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Differences in Health-Related Quality of Life after Traumatic Brain Injury between varying Patient Groups: Sensitivity of a Disease Specific (QOLIBRI) and a Generic (SF-36) Instrument.

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Abstract

Factors associated with health-related quality of life (HRQOL) in patients after TBI include severity of initial injury, different grades of trauma recovery, sociodemographic status and psychological characteristics. Yet, sensitivity of HRQOL instruments to such effects is often underexplored. Thus, we aimed to compare the capacity of the disease-specific instrument QOLIBRI (Quality of Life after Brain Injury) and the generic SF (Short Form)-36 to detect significant differences in HRQOL between patients.

Patients (N = 795) completed HRQOL, sociodemographic, clinical, psychological and health status questionnaires. Univariate (Wilcoxon-Mann-Whitney) and multivariate (Wei-Lachin) non-parametric analyses were conducted using the Wilcoxon-Mann-Whitney approach to compare the sensitivity of the QOLIBRI and the SF-36.

For both instruments, HRQOL was particularly influenced by patients' reliance on others, depression, anxiety, and recovery status, whilst smaller effects were found for living arrangements and participation in leisure activities. Both HRQOL instruments were sensitive to group differences, but the QOLIBRI was able to detect a greater number of and finer differences between specific patient groups, which is particularly important in clinical and therapeutic contexts. This finding is likely explained by the QOLIBRI's greater specificity to disease-specific aspects of consequences of TBI.

This head-to-head HRQOL instrument comparison resulted in a recommendation for the use of the QOLIBRI when detailed insight in the subjective consequences and impact of TBI on patients is required.

Keywords: QOLIBRI, health -related quality of life, SF-36, disease-specific, traumatic brain injury

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Introduction

The measurement of Health-Related Quality of Life (HRQOL) has seen many developments during the last 30 years; however, the study of disease-specific HRQOL in patients who have suffered a traumatic brain injury (TBI) has only recently gained pace. The construct HRQOL was developed to reflect an individual's perception of the effects of an illness and its treatment on their physical well-being, mental and cognitive state, and social and emotional functioning. Traditionally, HRQOL is measured as a patient-reported outcome, indicating that the perspective of the patient is of central importance.[1] Physical, psychological and social constraints following TBI have played an important role in the development within the field. The effects of TBI are often lasting and serious, and can affect, among other aspects, cognition, communication, physical health, behavior, personality and mood.[2] Cognitive impairments might affect TBI patients' ability to rate their own HRQOL, but this influence is often not recognized, or - worse - impaired patients simply get excluded from research studies without any further examination.[3]

Results from several studies have shown that individuals after TBI report reduced HRQOL compared to healthy controls.[2,4-7] Lower HRQOL has been reported after moderate or severe TBI compared to patients after mild TBI.[8,9] However, in some studies individuals after mild TBI reported a lower HRQOL compared to moderate or severe TBI, but confounding effects of depression may account for these findings.[7] Associations have been reported between a lower rating on the Glasgow Outcome Scale Extended (GOSE) and poorer HRQOL.[4,8-13] Furthermore, the presence of comorbid illnesses is common amongst TBI patients and has been associated with lower HRQOL.[7,8,14,15]

TBI can also affect HRQOL indirectly through other factors. Whereas patients make more rapid physical progress within the first six months, psychosocial problems following TBI have been highlighted as a persistent long-term problem.[10] Within TBI samples a significant increase in the prevalence of depression and anxiety after TBI over time was found[5,10,11,16-21] including an association with HRQOL,[7,10-12,21,22] where an improvement over time is observed for most aspects, except mental health domains.[8,12,23]

TBI patients seem to participate less in (social) leisure activities, despite the fact that such activities can improve HRQOL.[24] They often need physical help throughout the

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day, which itself can lead to reduced participation in social and leisure activities.[25] This reliance on others has been linked to poorer HRQOL, although some authors reported an indirect effect, with the need for assistance in daily living activities predicting depression, which in turn affected HRQOL.[12,25-27] Community integration and living independently without needing help were associated with better HRQOL.[11,19]

HRQOL measures can be either generic or disease-specific. Each approach has its advantages, depending on the objectives of the researcher or clinician.[13,28] Disease-specific instruments are likely to be more sensitive to specific consequences of a health-condition, and allow for collection of more focused and precise information. Most TBI research, however, has relied on generic instruments, which allow for comparison across disease states and with healthy individuals, but lack sensitivity and may be less relevant for TBI patients.[29-33]

