurological, EENT, lower gastrointestinal, and musculoskeletal conditions. PCS symptoms in the long-term were also found to be influenced by the occurrence of psychiatric, EENT and neurological conditions following injuries. Below, the unique factors specific for the TBI and orthopaedic groups are discussed in further detail.

Predictors of postconcussion symptoms among TBI participants

The main findings from the multivariate linear regression analyses were that, among TBI participants, younger age, higher-level education, and increased hospitalisation collectively explained 15% of variance in residual symptoms of PCS following TBI. Within the literature, certain demographic factors have been noted to determine the persistence of PCS symptoms among TBI patients, that typically include those who are of older age (above 40 years), female, have lower socioeconomic status, or low education level, and lack of social support (Iverson et al., 2017; King, 2014a, 2014b; Polinder et al., 2018; Stålnacke, 2007; Tator et al., 2016). Others have also found that stronger illness beliefs such as symptom endorsement attributed to the injury, emotional reactions to the injury, and the expectation of symptoms may play a contributing factor to the perception of symptom experience (Snell et al., 2011).

Contrary to these findings, the current TBI sample however, indicated that younger participants were more likely to report residual PCS symptoms. Previous reviews of the literature have found some, but not definitive support for a gradient in age and lingering of symptoms, although Iverson et al. (2017) assert that teenagers and high school years represent the greatest age of period of vulnerability for slow recovery. Although history of TBI was not asked among respondents in this sample, the finding that younger participants were more likely to report persistent symptoms may be partly explained by the higher likelihood of this group also experiencing multiple past TBIs, particularly sport-related concussions, as confirmed by various researchers (Barker et al., 2017; Covassin et al., 2008; Iverson et al., 2012; Tator et al., 2016). While others have highlighted the cumulative effects of multiple TBIs on delayed symptom resolution (Edna & Cappelen, 1987; Polinder et al., 2018; Ponsford et al., 2008; Theadom et al., 2016), the collective evidence for this relationships remains inconclusive, with some recent meta-analyses reporting a lack of significant evidence on the detrimental effects of past multiple mild TBIs, especially on cognitive and neuropsychological functioning (Belanger et al., 2010; Yumul & McKinlay, 2016).

There is variable evidence suggesting also that females and those who are unemployed are more likely to report a higher rate of symptoms (Bazarian et al., 2010; Silverberg et al., 2015; Wall, 2012). The current study however, found a lack of significance for these characteristics as explanatory factors of PCS symptoms, which is in line with studies by Tator et al. (2016), Jacobs et al. (2010), Theadom et al. (2018) and Thornhill et al. (2000). Interestingly, injury severity factors provided no prognostic value in long-term symptoms in the TBI group in this study, and a review of the literature by Polinder et al. (2018) collectively indicated the presence of a weak relationship between injury severity and PCS symptoms, particularly among longitudinal studies. Factor analysis and more recently emerging modern techniques such as Generalisability theory have pointed to the presence of acute symptoms in the first three months, and a relative stability in symptoms after 6–12 months, which may offer some explanation for this weak relationship (Barker-Collo et al., 2018; Medvedev, Theadom, et al., 2018).

Whilst previous studies have largely looked at the classic factors such as demographic and injury characteristics, the present study has gone beyond this general understanding and investigated the role of comorbidities, and specifically explored which comorbidities have the strongest influence on long-term residual symptoms. In the TBI sample, higher RPQ scores were also explained by pre-existing neurological and EENT problems, with most common complaints around migraines, headaches, and a smaller proportion with minor hearing impairment. These results are in line with evidence from a handful of studies that have found that prior history of migraines and headaches can contribute to ongoing PCS symptoms (Meehan et al., 2014; Mickevičiene et al., 2004; Register-Mihalik et al., 2018). However, after assessing the evidence in a systematic review, Iverson et al. (2017) argued against there being a consistent relationship between neurological history and postconcussive symptoms. It is important to note that a quarter of PCS symptoms such as headaches, dizziness, memory and concentration difficulties have neurologic aetiology, and therefore may be confounding this observed association with postconcussive symptoms. Within the literature, there is a stronger base of evidence supporting psychiatric history and persistent symptoms, than for any other comorbidity that has been previously investigated (King & Kirwilliam, 2011; Meares et al., 2011; Polinder et al., 2018; Silverberg et al., 2015). In the present study, pre-existing mental health was not deemed as important as post-injury psychological factors, which was also confirmed by Tator et al, (2016). The lack of significance for pre-injury mental health issues, however, may have been affected by recall bias in the

study—at the time of assessment participants were asked to subjectively recall if they had experienced any psychiatric problems prior to their injuries, that elapsed from anywhere between 1 to 5 years prior to their TBI.

Whilst there is an abundance of evidence linking psychiatric disorders to postconcussion symptoms, there remains to date a lack of knowledge on other conditions that may be important to consider. This study highlights that in addition to psychiatric difficulties, other post-injury difficulties related to the neurological, genitourinary and musculoskeletal systems play an important role in the presentation of long-term symptoms. Findings from this study also suggest that the persistence of PCS symptoms can mirror difficulties associated with other health conditions, that may not necessarily be relating to the experience of a brain injury. There is a growing body of literature supporting these assumptions. In an analysis of TBI and non-TBI trauma controls, Meares et al. (2011) confirmed that, whilst mild TBI did not predict PCS symptoms, pre-injury depressive and anxiety disorders were early markers of these symptoms regardless of whether TBI had occurred or not. Studies by Mickeviciĕnce et al. (2004), Snell et al. (2018), and Dikmen et al. (2010), give corroborating evidence for the occurrence of symptoms among non-TBI participants, in which Mickeviciĕnce's study found that after one year post-injury the vast majority of symptoms between the TBI and minor injury patients did not differ significantly. An unexpected result in the present study was the negative correlation between genitourinary conditions and PCS symptoms, that seems to suggest that a participant with genitourinary difficulties is likely to report lower PCS symptoms. Similarly, the relationship between prior EENT problems (e.g. visual disturbances, noise sensitivity) and lower PCS symptoms after injuries, is an unexpected finding given the overlap of symptoms. As there is no evidence to corroborate these findings, replication of this study is needed to determine if these relationships arise in other studies or are simply an anomalous result in the current analysis due to the small sample size and/or a large number of statistical tests.

The overall model in the TBI sample explained only 40% of variance in RPQ scores, which is similar to models reported by other studies (Tator et al., 2016; Theadom et al., 2018). However, this also means that approximately 60% of variance in PCS symptoms among individuals is unexplained in current predictive models, and points to the existence of other important variables that merit further investigation.

Predictors of PCS among orthopaedic participants

Research to date has only begun to compare the prevalence of postconcussion-like symptoms beyond TBI samples such as in the general population (Theadom et al., 2018), chronic pain patients (Smith-Seemiller et al., 2003; Snell et al., 2018), depressed versus non-depressed groups (Chan, 2001), and minor injury groups (Dikmen et al., 2010; Iverson et al., 2017). The current study's findings also add to the growing body of literature on PCS symptoms and confirm the existence of symptoms in orthopaedic patients, that persist even after 2.50 years following injuries. These findings are in line with some authors' observations that having a TBI is not a requisite for the development of symptoms (Dean et al., 2012; Lagarde et al., 2014; Meares et al., 2011). Unlike past studies, which have merely looked at rates of PCS symptoms, the present study extends the investigation by exploring the different factors, including comorbidity factors, that may contribute to the presentation of symptoms in the non-TBI population.

Similar to the TBI sample discussed earlier, younger age, and longer hospital stay, predicted higher PCS symptoms among orthopaedic participants in this study. Among 14 categories of pre-existing health conditions, lower gastrointestinal (e.g. past hernia operation, appendectomy) and musculoskeletal conditions (e.g. general mild discomfort related or unrelated to injuries), collectively predicted a small proportion of RPQ score variance (approximately 14% variance in the model). As with TBI participants, post-injury psychiatric (anxiety/depression), and neurological disturbances (e.g. tingling/numbness, migraines, post-injury concussions) also contributed to higher PCS symptoms following orthopaedic injuries, together explaining just under 10% of variance. These findings highlight that both TBI and orthopaedic participants share similar experiences of psychological and neurological disturbances after injuries. In fact, Lagarde et al. (2014) found that at one week and three months post-injury, there were no significant differences in the rates of posttraumatic stress disorder, anxiety, depression, and pain between TBI and mild injury patients. Others have shown that even after two years, orthopaedic injury patients continue to report psychological distress, posttraumatic stress disorder, anxiety, and depression (Bhandari et al., 2008; Ponsford et al., 2008; Starr et al., 2004).

Neurological deficits such as tingling and numbness are a common occurrence of orthopaedic injuries, as noted by Balogh et al. (2012) and Robinson (2000), and are likely to exacerbate specific postconcussive symptoms related to fatigue and sleep difficulties. Interestingly, the experience of post-injury musculoskeletal problems was

deemed not a determining factor of PCS among orthopaedic participants in the current study, while it was for the TBI group, which may suggest that musculoskeletal problems in the orthopaedic group may have resolved at the time of interview. In contrast, in the TBI group, post-injury musculoskeletal problems had a greater impact on associated PCS symptoms. However, it is unknown whether these musculoskeletal problems are injury-related sequelae or if they developed independently as a result of other causes. Further complicating the picture is the finding that similar to the TBI group, overall injury severity was a not predictive factor of PCS symptoms in the orthopaedic sample. It may be, as Meares et al. (2011) suggest, that injury severity may only be relevant to symptoms in the early stages of recovery, and becomes less meaningful as a prognostic factor as symptoms resolve over time. As noted earlier with the TBI group, the finding of prior gastrointestinal issues (e.g. hernia operations) as a predictor of PCS symptoms also in the orthopaedic sample remains unclear, and is an association that needs to be explored further in future studies.

The findings above are a novel contribution to the current burgeoning knowledge of postconcussion symptoms, which has only recently begun to acknowledge the presence of similar symptoms in non-TBI populations (Chan, 2001; Iverson & Lange, 2011; Smith-Seemiller et al., 2003). Furthermore, there is ongoing debate as to the underlying mechanisms and non-specificity of PCS symptoms, where some have argued that these symptoms elicit hyperarousal activity, which shares a similar aetiology in posttraumatic stress associated with the injury experience (Lagarde et al., 2014; Rees, 2003). Therefore, it is unsurprising that individuals with depression, as well as chronic pain patients also report high rates of PCS (Iverson, 2006; Smith-Seemiller et al., 2003; Snell et al., 2018). The differences observed by Smith-Seemiller et al. (2003) among mild TBI patients is that this group is more likely to endorse cognitive symptoms of memory and light/noise sensitivity than pain patients. Some have also asserted that the pursuit of financial compensation regarding insurance claims on ongoing medical costs may exacerbate stress levels and consequently lead to an increased level of symptom reporting after mild TBI (Paniak et al., 2002). The picture is further muddied by the finding that there is a base rate of postconcussion symptoms even in the healthy population as has been documented by several studies (Chan, 2001; Iverson & Lange, 2003; Theadom et al., 2018). Theadom et al. (2018) in fact found no significant differences in overall PCS symptoms, especially in the emotional and somatic symptom clusters between mild TBI patients at four years post-injury, and the healthy population.

The only difference between these two groups was observed for the cognitive symptom cluster, which was more likely to be endorsed by the TBI group. In a recent study, the authors also explored the factor structure of the RPQ and found no significant differences in symptom clusters between mild TBI at four years post-injury and healthy controls (Barker-Collo et al., 2019). The healthy controls also appeared to endorse 'acute TBI symptoms', comprising of headaches, nausea/vomiting, dizziness and slowed thinking, which were compared to flu-like or hangover symptoms. A similar exploratory factor analysis to compare clusters of symptoms between TBI and orthopaedic groups in the current study, would have shed some important observations into the current findings, but due to the small sample size is beyond the scope of this study.

Section summary

No studies to date have attempted to identify the different predictors of PCS symptoms between TBI and non-TBI populations. Results from this study show that TBI participants with previous neurological disturbances and orthopaedic participants with previous musculoskeletal problems were more likely to report prolonged PCS symptoms after injuries. The results also indicated that TBI and orthopaedic participants share common post-injury ailments such as psychiatric and neurological difficulties that may lengthen symptom duration. These findings confirm previously tested hypotheses that firstly, TBI is not a requisite for the occurrence of PCS and secondly, that symptoms may actually be indicative of symptoms related to posttraumatic stress related to injuries (Lagarde et al., 2014; Meares et al., 2011). The current study serves as an exploratory foundation in identifying predictors of long-term postconcussion symptoms in different injury groups, but further research employing larger samples sizes is needed to substantiate the preliminary evidence gathered in this study.

Identifying predictors of long-term quality of life after injuries

The main findings from the multivariate linear regression analyses indicated that only a small portion of variance in WHOQoL-BREF scores was predicted by demographic characteristics, where a person's marital status, especially cohabitation or being married was noted to be the only significant demographic predictor of higher quality of life overall. In the TBI group, for example, marital status was important for the psychological QoL, whereas among orthopaedic participants, marital status only affected scores on the social domain. Being married or being in a relationship offers important psychosocial support, and has been linked to better mental health and

adjustment after injuries (Gopinath et al., 2017; Steadman-Pare et al., 2001). Additionally, older orthopaedic participants in this sample were more likely to perceive their environmental quality of life more favourably than their younger counterparts; a finding that was also supported by Feder et al. (2015). The underlying association suggested by the authors linked environmental satisfaction to accessibility of good housing conditions, and time availability for leisure activities in older aged participants.

In line with a few other studies, injury characteristics for the predominantly mild injury participants ceased to be of any importance as determinants of long term quality of life (Nestvold & Stavem, 2009; Ponsford et al., 2008). Other studies have highlighted that injury severity becomes an important factor for major or multiply-injured trauma patients particularly as a predictor of long-term disability (Airey et al., 2001; Holtslag et al., 2007). Studies by Hetherington et al. (1995) and Polinder et al. (2007), noted that increased length of hospitalisation among severe injury or major trauma patients were also predictive of poor quality of life. In the current study, this association remained even among relatively minor TBI and orthopaedic injury patients, where increased length of hospital stay was likely to predict lower QoL on average 2.50 years after injury. Furthermore, length of hospitalisation predicted to a small extent variance in the social and environmental domain scores within the TBI group, and physical domain scores in the orthopaedic group.

Premorbid history of health conditions and post-injury comorbidities (after controlling for prior history) were both seen to have adverse effects on overall quality of life among injury patients studied in this sample. Although a handful of studies have acknowledged a dose-response relationship existing between comorbidities and quality of life in injury studies (Haagsma et al., 2011; Polinder et al., 2007; Van Son et al., 2017), none to date have explored the role of specific comorbidities at the pre-injury and post-injury stages and their potential impact on long-term quality of life after injury. The present study analysed the impact of specific comorbidities on long-term quality of life with comparisons between TBI and orthopaedic groups. These results are discussed next in the following sub-sections.

Predictors of long-term quality of life after TBI

Different patterns emerged between TBI and orthopaedic groups, placing emphasis on different health conditions affecting quality of life after injury. In the TBI sample, prior neurological problems such as headaches or migraines, appeared as a consistent

predictor of overall QoL, as well as for each of the physical, psychological, social and environmental dimensions related to quality of life. In the general population, it has been shown that prior history of migraines and vertigo disorders is associated with reduced quality of life (HRQoL), among both adults and children (Deissler et al., 2017; Vladetić et al., 2017). As addressed earlier in the discussion, individuals with prior history of migraines or headaches tend to report more PCS symptoms (Meehan et al., 2014; Mickevičiene et al., 2004; Register-Mihalik et al., 2018), but there is a paucity in the literature regarding the extent to which prior neurological disturbances impact on quality of life after TBI. Testing for interaction effects between migraine/headache history and PCS symptoms, also yielded no significant results on QoL scores for the TBI group. Nevertheless, the present study does highlight that prior and post-injury neurological problems remain relevant risk factors of poor long-term quality of life after TBI.

In this sample, prior psychiatric difficulties such as anxiety and depression only predicted scores on the psychological domain, and are similar to findings by Lin et al. (2010). Nestvold and Stavem (2009) found that a history of headaches (i.e. headaches >1 day per month), and psychiatric problems, were also predictors of mental health aspects of HRQoL in the first few months after TBI, while Davis et al. (2012) noted that pre-injury psychiatric problems and substance abuse disorders predict lower satisfaction with life in the first 12 months after TBI.

In the current study, it was shown that past history, and not persistent respiratory problems (e.g. most commonly asthma problems), predicted scores on environmental QoL for the TBI group. As many of the participants in the respiratory category self-reported only experiencing mild asthma previously, it may suggest that for many respondents, this condition was perhaps under control after injuries, and thus the impact on quality of life was minimal. This was supported by a study by Chen et al. (2007) who found that asthma severity and asthma control although related concepts, each contributed independently to HRQoL. Similarly, Sundh et al. (2017) also found that self-management of asthma was linked with higher HRQoL, while the burden of moderate or severe asthmatic disease was associated with lower HRQoL.

The most commonly occurring post-injury predictors of quality of life in the TBI sample were musculoskeletal, neurological and psychiatric conditions. Musculoskeletal conditions as a post-injury predictor explained the most variance in the regression

models, especially in the physical domain. This is not an uncommon finding as TBIs are usually associated with injuries to the musculoskeletal system particularly in motor vehicle-related accidents (Holcomb et al., 2012), which accounted for the majority of TBI events in this study. Research has identified that concurrent extremity injuries after TBI impact on physical disability, and prolong diminished quality of life (Gabbe et al., 2012; Ponsford et al., 2008). Persisting neurological problems commonly reported by the current TBI group related to posttraumatic headaches and migraines, which were found in the regression analyses to have a detrimental effect on perceived quality of life, especially in the psychological and environmental domains. Posttraumatic headaches are a common complaint among TBI patients with 18–33% reporting persistence of headaches beyond the first year (Lew et al., 2006). These have been associated with higher symptoms of depression and anxiety, posttraumatic stress disorder, as well as lower quality of life (Martins et al., 2012; Sawyer et al., 2015). Symptoms of headaches and migraines may also overlap with postconcussion symptoms (Bigler, 2008), which was also identified as a predictive factor for poor quality of life in this study, as well as in other research in TBI patients (Emanuelson et al., 2003; Voormolen, Polinder, et al., 2018). Neurological difficulties can also come in the form of traumatic neuropathic pain caused by injuries to the extremities, which can sometimes result in tingling, numbness or burning sensations in or near the location of the injury, and known to decrease quality of life (Yao et al., 2017). The present study also confirmed previously established relationships between post-injury psychiatric difficulties and their deleterious long-term effects on quality of life that can last up to 10 years after TBI (Andelic et al., 2009; Cnossen et al., 2017; Haagsma et al., 2012; Haagsma et al., 2015).

One of the strongest findings of this study is that a notable proportion of variance in quality of life scores was explained by residual symptoms of PCS among individuals with TBI, even after having adjusted for demographic, injury variables as well as prior and post-injury comorbidities. In fact, persistent PCS symptoms were found to be the most significantly predictive factor in the model explaining between 13–16% of variance alone in the physical, psychological and the environmental domains. These results align with findings from other studies that have commented on the inverse relationship between PCS symptoms and quality of life particularly after mild TBI, although this area has only recently gained attention (Emanuelson et al., 2003; Voormolen, Polinder, et al., 2018). In a recent study by Voormolen et al. (2018), the authors noted that mild TBI patients diagnosed with ‘postconcussion syndrome’ (using

ICD-10 criteria), were more likely to score lower in the physical and mental QoL components at six months than their counterparts who did not have postconcussion syndrome. Correlations between PCS and Short-Form (SF) 36 subscales were strongest between fatigue and vitality, social functioning and role limitations related to physical functioning, while psychological and emotional symptoms of depression, irritability and frustration were strongly linked with social functioning, and mental/emotional health domains. Caution should however be exercised to attribute PCS symptoms solely to the experience of injuries, as this study also demonstrated that the presence of comorbidities does additionally contribute to the persistence of symptoms. Therefore, this overlap in symptoms needs to be examined carefully.