A recent systematic review identified 61 articles that assessed HRQOL in patients after TBI, of which only nine aimed to examine the validity of HRQOL instruments in this population. The most commonly administered generic instrument is the SF-36 (used overall in 61 studies since its creation until the writing of this paper). This measure could differentiate well between mild and severe TBI, showed moderate internal consistency for all subscales, but also floor and ceiling effects in multiple domains.[34] The QOLIBRI is the first disease-specific measure of HRQOL in TBI. It is of newer date than the SF-36 and has been applied in 35 studies in different validation and clinical contexts since its creation. Psychometric properties and validity of the QOLIBRI were tested within an international TBI population and norms were met for all subscales, even when applied in a subgroup of patients with lower cognitive functioning.[9,35] Even though both instruments (the SF-36 and the QOLIBRI) appear reliable and valid when administered in TBI, the issue of sensitivity is not yet sufficiently investigated.

Which dimension of which instrument is better able to detect differences in the effects of sequelae after TBI? To some extent two previous studies have investigated this question. The first reported that both scales were associated with the GOSE functional outcome scores, although a stronger correlation was found and additional information was captured by the QOLIBRI instrument.[9] The second publication compared the discriminative power or absolute informativity of the QOLIBRI and SF-36, as indicated by the Shannon

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index H' *within* a patient group.[13] All QOLIBRI subscales showed a high Shannon index H', whereas several SF-36 subscales scored lower on this index, and this pattern was repeated within multiple differentiations in groups defined by predictor variables of HRQOL.[13]

Given that HRQOL is an important outcome after TBI for individuals and their families, as well as research contexts, clinical contexts, drug approval, epidemiology, and health political decisions, it is important to examine the validity of instruments measuring disease-specific and generic HRQOL after TBI.[26] Therefore, we aimed to examine the ability of QOLIBRI and that of SF-36 to detect significant differences in HRQOL between patient groups characterized by different grades of trauma recovery, depression, anxiety, and other clinical and socio-demographic characteristics. For this purpose, the discriminative power *between* different TBI patient groups and predictive variables were compared for both instruments. A head to head comparison within the same study population allows for better assessment of discriminant ability. It was hypothesized that the QOLIBRI subscales discriminate better between groups in comparison to SF-36 subscales, especially for those dimensions that play important roles in the lives of TBI patients.

Materials and Methods

Participants

A total of 921 participants who had suffered a TBI were recruited, according to the following inclusion criteria: having an ICD-10 diagnosis of TBI, age range between 17-68 years at interview or postal answer, minimum age of 15 years at injury, being 3 months to 15 years post-injury, an out-patient status, and an ability to give informed consent. Participants were excluded if they had a GOSE score < 3, suffered a spinal cord injury, had a terminal illness, were unable to understand, cooperate or answer questions, or a significant current or pre-injury psychiatric condition was present. Nine countries (6 languages; Dutch, English, Finnish, French, German, and Italian) took part in this original validation study: Australia (*N* = 64), Belgium (*N* = 33), Finland (*N* = 171), France (*N* = 135), Germany (*N* = 172), Italy (*N* = 150), the Netherlands (*N* = 118), U.K. (*N* = 41), and USA (*N* = 25). As GOSE and GCS[38] (for more detail, see Measures) were missing for 126 participants, these were excluded from subsequent analyses. For other variables, missing data was

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limited to 0-8 %. The demographic characteristics of the final sample (*N* = 795) are shown in Table 1.

Procedure

Participants were internationally recruited; details are reported elsewhere.[9,34] Most centers used convenience sampling and recruited participants from rehabilitation clinics. In Germany and Australia random sampling was applied using outpatients of hospital registries. Each collaborating center obtained an ethics clearance and informed consent from every patient.

Mainly, questionnaires were sent by mail and returned after self-completion without help (*N* = 325). The GOSE and clinician checklist of inclusion/exclusion criteria were completed in a telephone interview, while the GCS was obtained from patient record forms. Participants who needed support either completed the questionnaires at the clinic via self-report (*N* = 240), answered the questions during a face-to-face interview (*N* = 215), or through a telephone interview (*N* = 13). In these cases, all measures were obtained in one session.