Predictors of long-term quality of life after orthopaedic injuries

Results for the orthopaedic sample revealed mainly that prior and post-injury musculoskeletal difficulties and psychological disorders were consistent predictors of quality of life after two years. Pre-existing musculoskeletal conditions affected overall quality of life, and specifically the physical, psychological and environmental domains. This is to be expected as even minor musculoskeletal discomfort can inhibit functional outcome, which can be challenged by more demanding environmental conditions (e.g., walking uphill, manoeuvering away from physical barriers), and also affect one's mobility within the social and community environment (Keysor et al., 2009). As reported by Bhandari et al. (2008), associated musculoskeletal pain or discomfort following an orthopaedic injury may also accompany additional psychological distress. Musculoskeletal problems reported in the current sample of orthopaedic participants in post-injury phase, however only appeared to marginally affect physical quality of life, with only 3% of variance explained in the model. One reason may be related to emotional adjustment of prior difficulties, which in combination with adoption of positive coping strategies, may buffer the impacts of a subsequent injury. In fact, Curran, Ponsford and Crowe (2000) found that coping strategies between severe TBI and orthopaedic patients after one to five years were not significantly different, and also noted that higher emotional adjustment was associated with lower anxiety/depressive symptoms after injuries.

Relatively little is known about the outcomes for orthopaedic patients who suffer from previous psychological problems, but it is recognised that up to 50% of patients with clinical depression are missed due to a lack of screening in the trauma setting (Crichlow et al., 2006). In line with evidence from past studies, the present study highlighted that

history of anxiety or depression contributes to diminished quality of life, with similar effects between TBI and orthopaedic participants (Haupt et al., 2018; Ponsford et al., 2011). Specifically, these studies found that there were no significant differences in the reported rates for lifetime anxiety, depression and substance abuse between mild TBI and trauma control patients. Furthermore, a preinjury psychiatric diagnosis has also been found by some studies to predispose patients to sustaining more severe injuries, and developing post-injury depression (Becher et al., 2014; Ponsford et al., 2011).

In the post-injury phase, people who have experienced an orthopaedic injury are known to continuously experience psychological symptoms of emotional distress associated with injury-related pain (Archer et al., 2016), with some researchers reporting no discernible differences between TBI and orthopaedic patients (Curran et al., 2000). In a recent large multinational study by the TRACK-TBI collaborators, the evidence revealed that risk of posttraumatic stress disorder and major depression were significantly and consistently elevated for mild TBI patients at three and six months, compared with orthopaedic controls (Stein et al., 2019). Results on the differences on the risks between the two groups at 12 months post-injury were however, inconclusive. Similarly, in an earlier study Hanks et al. (1999) reported that, while TBI individuals differed significantly in emotional and behavioural maladjustment from community controls, levels of psychological difficulties between TBI and non-TBI patients appeared to be similar at one year after injury. As observed by Archer et al. (2016) and Ponsford et al. (2008), quality of life following orthopaedic trauma is reported to be worse among those who develop anxiety or depression, even after adjusting for severity of physical injuries. The current study confirms these findings and shows that, after taking into account injury factors and prior psychological history, symptoms of anxiety and depression persist and continue to impact on quality of life even at 2.50 years after injuries. Nota et al. (2015) showed that depression after 1–2 months of musculoskeletal trauma significantly predicted functional disability at 5–8 months. A similar finding was echoed in this study, where pre- and post-injury psychological disturbances were also found to predict poor physical quality of life.

An important finding highlighted by this study is the pertinence of measuring PCS symptoms in the orthopaedic group, which were found to be a significant predictor of physical, psychological, and overall quality of life, after controlling for demographic, injury, premorbid health and post-injury health difficulties. This is a novel contribution to the literature, which has to date minimal evidence on the prevalence of PCS

symptoms in non-TBI populations, especially among general injury patients (Dikmen et al., 2010; Ponsford et al., 2011). Ponsford et al. (2011) noted that PCS symptoms were at similar levels between TBI and trauma controls (3.4% vs. 3.8%), at three months post-injury. Although there only were minor differences in the rates of PCS symptoms between TBI and orthopaedic participants in the present study, the current findings emphasise that PCS symptoms continue to impact on long-term quality of life regardless of the type of injury. Further investigation into the overlap between symptoms of posttraumatic stress and PCS among injury patients, as suggested by Meares et al. (2011), may provide important clarification on the non-specificity of PCS symptoms, and their contribution as a risk factor of poor outcomes after injury.

Lastly, some anomalous results came to the fore in the regression results which should be acknowledged. In the present study, previous lower gastrointestinal issues (e.g. past appendectomy or hernia operation) appeared to affect overall quality of life after injury, while prior endocrine-metabolic problems (e.g. elevated cholesterol or type 2 diabetes), were found to affect physical QoL. Post-injury genitourinary problems (e.g. prostate problems) also appeared to be a significant predictor of scores on the social domain. While these factors may well be spurious results arising from the small sample size in this study, these associations merit further investigation by the use of larger sample sizes.

Section summary

The multivariate linear regression analyses presented preliminary results that highlighted key pre-existing illnesses and post-injury conditions that prolong diminished quality of life after injuries. In the TBI group prior conditions such as neurological, psychiatric/behavioural, and respiratory conditions, impacted on different components of quality of life in the long-term, whereas among orthopaedic participants pre-existing musculoskeletal problems seemed to affect predominantly the physical domain. In both groups, prior psychiatric history resulted in poorer quality of life. The preliminary results also revealed common ailments experienced by both TBI and orthopaedic participants following injuries, namely psychological disturbances and musculoskeletal difficulties, both of which negatively impacted on quality of life. Interestingly, post-injury musculoskeletal issues appeared to occupy greater significance in predicting QoL for TBI participants than for the orthopaedic injury group. Additionally, the TBI group also reported experiencing more post-injury neurological problems which contributed to lower quality of life. One of the most significant findings

from the regression analysis is that, after adjusting for baseline and injury differences, and pre- and post-injury health conditions, residual PCS symptoms remained an important contributing factor affecting quality of life among both TBI and orthopaedic participants, even after 2.50 years since injuries. These findings, together with evidence from past research therefore, present a strong argument for paying attention to PCS symptoms as an important contributing factor in the recovery process between these two populations.

Exploring relationships between comorbidities, postconcussive symptoms and quality of life after injuries

The multiple linear regression analyses in the preliminary data analytical steps of Study 2 explored the effects of individual comorbidity categories on PCS symptoms and quality of life. These analyses were used to identify important predictors, that subsequently informed the development of an empirically-derived model, demonstrating the relationships existing between predictors and outcomes, using structural equation modelling methods. These models incorporated demographic and injury-related factors, as well as post-injury comorbidities, and their observed direct and indirect effects on PCS symptoms and quality of life, including on the physical, psychological, social and environmental domains.

Generally, fit indices of models indicated that the models fit the data well. Results from the SEM analysis confirmed previous findings from the regression analysis, and other similar studies by Polinder et al. (2018) and Tator et al. (2016), that age is a direct predictor of PCS symptoms in TBI patients. In terms of quality of life, age was also found to have direct relationships with physical and social QoL, whereas marital status was a more consistent predictor of QoL across different domains. Structural relationships explored by other authors have revealed that factors such as age, education, ethnicity, employment, access to family support, and family satisfaction tend to have small to moderate direct and indirect effects on perceived quality of life among TBI patients (Azouvi et al., 2016; Novack et al., 2001; Webb et al., 1995; Williamson et al., 2013). In the orthopaedic group, age was found to demonstrate a direct relationship with PCS symptoms, but seemed to directly impact only on some components of quality of life, namely those relating to the social and environmental domains. Additionally, it was shown that among orthopaedic participants, marital status bears some impact on social domain scores. These results are somewhat incongruent with analyses by Ponsford (2008) and Bhandari (2008), whose findings have associated age with small

effects on quality of life among orthopaedic injury patients, but only within the physical domain. Neither study investigated the effects of marital status on quality of life after orthopaedic injury.

The SEM analyses confirmed the previous results from Study 1, that neither TBI severity nor overall injury severity is predictive of long-term PCS symptoms or quality of life for either TBI or orthopaedic participants. Dikmen et al. (1995) previously asserted that injury severity is a better prognostic indicator for objective measures e.g. employment status, than of self-perceived psychosocial limitations. With respect to clinical characteristics, length of hospitalisation was seen to indirectly affect quality of life through PCS symptoms as a mediating variable, but only for the orthopaedic sample. In comparison, length of hospitalisation in the TBI group bore no significance on PCS or on quality of life. Length of stay may be a prognostic indicator of quality of life for patients with functional impairment or more severe brain injuries which require longer medical intervention—a finding which has been supported by Azouvi et al. (2016). In contrast, most TBI participants in this study had sustained mild TBI, for whom longer hospitalisation was significantly shorter than for the orthopaedic sample. The following sections discuss the main findings from the SEM analyses regarding the contribution of post-injury comorbidities on outcomes, with the aim to highlight conditions that are unique to TBI and orthopaedic groups.

Factors unique to different injury groups

Psychiatric/behavioural difficulties

In the extant literature, the few existing SEM analyses on outcomes after TBI have highlighted that previous psychological problems are significant predictors of poor quality of life (Azouvi et al., 2016; Webb et al., 1995; Williamson et al., 2013). SEM analyses in the current study, highlighted the importance of post-injury psychiatric/behavioural difficulties as having prolonged effects on long-term postconcussive symptoms and QoL in both TBI and orthopaedic participants, even after 2.50 approximately years since injuries. The effects of psychiatric/behavioural problems on QoL were also mediated by the presence of PCS symptoms. In the TBI sample, psychiatric difficulties only seemed to exert a strong influence on the psychological domain, whereas in the orthopaedic sample psychiatric problems affected not only overall QoL, but also consistently across all domains, with total effects ranging between moderate and strong. Interestingly, unlike in the TBI sample, the analyses for the

orthopaedic sample in the present study showed that, psychological problems had similar direct impacts on both PCS symptoms and quality of life.

Similarly, previous SEM analyses have highlighted that prior psychiatric history of alcohol/drug dependence and mood disorders after injury, are significant predictors of poor quality of life after TBI, although these studies are mainly comprised of moderate to severe TBI patients (Azouvi et al., 2016; Webb et al., 1995; Williamson et al., 2013). In a study, Williamson et al. (2013) demonstrated that depression at 24 months among moderate to severe TBI patients, has a moderate direct relationship with HRQoL, while Lin et al. (2010), showed that TBI patients with depressive status and poor functional independence experienced poorer QoL improvements in the psychological and social domains between 6 and 12 months after injury. An SEM analysis of severe TBI patients by Azouvi et al. (2016), showed that only mood disorders and cognitive function directly impacted on quality of life after four years. Similar findings were confirmed in the current study, which additionally demonstrated that the effects of psychological disturbances on quality of life are also mediated by the presence of PCS symptoms. This is in accordance with results reported by a NZ study by Theadom et al. (2018), who confirmed the strong relationship existing between psychological problems and long-term postconcussive symptoms.

The discrepancies between the two injury groups, where the influence of psychological problems on quality of life was stronger for the orthopaedic than for the TBI group, are not unusual, albeit unexpected. Previous studies as described earlier, have noted that psychological symptoms such as anxiety and depression are also prevalent among those who have suffered an orthopaedic injury, and do not differ with those from TBI patients in the first year after injury (Archer et al., 2016; Curran et al., 2000; Hanks et al., 1999; Stein et al., 2019). These difficulties have been linked to poor outcomes including diminished quality of life among orthopaedic patients (Archer et al., 2016; Ponsford et al., 2008). Whilst these studies have primarily been interested in the first 12 months of injury, the current study extends previous findings by highlighting that psychological difficulties can impact on quality of life also in the long-term, beyond 2.50 years post-injury.

Musculoskeletal problems

Post-injury musculoskeletal problems were another common ailment reported by both TBI and orthopaedic participants, and which portrayed both direct and indirect

relationships with postconcussion symptoms and quality of life. The direct effects on quality of life was mostly pronounced in the physical domain for the TBI group, for whom the total effects on quality of life was through PCS symptoms as a mediating factor. This highlights that for the TBI group, their physical quality of life was likely impacted due to the compounded effects of extracranial difficulties. Musculoskeletal-related pain often accompanies TBI and results in poor quality of life, in direct and indirect ways (Azouvi et al., 2016; Williamson et al., 2013). Rees (2003), and Lin et al. (2010) have argued that TBI severity (measured by GCS), may not be an appropriate predictor of quality of life in mild TBI patients, whereas duration of post-traumatic amnesia and functional independence may instead serve as better prognostic indicators of quality of life. In comparison, musculoskeletal effects in the current orthopaedic group were more subdued, which showed only a marginal direct effect on physical QoL. It may suggest that these participants, whose overall injury severity was lower than for the TBI group, had likely recovered from their minor injuries, and any residual pain or associated discomfort only had a minimal impact on their quality of life. These findings are in accordance with Bhandari et al. (2008), who found that other than fracture location, clinical factors relating to the injury such as severity did not predict QoL scores on the SF-36. Similarly, Ponsford et al. (2008) also confirmed that injury severity was not a predictor of quality of life at one and two years, but instead, ongoing pain especially among lower limb fracture patients was shown to be a better predictor of poor physical quality of life.

Neurological problems

Post-injury neurological problems such as migraines and headaches appeared as a consistent predictor of quality of life across domains, in both groups, but only demonstrated a small direct effect on PCS symptoms among TBI participants. In the psychological domain, the total effects of neurological disturbances on quality of life for the TBI group (including indirectly through PCS symptoms), were moderate. This relationship may have been confounded by the presence of PCS symptoms, which are known to share similar symptomology with neurological disorders. The present study also confirms the strong significant relationship existing between PCS symptoms and lower quality of life, with the largest effects mainly observed in the physical and environmental domains for the TBI group. Few studies have highlighted the persistence of symptoms many years after injuries (Åhman et al., 2013; Bohnen et al., 1994; Theadom et al., 2018), and there is limited published evidence regarding the links

between residual postconcussion symptoms and poor quality of life in the first year after TBI (Emanuelson et al., 2003; Voormolen, Polinder, et al., 2018). The current study extends this evidence by noting the significance of the association between PCS symptoms and quality of life as persisting beyond the first year of injury, and additionally noting the influence of neurological conditions on this relationship. In comparison, in the orthopaedic sample, post-injury neurological problems had only minor effects on quality of life domains, with PCS symptoms acting as an intermediary variable. Nevertheless, the relationship between postconcussion symptoms and quality of life remained significant for the orthopaedic group, with effects most notable in the physical domain. There is a paucity in the data regarding the impact of neurological problems, postconcussive symptoms and quality of life in the orthopaedic population, and therefore comparison of these novel findings to existing literature is not possible.

Other post-injury comorbidities

Lastly, other post-injury comorbidities such as the presence of respiratory conditions (e.g. asthma), also appeared to have minimal but significant effects on PCS symptoms and environmental quality of life among orthopaedic participants. While respiratory conditions have been known to lower HRQoL (Chen et al., 2007; Sundh et al., 2017), there are have been no previous links drawn between PCS symptoms and respiratory problems. It can be assumed that difficulties in breathing can lead to sleep disturbances (Molzon et al., 2013), while laboured breathing due to inadequate oxygen circulation may also induce fatigue (Small & Lamb, 1999)—both symptoms of sleep disturbances and fatigue also feature under the PCS constellation. As mentioned earlier in the discussion, the direct effects of genitourinary problems on social QoL for both groups, and additional effects on environmental QoL for the TBI sample, is unclear. This unexpected relationship may be explained by age, which was a moderate covariate in the models. These observed results may well be spurious; however, further research is needed to clarify on the associations (if any), between respiratory difficulties, genitourinary conditions, postconcussion symptoms and quality of life.

The effect of interval versus ordinal measures on relationships between variables

A secondary aim within the SEM analyses was to compare the use of ordinal versus Rasch-transformed interval-level measures derived for the RPQ and the WHOQoL-BREF, and their effects on strengths of associations in the models. The different iterations of the overall model using interval-level and ordinal-level measures, generally

yielded minimal and inconsistent differences in weights of beta coefficients and model fit indices. The use of interval-level measures in some instances resulted in marginally lower model fit and lower strength of associations, whereas for other associations, it led to a slight increase in beta coefficients. Fit indices in the interval scales model, when compared with the ordinal scales model, were only slightly lowered, but maintained good theoretical fit to the data. Overall however, the inconsistencies in the patterns suggested no discernible differences in weights of relationships when interval-measures are used in place of ordinal scales. The rationale for utilising Rasch measures in lieu of ordinal-level measures lies in its advantage in increasing precision by reducing measurement error as argued by Tennant et al. (2004), which therefore results in marginally smaller coefficients. Moreover, given that SEM is underpinned by a linear model, any measures that are entered into the analyses should also ideally reflect this property in order to produce the most reliable estimates. Although there is strong theoretical justification for using Rasch-transformed interval measures in outcome measurement (Hobart et al., 2007), the empirical results in this study were not able to provide conclusive evidence to support this argument. This may be partly due to the small sample sizes used in the models, which consisted of 108 TBI and 114 orthopaedic participants, analysed separately for the SEM analyses. Therefore, it is likely that the respective samples were underpowered to detect small differences in effect sizes. A much larger sample size would have been required to explore the differences in ordinal and interval scales on SEM analyses in greater detail, and to demonstrate smaller effect sizes between observed relationships.

Implications of findings

Study 2 presented novel findings, by highlighting that underlying health problems, that occur before and after injuries, explain a considerable portion of residual PCS symptoms and diminished quality of life, independent of the type of injuries. In addition to psychiatric problems explored exhaustively by literature, this study found that other conditions such as, neurological and musculoskeletal difficulties are a common burden to both TBI and orthopaedic groups, which should be taken into consideration in treatment efforts for postconcussive symptoms. Contrary to previous assumptions that those with relatively minor injuries make a full recovery in the first few months (Rohling et al., 2012), these results highlight that people who have experienced even ‘minor’ injuries can continue to experience common health problems that have deleterious effects on quality of life. Clinically, this also allows clinicians to identify

and predict those individuals with pre-existing psychiatric, neurological and musculoskeletal problems, that are likely to experience worse symptoms and adjustment following the experience of an injury. By doing so, it may enable health practitioners to target treatment regimens early to help minimise PCS symptoms and improve recovery.

Based on the most current guidelines on mild TBI management, management of persistent symptoms should begin with a thorough investigation of the patient's medical history to rule out any underlying conditions as confounding factors in the diagnosis (Ontario Neurotrauma Foundation, 2018). This is followed by investigating treatable causes of persistent dizziness, vision problems, sleep disturbance, and fatigue. This can involve for example, assessment of vertigo and/or ocular examination for visual accommodation, and/or medical investigation of persistent fatigue (such as medication side-effects or bloodwork for metabolic and electrolyte abnormalities) (Ontario Neurotrauma Foundation, 2018). Management of physical symptoms such as headaches may include the use of non-steroidal anti-inflammatory analgesics, which is still the most commonly recommended pharmaceutical treatment for PCS symptoms (Mittenberg et al., 2001). Screening for the presence of psychological symptoms such as anxiety and depression should take precedence in the investigation, given that mood disturbances are the most commonly reported among postconcussion symptoms, and remain to be the most powerful predictors of recovery as confirmed in this study and elsewhere (Cnossen et al., 2017; Silverberg et al., 2015). Patients who have had a history of anxiety or depression, and who report continuing psychological difficulties in addition to PCS symptoms, may be recommended cognitive behavioural therapy, which has been shown to have some effectiveness in managing symptoms. However, larger randomised controlled trials are needed to produce definitive evidence on its efficacy (Al Sayegh et al., 2010).

Psychotropic medication such as serotonin reuptake inhibitors or tricyclic antidepressants, continue to be routinely recommended first-line treatments for management of anxiety and depression post-TBI, and additionally have been shown to concurrently reduce symptoms of irritability, headaches, fatigue, and concentration difficulties (Mittenberg et al., 2001; Silverberg & Panenka, 2019). However, current guidelines do acknowledge the 'catch-22' here, given the contribution of medication overuse (defined as greater than 15 days of continuous use), to the persistence of symptoms. For example, excessive use of pain medications can inadvertently perpetuate the occurrence of posttraumatic headaches (Gladstone, 2009). Similarly, it is just as

important to recognise the role that prescribed medications for pre-existing illness may play in influencing PCS symptoms. Anecdotal evidence gathered from participants in the present study indicated that many were receiving medications for common pre-existing conditions, such as anxiety and depression, type 2 diabetes, and cardiovascular problems. Many of these medications are known to have unintended side effects, which can either be mirroring or exacerbating PCS symptoms. For example, anxiolytics, antidepressants and antiarrhythmic drugs commonly prescribed for anxiety, depression, and heart problems, respectively, have known side effects including neurological effects (e.g. dizziness, loss of consciousness, cognitive impairment, headaches), as well as fatigue, nausea/vomiting, and mood problems (Joint Formulary Committee, 2020; Wooten et al., 2000). It is currently unknown whether there are complex interactions between medication use and persistence of PCS symptoms. Future studies need to collect adequate data on medication use and consider this as a potential predictor when assessing the prevalence of PCS symptoms following TBI or orthopaedic injury.