< Table 1 here >

Measures

Socio-demographic information: Participants completed a socio-demographic questionnaire recording their gender, age, relationship status, educational level and former and current employment status. In addition, participants rated their engagement in leisure, hobbies, and social activities (five-point Likert scale, 'never'-to-'daily'). Participants were also asked to rate the degree of 'Help Needed' or reliance on other people on a five-point Likert scale ('no help needed' – to – 'constant help needed'), covering 'basic personal needs', 'basic mobility', 'daily activities', 'transportation', and 'organization and management of things in life'. In the present study, these variables were dichotomized to enable group comparisons (e.g., those who needed help in ≥ 2 areas of life vs. those who needed help in < 2 areas).

Medical information: Clinical information checklist: Information on the patient's clinical background was completed by medical professionals. This checklist contained the TBI diagnosis, severity of the TBI, patients' current age and age at time of injury, presence

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of spinal cord injury, current or pre-injury psychiatric problems, drug/alcohol dependence, terminal illness, level of understanding and communication abilities, interview mode, and outpatient status. Inclusion in the study was based on this checklist.

Self-reported Health-Status List[36]: Participants indicated whether items from a list of 29 symptoms and possible comorbid health conditions applied to them (yes/no answer). Three subscales were identified: 'comorbidity', 'sensory/ psychosomatic complaints' and 'muscular-skeletal complaints'.

Glasgow Coma Scale (GCS)[37]: The GCS is the most common scoring system for assessing the level of consciousness impairment and coma in a person following a TBI. It is commonly used in emergency or intensive care units and entails the patients' most severe GCS score 24h post injury. Three aspects are measured: behavioural/motor responsiveness, verbal performance, and eye-opening. Brain injuries are classified according to GCS scores as mild (GCS 13-15), moderate (GCS 9-12) and severe (GCS-8).

Glasgow Outcome Scale Extended (GOSE)[38]: This eight stage measure of the grade of disability and recovery is commonly recommended as an outcome measure in TBI.[39] Here, the eight categories (ranging from 'dead' to 'upper good recovery') were used to create three subgroups of patients: those with a severe disability (GOSE 3-4), moderate disability (GOSE 5-6) and good recovery (GOSE 7-8).

Hospital Anxiety and Depression Scale (HADS)[40]: This self-rated questionnaire was administered to assess patients' levels of anxiety and depression. Three categories were differentiated: mild (scores 8-10), moderate (scores 11-15) and severe symptoms (scores ≥ 16). This instrument demonstrates good internal consistencies and moderate content validities when used within a TBI population.[41]

Disease-specific and generic HRQOL Instruments

Quality of Life after Brain Injury (QOLIBRI): The QOLIBRI is a 37-item questionnaire for adults with six scales, and a six-item screening instrument for overall HRQOL after brain injury (QOLIBRI-OS). Four subscales measure *satisfaction*, including 'Cognition', 'Self', 'Daily Life and Autonomy' and 'Social Relationships', and two the extent to which participants felt *bothered* by a variety of issues, including 'Emotions' and 'Physical Problems'. Items are rated on a five-point Likert scale (*'not at all'*- to -*'very'*). The scores are converted to a 0

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to100 scale, so that subscale scores vary from 0 (the worst possible HRQOL) to 100 (the best possible HRQOL). A total QOLIBRI score can be calculated as the mean of all individual items. For the present analyses, mean substitution per subscale was applied in case of missing values.

MOS 36-Item Short Form Health Survey (SF-36, version 1): The SF-36 is a generic, commonly used measure of subjective health status/HRQOL. It was validated extensively in the general population and is able to distinguish various medical and psychological patient groups.[42-46] The questionnaire contains 36 items, recording participants' subjective views on eight health domains: 'Physical Functioning' (PF), 'Role Physical' (RP, comprising limitations in usual role activities because of physical health problems), 'Bodily Pain' (BP), 'General Health' (GH), 'Vitality' (VT), 'Social Functioning' (SF), 'Role Emotional' (RE, assessing limitations in usual role activities because of emotional problems), and 'Mental Health' (MH). Most often questions ask participants to rate how they have felt over the last four weeks, using Likert-type scales (two-, three-, five-, and six-point scales). For each subscale, items are summed and transformed into a score ranging from 0 to 100. In addition, two summary scales can be calculated: a Physical Component Summary (PCS) and a Mental Component Summary (MCS). In this study, overall mean substitution per subscale was adopted in case of missing values. (Version 2 of the SF-36 was administered to 62 Australian patients, with subsequently transformed data used).[42-44]

Data Analysis

The examination of psychometric properties of the SF-36 and the QOLIBRI using methods from classical and modern test theory are reported elsewhere.[9,13,35] Normality of the data was assessed with Kolmogorov-Smirnov and Shapiro-Wilk tests. Several subscales of both HRQOL instruments and most predictor variables were not normally distributed. Non-parametric analyses were therefore applied. To investigate to what extent the two instruments measured the same construct, convergent validity was calculated for the SF-36 and the QOLIBRI.