Lastly, current treatment protocols mandate the need for non-pharmaceutical interventions, in order to steer away from the over-reliance of pharmaceutical interventions for symptom management (Ontario Neurotrauma Foundation, 2018). Primarily, this is in the form of education, that includes both verbal and printed information on TBI, its associated symptoms and expected outcomes (Comper et al., 2005). Due care needs to be taken to emphasise on the normalcy of common symptoms to alleviate concerns, without overly raising expectations of recovery in patients. Furthermore, patients should be encouraged to engage in a gradual return to activities (either in daily life or employment), in a way that does not compromise current therapy or exacerbate symptoms. Advice may also include techniques to manage stress, such as with light exercise, or mind-body approaches such as yoga, Tai-Chi and mindfulness, which have been shown to have beneficial gains for stress management (Hanna-Pladdy et al., 2001; Lucke-Wold et al., 2018). Other nontherapeutic interventions might include, expanding a person's social support network for mental wellbeing, self-management techniques (e.g. list-making, using a calendar for remembering appointments, scheduled rest periods, and meditation) to improve fatigue and concentration, and occupational or physical therapies to improve functional outcomes. These interventions have all shown to yield benefits and improvements in quality of life among those living with lingering PCS symptoms (Ala'a et al., 2019). In summary, by identifying high risk individuals through prognostic modelling, appropriate

rehabilitation strategies can be planned and implemented early to mitigate the impact of PCS symptoms, and to help better adjustment in normal life after injuries.

Limitations

It is important to acknowledge that while SEM allows researchers to test complex models and to observe structural relationships existing between predictors, it does not prove causality, and different iterations of a model might fit a given set of data equally well. It should also be recognised that outcome after either TBI or orthopaedic injury is influenced by a host of factors, which, were not all accounted for in the models presented in this thesis. Other limitations have already been addressed in this chapter, which include the small sample size comprising of approximately 110 participants per injury group. Sample size limitations therefore restricted the number of factors that could be tested in the SEM analyses. This may explain some discrepancies that were observed between SEM and the regression model, in which some significant associations in the regression model were subsequently found to be non-significant in the SEM model. Nevertheless, it is encouraging that even a small sample size yielded high fit indices and suggests the feasibility of the developed models in this thesis. These models, however, need to be subjected to further testing using much larger samples which is recommended for the conduct of SEM analysis (Wolf et al., 2013). Another limitation to be noted is the absence of TBI severity as a variable in the SEM model, given its high rate of missing data in the TBI sample. The inclusion of TBI severity would have permitted the analyses to delineate any relationships that are affected by the severity of the brain injury. Furthermore, as these results represent predominantly mild injuries (for both TBI and orthopaedic groups), future studies could consider comparing how the impact of comorbidities would differ in samples that contained more severely injured participants. It may well be the case that strengths of relationships would be more pronounced in patients with more severe injuries, but also highlight other comorbidities that should be considered risk factors of prolonged postconcussion symptoms and poor quality of life.

8.5 Chapter summary

To summarise, this study has pointed to some key findings regarding the importance of the role of comorbidities in predicting outcomes after injury. The preliminary multiple linear regression analyses found that TBI participants with prior neurological problems were at most risk from experiencing higher rates of PCS symptoms after injury, whereas individuals who had sustained an orthopaedic injury and who had previous

musculoskeletal issues were equally at high risk of symptoms. It was also found that, both groups commonly experienced pre-injury psychiatric and neurological difficulties, both of which were likely to contribute to lingering symptoms in the long-term. With regards to quality of life, TBI participants who reported having a history of neurological and psychiatric problems, were more likely to have worse long-term physical and psychological quality of life, whereas among orthopaedic participants, prior musculoskeletal problems predicted lower scores relating to physical quality of life. The SEM analyses that followed confirmed that in both injury groups, the occurrence of post-injury psychological, musculoskeletal, and neurological problems, as well as PCS symptoms were not only common ailments, but also predicted poor long-term quality of life across various domains. These findings are a novel contribution to an area which is currently severely under-researched. The overall implications of the findings arising from this PhD will be addressed in the next chapter, with acknowledgments of limitations of the overall PhD study, and directions for future research.

Chapter 9 Integrated Discussion and Conclusion

The overarching goals of this PhD thesis were to enhance instrument precision in TBI outcome research, and to extend current knowledge regarding the predictors of long-term outcomes after TBI, elucidating specifically on the role of comorbidities. To achieve these aims, an age- and sex-matched case-control sample comprising of 109 TBI and 114 orthopaedic adult injury participants were recruited from a hospital trauma registry in the Waikato region of New Zealand. The first objective of this study was to evaluate the psychometric properties of three commonly used outcome measures and to determine their applicability for use in both TBI and orthopaedic injury populations. With the application of modern and rigorous methods of Rasch analysis, the psychometric properties of the Comorbidity Illness Rating Scale, the Rivermead Postconcussion Questionnaire and the WHO Quality of Life-BREF were evaluated in Study 1. Rasch analysis was also used to validate existing derivatives of the WHOQoL-BREF such as the EUROHIS-QOL-8 and the WHOQoL-5, as well as to inform the development of a 12-item version of the WHOQoL-BREF.

The second objective of the thesis, which comprises Study 2, was to explore the structural relationships existing between pre-injury, peri-injury and post-injury factors, to identify the most important contributors to long-term postconcussive symptoms and quality of life. With the application of multivariate linear regression and structural equation modelling techniques, an empirically-informed model was developed and tested the effects of pre-existing and post-injury comorbidities and other predictors on long-term outcomes for TBI and orthopaedic groups. Secondary analyses within Study 2 also examined and compared the effect of the use of ordinal versus interval measures on the strengths of relationships derived in the structural equation models.

The following sections will summarise the key findings from this thesis and discuss them in relation to existing knowledge, and future clinical implications arising from this work. Lastly, the overall study limitations will be addressed, concluding with a brief discussion on directions for future research.

9.1 Summary of major findings from this thesis

Study 1: Validation of the CIRS, RPQ and WHOQoL-BREF in TBI and orthopaedic populations

In the first of the Rasch analyses of Study 1, Chapter 5 described the comorbidity profiles of TBI and orthopaedic injury participants at the pre- and post-injury phases. Univariate analysis of comorbidity patterns using the CIRS revealed that TBI and orthopaedic participants have generally similar health profiles prior to their injuries, with the exception that the orthopaedic group had significantly higher pre-existing musculoskeletal and endocrine-metabolic related problems than TBI participants. In the post-injury phase, complaints of neurological disturbances such as frequent migraines and headaches were more prominent in the TBI group, however common ailments in both groups also related to musculoskeletal pain and psychological difficulties such as anxiety and depression. When the CIRS was evaluated using Rasch analysis, findings showed that, although the scale was unidimensional and met the assumptions of the Rasch model, it nevertheless fails to meet modern psychometric standards due to its poor instrument reliability. It was therefore concluded from this exercise that the scale's scores should be interpreted with caution, particularly when analysed as a total score. This finding however does not underscore the informational value contained within the individual comorbidity items of the scale, which does present useful data regarding the extent of specific comorbidities in an individual. In the extant literature, the evidence on the psychometric properties of the CIRS is sparse and where available is limited to studies of geriatric samples (Fabio et al., 2008; Parmelee et al., 1995). This study provided much needed detailed psychometric information regarding the usability of the CIRS to assess comorbidity within the injury context but presented concerns regarding the scale's lack of reliability. However, as the present findings were based on samples with low comorbidity levels, further validation work is required to ascertain if the instrument may perform better for populations with higher comorbidity levels.

In Chapter 6 within Study 1, Rasch methods were applied to validate the Rivermead Postconcussion Questionnaire in the TBI and orthopaedic samples. To the candidate's knowledge, this study was the first to have validated a TBI-specific instrument in a non-TBI population, by implementing a novel case-control design. Results from this analysis indicated that the RPQ is a reliable measure of long-term PCS symptoms in both the TBI and orthopaedic populations. The measure demonstrated strong reliability with good coverage across the TBI sample, although item-person targeting was less than

ideal for the orthopaedic sample, who generally presented with low symptom prevalence. DIF analyses indicated that all items operated invariably irrespective of injury type, and therefore the measure is suitable to be administered across the wider injury population. Additionally, a PSI value of .87 provided evidence for the measure's usefulness across group comparisons, as well as its clinical utility for the individual assessment of symptoms. A major strength of this work was the clarification on the construct validity of the RPQ, on which previous Rasch analyses and factor analyses have so far failed to achieve consensus. This study presented strong evidence for the unidimensional construct of PCS symptoms in both TBI and orthopaedic participants, which permits the appropriate use of total scores according to the fundamental principles of measurement. The conversions from ordinal to interval-level total scores presented in this thesis, can be used to assess response shift and to compare scores across individuals. Evidence from this study and others does seem to call into question the validity of the nomenclature of this set of symptoms (i.e. post-'concussion symptoms') that misaligns it with experience of a concussion, when symptoms have been documented in various non-TBI samples.

In Chapter 7 within Study 1, the properties of the WHOQoL-BREF were evaluated for feasibility as a quality of life instrument across TBI, orthopaedic participants and an additional general population sample (n=140), using Rasch approaches. The findings from this study showed that the WHOQoL-BREF met the expectations of the Rasch model, demonstrating high internal consistency, excellent item-to-person coverage and invariant performance across injury/healthy groups and demographic characteristics. Supplementary analyses of shorter existing versions such as the EUROHIS-QOL-8 and the WHOQoL-5 revealed that only the EUROHIS-QOL-8 upheld the strong psychometric properties of the parent WHOQoL-BREF. Further work is needed to enhance the performance of the WHOQoL-5 before it can be used as a reliable scale in outcome assessment. A novel contribution of this chapter is the additional development of a 12-item WHOQoL version which met the criteria of the Rasch model and demonstrated sound psychometric properties. Variations in short-scale measurements permit researchers and clinicians to select versions that are most appropriate for used in time-restrained settings and where reducing response burden in participants (such as in individuals with cognitive deficits) is a priority. In the 12-item proposed version, researchers have the additional benefit of exploring domain-level scores and the advantage of conducting factor analysis which is not currently possible with the

EUROHIS-QOL-8 or the WHOQoL-5 formats. Similar to the RPQ, the provision of ordinal-to-interval conversion tables for the WHOQoL-BREF, EUROHIS-QOL-8 and the WHOQoL-5 is a notable contribution towards improving precision of these commonly used instruments.

Study 2: Modelling the effect of comorbidities on long-term outcomes: A case-control analysis

Employing multivariate linear regression and structural equation modelling techniques, Study 2 in Chapter 8, pointed to some key findings regarding the impact of prior and post-injury comorbidities on long-term postconcussive symptoms and quality of life after TBI and orthopaedic injuries. Multivariate linear regression showed that among TBI participants, prior neurological problems was a risk factor for delayed PCS symptom resolution, while both prior neurological and psychiatric difficulties such as anxiety and depression contributed to diminished long-term physical and psychological quality of life. Among those who had suffered an orthopaedic injury, pre-existing musculoskeletal problems were most predictive of longer PCS symptoms, although the presence of prior psychiatric and/or neurological problems were also identified as risk factors. Furthermore, premorbid as opposed to post-injury musculoskeletal conditions, were found to predict poor long-term physical quality of life among orthopaedic participants. SEM analyses were subsequently conducted to illustrate a model depicting the relationships between post-injury comorbidities and long-term outcomes. The models showed that, in both TBI and orthopaedic participants, the presence of post-injury psychological, musculoskeletal and neurological problems contributed directly to long-term PCS symptoms, and indirectly to poor quality of life on physical, psychological, social and environmental domains. Among TBI participants, post-injury musculoskeletal difficulties in particular, was seen to be an important factor for physical quality of life than for orthopaedic participants. A key finding produced from Study 2 is the relevance of PCS symptoms as a predictor of QoL in both TBI and orthopaedic groups. Symptoms appeared to have moderate to strong effects on QoL for participants who had experienced TBI, rather than for those with orthopaedic injuries.

9.2 Strengths and implications of study findings

There are several strengths arising from the results of this thesis. The first methodologically important contribution of this thesis is to outcome assessment, with the application of Rasch methods to produce linear scales of commonly used outcome measures, such as the RPQ and the WHOQoL-BREF. As detailed in Chapter 4, Rasch

analysis unlike CTT-based factor analysis allows normally ordinal-based scales to be transformed to a linear measurement when the core expectations of the Rasch model are achieved. In addition, validation of scales was conducted across diverse groups consisting of TBI, orthopaedic and general population samples to demonstrate the versatility of these instruments. In the case of the RPQ, two age- and sex-matched injury samples of TBI and orthopaedic subjects were used, whereas the analysis of the WHOQoL-BREF was supplemented by an additional general population group. In past works, the RPQ has only been evaluated with Rasch methods within the TBI population (Eyres et al., 2005; Lannsjö et al., 2011), whereas the present study extends previous efforts by demonstrating that the RPQ can be reliably administered to the non-TBI population as a suitable measure of PCS symptoms. Similarly, this study extends existing evidence by demonstrating the efficacy of the WHOQoL-BREF and shorter versions for assessing quality of life across the healthy and the injury populations. This includes the development of a 12-item version of the WHOQoL that can be used as a reliable alternative scale for exploring domain-level scores and conducting factor analysis in these populations.

Unlike some previous Rasch studies noted throughout the thesis, this PhD work adhered to the current recommended guidelines for the conduct of Rasch evaluation as proposed by Leung et al. (2014). This included specific testing of unidimensionality, which is argued by researchers as a statistical requirement for the calculation of a total score (Tennant & Conaghan, 2007). Also, unlike previous validation efforts that are largely based on CTT methods, the use of Rasch analysis in this thesis also presented detailed information on the performance of individual items, and indication of item performance by sub-group. Using a case-control design presented an additional strength of the study in this respect, because it enabled the evaluation of differential item performance by a disease condition group, which is rarely conducted. This meant that it was possible to evaluate whether items on the RPQ and the WHOQoL-BREF functioned differently for participants who had a TBI than those who had sustained an orthopaedic injury. Similar DIF analyses were applied for the evaluation of the WHOQoL scales, in which additional comparisons to the general/healthy population were made. Conducting DIF analyses by disease group is a novel approach not previously seen in Rasch validation studies and it is recommended that future studies consider employing similar DIF analyses beyond those of the common demographic features such as age, sex and country.

Another strength of the Rasch work demonstrated in this thesis is that minimal modifications were applied within the Rasch analyses to enhance the model parameters, that is in line with current strategies recommended by Leung et al. (2014). Previous conventions for dealing with items that deviated from model assumptions (e.g. due to model misfit, disordered thresholds, DIF, local item dependency), involved either item rescoring, and where necessary, deletion of misfitting items altogether. These strategies were often employed to achieve a satisfactory model fit, at the expense of items being deleted, and is recommended only as a last resort strategy where misfit cannot be addressed in any other way, or in cases where items do not have conceptual relevance (Cohen et al., 2013). Crişan et al. (2017), in fact, found that that the deletion of misfitting items can only improve results in cases of severe multidimensionality or where there is a large proportion of misfitting items. Moreover, item deletion or item rescoring significantly alters the properties of the scale, and thus makes comparisons with other Rasch validation studies difficult. These approaches were employed in previous Rasch analyses for both the RPQ and the WHOQoL-BREF (Eyres et al., 2005; Pires et al., 2018; Rocha et al., 2012a), and the resulting alterations to the scale limit the pooling of estimates across studies. In contrast, this PhD thesis followed best practice guidelines of dealing with model misfit through the super-item (or subtest) approach as suggested by Lundgren Nilsson and Tennant (2011), which enabled the results to achieve satisfactory Rasch model fit, with only minimal modifications to the scale. As described in Chapter 4, the super-item approach essentially cancels out any bias arising due to contextual or method effects within misfitting items and therefore, enables the analysis to retain all items of the original scale. Lastly, in keeping with the best practice guidelines of outcome measurement, this thesis provided ordinal-to-interval conversion tables for the RPQ and WHOQoL-BREF that adjust raw total scores to Rasch-transformed total scores, and therefore optimise the performance of these instruments. The use of the ordinal-to-interval conversion table presented within the appendices has proven advantages such as improved precision of instruments through equal scaling. Adjustment to an interval scale therefore enables calculation of summary scores that can facilitate the interpretation of change scores in individuals, and permits the use of parametric statistics without violating principles of fundamental measurement (Leung et al., 2014). The provision of conversion tables in this thesis therefore represents an important contribution to outcome measurement in TBI and injury research.

Perhaps one of the most important features of this thesis, explored in Study 2, is the emphasis on a holistic understanding of different factors influencing the outcome pathway, which previous research has failed to address adequately. This research sought to create a theoretical model to depict the relationships between pre-injury factors such as pre-existing health conditions, peri-injury factors including injury severity, post-injury health problems, and their collective impact on ongoing symptom experience and quality of life. Notably, findings from Study 2 contradict the previous hypothesis that those with mild injuries, either due to a TBI or orthopaedic injury, necessarily make a full recovery within the first year (Rohling et al., 2012). The results presented here highlight that contrary to previous assumptions, 'mildly injured' patients can frequently continue to experience long-term PCS symptoms and diminished quality of life, several years after injuries. Whilst there exists an abundance of evidence on psychological disorders as risk factors of poor prognosis, this study provides an in-depth analysis into a range of somatic conditions that play an important role in recovering from an injury, and which should be considered in rehabilitation planning. Importantly, this study elucidates on the role of pre-existing medical conditions on injury outcomes, which is an area largely neglected by the injury literature. As an example, this study brought to attention that prior neurological problems can exacerbate the effects of TBI on PCS symptoms and quality of life – a finding that has not been documented to date. Similarly, the effects of previous musculoskeletal and psychological difficulties as important predictors of PCS and QoL among orthopaedic patients have not been documented prior to this study. While during the design of this study there was a notable gap in the literature regarding the role of comorbidities on TBI recovery, it is encouraging to see that this area has gained renewed attention in recent times with similar studies being published recently that confirm the value of this thesis' findings (Colantonio & Biscardi, 2018; Voormolen, Polinder, et al., 2018; Yue et al., 2019).

The findings from this thesis have implications reaching beyond that of the research context that can be applied to the clinical setting. From a clinical standpoint, these findings may assist health professionals to identify groups of injury patients with specific medical conditions who are likely to experience ongoing difficulties. In doing so, appropriate resources and interventions can be targeted early on to improve outcomes. Understanding the effects of comorbidities and injuries on outcome also means that treatment regimens and rehabilitation strategies can be individualised and modified accordingly for each patient. For instance, findings from this research suggest

that TBI patients with prior neurological or psychological problems, are likely to experience longer PCS symptoms and worse quality of life, and therefore should follow a modified rehabilitation plan that takes these factors into consideration.

Aside from the findings highlighted above, the features of the study design can also be considered to add to the overall strengths of this work. This thesis aimed to focus on understanding outcomes from a long-term perspective, for which evidence is generally limited in the extant literature. Many TBI and other injury studies are typically focussed on the hospital setting which commonly assess outcomes within the first 12 months after injury. One reason might be due to the low attrition rates that plague TBI longitudinal studies. It has been found that the between 30 to 50% of participants drop out of TBI follow-up studies after one year, which presents challenges for researchers seeking to understand long-term recovery (Corrigan et al., 2003). The current study therefore presents great value in assessing participants across a relatively wide timeframe; from injuries that occurred six months to six years prior. In doing so, it provides a cross-sectional snapshot of symptoms and difficulties experienced post-acute care, and furthers our understanding of the long-term sequelae of injuries.