We performed comparisons for the individual QOLIBRI subscales and the Total QOLIBRI score as well as for the SF-36 subscales, and its PCS and MCS scores. Discriminant validity or sensitivity of both measures was compared using the Wei-Lachin method.[47-49]

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Multiple comparisons were performed between patients with different living arrangements, degrees of Help Needed, social activities, internet activities and other hobbies, comorbid health conditions, sensory and psychosomatic complaints, motor-skeletal complaints, the GOSE recovery and the HADS depression and anxiety scores.

The Wei-Lachin procedure provides efficient multivariate Wilcoxon-Mann-Whitney difference analyses that can be applied simultaneously to outcomes using different scales (dichotomous, ordinal, etc.) without losing information. This highly efficient global test procedure considers the between-variable correlations and calculates standardized effect sizes (0-1.0) for outcome variables and combined results, which are easily interpreted. It fully controls alpha levels for the ensemble of a multivariate analysis (e.g. for the ensemble of HRQOL subscales), but not across Wei-Lachin procedures (e.g. across multivariate analyses: mild vs. moderate/mild vs. severe/moderate vs. severe, etc.). It is a non-parametric, distribution-free method that handles missing and censored data well. This procedure thus maintains generally accepted type I error probabilities, but has more power than traditional approaches to correct for multiple tests, such as Bonferroni or Sidak corrections.[49] Statistical analyses were performed using the statistical software package TESTIMATE, version 6.5 (idv). Combined Wei-Lachin statistics are reported for the ensemble of subscales, whereas for descriptive purposes subscale statistics are reported with Bonferroni-corrected significance adjustments (for the QOLIBRI subscales $\alpha/6 < .0083$ and for SF-36 subscales $\alpha/8 < .0063$).

Firstly, univariate non-parametric (Wilcoxon-Mann-Whitney-U Test - WMW) sensitivity analyses were performed, comparing all patient-groups for Total QOLIBRI scores and the SF-36 PCS and MCS scores only. Secondly, using a multivariate approach, correlation-sensitive analyses (Wei-Lachin procedure), comparisons of patient-groups for the ensemble of all QOLIBRI and SF-36 subscales were examined. Sensitivity was quantified by the Mann-Whitney effect size measure (MW), whereby MW = 0.50 represents equality, whereas higher or lower values indicate the degree of discrimination/sensitivity of the HRQOL instrument between the compared groups. The comparator and the test group differed for each predictor. For example, those individuals who did not need help (comparator) were compared to those who needed help (test), or those with mild anxiety symptoms (comparator) were compared to those who suffered from moderate/severe

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anxiety (test). Which patients represent which group is specified in the respective result tables. Table 2 gives an overview of thresholds for the MW effect sizes.

< Table 2 here >

Finally, to test effects concerning statistical significance, 38 meta-level direct comparisons of 19 subdomains of interest (distinct patient level contrasts) of disease-specific vs. generic HRQOL were conducted. The comparison by means of the Wei-Lachin contrast procedure was based on the corresponding areas under the receiver-operating characteristic (ROC) curves [48]. Results were adjusted for multiplicity by means of the Bonferroni correction (α_{adj}= 0.00132).

Results

Clinical Characteristics

Table 3 summarizes the clinical characteristics of the participants. It is noteworthy that a large percentage had been severely injured (GCS <8) and most were left with a moderate disability (GOSE 5-6).

< Table 3 here >

Psychometric Properties of HRQOL Instruments

Psychometric properties of QOLIBRI and SF-36 subscales in this sample have been reported elsewhere.[9,13,34] They were good to excellent for all QOLIBRI subscales and mostly good to satisfactory for the SF-36 subscales.

Convergent Validity of HRQOL Instruments

In order to investigate to what extent, the subscales of the respective instruments cover similar domains, correlations between the subscales of QOLIBRI and SF-36 were examined (see Table 4). All correlations were significant (ranging from *r* =.23 to *r* =.64), indicating that information was shared, albeit to different degrees, by both questionnaires. In general, the SF-36 subscales RP, PF, and BP with an emphasis on the physical domain showed lower correlations with the QOLIBRI subscales (except for 'Physical Problems' and the Total score) than the more psychologically/emotionally oriented subscales RE, MH, SF, VT, and also GH. Of the QOLIBRI subscales, Physical Problems demonstrated the highest correlations to all SF-36 subscales, Social Relationships the lowest.

< Table 4 here >

Sensitivity of HRQOL Instruments

Mann-Whitney effect sizes (MW) with confidence intervals using the Wilcoxon-Mann-Whitney approach were explored to assess the discriminant validity of the QOLIBRI and the SF-36 for different patient groups and variables. First, univariate non-parametric sensitivity analyses were performed comparing patient groups for the summary scores of both instruments only. Figure 1 shows the effect sizes for each comparison for the QOLIBRI total scores and SF-36 summary scores (PCS and MCS). Effect sizes towards the left side represent differentiation in favor of the groups noted on the left, and effect sizes towards the right side suggest more favorable HRQOL outcomes in the opposite group.

< Figure 1 here >

The total and the summary scores for both instruments were able to differentiate between most patient groups, although effect sizes varied. The QOLIBRI total score distinguished most groups significantly (CIs did not cross 0.5), except those living at home independently vs. those living in a nursing home: here, no differences were detected by the SF-36 summary scales either. Interestingly, those living at home supported by others rated their HRQOL more negatively compared to those living in a nursing home, although this effect was not observed for the MCS. Presence of comorbidity, hobbies, and home-supported vs. nursing home groups could not significantly be differentiated by PCS and MCS. The MCS discriminated patients with different levels of anxiety and depression better than the PCS, which in turn discriminated better between those patient groups with and without comorbid health conditions, or motor/skeletal complaints. Whilst a trend can be seen with the QOLIBRI data showing stronger effect sizes than the SF-36 summary scales when differentiating between 'leisure activity' groups and 'help needed' groups, overlapping confidence intervals suggest this difference was not significant. For most of these comparisons, sensitivity of the QOLIBRI and the SF-36 was comparable.

Secondly, multivariate, correlation-sensitive analyses were performed comparing, patient groups for the ensemble of QOLIBRI subscales and the SF-36 subscales (see Table 5-8). In general, a larger number of strong effect sizes was found for the QOLIBRI subscales (strong, *N*=35/26.3%]; medium, *N*=34/ 25.6%; small, *N*=53/39.8%) compared with the SF-

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36 subscales (strong, *N*=27/15.8%; medium, *N*=58/33.9%; small, *N*=58/33.9%). In total, for the QOLIBRI subscales in 111 of 133 comparisons a significant effect size was found (83.5%). For the SF-36 subscales a total of 130/171 comparisons had a significant effect size (76.5%). The results showed a substantial overlap of the QOLIBRI and SF-36 subscales (see CIs in Figure 1), thus, the interpretation of the results should be carried out with caution.

Like in the first analysis of the summary scores, the combined Wei-Lachin statistic (representing all QOLIBRI subscales taken together) reveals that the QOLIBRI and the SF-36 were able to significantly differentiate all patient groups, except those living at home independently and those living in a nursing home (see Table 5). The QOLIBRI subscale 'Daily Life and Autonomy' presented a medium sized difference for the comparison 'at home-independent' vs. 'at home-supported'. For the SF-36 instrument RF and PF indicated a total of three medium-sized effects. Effect sizes were small for other subscales/comparisons of living arrangements.

For the comparison of 'Help Needed' strong discriminatory effects were found for both instruments, with QOLIBRI subscales 'Daily Life and Autonomy', 'Cognition' and 'Physical Problems' identifying the strongest effects.

< Table 5 here >

Mostly small effects were observed comparing participants who engaged in leisure activities with those who did not (see Table 6), with the more physical subscales of the SF-36 detecting few differences for individual activities and hobbies. Stronger effects were detected for social activities, specifically for 'Physical Problems', 'Self and Daily Life/Autonomy' (QOLIBRI) and PF, GH, MH and VT (SF-36).

< Table 6 here >

With regards to patients' self-reported health status (Table 7), the QOLIBRI 'Physical Problems' subscale could best distinguish patient groups with and without comorbidity. BP and GH (SF-36) also differentiated comorbidity groups well. The QOLIBRI subscales appeared more sensitive to the effect of sensory/psychosomatic complaints on HRQOL than SF-36 subscales (however, confidence intervals overlapped). Motor/skeletal complaints demonstrated small effects for the 'Social Relationships' and 'Emotion' subscales and similarly, small effects for RE and MH (SF-36) were noticed.