With regards to psychometrics, the novel approach of using a case-control sample for the validation of outcome measures, is one that is rarely employed, in part due to the difficulty and costs of recruiting controls. A methodological strength of this study lies in the inclusion of age- and sex-matched TBI and orthopaedic injury participants which serves the goals of both phases of the thesis. Firstly, in Study1, the case-control design enabled validation of instruments in two injury samples concurrently, and also permitted the assessment of differential function of scale items by injury group. Secondly, the adoption of a case-control study design also suited the goals of Study 2. As there are certain psychological factors that are associated with the experience of injuries (e.g. posttraumatic stress), it was important to minimise the influence of these potential confounders, and other known confounders such as age and sex on outcomes, in order to produce clinically relevant findings and precise estimates. Utilising a case-control design enabled distinct comparisons to be made between the TBI and orthopaedic groups, which thus helped to isolate factors that were unique to the experience of a traumatic brain injury. Although case-control study designs are commonly used in TBI research, the most frequently used control group tends to be the general population, given the wider sampling frame and the greater potential for accessibility (e.g. through census data) compared with other populations. Miettinen

(1985) recommends that for the valid conduct of a case-control study, cases and controls must be representative of the same base experience. This guideline is an important one to bear in mind when designing a case-control study particularly for TBI studies, as the selection of improper controls may lead to potentially biased results (Marshall, 2008). The use of a general healthy population as a control group in TBI or injury studies can be questioned as they are not necessarily representative of the same denominator from which the cases are selected. It is therefore recommended that future studies consider, where appropriate, the selection of controls within the injury population, so as to adjust for the psychological experience of injuries, and to maintain comparability of outcomes from within an injury context.

9.3 Limitations

As with most research, certain limitations within this study need to be acknowledged for their potential bias in findings. One limitation in the study is the relatively small representation of certain ethnic denominations of Māori, Pacific, Asian and other groups, meaning that the results presented in this thesis are likely to be more representative of outcomes for the NZ European population. In the TBI sample, the ethnic representation of NZ Europeans was about 60%, followed by 24% Māori, 0.9% Pacific, 5% Asian and 10% other ethnicities. Proportions were similar for the orthopaedic sample which was biased towards a NZ European representation (72% of the total sample). A comparison with a population-based study in this region conducted using multiple-source recruitment strategies found that that NZ European individuals (61% of their sample) are overrepresented in the TBI spectrum, compared with Māori (31%), Pasifika (4%), Asian (3%) and 'Other' (1%) ethnic groups. The discrepancies in ethnic representation in TBI studies are worrisome as there is evidence to show that ethnic minority groups have increased risk of TBI (Lagolago et al., 2015), and may experience poor outcomes due to lower education levels and poor access to healthcare services (Bowman et al., 2007; Gary et al., 2009). Greater representation of 'hard-to-reach' populations in TBI studies is needed, and may be addressed by intensive recruitment approaches such as purposive sampling, or even indigenous field worker sampling which relies on formally trained investigators who are selected from local communities (Shaghaghi et al., 2011).

A frequently reported limitation in many TBI follow-up studies is the small sample size (Corrigan et al., 2003). Overall, the case-control study in this thesis was sufficiently powered to detect moderate differences in effect sizes, although, the relatively small

within-group sample sizes meant that TBI and orthopaedic participants had to be combined into an injury sample for the Rasch analyses. Overall, however, the study met minimum sample size requirements to estimate person measures to ± 0.5 logit within 99% confidence levels for Rasch analyses. Although large sample sizes are generally recommended for most types of quantitative data analysis, Smith et al., (2008) found in an exploratory study that Rasch model fit statistics are sample dependent, and that the increasing sample size inflates Type 1 error rate, and thus increases the number of misfitting items in the model. Therefore, careful consideration needs to be taken when identifying model misfit under large sample size simulations. Although the sample size in the current study was acceptable for DIF comparisons by injury type, a larger sample size would have enabled Rasch analyses to be conducted separately for the TBI and orthopaedic populations. This would have further strengthened the study by providing more detailed information on the psychometric performance of outcome measures separately for each injury group. Additionally, the sample size used in this study may have been underpowered for the separate SEM analyses for the TBI and orthopaedic participants, which generally favour larger sample requirements (Tarka, 2018). A small sample size also limited the number of relationships that were possible to include in the SEM path diagrams in Study 2. The use of a larger sample size may have yielded stronger relationships between factors and may have shown greater differences in the models' effect sizes between the ordinal and interval outcome measures. Furthermore, the relatively small sample size of the polytrauma group required that isolated and polytrauma TBI cases be combined to improve statistical power of the study. This may have introduced some degree of confounding to the results as polytrauma patients have more severe injuries and typically have worse outcomes than isolated TBI cases (Gross et al., 2012; Lippert-Grüner et al., 2007; McDonald et al., 2016). The inclusion of a larger sample of polytrauma TBI cases would have allowed for further sub-group analyses to be undertaken to demonstrate different outcome trajectories between isolated TBI and polytrauma TBI participants in the SEM analyses. Methods such as bootstrapping using partial least squares estimation can be employed here to improve the precision of model parameter estimates where sample sizes are small and where data are derived from non-normal conditions (Sharma & Kim, 2013).

Although this thesis attempted to capture important pre-injury demographic data, such as educational level as a proxy for socioeconomic status as is commonly seen in many prediction models (Lingsma et al., 2015; Silverberg et al., 2015), the results herein

indicated that education was not a predictor of long-term outcome after TBI nor orthopaedic injury. The data did not capture income level, which may serve as a better predictor of long-term outcome, although the results from other studies are indefinite (Humphries et al., 2020). Arguably, there may be more relevance of socioeconomic variables in healthcare systems that are large funded by private health insurance such as in the United States, where access to healthcare services is contingent on a person's socioeconomic position. In contrast, the context is different in New Zealand where access to healthcare for accidental injuries is primarily mediated by the country's public 'no-fault' personal accident insurance scheme, which allows greater access to health services, irrespective of a person's income level. Similar to the models presented in this thesis, it is acknowledged that current prediction models explain at most 30–40% of variability. There have been increased efforts into investigating the importance of other variables such as biological factors, genetics, and inflammatory markers such as APOE-4 and S-100B, although the latter have shown varying promise (Silverberg et al., 2015). Other factors such as the cumulative effects from recurrent mild TBIs have shown to predict higher frequency of PCS symptoms later on (Theadom et al., 2015), and may be included as a potential predictor in current prognostic models.

Other limitations within this study generally relate to data collection procedures. One limitation is that participants' medical histories and post-injury health problems were only ascertained at a single time-point during the one-off assessment. Ideally the collection of this information should be appropriately conducted at a minimum of two different timepoints. This is because in many cases, several years had elapsed since the injury, and therefore information on pre-injury comorbidity and severity of conditions is subject to significant participant recall bias. Cross-verification of patient medical history with hospital records was initially planned and would have further improved the accuracy of information, however due to the ethical constraints within the study, this was not possible. As measurement of outcomes was only limited to a single assessment after injury, the data can thus only be viewed as a cross-sectional snapshot of the difficulties experienced post-injury. Collection of outcome data from the outset of injury and at different timepoints (e.g. 1, 6, 12, 24 months) would have significantly strengthened the study by providing a longitudinal analysis of symptom experience and changes in QoL across the recovery trajectory. Furthermore, it is also acknowledged that important outcomes such as post-injury functional impairment and psychological functioning were only superficially addressed with the CIRS instrument, which only

measures these aspects as two single items on the scale. Given the importance of these factors on TBI outcome, more detailed information regarding physical function and psychological health using appropriate tools needs to be embedded within the proposed models to improve their predictive ability.

A common limitation encountered in many studies whose sampling frames are based on hospital registries is the high rate of missing or outdated patient information (Shivasabesan et al., 2018). In the current study, this applied to patient contact details that were missing or outdated in a third of participants, thereby leading to difficulties in reaching potential participants. Of concern was the relatively high degree of missing information on brain injury severity (GCS scores) where recorded scores were only available for 70% of all TBI participants, and merely 17% for the orthopaedic group. In some TBI participants in this study, including those who had sustained only orthopaedic injuries, anecdotal evidence during the interview suggested that there was a high possibility that some participants had suffered a TBI, but for whom a GCS score was not recorded in the registry. The high rate of missing GCS data and a lack of post-traumatic amnesia information, meant that brain injury severity was not able to be included as a predictor of outcomes in SEM analyses for TBI patients in Study 2, and represents a notable limitation in this study. The inclusion of this variable would have been important in assessing to what extent TBI severity influences the onset of PCS symptoms and quality of life in the context of comorbidities. The lack of rigour in consistent recording of GCS scores and misdiagnosed TBI cases is a common limitation in many hospital registry systems and is one that needs to be urgently addressed (Moore et al., 2005). In NZ, Feigin et al., (2013) found that the lack of consistent recording of GCS scores is worse in non-hospital cases. In their study it was noted that while 92% of hospitalised TBI cases had their GCS scores recorded at admission, this is in stark contrast with GCS scores available for cases at family practices and other services, where only 13% of individuals had their GCS scores recorded. Crucially, the lack of GCS data has implications for accurate diagnosis resulting in potentially misdiagnosed patients being excluded from receiving timely and appropriate clinical treatment for their injuries (Stratton, 2018).

Based on available injury details including both GCS and ISS measures in this study, the majority of both TBI and orthopaedic injuries had relatively mild injuries, and caution needs to be exercised when generalising the present findings to more moderate and severely injured individuals, who are likely to present with worse outcomes after

injuries. Furthermore, it should be noted that all injury cases and controls were recruited from hospitalisations recorded in the registry, which excludes individuals who either do not present to hospital or are only seen at the emergency department. In fact, a NZ population-based study in the Waikato region found that in the recruitment of TBI cases, hospitalisations only capture about two thirds of all TBI cases (for mild TBI, as well as for moderate and severe TBI). It also noted that 8% of cases present to family physician practices, and almost a third of cases can only be identified from others sources such as accident and medical clinics, compensation claims databases and self-referrals (Feigin et al., 2013). As both TBI and orthopaedic injuries in this study were based on hospitalisations, it is likely that the sample represents more 'complicated' injuries who may differ in symptom presentation than 'uncomplicated' mild injuries that do not present to hospital (Barker-Collo & Feigin, 2009).

Lastly, in more general terms it is also important to acknowledge the biases and challenges inherent in different data collection methods that may affect results. The shift from traditional formats of collecting information, such as through in-person assessment to other means such as web-based interview/questionnaire or telephone interviewing, has provided several advantages to researchers. The advantages offered by telephone interviews such as easy accessibility of participants across a wide geographical region, reduced time and travel costs, improvements in response rates and reduced missing responses (Feveile et al., 2007), provided a strong rationale for selecting telephone interviewing as the most feasible method of obtaining data for this study, albeit with some limitations which are addressed below.

One of the most notable limitations when conducting telephone interviews is the impact of response burden when interviewing participants who had experienced a TBI or who are of older age. *Response burden* refers to the difficulty involved in taking part in lengthy questionnaires and is particularly a challenge when conducting telephone assessments with participants who have reduced cognitive skills (Rolstad et al., 2011). For instance, participants in this study were required to pay close attention to the questions and response options spoken to them over the telephone, which required a certain level of mental effort to be sustained for an average 30–45 minute telephone questionnaire. Specific care thus needs to be taken to ensure that participant fatigue is minimised especially in participants dealing with the cognitive effects of TBI. Another bias in telephone interviews is the occurrence of *primacy* and *recency* effects, where the former refers to the tendency of respondents in being more likely to choose the first

response option presented to them, while the latter occurs when respondents are likely to recall (and therefore endorse) the last option read to them. In a study, Bowling (2005) found that the tendency for response order effects is more prevalent in telephone research which can lead to skewed results, given that subjects are asked to remember not only the question being asked, but also the different corresponding response options. A meta-analysis by Knauper (1999) revealed that recency effects were also more prominent in those aged 65 years and above, possibly as a result of cognitive changes that occur naturally with ageing. A more appropriate format for interviewing such participants may be to consider self-administered web-based questionnaires, or face-to-face assessments as alternative formats, where participants are able to complete the questionnaire at their own pace.

The difficulties of acquiring sensitive medical information through telephone interviewing presented a significant challenge to this study, as some participants perceived this as an intrusive procedure. This may have subsequently affected response rates in the study. The phenomenon of *social desirability bias* is also a possible limitation and refers to the tendency for survey respondents to report the most socially favourable response (Phillips & Clancy, 1972). This type of bias is known to occur in face-to-face surveys where there is a direct relationship between the interviewer and interviewee, although it can also occur in telephone research. In a comparative study, Holbrook et al. (2003) in fact found the converse to be true—that telephone respondents appear more sceptical about the interview process and are more likely to give socially desirable answers than face-to-face interviewees. For surveys on self-reported health, postal surveys offer the advantage of anonymity due the absence of an interviewer, and as such may more accurately capture self-reported health. Specifically, in the reporting of postconcussive symptoms some researchers have suggested that the method of interviewing has the potential to influence the number and type of self-reported symptoms. Villemure et al. (2011) found that participants reported fewer symptoms when asked to freely identify current symptoms than when they were given a standardised checklist of the most common PCS symptoms such as on the RPQ. This bias may be reinforcing the notion of *expectation bias* of symptoms, where TBI participants expect to experience certain symptoms as a result of their injury (Mittenberg et al., 1992). Expectation bias in combination with the “good old days bias”, where individuals, particularly those have had injuries, tend to view themselves

as being healthier and having less health problems in the past, can thus have a significant influence on symptom reporting (Iverson et al., 2010).

9.4 Conclusion and directions for future research

The current PhD study has made some notable contributions to outcome research and to the current limited understanding of the influence of comorbidities on outcomes after injuries. These findings serve as a foundation on which future studies can explore and build on existing knowledge. Replication of this study using larger sample sizes is key to achieving external validity of the findings presented here. Further study is needed to understand the impact of comorbidities in the more severely injured participants such as those with moderate or severe TBI, and TBI patients with extracranial injuries who may present with worse outcomes. To the candidate's knowledge, this thesis is to date the only study to have demonstrated that the RPQ can be used as a unidimensional measure of long-term PCS symptoms in TBI and orthopaedic patients alike, and which also correctly allows for the calculation of total scores using the ordinal-to-interval conversions provided within. Thus, the calculation of total scores may serve as a starting point for future development of cut-off total scores for determining clinical thresholds of PCS symptoms and diagnostic validity of the RPQ. However, this remains a challenge as evaluating the sensitivity and specificity of the scale requires there to be consensus on a gold standard of diagnosis for PCS, which to date still remains a heavily-debated topic. While studies have acknowledged the presence of PCS symptoms in other populations, further validation of the instrument is needed to ascertain its usability in other non-TBI samples, such as in the healthy population. This includes exploring the dimensionality of PCS in TBI and non-TBI groups in the short to medium term phases of injury recovery, and analysing longitudinal changes with the application of modern techniques such as Generalisability theory. Validation of the RPQ in severely injured samples, with DIF comparisons between mild and moderate/severe injury groups may be useful in evaluating the performance of instruments in the severely injured population. Findings from this thesis also confirmed the versatility of the WHOQoL-BREF as a generic QoL instrument that maintains strong performance across diverse contexts, that includes the injury population. Further work is however recommended for the shorter WHOQoL-5, which, in its current format falls below acceptable standards. A similar conclusion is drawn for the use of the CIRS, which serves its purpose as a comorbidity index, but requires further scrutiny into the reliability of the scale.

To conclude, the findings presented in this thesis have made valuable contributions to outcome research and existing knowledge on recovery after TBI and orthopaedic injuries. Importantly, this thesis acknowledges that understanding of the injury recovery journey should be approached holistically with a focus on factors in different phases of injury, especially with regards to the influence of premorbid and post-injury comorbidities in the presentation of symptoms, and impact on quality of life. It is hoped that using the suggestions provided in this thesis, future studies may be able to replicate and improve on current efforts of this research.

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Appendices

Appendix 1. Health and Disability Ethics Committee approval

Health and Disability Ethics Committees

Health and Disability Ethics Committees
Ministry of Health
Freyberg Building
20 Aitken Street
PO Box 5013
Wellington
6011

0800 4 ETHICS
hdecs@moh.govt.nz

17 December 2015

Miss Shivanthi Balalla
[redacted]
Northcote
Auckland 0627

Dear Miss Balalla

Re:	**Ethics ref:**	**15/NTA/173**
	Study title:	Impact of comorbidities on long-term recovery after traumatic brain injury

I am pleased to advise that this application has been *approved* by the Northern A Health and Disability Ethics Committee. This decision was made through the HDEC-Full Review pathway.

Conditions of HDEC approval

HDEC approval for this study is subject to the following conditions being met prior to the commencement of the study in New Zealand. It is your responsibility, and that of the study's sponsor, to ensure that these conditions are met. No further review by the Northern A Health and Disability Ethics Committee is required.

Standard conditions:

1. Before the study commences at *any* locality in New Zealand, all relevant regulatory approvals must be obtained.

2. Before the study commences at *a given* locality in New Zealand, it must be authorised by that locality in Online Forms. Locality authorisation confirms that the locality is suitable for the safe and effective conduct of the study, and that local research governance issues have been addressed.

After HDEC review

Please refer to the *Standard Operating Procedures for Health and Disability Ethics Committees* (available on www.ethics.health.govt.nz) for HDEC requirements relating to amendments and other post-approval processes.

Your next progress report is due by **19 December 2016.**

Participant access to ACC

The Northern A Health and Disability Ethics Committee is satisfied that your study is not a clinical trial that is to be conducted principally for the benefit of the manufacturer or distributor of the medicine or item being trialled. Participants injured as a result of treatment received as part of your study may therefore be eligible for publicly-funded compensation through the Accident Compensation Corporation (ACC).

Please don't hesitate to contact the HDEC secretariat for further information. We wish you all the best for your study.

Yours sincerely,

BJ Fergus

Dr Brian Fergus
Chairperson
Northern A Health and Disability Ethics Committee

Encl: appendix A: documents submitted
appendix B: statement of compliance and list of members

Appendix 2. Waikato District Health Board ethics approval

Waikato DHB Approval of Research

RD015127	Impact of comorbidities on long term injuries (Medical Conditions and Injuries)

Project Personnel

Principal Investigator:	Shivanthi Balalla Auckland University of Technology +64 9 921 9999 ext 7654 sbalalla@aut.ac.nz
Waikato DHB investigators:	Mr Grant Christey Grant.christey@waikatodhb.health.nz +64 7 839 8899
Primary contact name and details:	Shivanthi Balalla National Institute for Stroke and Applied Neurosciences AA254C, 90 Akoranga Drive, Northcote, Auckland 0627 School of Public Health and Psychosocial Studies Faculty of Health and Environmental Sciences Auckland University of Technology, North Shore Campus
Date Submitted:	01/12/2015
Type of Project:	Observational: quantitative/epidemiological
Multisite?	Not a multi-centre project
Department:	Trauma Registry
Service:	Surgical Services

Project Description:

Start: 01/03/2016
End: 31/12/2017
Sample Size: 800

Traumatic Brain Injury (TBI) has been found to affect up to 790 people per 100,000 in New Zealand every year. Previous research has highlighted a wide array of poor physical, emotional, cognitive and behavioural outcomes associated with TBI. However it is poorly understood whether the roles of pre-injury medical conditions, and concomitant injuries (additional physical injuries) sustained alongside a TBI potentially affects recovery. There is

also a lack of understanding on the likely increased risks of developing subsequent medical conditions in the TBI population. This PhD aims to investigate whether a) pre-injury medical conditions, and b) the existence of concomitant injuries affects recovery outcomes after TBI. The study also aims to investigate whether c) TBI patients are at increased risk of developing other medical conditions after injuries.

To answer the research questions a longitudinal study assessing recovery in a TBI population and people who have sustained an orthopaedic injury as a comparison group within the Waikato region will be conducted. This study will involve a cross sectional study of TBI participants to answer questions a) and b) and a case-control study (cases and controls being TBI and orthopaedic participants, respectively) will be used to answer question c. It is hoped that results arising from this PhD study will address current gaps in the understanding of factors affecting recovery after TBI. Importantly, a greater understanding of pre-injury, concomitant and post-injury factors affecting recovery after a TBI will enable health professionals to implement management guidelines to target optimal recovery for TBI patients with specific conditions. Therefore this PhD will add a unique contribution to understanding the role of pre-injury and post-injury factors in the recovery from brain injuries to assist in intervention planning post-TBI.

Access to Trauma registry and patient files will be required.

Management and Resource Sign-offs

This study requires HDEC review.

Locality Review – *the undersigned agree to the following statements:*

- The study protocol and methodology are ethical and scientifically sound.
- The local lead investigator is suitably qualified, experienced, registered and indemnified.
- Resources, facilities and staff are available to conduct this study, including access to interpreters if requested.
- Cultural consultations have occurred or will be undertaken as appropriate
- Appropriate confidentiality provisions have been planned for.
- Appropriate arrangements are in place to notify other relevant local health or social care staff about the study, and for making available any extra support that might be required by participants. (HDEC SOPs under Locality Authorisation requirements Section 10).
- Conducting this research will have no adverse effect on the provision of publicly funded healthcare.
- There is a stated intent that the results of the study will be disseminated and where practical and appropriate the findings of the study will be translated into evidence based care.

Queries about this research must be made to the Primary Contact person listed.

Dept/Service/ Org	Role	Name (print clearly)	Signature	Date signed
Surgical Services	Head of Surgery	Chris Holdaway	C Holdaway	25/1/16
Surgical & Critical Care	Director	Kevin Harris		22/1/16
Te Puna Oranga	Service Development Manager	Millie Berryman	See attached letter.	17/12/2015

Clinical Support Services Sign-offs

CROSS OUT/ADD SIGN-OFFS APPLICABLE TO THIS PROJECT

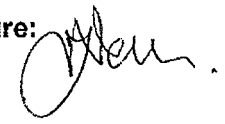
SIGNATORIES DECLARATION: We agree that appropriate resources are available in our service to support this project

Clinical Support Service	Name (print clearly)	Signature	Date signed
DHB Pharmacy	Rajan Ragupathy	N/A	
Laboratory	Kay Stockman	N/A	
Radiology	Dr Muthu	N/A	
Medical Records	Marilyn Hunt	MHunt	19/1/16.

Spoken to Shivanthi & explained that she needs to pull the 500 records — we will show her how to do it. MH

Please return to the Research Office (via Sarah Brodnax, 218A Pembroke Street) along with required documents as identified in the checklist for final approval.

Office use only:
Quality & Patient Safety, Waikato DHB

Signature:  **Date:** 26/1/16.

Name: Mo Neville
Director
Quality & Patient Safety

Position:

Appendix 3. Waikato District Health Board access to registry data form

Waikato District Health Board

recruitment service

Access to Information Declaration:

Obligations for Employees, External Personnel, Volunteers, Students, Temps, Contractors and Locums
Waikato District Health Board (Waikato DHB) recognises the valuable, sensitive and confidential nature of the information on its computer system and hospital files. This information is protected by the law, ethical standards and Waikato DHB policies.

Such information may include:
- Information relating to individual health and/or disability and his or her treatment,
- Personnel information (such as salaries, employment records, disciplinary actions, etc,)
- Information relating to governance management and administration (such as financial and statistical records, strategic plans, internal reports, memos, contracts, peer review information, communications and passwords).
- Third party information (such as computer programmes, client and vendor propriety information, source code, propriety technology, etc).

The purpose of this document is to help you understand your obligations and responsibilities in using and managing such information.

Access and Use of Information
As part of your employment, voluntary or learning activities you are entitled to access relevant information on a "need to know" basis. Further, you may only access and use this information consistent with the purposes for which it was obtained and consistent with your role as an employee, volunteer, student, temp, contractor or locum within Waikato DHB.

You are responsible for safely managing the information consistently with the law, ethical standards and Waikato DHB policy.

Misuse of Access Right and Information
If you access or use information for purposes:
- Not associated with your role; or
- Inconsistent with the purposes for which the information was collected (without obtaining specific consent).

You may be:
- Denied access to Waikato DHB information; and/or
- Subject to disciplinary action, including termination of employment.

This is in addition to any action which may brought under the law or by your professional body.

Misuse of information
You must advise the Waikato DHB person to whom you usually report or, if appropriate, a more senior Waikato DHB manager or supervisor, of any activities by any individual or entity that you suspect may have accessed or used information outside the scope of these obligations.

Continuation of access rights
Your access privileges to Waikato DHB information are subject to periodic review, revision and if appropriate renewal.

Your access to the Waikato DHB information systems will be audited daily. Any access or information you place or record in the Waikato DHB operated system may be subject to review.

Waikato DHB may at any time, including without notice, revoke your access code(s), other authorisation(s), or access to information.

please turn over

Your Confirmations

You confirm that:

- Your signature below and/or your access and use of the information indicates your agreement to and acceptance of your responsibilities regarding the safe management of Waikato DHB information.
- You have no rights or ownership interest in any information referred to in this document.
- Your obligations will continue after termination of your role as an employee/volunteer/student/temp/contractor/locum.
- The information accessed through all Waikato DHB information systems contains valuable, sensitive and confidential patient care, business, financial and hospital employee information, and that you will not disclose that information other than to those authorised to recieve it.

You undertake:

- To only access information which you have a need to know in your role with Waikato DHB.
- Not to in any way divulge, copy, release, sell, loan, review, alter or destroy any information except as properly authorised within the scope of your activities as an employee/volunteer/student/temp/contractor/locum with Waikato DHB.
- Not to misuse information or carelessly manage information.
- Not to knowingly include or cause to be included in any record or report, a false, inaccurate, or misleading entry.
- Not to divulge any information without proper authority to do so, and in particular any information which identifies a patient or person in the care of Waikato DHB.
- Not to seek personal benefit or permit others to benefit personally through the use of any information or equipment available through your work as an employee/volunteer/student/temp/contractor/locum at Waikato DHB.
- To only use information and Waikato DHB equipment strictly for Waikato DHB work purposes.
- To only use information for the purpose it was collected unless you have explicit consent.
- Not to make unauthorised copies of software or allow unauthorised persons to access software.
- To comply with all software and other licence and access terms imposed on Waikato DHB, and not to cause Waikato DHB to breach those terms.
- To follow the procedures established to manage the use of any information system.
- To comply with the requirements of the Copyright Act (available through the Waikato DHB library).
- To safeguard accidental or inadvertent disclosure any access code(s) or other information necessary for authorised access to information.
- Not to deliberately disclose such codes or information except as authorised by Waikato DHB.
- Not to attempt to overcome, bypass, or make inoperable any security measure that Waikato DHB implements to safeguard information or computing resources.

By signing this, I agree that I have read, understand and will comply with these obligations.

Signature Balalla

Printed Full Name SHIVANTHI KUMARI BALALLA

Date 03/12/2015

Witness Signature A Meadows

Printed Full Name of Witness ALICE MAY MEADOWS

Contact Number 09 921 9999 x 7805

Appendix 4. Waikato District Health Board Māori Consultation Research Review Committee approval

Te Puna Oranga Māori Consultation Research Review Committee
TPOMCRRC

17 December 2015
Shivanthi Balalla
Re: Māori Consultation for "Impact of comorbidities on long term injuries"

Tēnā Koe Shivanthi,

Thank you for submitting the above research proposal to the Waikato DHB Te Puna Oranga Māori Health Research Committee for Māori consultation.

The Committee has reviewed the research application form and acknowledges the effort you have taken to consult with and include Māori in this research to improve health outcomes for Māori and to reduce inequalities.

1. The Committee acknowledges the research team for collecting ethnicity data as part of a demographic background of the participant. Ethnicity is an important determinant of health independent of age and socio –economic position.

2. The Committee acknowledges the research application has not identified inequalities in this area however monitoring health care by ethnicity supports inequality reduction.

3. The Committee encourages the research team to aim to actively recruit equal numbers of Māori and Non Māori participants in this research, which is more likely to contribute to the reduction of health inequalities for Māori. The Māori participants would require sufficient face to face time with the researchers for informed consent to participate in the research. Inclusion of the whānau of the Māori participant can be encouraged for fully informed consent.

4. The Committee acknowledges the researcher for the effort that the researcher will take to fully inform the Māori participants regarding the detail of the tissue collection. If cultural issues arise for the Māori participant during this research, they will inform the research team during the study that cultural issues have arisen. Cultural issues may not be obvious to the participant or the researcher prior to starting the research.

5. The Committee acknowledges the time and effort that the research team will take to fully engage and communicate with Māori participants and their whānau in an effort to contribute to reducing inequalities for Māori and improving health outcomes.

6. The Committee encourages the research team to continue to consult with Te Puna Oranga, Māori Health service, should they have any further queries.

Millie Berryman
Pou Whakahaere
Te Puna Oranga-Maori Health Service
Millie.Berryman@waikatodhb.health.nz

Appendix 5. Auckland University of Technology Ethics Committee approval

AUTEC Secretariat

Auckland University of Technology
D-88, WU406 Level 4 WU Building City Campus
T: +64 9 921 9999 ext. 8316
E: ethics@aut.ac.nz
www.aut.ac.nz/researchethics

1 December 2015

Alice Theadom
Faculty of Health and Environmental Sciences

Dear Alice

Ethics Application: **15/454 Impact of medical comorbidities on long term recovery after injury.**

Thank you for submitting your application for ethical review to the Auckland University of Technology Ethics Committee (AUTEC). I am pleased to confirm that your ethics application has been approved for three years until 30 November 2018.

As part of the ethics approval process, you are required to submit the following to AUTEC:

- A brief annual progress report using form EA2, which is available online through http://www.aut.ac.nz/researchethics. When necessary this form may also be used to request an extension of the approval at least one month prior to its expiry on 30 November 2018;
- A brief report on the status of the project using form EA3, which is available online through http://www.aut.ac.nz/researchethics. This report is to be submitted either when the approval expires on 30 November 2018 or on completion of the project;

It is a condition of approval that AUTEC is notified of any adverse events or if the research does not commence. AUTEC approval needs to be sought for any alteration to the research, including any alteration of or addition to any documents that are provided to participants. You are responsible for ensuring that research undertaken under this approval occurs within the parameters outlined in the approved application.

AUTEC grants ethical approval only. If you require management approval from an institution or organisation for your research, then you will need to obtain this. If your research is undertaken within a jurisdiction outside New Zealand, you will need to make the arrangements necessary to meet the legal and ethical requirements that apply there.

To enable us to provide you with efficient service, we ask that you use the application number and study title in all correspondence with us. If you have any enquiries about this application, or anything else, please do contact us at ethics@aut.ac.nz.

All the very best with your research,

Kate O'Connor
Executive Secretary
Auckland University of Technology Ethics Committee

Cc: Shivanthi Balalla sbalalla@aut.ac.nz

Appendix 6. Study participant information sheet

MIDLAND TRAUMA SYSTEM

AUT

Participant Information Sheet

Study title:	***Medical conditions and injuries***		
Locality:	**Auckland, New Zealand**	Ethics committee ref.:	**15/NTA/173**
Lead investigator:	**Shivanthi Balalla**	Contact phone number:	**+64 9 921 9999 ex 7654**

You are invited to take part in a study that is looking at how other medical conditions may have affected recovery after injury. We will also be looking at the conditions people may go on to develop after their injury. Whether or not you take part is your choice. If you don't want to take part, you don't have to give a reason, and it won't affect the care you receive. If you do want to take part now, but change your mind later, you can pull out of the study at any time.

This Participant Information Sheet will help you decide if you'd like to take part. It sets out why we are doing the study, what your participation would involve, what the benefits and risks to you might be, and what would happen after the study ends. We will go through this information with you and answer any questions you may have. You do not have to decide today whether or not you will participate in this study. Before you decide you may want to talk about the study with other people, such as family, whānau, friends, or healthcare providers. Please feel free to do this.

Once you have had some time to read and understand the information on the sheet, you will be contacted after 1 week by a researcher by telephone who will ask about your interest in taking part in this study. If you agree to take part in this study, you will be asked to provide agreement over the phone which will be audio-taped as a part of ethics requirements. This copy of both the Participant Information Sheet and the Consent Form are for you to keep.

This document is 6 pages long, including the Consent Form. Please make sure you have read and understood all the pages.

WHAT IS THE PURPOSE OF THE STUDY?

I am a PhD student at Auckland University of Technology (AUT) and I am working with the trauma registry team at Waikato Hospital. I am investigating how other medical conditions may be linked to recovery from injury as part of my PhD.
This study aims to investigate:

a) How any health conditions you had before your injury might affect your recovery afterwards.
b) How different injuries and their severity might affect your recovery afterwards.
c) How experiencing your injury may affect your risk of developing other health conditions afterwards.

There is very little information available on how medical conditions affect individuals who have had injuries, in recovering from ongoing symptoms and how they affect their quality of life afterwards. Yet we know that many people have other medical conditions. It is important for us to understand your views about how your injury has affected your life and what other medical conditions you may have and when you developed them. This information will allow health professionals (such as doctors, nurses, physiotherapists, psychologists and support workers) to improve early treatment and long-term support care to help people cope with life after having an injury.

This study will be carried out as a part of a PhD degree at AUT and is funded by the University. This study has been approved by the Health and Disability Ethics Committee (ref 15/NTA/173).

If you have any questions about the study please contact the primary investigator:

Shivanthi Balalla
Phone: (+64) 9 921 9999 extension 7654
Email: sbalalla@aut.ac.nz

WHAT WILL MY PARTICIPATION IN THE STUDY INVOLVE?

Hospital records at the Waikato Hospital show that you experienced an injury and went to the hospital for treatment between 1st January 2012 and 31st December 2014. I am interested in finding out how you are doing after your injury and to ask about other medical conditions you have and when you developed them. Approximately 800 participants who have had injuries are expected to be interviewed for this study.

After 1 week of you receiving this information sheet, a researcher will get in touch with you to give you the opportunity to ask any questions you may have about the study and to see if you would like to take part. If you would like to take part, a suitable time will be arranged with you to talk to a researcher. Your agreement to take part in the study will be recorded over the phone.

During the telephone interview, you will be asked questions about any medical conditions you had before your injuries or that you have since developed. You will also be asked about any ongoing symptoms and your overall quality of life since your injuries. The researcher will also ask you to confirm your details such as your name, date of birth, gender, ethnicity, education, marital status and contact details. This interview is estimated to take no longer than 30 minutes. You will be able to have support people with you during the interview. If you prefer, you can complete the assessment over multiple sessions, or in person if you would find it difficult to complete the interview over the phone. As part of the study we will also ask for your permission to access your medical history from medical records.

Data collection for this study is aimed to be completed by December 2016.

MIDLAND TRAUMA SYSTEM

AUT

WHAT ARE THE POSSIBLE BENEFITS AND RISKS OF THIS STUDY?

Some people find it helpful to talk about their experience after injury. Your views on your recovery from your injury will help us to understand if you are experiencing any ongoing difficulties, and if you would benefit from additional support from community services such as physiotherapy, GP services, mental health services, employment support services etc.
There are no known risks caused by this study, however you may find it uncomfortable to answer some questions or you may feel embarrassment. You do not have to answer any questions you do not wish to do so.
Your usual medical care will not be affected in any way by taking part in the study, or withdrawing from the study at any stage. You will be able to continue with any medical treatments you are receiving. Your participation in this study will be stopped if you experience any harmful effects or if the doctor feels it is not in your best interests to continue.

WHO PAYS FOR THE STUDY?

There should be no direct costs to you in taking part in this study. If for some reason you are unable to complete the telephone assessment, you have the option of completing the assessment in-person with a researcher at your home or other accessible location.
As appreciation of your time in taking part in this study, your details will be put in a draw of 10 prizes of vouchers, worth $100 each.

WHAT IF SOMETHING GOES WRONG?

It is unlikely you will be at risk of harm from taking part in this study. If something goes wrong please contact the primary investigator (Shivanthi Balalla) as soon as possible on (+64) 9 921 9999 extension 7654.

WHAT ARE MY RIGHTS?

Your choice to participate in this study is entirely your choice and you will be able to withdraw from the study at any stage. Your choice to withdraw won't affect you in any negative way, or affect any access to health care services now or in the future.
All data that is collected will be treated with strict confidentiality. Any personal information collected for this study will be stored separately in a lockable, secure cabinet and only be accessed by the primary investigator and the supervisor (contact details on page 4). Any results published using this data will be removed of any information such as your name and contact details that could identify you. You will be able to access your information collected as part of the study if you wish to do so. The primary investigator will contact you to let you know if any new information about negative or beneficial effects related to the study become available during the study that may have an impact on your health.

WHAT HAPPENS AFTER THE STUDY OR IF I CHANGE MY MIND?

After the study has been completed your records will be stored for 16 years in a locked cabinet at AUT University in Auckland by the primary investigator. All computer records will

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be password protected. Any identifying information will not be shared outside of the research team without your permission first. After 16 years all electronic information will be deleted and destroyed.

If at any point you decide to withdraw from the study please let the primary investigator know as soon as possible. No information will be shared beyond the hospital trauma registry without your permission.

If you would like a summary of the results from this study, these will be sent to you after data has been collected and analysed in early 2017. We will not be able to give individual clinical advice on whether medical conditions affect injuries and vice versa. If you would like to receive a copy of the results, the findings will be reported at a group level.

WHO DO I CONTACT FOR MORE INFORMATION OR IF I HAVE CONCERNS?

If you have any questions, concerns or complaints about the study at any stage, you can contact:

Shivanthi Balalla, PhD student (Primary Investigator)
Telephone: (+64) 9 921 9999 extension 7654
Email: sbalalla@aut.ac.nz

Dr Alice Theadom, PhD supervisor
Senior Research Fellow
Telephone: (+64) 9 921 9999 extension 7805

If you want to talk to someone who isn't involved with the study, you can contact an independent health and disability advocate on:

Phone: 0800 555 050
Fax: 0800 2 SUPPORT (0800 2787 7678)
Email: advocacy@hdc.org.nz

For Māori health support please contact:

Te Puna Oranga (Waikato DHB Māori Health Unit),
Hockin Building, Level 1, Pembroke St, P.O.Box 934, Hamilton.
Phone: 07 834 3644.
Fax: 07 834 3619.

You can also contact the health and disability ethics committee (HDEC) that approved this study on:

Phone: 0800 4 ETHICS
Email: hdecs@moh.govt.nz

Please keep this for your information.
Thank you for interest in this study

Appendix 7. Participant consent form

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Consent Form

If you need an INTERPRETER, please let us know

Please tick to indicate you consent to the following

I have read, or have had read to me in my first language, and I understand the Participant Information Sheet.	Yes ☐
I have been given sufficient time to consider whether or not to participate in this study.	Yes ☐
I have had the opportunity to use a legal representative, whanau/ family support or a friend to help me ask questions and understand the study.	Yes ☐
I am satisfied with the answers I have been given regarding the study and I have a copy of this consent form and information sheet.	Yes ☐
I understand that taking part in this study is voluntary (my choice) and that I may withdraw from the study at any time without this affecting my medical care.	Yes ☐
I consent to the research staff collecting and processing my information (including tape-recording verbal consent), including information about my health.	Yes ☐
If I decide to withdraw from the study, I agree that the information collected about me up to the point when I withdraw may continue to be processed.	Yes ☐ No ☐
I consent to my GP or current provider being informed about my participation in the study and of any significant abnormal results obtained during the study.	Yes ☐
I agree to an approved auditor appointed by the New Zealand Health and Disability Ethic Committees, or any relevant regulatory authority or their approved representative reviewing my relevant medical records for the sole purpose of checking the accuracy of the information recorded for the study.	Yes ☐
I understand that my participation in this study is confidential and that no material, which could identify me personally, will be used in any reports on this study.	Yes ☐
I know who to contact if I have any questions about the study in general.	Yes ☐
I understand my responsibilities as a study participant.	Yes ☐
I wish to receive a summary of the results from the study.	Yes ☐ No ☐

Declaration by participant:
I hereby consent to take part in this study. I agree to my consent being audio-taped.

Participant's name: _____

Signature: _____ Date: _____

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Declaration by member of research team:

I have given a verbal explanation of the research project to the participant, and have answered the participant's questions about it.

I believe that the participant understands the study and has given informed consent to participate.

Researcher's name: _____

Signature: _____ Date: _____

Appendix 8. Study questionnaire comprising of demographic questions (page 1), the Cumulative Illness Rating Scale (page 2), the Rivermead Postconcussion Questionnaire (page 3) and the WHO Quality of Life BREF (pages 4-6)

Study registration number: **Participant Initials:** **Researcher Initials:**

General questions

Date of Birth:	_____(DD)_____(MM)_____(YYYY)		
Gender (circle one):	Male	Female	
Area of residence (circle one):	Resident of Hamilton	Resident of Waikato	Other:_____
Ethnic identity (circle **all** that apply):	New Zealand European	Māori	Samoan
	Cook Island Maori	Tongan	Niuean
	Chinese	Indian	
	Other (please specify)_____		
Highest education received (circle one):	Primary School	High School	
	Polytechnic/ College	University	
Current marital status (circle one):	Married/ Civil Union / De Facto		Separated/ Divorced / Widowed
	Never Married (Single)		Unknown

Study registration number: **Participant Initials:** **Researcher Initials:**

Cumulative Illness Rating Scale Questionnaire

Each system is rated as follows:

0 = No problem affecting that system; or past problem without clinical relevance

1 = Current mild problem / past significant problem

2 = Moderate disability or morbidity / requires first line therapy

3 = Severe problem / constant and significant disability / hard to control chronic problems (complex therapeutic regimen).