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The GOSE disability groups could be differentiated well by both instruments, but HRQOL scores distinguished less strongly between patient groups with severe disability vs. moderate disability.

< Table 7 here >

Discrimination between patient groups suffering or not from anxiety or/and depression assessed with the HADS was very good for the QOLIBRI and SF-36 subscales, with smaller effects identified for the comparison of patients with mild vs. moderate/severe anxiety and depression (see Table 8).

< Table 8 here >

Meta-level Comparison of sensitivity of sum scores of the QOLIBRI and the SF-36

To test the above reported effects for statistical significance, 38 meta-level direct comparisons of disease-specific vs. generic have been performed in 19 subdomains of interest (distinct patient level contrasts) for (a) QOLIBRI total vs. SF-36 PCS; and (b) QOLIBRI total vs. SF-36 MCS. In nine out of the 19 subdomains, the QOLIBRI performed significantly better than either the physical (PCS) or the mental (MCS) scales of the SF-36. The QOLIBRI performed significantly better compared to MCS in distinguishing the domains of 'Help Needed', Comorbidities, and GOSE. QOLIBRI also performed better compared to PCS in distinguishing for the HADS domains. In none of the subdomains did the SF-36 perform significantly better than the QOLIBRI, neither PCS nor MCS. The results were adjusted for multiplicity by means of the Bonferroni correction for 38 comparisons (α_{adj}= 0.00132). For details see Table 9.

< Table 9 here >

Discussion

The present study compared the validity and sensitivity of a disease-specific and a generic HRQOL instrument in a large international sample of patients after TBI. Sensitivity was assessed for various correlates of HRQOL by applying the Wei-Lachin multivariate one-sided test for multiple outcomes.[9,13] First, univariate WMW sensitivity analyses showed that summary scores of both measures were sensitive to most group differences. A more detailed Wei-Lachin analysis of all subscales showed a higher number of significant and stronger effect sizes for the disease-specific QOLIBRI instrument compared to the generic

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SF-36 instrument, which suggests greater sensitivity for the QOLIBRI subscales. The physically oriented subscales of the SF-36 were found to be more sensitive to health states, whereas psychologically oriented scales showed stronger effects for depression and anxiety classifications. Both instruments discriminated very well between 'help-needed', anxiety and depression and GOSE disability groups, although, regarding the latter, smaller effects were noted for mild vs. moderate/severe comparisons. Less sensitivity to patients' living arrangements and leisure activities was found, with mostly small effect sizes observed across instruments.

This assumption that the disease-specific QOLIBRI instrument is able to detect subtle differences that are not identified as efficiently by a more generic measure was supported statistically. Previous findings showed higher discriminatory power *within* specific patient groups (Shannon Indexes H') for the QOLIBRI subscales compared with the SF-36 scales.[13] The present study demonstrates that the QOLIBRI is more sensitive to differences *between* groups as well, which is likely explained by the specificity of the QOLIBRI to disease-specific aspects of the consequences of the TBI. This is particularly relevant in the clinical and rehabilitation context.

The QOLIBRI proved to be a valid measure of HRQOL, since there was sufficient correlational congruency with the SF-36 subscales (i.e., convergent validity). Long-term psychosocial and emotional problems are an important clinical feature of patients that have sustained a TBI. [50] The higher correlation of the QOLIBRI with MCS compared to PCS summary scales reflects this. Moreover, the relative importance of psychological problems in determining HRQOL might increase with time since the injury.[51] For most patients in our sample the TBI occurred over two years ago (and up to 18 years ago), and unsurprisingly both the QOLIBRI and the SF-36 were sensitive to psychological predictors of the HRQOL. Both instruments distinguished clearly between normal vs. moderate/severe patients classified by the HADS anxiety and depression scales; however, the in general less affected patient groups (normal vs. mild) were differentiated better by QOLIBRI subscales. Differences in the HRQOL are likely smaller for these comparisons, and the more specific focus of the QOLIBRI on emotional and social aspects of the HRQOL may have contributed to its better ability to detect smaller differences.[2] Since with time, psychosocial problems tend to outweigh the burden of physical issues [52], the QOLIBRI can be especially relevant in

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a longitudinal perspective, as a prognostic tool or for patients whose TBI lays further back in the past. The SF-36 summary score MCS was much more sensitive to HADS anxiety and depression classifications than the PCS scale, while the reverse was found for health status comparisons.