4 = Extremely severe problem / immediate treatment required / organ failure / severe functional impairment

	Comorbidities	Pre-injury score	Post-injury score
Item 1	Cardiac (heart only)		
Item 2	Hypertension (rating is based on severity; organ damage is rated separately)		
Item 3	Vascular (blood, blood vessels and cells, marrow, spleen, lymphatics)		
Item 4	Respiratory (lungs, bronchi, trachea below the larynx)		
Item 5	EENT (eye, ear, nose, throat, larynx)		
Item 6	Upper GI (esophagus, stomach, duodenum, biliary and pancreatic trees; do not include diabetes)		
Item 7	Lower GI (intestines, hernias)		
Item 8	Hepatic (liver and biliary tree)		
Item 9	Renal (kidneys only)		
Item 10	Other GU (ureters, bladder, urethra, prostate, genitals)		
Item 11	Musculo-skeletal-integumentary (muscles, bone, skin)		
Item 12	Neurological (brain, spinal cord, nerves; do not include dementia)		
Item 13	Endocrine-Metabolic (includes diabetes, thyroid, breast, systemic infections, toxicity)		
Item 14	Psychiatric/Behavioral (includes depression, anxiety, agitation, psychosis, not dementia).		

TOTAL NUMBER CATEGORIES ENDORSED.....

TOTAL SCORE.....

Severity Index: (Total score/total number of categories endorsed).....

Number of categories at Level 3 severity.....

Number of categories at Level 4 severity.....

Study registration number: **Participant Initials:** **Researcher Initials:**

The Rivermead Post-Concussion Symptoms Questionnaire

After a head injury or accident some people experience symptoms which can cause worry or nuisance. We would like to know if you now suffer from any of the symptoms given below. As many of these symptoms occur normally, we would like you to compare yourself now with before the accident. For each one, please circle the number closest to your answer.

0 = Not experienced at all

1 = No more of a problem

2 = A mild problem

3 = A moderate problem

4 = A severe problem

Compared with before the accident, do you now (i.e., over the last 24 hours) suffer from:

Item 1	Headaches	0	1	2	3	4
Item 2	Feelings of dizziness	0	1	2	3	4
Item 3	Nausea and/or vomiting	0	1	2	3	4
Item 4	Noise sensitivity, easily upset by loud noise	0	1	2	3	4
Item 5	Sleep disturbance	0	1	2	3	4
Item 6	Fatigue, tiring more easily	0	1	2	3	4
Item 7	Being irritable, easily angered	0	1	2	3	4
Item 8	Feeling depressed or tearful	0	1	2	3	4
Item 9	Feeling frustrated or impatient	0	1	2	3	4
Item 10	Forgetfulness, poor memory	0	1	2	3	4
Item 11	Poor concentration	0	1	2	3	4
Item 12	Taking longer to think	0	1	2	3	4
Item 13	Blurred vision	0	1	2	3	4
Item 14	Light sensitivity, easily upset by bright light	0	1	2	3	4
Item 15	Double vision	0	1	2	3	4
Item 16	Restlessness	0	1	2	3	4

Are you experiencing any other difficulties? (Please state and give a score)

Item 17		0	1	2	3	4
Item 18		0	1	2	3	4

Study registration number: **Participant Initials:** **Researcher Initials:**

World Health Organization Quality of Life – BREF

ABOUT YOU

Before you begin we would like to ask you to answer a few general questions about yourself: by circling the correct answer or by filling in the space provided.

What is your **gender**? Male Female

What is you **date of birth**? _____(Day)/ _____(Month)/_____(Year)

What is the highest **education** you received? None at all Primary school

Secondary school Tertiary

What is your **marital status**? Single Separated

Married Divorced

Living as married Widowed

Are you currently **ill**? Yes No

If something is wrong with your health what do you think it is?_____illness/ problem

INSTRUCTIONS

This assessment asks how you feel about your quality of life, health, or other areas of your life. **Please answer all the questions**. If you are unsure about which response to give to a question, **please choose the one** that appears most appropriate. This can often be your first response.

Please keep in mind your standards, hopes, pleasures and concerns. We ask that you think about your life **in the last two weeks**. For example, thinking about the last two weeks, a question might ask:

		Not at all	Not much	Moderately	A great deal	Completely
Example 1	Do you get the kind of support from others that you need?	1	2	3	4	5

You should circle the number that best fits how much support you got from others over the last two weeks. So you would circle the number 4 if you got a great deal of support from others as follows.

You would circle number 1 if you did not get any of the support that you needed from others in the last two weeks.

Please read each question, assess your feelings, and circle the number on the scale for each question that gives the best answer for you.

		Very poor	Poor	Neither poor nor good	Good	Very good
1 (G1)	How would you rate your quality of life?	1	2	3	4	5

Study registration number: Participant Initials: Researcher Initials:

		Very dissatisfied	Dissatisfied	Neither satisfied nor dissatisfied	Satisfied	Very satisfied
2 (G4)	How satisfied are you with your health?	1	2	3	4	5

The following questions ask about <u>how much</u> you have experienced certain things in the last two weeks.

		Not at all	A little	A moderate amount	Very much	An extreme amount
3 (F1.4)	To what extent do you feel that physical pain prevents you from doing what you need to do?	1	2	3	4	5
4 (F11.3)	How much do you need any medical treatment to function in your daily life?	1	2	3	4	5
5 (F4.1)	How much do you enjoy life?	1	2	3	4	5
6 (F24.2)	To what extent do you feel your life to be meaningful?	1	2	3	4	5

		Not at all	A little	A moderate amount	Very much	Extremely
7 (F5.3)	How well are you able to concentrate?	1	2	3	4	5
8 (F16.1)	How safe do you feel in your daily life?	1	2	3	4	5
9 (F22.1)	How healthy is your physical environment	1	2	3	4	5

The following questions ask about <u>how completely</u> you experience or were able to do certain things in the last two weeks.

		Not at all	A little	Moderately	Mostly	Completely
10 (F2.1)	Do you have enough energy for everyday life?	1	2	3	4	5
11 (F7.1)	Are you able to accept your bodily appearance?	1	2	3	4	5
12(F18.1)	Have you enough money to meet your needs?	1	2	3	4	5
13(F20.1)	How available to you is the information that you need in your day-to-day life?	1	2	3	4	5
14(F21.1)	To what extent do you have the opportunity for leisure activities?	1	2	3	4	5

		Very poor	Poor	Neither	Good	Very good
15(F9.1)	How well are you able to get around?	1	2	3	4	5

Study registration number: **Participant Initials:** **Researcher Initials:**

The following questions ask you to say how good or satisfied you have felt about various aspects of your life over the last two weeks.

		Very dissatisfied	Dissatisfied	Neither satisfied nor dissatisfied	Satisfied	Very satisfied
16(F3.3)	How satisfied are you with your sleep?	1	2	3	4	5
17(F10.3)	How satisfied are you with your ability to perform your daily living activities?	1	2	3	4	5
18(F12.4)	How satisfied are you with your capacity for work?	1	2	3	4	5
19(F6.3)	How satisfied are you with yourself?	1	2	3	4	5
20(F13.3)	How satisfied are you with your personal relationships?	1	2	3	4	5
21(F15.3)	How satisfied are you with your sex life?	1	2	3	4	5
22(F14.4)	How satisfied are you with the support you get from your friends?	1	2	3	4	5
23(F17.3)	How satisfied are you with the conditions of your living place?	1	2	3	4	5
24(F19.3)	How satisfied are you with your access to health services?	1	2	3	4	5
25(F23.3)	How satisfied are you with your transport?	1	2	3	4	5

The following question refers to how often you have felt or experienced certain things in the last two weeks.

		Never	Seldom	Quite often	Very often	Always
26(F8.1)	How often do you have negative feelings such as blue mood, despair, anxiety, depression?	1	2	3	4	5

Did someone help you to fill out this form?.....

How long did it take to fill this form out?.....

Do you have any comments about the assessment?

.....

.....

THANK YOU FOR YOUR HELP

DATE COMPLETED_____(DD)_____(MM)_____(YYYY)

Signature_____

Appendix 9. Skewness and kurtosis of variables in the dataset (*n*=223)

Variables	Missing	Mean	Median	SD	Skewness	Std. Error of skewness	Kurtosis	Std. Error of kurtosis
Age, years	0	48.36	51.17	19.645	-0.073	0.163	-1.317	0.324
Time since injury, years	0	2.59	2.53	0.992	0.757	0.163	1.332	0.324
ISS	0	9.90	6.00	8.611	1.345	0.163	1.227	0.324
GCS	129	12.86	14.00	3.481	-1.884	0.249	2.319	0.493
LOS	0	7.58	5.00	7.802	2.716	0.163	10.921	0.324
Pre-cardiac score	0	0.18	0	0.628	3.701	0.163	13.087	0.324
Pre-hypertension score	0	0.27	0	0.697	2.478	0.163	4.906	0.324
Pre-vascular score	0	0.17	0	0.687	4.645	0.163	21.711	0.324
Pre-respiratory score	0	0.11	0	0.381	3.609	0.163	12.991	0.324
Pre-EENT score	0	0.22	0	0.628	3.098	0.163	9.052	0.324
Pre-upper GI score	0	0.12	0	0.454	4.278	0.163	19.46	0.324
Pre-lower GI score	0	0.06	0	0.302	5.516	0.163	30.799	0.324
Pre-hepatic score	0	0.05	0	0.318	9.557	0.163	109.714	0.324
Pre-renal score	0	0.09	0	0.446	6.852	0.163	53.892	0.324
Pre-GU score	0	0.16	0	0.521	3.861	0.163	16.036	0.324
Pre-musc score	0	0.33	0	0.589	1.764	0.163	2.669	0.324
Pre-neuro score	0	0.15	0	0.425	2.986	0.163	8.545	0.324
Pre-endocrine score	0	0.33	0	0.715	2.027	0.163	2.916	0.324
Pre-psych score	0	0.42	0	0.855	1.92	0.163	2.409	0.324
Pre-injury CIRS total score	0	2.65	1	3.542	2.707	0.163	12.245	0.324
Post-cardiac score	0	0.26	0	0.730	2.922	0.163	7.457	0.324

Variables	Missing	Mean	Median	SD	Skewness	Std. Error of skewness	Kurtosis	Std. Error of kurtosis
Post - hypertension score	0	0.33	0	0.769	2.045	0.163	2.640	0.324
Post -vascular score	0	0.20	0	0.733	4.103	0.163	16.746	0.324
Post - respiratory score	0	0.15	0	0.475	3.730	0.163	15.139	0.324
Post -EENT score	0	0.35	0	0.736	2.425	0.163	5.884	0.324
Post -upper GI score	0	0.13	0	0.451	4.096	0.163	18.505	0.324
Post -lower GI score	0	0.10	0	0.383	3.925	0.163	15.131	0.324
Post -hepatic score	0	0.05	0	0.318	9.557	0.163	109.714	0.324
Post -renal score	0	0.09	0	0.450	6.674	0.163	51.653	0.324
Post -GU score	0	0.20	0	0.569	3.245	0.163	10.929	0.324
Post -musc score	0	0.84	1	0.858	0.869	0.163	0.786	0.324
Post -neuro score	0	0.38	0	0.672	1.805	0.163	2.762	0.324
Post-endocrine score	0	0.41	0	0.828	1.798	0.163	1.876	0.324
Post -psych score	0	0.66	0	1.022	1.285	0.163	0.317	0.324
Post-injury CIRS total score	0	4.15	3.00	4.105	2.217	0.163	9.273	0.324
RPQ16 total ord	0	10.95	8.00	9.943	0.978	0.163	0.333	0.324
RPQ16 total interv	0	21.47	22.57	11.915	-0.277	0.163	-0.946	0.324
WHOQoL24 total ord	1	96.89	98.00	14.604	-0.347	0.163	-0.731	0.325
WHOQoL24 total interv	1	83.59	82.70	11.672	0.252	0.163	-0.734	0.325
Physical Domain interv	1	22.86	21.84	4.083	0.540	0.163	-0.414	0.325
Psychological Domain interv	1	23.14	23.21	3.560	0.107	0.163	-0.565	0.325
Social Domain interv	1	10.03	10.43	2.308	-0.367	0.163	-0.831	0.325
Environmental Domain interv	1	27.56	26.94	3.617	0.201	0.163	-0.656	0.325
WHOQol12 total ord	1	48.30	50.00	7.789	-0.556	0.163	-0.469	0.325
WHOQol12 total interv	1	44.19	43.77	6.056	0.635	0.163	0.091	0.325

Appendix 10. RPQ ordinal-to-interval transformed scores

Ordinal	Interval		Ordinal	Interval	
Score	Logits	Scale	Score	Logits	Scale
0	-5.35	0.00	33	0.37	39.68
1	-4.48	6.08	34	0.43	40.11
2	-3.86	10.40	35	0.49	40.53
3	-3.41	13.46	36	0.55	40.95
4	-3.07	15.88	37	0.61	41.36
5	-2.77	17.90	38	0.67	41.77
6	-2.52	19.65	39	0.72	42.16
7	-2.30	21.19	40	0.78	42.56
8	-2.10	22.57	41	0.84	42.95
9	-1.92	23.82	42	0.89	43.33
10	-1.75	24.97	43	0.95	43.71
11	-1.60	26.04	44	1.00	44.08
12	-1.46	27.03	45	1.06	44.46
13	-1.33	27.95	46	1.11	44.83
14	-1.20	28.81	47	1.16	45.19
15	-1.08	29.62	48	1.21	45.55
16	-0.97	30.38	49	1.27	45.92
17	-0.87	31.11	50	1.32	46.30
18	-0.77	31.80	51	1.38	46.69
19	-0.68	32.45	52	1.43	47.07
20	-0.59	33.08	53	1.49	47.49
21	-0.50	33.69	54	1.56	47.93
22	-0.42	34.26	55	1.62	48.41
23	-0.33	34.82	56	1.70	48.93
24	-0.26	35.36	57	1.79	49.52
25	-0.18	35.89	58	1.88	50.21
26	-0.11	36.40	59	2.00	51.03
27	-0.03	36.91	60	2.15	52.05
28	0.04	37.40	61	2.35	53.41
29	0.11	37.87	62	2.63	55.38
30	0.17	38.34	63	3.10	58.64
31	0.24	38.79	64	3.87	64.00
32	0.30	39.24			

Appendix 11. Co-authored works from the PhD thesis

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ORIGINAL RESEARCH

Validation of the WHOQOL-BREF and Shorter Versions Using Rasch Analysis in Traumatic Brain Injury and Orthopedic Populations

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Abstract

Objective: To use Rasch analysis to validate the World Health Organization Quality of Life-BREF (WHOQOL-BREF) and existing short versions in individuals with traumatic brain injury and orthopedic injuries, with comparisons to a general population group.

Design: The Partial Credit Rasch model was applied to evaluate the WHOQOL-BREF as well as shortened versions using a cross-sectional study design.

Setting: Regional hospital, and national electoral sample in New Zealand.

Participants: Individuals with traumatic brain injury (n=74), individuals with orthopedic injuries (n=114), general population (n=140).

Interventions: None.

Main Outcome Measure: WHOQOL-BREF.

Results: The WHOQOL-BREF met expectations of the unidimensional Rasch model and demonstrated good reliability (person separation index [PSI] =0.82) when domain items were combined into physical-psychological, social, and environmental superitems. Analysis of shorter versions, the EUROHIS-QOL-8 and World Health Organization Quality of Life-5 (WHOQOL-5), indicated overall acceptable fit to the Rasch model and evidence of unidimensionality. The EUROHIS-QOL-8 showed good reliability (PSI=0.81); however, reliability of the WHOQOL-5 (PSI=0.68) was below acceptable standards for group comparisons, in addition to demonstrating poor person-item targeting.

Conclusions: The WHOQOL-BREF and the 8-item EUROHIS-QOL-8 version are both reliable and valid in the assessment of quality of life in both injury and general populations. Ordinal-interval conversion tables published for these validated scales as well as for the WHOQOL-5 can be used to improve precision of assessment. The transformation of ordinal scale scores into an interval measure of health-related quality of life also permits the calculation of a single summary score for the WHOQOL-BREF, which will be useful in a wide range of clinical and research contexts. Further validation work of the WHOQOL-5 is needed to ascertain its psychometric properties.

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Injury patients often experience a multitude of difficulties including functional disability,[1,2] poor cognition,[3,4] and psychological distress,[5-8] which can delay return to employment[9,10] and adversely affect health-related quality of life.[8,11-13] One of the challenges inherent in collecting quality of life information from injury participants such as those who have experienced a traumatic brain injury (TBI) is that any presence of impaired cognition and/or mental fatigue is likely to require strenuous effort on the individual to take part in lengthy questionnaires—a phenomenon referred to as 'response burden'.[14] This can present a barrier to routine assessment of patient-reported outcomes and health-related quality of life and provides a rationale for producing briefer scale versions of existing measurement scales.[15] The World Health Organization Quality of Life-BREF (WHOQOL-BREF)[16] is a widely used quality of life questionnaire that has been previously shown to be a valid and reliable health-related quality of life measure in the general population,[17-21] cancer survivors,[22-24] and patients with psychological disorders.[25-27] Previous psychometric evaluation in trauma patients,[28] including head and spinal

Disclosures: none.

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cord injury patients,[29,30] has confirmed good internal consistency, test-retest reliability, and discriminant and convergent validity of the measure; however, the dimensionality of the instrument has not yet been evaluated in this population. Shorter versions such as the EUROHIS-QOL-8[31] and World Health Organization Quality of Life-5 (WHOQOL-5)[32] have also been developed, but their psychometric properties and their clinical use in the injury population has not been assessed to date.

Rasch analysis is a robust modern psychometric method that is part of the family of models based on item-response theory and has been used in the development of many quality of life instruments.[33,34] The underlying principle of the Rasch unidimensional model asserts that the probability of a person passing or endorsing an item is related to (1) the difficulty of an item (item parameter), and (2) how much of a latent trait or construct is held by a person (person parameter), both of which are represented on the same logarithmic interval scale. It therefore follows that the higher the amount of a construct a person has (eg, quality of life), the more likely they will pass (endorse) an item than an individual with a lower level of the construct. Rasch analysis offers detailed information about the performance of individual items, and the ability to evaluate to what extent an item measures the latent trait for individuals of the same ability, of a separate subgroup.[33] The latter is referred to as 'differential item functioning' (DIF). Fundamentally, when a scale has achieved the core criteria of the Rasch model, an ordinal scale can be transformed to an interval-level measure that permits the calculation of total scores and the use of parametric statistics, which would normally be violating statistical assumptions if ordinal scores are used.

The present study is the first to assess the psychometric properties of the WHOQOL-BREF using Rasch analysis within a TBI and orthopedic population compared with the general population. The study also examined the properties of shorter existing versions, namely the EUROHIS-QOL-8[31] and WHOQOL-5.[32] Lastly, we have provided ordinal-to-interval conversion tables to improve precision of scoring and to allow for calculation total interval scores of the scales.

Methods

Participants

Participants with confirmed TBI (n=432) and orthopedic injuries (n=658) aged 16 years and older at time of injury and discharged alive between 2012 and 2016 were recruited from a regional hospital registry in the Waikato region of New Zealand and contacted for follow-up at 0.5-6 years. Injuries were defined according to the Abbreviated Injury Scale 2005 update 2008.[35] A TBI was defined in accordance with the World Health Organization guidelines[7] as an acute brain injury resulting from external physical forces and not due to drugs, alcohol, medications, other injuries or treatment for other injuries (eg, systemic injuries, facial injuries, or intubation), or other problems (eg, psychological trauma, language barrier, or coexisting medical conditions). Any of the following indicators were taken as evidence of a confirmed TBI diagnosis by a trauma specialist: cerebellum injury, hematoma, contusion, diffuse axonal injury, brain swelling, any loss of consciousness, alteration of mental state, or presence of post-traumatic amnesia.

Orthopedic injuries included joint injuries relating to fractures, dislocations, or sprains to the pelvic region and upper and lower extremities. Injuries due to insufficiency fractures (ie, those resulting from physiologic stress on weakened bone), periprosthetic fractures, exertion injuries with no external force, hanging, drowning, asphyxiation, poisoning without evidence of external force, ingestion of foreign bodies, or injuries as a result of a pre-existing medical condition (eg, epilepsy, Parkinson's disease, etc.) were excluded. Participants unable to give consent or with severe injuries (eg, amputations, crushes, severe fractures) were excluded because of the likely presence of significant psychological trauma, as well as to match the mild category of the TBI sample.

Final response rates for both clinical samples (17% per group) yielded n=74 TBI and n=114 orthopedic consenting participants who completed questionnaires via telephone interview administered by a researcher. Clinical injury details and demographic information were obtained from the hospital and cross-verified during the interview. The comparison group of general population residents was a subset (n=140) selected from a national (New Zealand) validation study of the WHOQOL-BREF, where participants had been randomly sampled using the national electoral register and through purposive convenience sampling.[17] Informed consent for the 2 clinical samples was either written or audiotaped. Ethical approval was granted by the national, hospital, and authors' institutional ethics committees.

List of abbreviations:

DIF	**differential item functioning**
HRQOL	**health-related quality of life**
PSI	**person separation index**
TBI	**traumatic brain injury**
WHOQOL-5	**World Health Organization Quality of Life-5**
WHOQOL-BREF	**World Health Organization Quality of Life-BREF**

Outcome measure

The WHOQOL-BREF is a 26-item questionnaire designed to measure quality of life, comprising items on physical, psychological, social, and environmental quality of life domains.[16] Items are rated on a 5-point ordinal scale with higher scores denoting higher quality of life for most items, except for items 3, 4, and 26, which need to be reverse coded prior to data analysis.

Although not asked as separate questions, the data could also be analyzed in terms of shorter existing variations of the WHOQOL-BREF, such as the EUROHIS-QOL 8-item and WHOQOL-5 versions, which were developed as economic screening measures and derived from items within the previous WHOQOL-100 and WHOQOL-BREF.[31,32]

Data analysis

Missing data were approximately 2% and at random fashion. Descriptive statistics were conducted using SPSS version 25.[a] Similar procedures outlined by Lundgren-Nilsson[36] and Medvedev et al[37] were adopted for Rasch analysis. Detailed explanations of Rasch theory for further reading are provided elsewhere.[33,38,39] A likelihood ratio test did not support the use of a Rasch Rating Scale Model ($\chi^2[74]=298.67$; $P<.001$), and thus the polytomous (>2 response options) Partial Credit Rasch model[40] was applied using RUMM2030[41] to test (1) the WHOQOL-BREF items and domains, (2) EUROHIS-QOL-8, and (3) WHOQOL-5 following the procedures outlined in table 1. In line with current

Table 1 Steps of Rasch analyses with descriptions of procedures

Concept Examined	Description of Procedure
Overall Rasch model fit	Overall fit to the Rasch model was evaluated by observing χ^2 statistics for item-trait interaction, item, and person fit residuals. Under ideal fit conditions, item-trait interaction is not significant (Bonferroni adjusted $P>.05$), and means and standard deviations for overall item and person fit residuals are close to 1.00 and 0.00, respectively. Where the χ^2 is significant, it reflects that the hierarchical ordering of items (item difficulty) varies across the trait or construct. Individual items were also scrutinized for performance, with fit residuals within the range of −2.50 to +2.50 indicating acceptable fit to the Rasch model.[38]
Unidimensionality	Unidimensionality was tested for by way of principal component analysis of residuals excluding the latent trait component (Rasch factor) to detect if there are any further remaining associations between items.[38] An independent t test where the percentage of significant t tests beyond ±1.96 CIs is <5% and/or if the lower bound CI of significant tests overlaps the 5% mark, gives supporting evidence that the scale is unidimensional, or measures only 1 construct.[31]
Reliability	The PSI, equivalent to Cronbach's α, gives an indication of scale reliability with ideal values >0.70 that allow for group comparisons and values >0.85 that allow for individual assessment.[38]
Targeting of persons and items	Person-to-item targeting reflects how well targeted a measure is, and ideally the mean location should be centered around 0.00. Positive values suggest that the sample is located at a higher level of the construct, compared with the average of the scale, while the converse would be true for negative values.
DIF	Items were inspected for the presence of DIF, which describes the effect that item performance is not invariant across demographic groups such as age, sex, marital status (single/living as married), health status (well/unwell) at time of interview, and injury/noninjury groups. We have also distinguished between real DIF (or significant DIF) and artificial DIF whereby the latter may occur spuriously as an artefact of the method for detecting DIF.[42] A post hoc sign test of significance[43] gives indication of artificial DIF.
Ordering of response thresholds	The presence of significantly disordered response thresholds (which indicates that item response categories do not work as intended) was examined visually with category probability curves.
Local dependency	As a guide, the pattern of local item dependency (item responses influencing one another) can be examined by looking at values exceeding the margin of ±0.20 of mean residual correlations.[44]
Merging of related items: superitems	Issues concerning DIF, local dependency, and threshold disordering were addressed with the pairing of related items (such as based on their correlations) to create superitems.[45] As per Krägeloh et al, superitems were also created by combining related items belonging to each of the domains: physical, psychological, social, and environmental.[17]

Abbreviation: CI, confidence interval.

recommendations for Rasch analyses,[46] transformation of ordinal to interval-level scores are presented as conversion tables for the WHOQOL-BREF, EUROHIS-QOL-8, and WHOQOL-5 (appendix 1 and 2).

Results

Rasch analysis of the WHOQOL-BREF

Table 2 presents the demographic characteristics of the sample. There were no significant differences across the sample, with the exception of mean time since injury between TBI and orthopedic groups ($P=.015$), and sex ($P=.006$) whereby men were over-represented in the experience of injuries. Glasgow Coma Scale scores were only available in approximately 66% of TBI cases. Head injury participants were predominantly in the mild TBI category (median Glasgow Coma Scale score = 14.00) but had significantly higher injury severity (mean Injury Severity Score=12.68±10.0) than orthopedic participants (mean Injury Severity Score=6.26±6.21; $t[109.93]=4.95$; $P<.001$).

Summary fit statistics for the overall Rasch model fit, PSI, and unidimensionality tests are presented in table 3. Initial analysis that included all 26 items of the WHOQOL-BREF showed overall significant misfit to the Rasch model and lack of unidimensionality (21.49% significant t tests; lower bound confidence interval, 19.25), although scale reliability was already high (PSI=0.92). Similarly, initial analysis with 24 items (excluding anchor items 1 and 2) demonstrated a poor overall fit to the model and lack of unidimensionality but demonstrated excellent reliability. Across domains, the reliability for the physical (PSI=0.78), psychological (PSI=0.77), and environmental (PSI=0.75) components were satisfactory, with the exception of the social domain (PSI=0.57), which was below acceptable.

Table 4 presents the Rasch model statistics for the individual item fit of the initial 24-items analysis. Closer examination of individual items revealed that participants found items 16 (satisfaction with sleep) and 21 (satisfaction with sex life) were the most difficult to score highly in, with fit locations 0.77, SE=0.06 and 0.77, SE=0.05, respectively. The easiest item to score was item 5 (enjoyment of life) with a location of −0.64, SE=0.08. Seven items (3, 4, 5, 17, 19, 21, and 24) showed significant misfit to the Rasch model, with item-fit residuals exceeding the acceptable threshold of ±2.50. Some artificial DIF effects by diagnosis and age were observed across several items. The presence of real DIF (item bias) was seen by age

Table 2 Sample characteristics, shown separately for the TBI sample, the orthopedic sample (labeled here as Ortho), and the general population sample drawn from Krägeloh et al[17] (labeled here as Healthy)

Characteristic	TBI % (n=74)	Ortho % (n=114)	Healthy % (n=140)	Sig†
Sex				
Male	60.8	64.9	45.7	.01*
Female	39.2	35.1	54.3	
Age group				
≤30 y	32.4	36.0	31.6	.18
31-60 y	28.4	30.7	41.9	
>60 y	39.2	33.3	26.5	
Education				
Primary/high school	51.4	43.9	52.1	.21
Polytechnic/university	48.6	56.1	47.9	
Marital status				
Single	49.3	40.7	37.0	.22
Living as married	50.7	59.3	63.0	
Health status				
Unwell	13.5	9.7	13.7	.60
Well	86.5	90.3	86.3	
Time since injury, mean ± SD, y	2.26±1.32	2.66±0.04	-	.02*,‡

NOTE. Health status refers to participant reporting whether feeling well or unwell at time of assessment.

* Denotes statistical significance at $P<.05$.

† Refers to the P value from the results of the χ^2 test for proportions.

‡ t test comparison between TBI and orthopedic groups for time elapsed since injury.

(item 21), sex (item 11), marital status (item 20), and well/unwell groups (item 17). Item responses between items 6, 12, 15, 16, and 21 were correlated and thereby indicated local dependency.

The creation of superitems for the 4 domains in the subsequent step to correct for item misfit, DIF, and local dependency resulted in the best model fit ($\chi^2[36]=35.15$; $P=.51$), achieving strict unidimensionality and strong reliability (PSI=0.84). However, DIF by diagnosis was present for the physical ($F_{2,361}=19.29$; $P<.01$) and psychological ($F_{2,361}=20.16$; $P<.01$) domain superitems. DIF was also observed by age for the physical ($F_{2,361}=15.25$; $P<.01$), psychological ($F_{2,361}=7.52$; $P<.01$), and environmental ($F_{2,361}=25.20$; $P<.01$) domain superitems. According to item fit residuals (see table 3), the superitem representing the social domain was the most readily endorsed (item location −0.05, SE=0.03), and environment was the second easiest domain to endorse (−0.04, SE=0.02). The physical domain was the most difficult domain to score high on (0.10, SE 0.02), followed by the psychological domain (0.00, SE=0.02). Upon inspection of the pattern of local dependency, residual correlations were found between the psychological and physical superitems. After these superitems were combined into a physical-psychological superitem, the data met the assumptions of the Rasch model and achieved strict unidimensionality ($\chi^2[27]=11.35$; $P=.99$) with good reliability (PSI=0.82) and no DIF by diagnosis. While DIF effects by age still remained for the environmental domain superitem ($F_{2,361}=26.71$; $P<.01$), a post hoc sign test indicated that DIF between individual age groups was not significant ($P>.05$). Thus, the final analysis for the WHOQOL-BREF showed no individual item bias (ie, no DIF), and none of

Table 3 Summary of fit statistics for the initial and the final Rasch analyses of existing versions the 26-Item WHOQOL-BREF, 24-item WHOQOL-BREF (excluding anchor items 1 and 2), EUROHIS-QOL-8, and WHOQOL-5 (n=363)

	Item Fit Residual	Person Fit Residual	Goodness of Fit			Significant t Tests (Unidimensionality)	
Analyses	Value ± SD	Value ± SD	X^2 (df)	P Value	PSI	%	Lower Bound CI
WHOQOL-BREF							
Initial (26)	0.22±2.44	-0.20±1.61	449.19 (234)	.00	0.92	21.49	19.25 (No)
Initial (24)*	0.24±2.46	-0.20±1.58	446.95 (216)	.00	0.91	16.25	14.01 (No)
4 Domain superitems	-0.12±2.05	-0.39±1.01	35.49 (36)	.51	0.84	3.86	1.61 (Yes)
Final 3 domain superitems	-0.42±2.52	-0.48±1.00	11.35 (27)	.99	0.82	4.56	2.28 (Yes)
EUROHIS-QOL-8							
Initial/final	0.03±1.76	-0.30±1.12	84.18 (72)	.15	0.81	6.06	3.82 (Yes)
WHOQOL-5							
Initial/final	-0.14±1.37	-0.34±0.98	54.66 (40)	.06	0.68	2.76	0.25 (Yes)

Abbreviation: CI, confidence interval.

* Initial analysis excluding anchor items G1 and G2 of the WHOQOL-BREF.

Table 4 Rasch model fit statistics with item locations, fit residuals, and χ^2 for the 24-Item WHOQOL-BREF before and after creating superitems for domains (n=363)

Item	Location	SE	Fit Resid	χ^2	Prob
3 Extent physical pain prevents what you need to do	0.07	0.06	3.26*	33.20	.00
4 Medical treatment to function in daily life	0.20	0.06	7.25*	118.79	.00
5 How much do you enjoy life	−0.64	0.08	−2.59*	30.06	.00
6 Extent life is meaningful	−0.13	0.07	−1.21	8.96	.44
7 How well are you able to concentrate	0.11	0.07	−0.75	11.46	.25
8 Safety in daily life	−0.51	0.07	−0.81	15.39	.08
9 How healthy is physical environment	−0.60	0.08	−0.50	8.77	.46
10 Enough energy in everyday life	0.01	0.07	−1.21	10.40	.32
11 Able to accept bodily appearance	0.07	0.07	1.25	6.75	.66
12 Enough money to meet needs	0.42	0.06	1.30	4.13	.90
13 Information needed in daily life	−0.32	0.07	−1.93	12.52	.19
14 Opportunity for leisure activities	0.39	0.06	0.38	10.64	.30
15 Ability to get around	−0.63	0.07	0.38	5.61	.78
16 Satisfied with sleep	0.77	0.06	1.85	6.07	.73
17 Satisfied with ability to perform daily activities	−0.04	0.07	−3.04*	23.99	.00
18 Satisfied with capacity for work	0.28	0.06	−1.64	12.62	.18
19 Satisfied with yourself	0.30	0.07	−2.76*	34.55	.00
20 Satisfied with personal relationships	0.05	0.06	−0.77	5.16	.82
21 Satisfied with sex life	0.77	0.05	4.95*	43.58	.00
22 Satisfied with support from friends	−0.28	0.07	−1.10	9.78	.37
23 Satisfied with conditions of living place	−0.45	0.07	−0.86	8.13	.52
24 Satisfied with access to health services	0.21	0.06	2.64	5.71	.77
25 Satisfied with transport	−0.23	0.07	1.60	14.35	.11
26 How often do you have negative feelings	0.19	0.07	0.05	6.35	.70
4 Domain Superitems					
Physical	0.10	0.02	1.81	10.20	.33
Psychological	0.00	0.02	−2.49	16.46	.06
Social	−0.05	0.03	1.36	4.96	.84
Environmental	−0.04	0.02	−1.17	3.53	.94

* Significant misfit to the Rasch model, $P<.01$.

the individual superitems showed misfit to the Rasch model (see table 1). The item-person plot (fig 1) shows coverage for >95% of the sample with minor ceiling effects, although the item-person targeting (mean score, 0.70±0.60) was marginally acceptable as values were not close to 0, towards the center of the scale. By subgroup, targeting was better for the general population (person-item mean, 0.57±0.45), followed by the TBI group (mean, 0.75±0.70) and slightly worse for the orthopedic sample (mean,

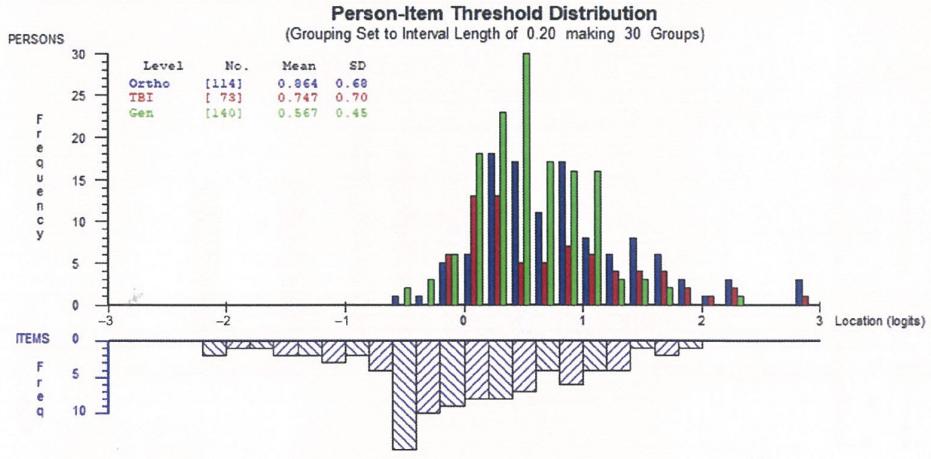

Fig 1 Person-item threshold distribution for the WHOQOL-BREF, by group.

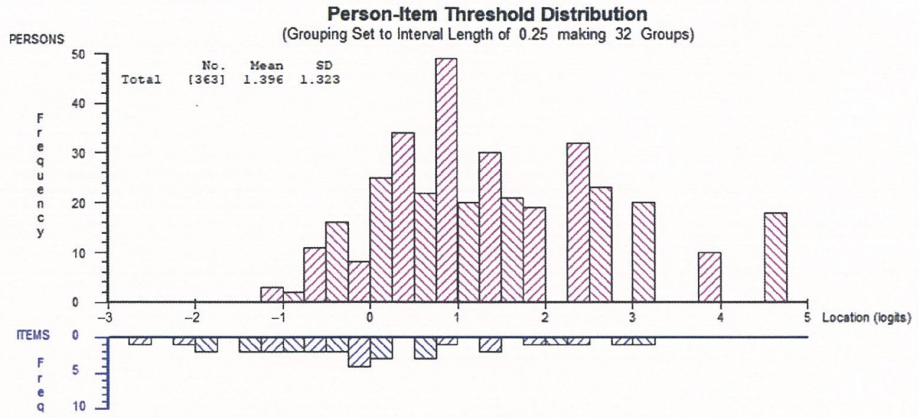

Fig 2 Person-item threshold distribution for the EUROHIS-QOL-8.

0.86±0.68). Overall, this seems to suggest that the WHOQOL-BREF is perhaps not well suited to distinguishing between sample respondents located within the uppermost levels of quality of life.

Rasch analysis of EUROHIS-QOL-8 and WHOQOL-5

Our supplementary analysis of the EUROHIS-QOL-8 indicated overall acceptable model fit ($\chi^2[72]=84.11$; $P=.15$), no significant DIF, and evidence of unidimensionality (see table 1). The PSI indicated good scale reliability (0.81) suitable for group comparisons. Person-item targeting was however suboptimal with a person mean of 1.40±1.32, and minor ceiling effects were noticeable with about 8% of the sample not covered by item thresholds (fig 2).

Results from the WHOQOL-5 analysis showed overall satisfactory fit to the Rasch model ($\chi^2[40]=54.66$; $P=.06$), confirmation of unidimensionality, and no significant DIF. Scale reliability (PSI=0.68) was below acceptable thresholds for group comparisons. The sample was not adequately covered by item thresholds, with about 16% of the sample outside the scale range, and poor person-item targeting with a person-item mean of 1.49±1.31 (fig 3). Table 5 details the item fit statistics for the EUROHIS-QOL-8 and the WHOQOL-5.

Discussion

The present study is the first to evaluate the WHOQOL-BREF in a sample of TBI and orthopedic participants using Rasch methods to assess its feasibility as a HRQOL measure in an injury population compared with a general population sample. The creation of the 3 superitems physical-psychological, social, and environmental, permitted the analyses to meet the expectations of the Rasch model, unidimensionality, good reliability, and 95% coverage of the sample. While the superitem method does not necessarily challenge the validity of the standard practice of calculating separate ordinal-level scores for the physical, psychological, social, and environmental domains of the WHOQOL-BREF, it detected the presence of a potential method effect between the physical and psychological items, as indicated by the presence of local dependency between these domains. Significantly, our

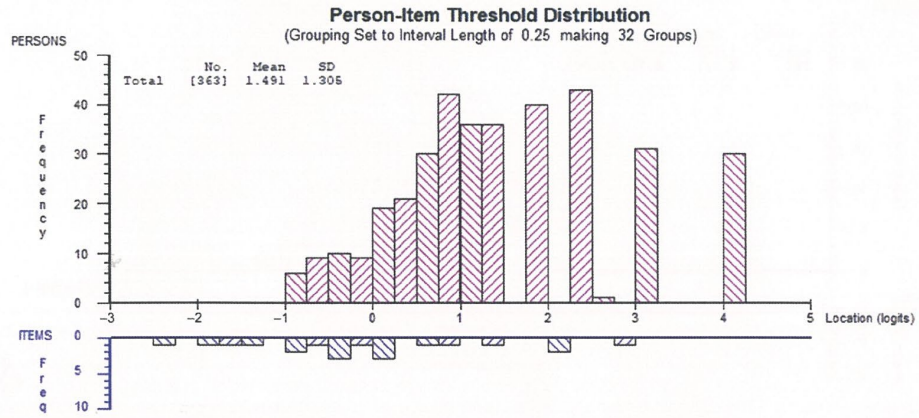

Fig 3 Person-item threshold distribution for the WHOQOL-5.