Furthermore, physical predictors had a stronger effect on physical aspects of the HRQOL, whereas psychological aspects were affected less. Comorbid conditions were stronger associated with physical aspects of HRQOL (QOLIBRI: 'Physical Problems'; SF-36: BP and GH) reflected by medium effects, suggesting that comorbid conditions affected physical aspects of the HRQOL but did not impact more psychological, social, and cognitive aspects (small effects only). Slightly stronger effects were identified for motor/skeletal complaints, although psychosocial aspects were less affected than other domains of the HRQOL, as indicated by small effects for these subscales (QOLIBRI: 'Social Relationships', 'Emotions'; SF-36: RE and MH). Surprisingly, the QOLIBRI was more sensitive to sensory/psychosomatic complaints, displaying medium to large effect sizes, whereas only few subscales of the SF-36 were sensitive to these effects (RP and MH). These stronger effect sizes can be explained by the fact that symptoms included in the sensory/psychosomatic category contained more psychological items such as nervousness, depression, and lack of energy, which are covered by the QOLIBRI. Finally, the QOLIBRI (and especially the 'Physical Problems' scale) and the SF-36 subscales were sensitive to the GOSE classifications, although some subscales identified small to medium effects only (QOLIBRI: 'Social Relationships' and 'Emotions'; SF-36: RE, MH, and SF).

In the literature, the 'reliance on others' has been linked to poorer HRQOL[12,26,53,54] This finding was verified by comparison between individuals 'needing' and individuals 'not needing help'. The QOLIBRI was more sensitive, showing especially large effects on 'Cognition', 'Daily Life/Autonomy' and 'Physical Problems', whereas SF-36 captured mostly medium effects. This would suggest a high prognostic and rehabilitation value of the QOLIBRI scales. Small effects were identified for the subscales 'Social Relationships' and RE, suggesting that these subscales are less sensitive to the effect of dependence on others on HRQOL. Similarly, those living at home independently showed better HRQOL compared with those who required support at home. However, surprisingly there was little difference between those living at home independently and those living in a nursing home.

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Interestingly, those living in a nursing home reported better HRQOL than those who were depended on support at home. Whilst this seems counterintuitive, given that in general the condition of those who need sheltered accommodation is expected to be worse, it is possible that professional care improves HRQOL in comparison to family care and the appeal of living at home. This is in line with findings by Lamontagne and colleagues and suggests that more resources are necessary to support care at home for patients.[55-57] Therefore, apart from physical aspects, other more psychological and social factors also should be considered before sending a patient home, especially if they are dependent on the support of others.

Furthermore, the direct association between participation in leisure activities and HRQOL was investigated. The QOLIBRI detected significant small effects of participation, whereas only few significant effects were identified by the SF-36. Some medium effects of social activities were reported for Self, Daily Life/Autonomy and Physical Problems, and PF, GH, MH and VT, suggesting that a lack of participation in social activities is more problematic than a lack of individual activities and hobbies. This could present a therapeutic opportunity in itself, which currently is not being utilized enough. Patients should be motivated and supported to take part in social activities, privately, as well as part of therapy.

Limitations

Some limitations of this study are to be addressed. Whilst a stronger effect size was interpreted as indicative of better sensitivity of the respective instrument, it must be acknowledged that this was based on the assumption that actual differences between categories existed. Whilst for most predictors and correlates clear associations with poor HRQOL had been reported before, the influence of living arrangement and leisure activities has received less attention. It is possible that for these aspects in reality the HRQOL did not greatly differ for certain groups and in such a case a smaller effect size would be valid. Therefore, the deduction of validity interpretations based on these associations requires caution. On a positive note, in terms of further research, living arrangement leisure and social activities seem to offer a potential underexplored area related to the HRQOL in TBI.

Furthermore, whilst the strength of this study is the large sample size and international recruitment, it must be remembered that most centers recruited

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convenience samples. Therefore, individuals after TBI with a good recovery and less clinical contact are underrepresented in this sample, limiting the generalizability of the findings. A large range of patients was included, which varied widely in the time since the injury occurred (ranging from < 1 year to 18 years), although in most patients the injury occurred over two years ago (75%). Over time, patients' coping and adaptation likely increased, possibly confounding results.