Table 5 Rasch model fit statistics with item locations, fit residuals, and χ^2 for the EUROHIS-QOL-8 and WHOQOL-5 (n=363)

EUROHIS-QOL-8 Item	Location	SE	Fit Resid	χ^2	Prob
1 Quality of life	−0.50	0.08	−1.62	13.83	.13
2 Satisfied with health	0.37	0.07	1.76	9.09	.43
10 Enough energy in everyday life	−0.04	0.08	0.39	5.42	.80
12 Enough money to meet needs	0.41	0.06	2.45	11.88	.22
17 Satisfied with ability to perform daily activities	−0.08	0.07	−2.12	14.92	.09
19 Satisfied with yourself	0.28	0.08	−1.89	14.19	.12
20 Satisfied with personal relationships	0.03	0.07	1.34	6.69	.67
23 Satisfied with conditions of living place	−0.48	0.07	−0.10	8.16	.52
WHOQOL-5 Item					
1 Quality of life	−0.37	0.08	−1.71	18.82	.02
2 Satisfied with health	0.51	0.07	1.30	7.31	.50
17 Satisfied with ability to perform daily activities	0.05	0.07	−1.39	12.63	.13
20 Satisfied with personal relationships	0.16	0.07	1.05	8.71	.37
23 Satisfied with conditions of living place	−0.36	0.07	0.05	7.20	.52

results are the first to compare and show that the WHOQOL-BREF items perform well and invariably across injury groups as well as healthy populations, although person-item distribution by diagnosis group reflects that most participants had likely recovered from their injuries.

Evidence for TBI and injury populations is limited to 3 studies that used classical test-based methods, 2 of which used the translated Taiwanese version with national items.[28-30] Comparable with our findings, the authors found symmetrical distribution across most domains, low floor and ceiling effects (0%-10.2%), and good internal consistency (α=0.74-0.89). Estimates from other samples also indicate acceptable to good reliability across domains (α=0.70-0.89),[17,19,20,26,47] with the exception of the social domain, which generally shows unsatisfactory reliability (α=0.54-0.68).[19,26,28,30] Our findings that the WHOQOL-BREF is underpinned by a unidimensional construct are similar to previous findings,[17,20-22,25,27] although Rocha et al[26] found that the social domain failed to meet the Rasch unidimensional model because of its poor psychometric properties. The evidence obtained from these studies is not confirmatory, however, in which the authors did not specifically test for unidimensionality as in our study. Also, unlike previous studies that traditionally dealt with the presence of DIF, local dependency, or misfitting items by deleting items, we were able to overcome these deviations of the Rasch model by using the superitem approach, and therefore retain all items. This method follows the recommendations by Lundgren-Nilsson and Tennant,[36] who argue that the creation of superitems attenuates measurement error inherent within individual items without needing to reorder thresholds or delete items.

Our supplementary Rasch analysis of the EUROHIS-QOL-8 indicates that it retains the psychometric properties of its parent WHOQOL-BREF with acceptable fit to the Rasch model, good reliability (PSI=0.81), and unidimensionality. However, poor person-item targeting and minor ceilings effects in our sample suggested that it was not able to discern between individuals who scored on the lowest end of the spectrum. Reliability of the EUROHIS-QOL-8 in our study is consistent with findings from 4 other studies that have reported values between 0.72 and 0.86[31,48-50]; however, there is inconsistent evidence regarding the property of unidimensionality. In studies by Schmidt,[31] Rocha,[49] and Pires[48] there was a lack of strong evidence for unidimensionality, which was not specifically tested for in their samples (and only implied within the Rasch unidimensional model). Only 1 other study produced evidence of unidimensionality in a sample of largely geriatric patients undergoing joint replacement; however, the authors did also note some evidence for multidimensionality.[50] In addition, in 2 of the studies,[31,48] Rasch model expectations were not met overall or for some items, while Rocha et al[49] were only able to achieve Rasch model fit through deletion of items. Person-item targeting in our study appeared to be similar to that for Rocha, although there were discrepancies in the other 2 studies[31,48] in which the authors observed a large variation of floor and ceiling effects across items (1.37%-27.46%). Few validation studies are available for the EUROHIS-QOL-8, but the existing evidence from varied contexts such as large cross-national studies, depressed patients to patients undergoing minor surgery, and the current study's evidence in injury and healthy participants point to the clinical utility of the scale across diverse groups.

Evaluation of the WHOQOL-5 in our dataset indicated below acceptable reliability that is not able to distinguish between healthy and injury groups, despite obtaining evidence of satisfactory model fit and unidimensionality. Furthermore, poor targeting and ceiling effects across the sample indicated that the WHOQOL-5 is unable to measure higher levels of quality of life very well. The assumption of unidimensionality was implied (although not specifically tested for) in just 1 study available by Geyh et al[32] who conducted Rasch analysis on the WHOQOL-5 in a multicenter spinal cord injury sample and who were able to achieve much higher reliability (PSI=0.76) than our sample. Despite its appeal as a 5-item version that can be quickly administered as a quality of life measure, further validation studies of the WHOQOL-5 are needed to demonstrate its utility as a psychometrically robust measurement.

The strength of this study lies in the inclusion of the TBI and orthopedic cohorts in addition to a comparative healthy sample, and our results have demonstrated that the WHOQOL-BREF and the EUROHIS-QOL-8 perform invariably and effectively across general and clinical populations. Additionally, conversion of ordinal to interval scores for the WHOQOL is produced by few[51] and is recommended by current conventions of Rasch articles. The provision of conversion tables (appendix 1 and 2) for the

WHOQOL-BREF, EUROHIS-QOL-8, and WHOQOL-5 therefore enables the interpretability of summary scores that are useful in clinical practice.

Study limitations

A limitation of this study is that in addition to the small sample size and variable length of follow-up between TBI and orthopedic participants (0.5-6 years), the injury sample consisted predominantly of mildly injured participants with an underrepresentation of severe injuries. Thus, the ability to generalize our findings to all people with TBI or orthopedic injuries should be done with caution as the HRQOL of people with severe injuries may have different recovery paths following an injury. Furthermore, the cross-sectional design does not enable capture of longitudinal data on health-related quality of life across the recovery trajectory of injured samples. Collection of quality of life information from the outset of injury and at different time points (eg, 1, 6, 12, and 24 months) would provide useful comparisons to explore if the scale is sufficiently sensitive to detect minimal changes in HRQOL across the recovery path.

Conclusions

To our knowledge, this study is the first to apply Rasch methods to validate the WHOQOL-BREF and its existing derivatives the EUROHIS-QOL-8 and WHOQOL-5 within an injury and healthy population, with results of the WHOQOL-BREF supporting its ubiquity as a HRQOL measure across these populations. The shorter EUROHIS-QOL-8 is psychometrically robust for use in national surveys containing multiple measurements or time-constrained clinical settings; however, the WHOQOL-5 did not meet modern psychometric standards with below acceptable reliability. Future studies should attempt to ameliorate the above limitations in a larger sample size with assessment across more severe injury groups and evaluation of cross-cultural validity in representative samples internationally.

Supplier

a. SPSS version 25; IBM.

Keywords

Psychometrics; Quality of life; Rehabilitation; Brain injuries, traumatic; Orthopedics

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Appendix

Appendix 1 Conversion Table for Ordinal to Interval Scores for the WHOQOL-BREF

Ordinal Raw Score	Interval Logits	Interval Scale	Ordinal Raw Score	Interval Logits	Interval Scale
24	−2.88	24.00	73	−0.04	71.14
25	−2.42	31.63	74	−0.02	71.54
26	−2.12	36.61	75	0.00	71.94
27	−1.92	39.85	76	0.03	72.34
28	−1.77	42.37	77	0.05	72.74
29	−1.65	44.47	78	0.08	73.14
30	−1.53	46.33	79	0.10	73.56
31	−1.43	48.01	80	0.13	73.97
32	−1.34	49.58	81	0.15	74.39
33	−1.25	51.04	82	0.18	74.81
34	−1.17	52.41	83	0.20	75.22
35	−1.09	53.67	84	0.23	75.66
36	−1.02	54.84	85	0.25	76.10
37	−0.96	55.92	86	0.28	76.55
38	−0.90	56.90	87	0.31	77.00
39	−0.85	57.79	88	0.34	77.47
40	−0.80	58.59	89	0.36	77.94
41	−0.76	59.29	90	0.39	78.42
42	−0.72	59.90	91	0.42	78.92
43	−0.69	60.45	92	0.45	79.42
44	−0.66	60.93	93	0.48	79.93
45	−0.63	61.37	94	0.52	80.47
46	−0.61	61.78	95	0.55	81.02
47	−0.58	62.15	96	0.58	81.58
48	−0.56	62.52	97	0.62	82.15
49	−0.54	62.85	98	0.65	82.75
50	−0.52	63.18	99	0.69	83.37
51	−0.50	63.50	100	0.73	84.00
52	−0.49	63.80	101	0.77	84.65
53	−0.47	64.12	102	0.81	85.33
54	−0.45	64.41	103	0.85	86.03
55	−0.43	64.71	104	0.89	86.76
56	−0.41	65.03	105	0.94	87.53
57	−0.39	65.35	106	0.99	88.33
58	−0.37	65.65	107	1.04	89.16
59	−0.36	65.96	108	1.09	90.06
60	−0.34	66.30	109	1.15	90.99
61	−0.32	66.63	110	1.21	91.99
62	−0.30	66.96	111	1.27	93.07
63	−0.27	67.33	112	1.34	94.24
64	−0.25	67.68	113	1.42	95.52
65	−0.23	68.05	114	1.51	96.94
66	−0.21	68.43	115	1.60	98.55
67	−0.18	68.81	116	1.72	100.48
68	−0.16	69.19	117	1.86	102.88
69	−0.14	69.58	118	2.06	106.16
70	−0.11	69.98	119	2.38	111.46
71	−0.09	70.36	120	2.89	120.00
72	−0.07	70.76			

NOTE. Conversion table is only for total scores. For domain level ordinal-to-interval conversion scores, please refer to Krägeloh et al.[51]

Appendix 2 Conversion Table for Ordinal-to-Interval Scores for the EUROHIS-QOL-8 and WHOQOL-5

EUROHIS-QOL-8 Ordinal	Interval		WHOQOL-5 Ordinal	Interval	
Raw Score	Logits	Scale	Raw Score	Logits	Scale
8	−5.08	8.00	5	−3.78	5.00
9	−3.75	12.41	6	−2.95	7.08
10	−2.92	15.13	7	−2.37	8.57
11	−2.41	16.82	8	−1.95	9.63
12	−2.05	17.99	9	−1.61	10.49
13	−1.78	18.87	10	−1.31	11.23
14	−1.57	19.56	11	−1.05	11.90
15	−1.40	20.13	12	−0.80	12.53
16	−1.25	20.62	13	−0.56	13.13
17	−1.12	21.05	14	−0.33	13.72
18	−1.00	21.46	15	−0.09	14.31
19	−0.88	21.86	16	0.15	14.92
20	−0.76	22.25	17	0.40	15.54
21	−0.63	22.66	18	0.66	16.21
22	−0.50	23.08	19	0.94	16.92
23	−0.36	23.54	20	1.26	17.72
24	−0.21	24.03	21	1.61	18.62
25	−0.05	24.56	22	2.03	19.67
26	0.12	25.12	23	2.54	20.96
27	0.29	25.70	24	3.22	22.68
28	0.48	26.30	25	4.14	25.00
29	0.67	26.93			
30	0.86	27.58			
31	1.07	28.26			
32	1.29	28.97			
33	1.52	29.73			
34	1.77	30.55			
35	2.04	31.45			
36	2.35	32.46			
37	2.70	33.64			
38	3.15	35.10			
39	3.77	37.15			
40	4.64	40.00			

NOTE. Conversion table is only for total scores.

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Appendix 12. WHOQoL-24 item ordinal-to-interval scores conversion tables

Ordinal	Interval		Ordinal	Interval	
Raw score	Logits	Scale	Raw score	Logits	Scale
24	-2.88	24.00	73	-0.04	71.14
25	-2.42	31.63	74	-0.02	71.54
26	-2.12	36.61	75	0.00	71.94
27	-1.92	39.85	76	0.03	72.34
28	-1.77	42.37	77	0.05	72.74
29	-1.65	44.47	78	0.08	73.14
30	-1.53	46.33	79	0.10	73.56
31	-1.43	48.01	80	0.13	73.97
32	-1.34	49.58	81	0.15	74.39
33	-1.25	51.04	82	0.18	74.81
34	-1.17	52.41	83	0.20	75.22
35	-1.09	53.67	84	0.23	75.66
36	-1.02	54.84	85	0.25	76.10
37	-0.96	55.92	86	0.28	76.55
38	-0.90	56.90	87	0.31	77.00
39	-0.85	57.79	88	0.34	77.47
40	-0.80	58.59	89	0.36	77.94
41	-0.76	59.29	90	0.39	78.42
42	-0.72	59.90	91	0.42	78.92
43	-0.69	60.45	92	0.45	79.42
44	-0.66	60.93	93	0.48	79.93
45	-0.63	61.37	94	0.52	80.47
46	-0.61	61.78	95	0.55	81.02
47	-0.58	62.15	96	0.58	81.58
48	-0.56	62.52	97	0.62	82.15
49	-0.54	62.85	98	0.65	82.75
50	-0.52	63.18	99	0.69	83.37
51	-0.50	63.50	100	0.73	84.00
52	-0.49	63.80	101	0.77	84.65
53	-0.47	64.12	102	0.81	85.33
54	-0.45	64.41	103	0.85	86.03
55	-0.43	64.71	104	0.89	86.76
56	-0.41	65.03	105	0.94	87.53
57	-0.39	65.35	106	0.99	88.33
58	-0.37	65.65	107	1.04	89.16
59	-0.36	65.96	108	1.09	90.06
60	-0.34	66.30	109	1.15	90.99
61	-0.32	66.63	110	1.21	91.99
62	-0.30	66.96	111	1.27	93.07
63	-0.27	67.33	112	1.34	94.24
64	-0.25	67.68	113	1.42	95.52
65	-0.23	68.05	114	1.51	96.94
66	-0.21	68.43	115	1.60	98.55
67	-0.18	68.81	116	1.72	100.48
68	-0.16	69.19	117	1.86	102.88
69	-0.14	69.58	118	2.06	106.16
70	-0.11	69.98	119	2.38	111.46
71	-0.09	70.36	120	2.89	120.00
72	-0.07	70.76			

Note: Conversion table is only for total scores. For domain level ordinal-to-interval conversion scores please refer to Krägeloh et al. (2013)

Appendix 13. EUROHIS-QOL-8 and WHOQoL-5 ordinal-to-interval scores conversion tables

EUROHIS-QOL-8 Ordinal Raw score	Interval Logits	Interval Scale	WHOQoL-5 Ordinal Raw score	Interval Logits	Interval Scale
8	-5.08	8.00	5	-3.78	5.00
9	-3.75	12.41	6	-2.95	7.08
10	-2.92	15.13	7	-2.37	8.57
11	-2.41	16.82	8	-1.95	9.63
12	-2.05	17.99	9	-1.61	10.49
13	-1.78	18.87	10	-1.31	11.23
14	-1.57	19.56	11	-1.05	11.90
15	-1.40	20.13	12	-0.80	12.53
16	-1.25	20.62	13	-0.56	13.13
17	-1.12	21.05	14	-0.33	13.72
18	-1.00	21.46	15	-0.09	14.31
19	-0.88	21.86	16	0.15	14.92
20	-0.76	22.25	17	0.40	15.54
21	-0.63	22.66	18	0.66	16.21
22	-0.50	23.08	19	0.94	16.92
23	-0.36	23.54	20	1.26	17.72
24	-0.21	24.03	21	1.61	18.62
25	-0.05	24.56	22	2.03	19.67
26	0.12	25.12	23	2.54	20.96
27	0.29	25.70	24	3.22	22.68
28	0.48	26.30	25	4.14	25.00
29	0.67	26.93			
30	0.86	27.58			
31	1.07	28.26			
32	1.29	28.97			
33	1.52	29.73			
34	1.77	30.55			
35	2.04	31.45			
36	2.35	32.46			
37	2.70	33.64			
38	3.15	35.10			
39	3.77	37.15			
40	4.64	40.00			

Note: Conversion table is only for total scores

Appendix 14. Zero-order correlations (Pearson's *r*) between sample characteristics and outcome variables—TBI group (*n*=109) bottom half, orthopaedic group (*n*=114) top half

	Sex†	Age	Injury time, years	Ethnic†	Educ†	Marital†	Employ†	ISS	GCS	LOS	Pre CIRS Total	Post CIRS Total	RPQ	Physical	Psych	Social	Environ	WHO QOL Total
Sex																		
Age			.352	-.350		.415					.558	.448	-.272				.310	
Injury time, years						.192*					.233	.187					.248	
Ethnic†		.305										-.199*						
Educ†	.249																.208*	
Marital†		.367											-.200*			.196*		
Employ†						-.249*				.198*	.225*							
ISS									-.458*	.522			.311					
GCS		.252*																
LOS				.235*				.595	-.348			.207*	.402	-.233*		-.191*	-.192*	-.216*
Pre CIRS Total		.497		-.192*			.266					.846		-.419	-.256	-.279		-.321
Post CIRS Total		.431	.197*								.712		.293	-.518	-.326	-.346	-.230*	-.419
RPQ		-.253			.195*									-.467	-.392	-.326	-.433	-.481
Physical											-.255	-.475	-.523		.722	.504	.628	.864
Psych						.298						-.400	-.614	.691		.650	.797	.928
Social						.265		-.219*	.260*	-.238*		-.254	-.297	.475	.621		.564	.739
Environ		.203*				.270				-.210*	-.190*	-.367	-.593	.642	.768	.586		.881
WHOQOL Total						.310					-.237*	-.452	-.612	.854	.909	.743	.885	

All values are significant at $p<.05$; *denotes significance at $p<.001$; †Spearman's *rho*

Appendix 15. Partial correlations (adjusted by age) between log10 transformed pre- and post-injury CIRS categories, Rasch transformed interval RPQ total scores, and WHOQoL-BREF total and domain scores, disaggregated by TBI (n=109) and orthopaedic (n=114) groups

	TBI						Ortho					
CIRS category	**Physical Domain**	**Psych Domain**	**Social Domain**	**Environ Domain**	**WHOQOL TotalInterv**	**RPQ Interv**	**Physical Domain**	**Psych Domain**	**Social Domain**	**Environ Domain**	**WHOQOL TotalInterv**	**RPQ Interv**
Pre cardiac		-.199										
Pre hypertension												
Pre vascular							-.221			-.235	-.208	.231
Pre respiratory				-.294			-.248	-.253	-.194	-.274	-.283	.277
Pre EENT						-.213	-.198				-.192	
Pre upper GI							-.194	-.207			-.192	
Pre lower GI							-.268	-.299	-.281	-.364	-.347	.276
Pre hepatic												.202
Pre renal										-.198		.256
Pre genitourinary									-.195			
Pre musculoskeletal	-.200			-.198			-.225	-.245		-.227	-.254	.279
Pre neurological	-.276	-.295		-.324	-.320	.282						.214
Pre endocrine							-.280	-.219			-.243	
Pre psych/behavioural		-.305			-.210	.244	-.323	-.298	-.316	-.334	-.364	.190

	TBI						Ortho					
CIRS category	**Physical Domain**	**Psych Domain**	**Social Domain**	**Environ Domain**	**WHOQOL TotalInterv**	**RPQ Interv**	**Physical Domain**	**Psych Domain**	**Social Domain**	**Environ Domain**	**WHOQOL TotalInterv**	**RPQ Interv**
Post cardiac	-.297	-.297		-.196	-.262			-.216				
Post hypertension												
Post vascular							-.187			-.191		.225
Post respiratory							-.263	-.229		-.276	-.286	.303
Post EENT				-.287	-.233*		-.226*		-.215*		-.209*	.200*
Pre upper GI							-.208*					
Post lower GI							-.342	-.290	-.303	-.364	-.376	.254
Post hepatic												.202*
Post renal												.267
Post genitourinary			-.201*						-.272			.206*
Post skin/musculoskeletal	-.537	-.321	-.267	-.414	-.462	.287	-.384	-.287		-.284	-.325	.290
Post neurological	-.255	-.381	-.237*	-.372	-.364	.355	-.203*	-.237*		-.230*	-.192*	.377*
Post endocrine							-.267				-.248	
Post psych/behavioural	-.257	-.476	-.222*	-.383	-.393	.383	-.402	-.427	-.426	-.435	-.482	.376
Pre-injury total comorbidity	-.221*	-.318		-.342	-.310		-.495	-.430	-.273	-.392	-.475	.305
Post-injury total comorbidity	-.468	-.535	-.267	-.514	-.532	.329	-.572	-.457	-.342	-.434	-.536	.432

All values are Pearson *r* correlation coefficients, and significant at $p<.05$; *denotes significance at $p<.001$