Of note, all described results and trends were obtained by comparison with SF-36 version 1Results described in this study can therefore not be generalized to the SF-36 version 2, which addresses some of the psychometric problems, especially of the physical scales.[44] In future, the validity of this version might however be tested in the context of the currently conducted prospective longitudinal Center-TBI study[58].

Conclusion

The choice of the best suited instrument depends on the goal of the researcher or clinician. For the assessment of HRQOL after TBI, the QOLIBRI is more sensitive than the SF-36 for contrasts on a great number of subscales, and shows fewer floor and ceiling effects. However, the SF-36 is also sensitive to most comparisons. The QOLIBRI provides a measure that includes dimensions of the HRQOL found to be especially meaningful in TBI populations, such as emotional, physical, and cognitive problems, changes in social relationships, self-concept, and restrictions in participation and activity.[52-62] If the aim of the researcher is to assess the HRQOL between different groups of patients after a TBI, a generic instrument might not capture all these aspects, whilst they are covered by the QOLIBRI. Our results demonstrated that the SF-36 provides a valid measure for comparisons of the HRQOL between patients with different diseases and it is better suited for application across health states. However, discrimination between different patient groups within a TBI population would be more refined when using a disease-specific instrument, such as the QOLIBRI.

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Author Disclosure Statement

Nicole von Steinbüchel: planned and wrote and revised the paper, no competing financial interests exist

Mirjam Meeuwsen; analysed wrote and revised, no competing financial interests exist

Marina Zeldovich: revised and wrote, no competing financial interests exist

Johannes C. Vester: analyzed and wrote, no competing financial interests exist

Andrew Maas: revised and wrote, no competing financial interests exist

Sanna Koskinen: revised and wrote, no competing financial interests exist

Amra Covic: revised and wrote, no competing financial interests exist

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This paper has been peer-reviewed and accepted for publication, but has yet to undergo copyediting and proof correction. The final published version may differ from this proof.

References

1. Bandayrel, K.,and Johnston, B.C. (2014). Recent advances in patient and proxy-reported quality of life research. Health Qual. Life Outcome 12 (110), 1-9.
2. Dijkers, M.P. (2004). Quality of life after traumatic brain injury: a review of research approaches and findings. Arch. Phys. Med. Rehabil. 85 (2), 21-35.
3. Von Steinbüchel, N., Petersen, C., Bullinger, M., and the QOLIBRI Group (2005). Assessment of health-related quality of life in persons after traumatic brain inury – development of the QOLIBRI, a specific measure. Acta Neurochir. 93, 43-49.
4. Jacobsson, L.J., Westerberg, M., & Lexell, J. (2010). Health-related quality-oflife and life satisfaction 6–15 years after traumatic brain injuries in Northern Sweden. Brain Inj. 24, 1075–1086.
5. Arango-Lasprilla, J.C., Krch, D., Drew, A., De Los Reyes Aragon, C.J., & Stevens, L.F. (2012). Health-related quality of life of individuals with traumatic brain injury in Barranquilla, Colombia. Brain Inj. 26 (6), 825-833.
6. Beseoglu, K., Roussaint, N., Steiger, H., & Hänggi, D. (2013). Quality of life and socio-professional reintegration after mild traumatic brain injury. Br. J. Neurosurg. 27 (2), 202-206.
7. Findler, M., Cantor, J., Haddad, L., Gordon, W., & Ashman, T. (2001). The reliability and validity of the SF-36 health survey questionnaire for use with individuals with traumatic brain injury. Brain Inj. 15 (8), 715–723.
8. Scholten, A.C., Haagsma, J.A., Andriessen, T.M.J.C., Vos, P.E., Steyerberg, E.W., van Beeck, E.F., & Polinder, S. (2015). Health-related quality of life after mild, moderate and severe traumatic brain injury: patterns and predictors of suboptimal functioning during the first year after injury. Injury 46 (4), 616-624.
9. Von Steinbüchel, N., Wilson, L., Gibbons, H., Hawthorne, G., Höfer, S., Schmidt, S., Bullinger, M., Maas, A., Neugebauer, E., Powell, J., von Wild, K., Zitnay, G., Bakx, W., Christensen, A.L., Koskinen, S., Formisano, R., Sarajuuri, J., Sasse, N., Truelle, J.L., & the QOLIBRI Task Force (2010b). Quality of Life after Brain Injury (QOLIBRI): scale validity and correlates of quality of life. J. Neurotrauma 27 (7), 1157-1165.

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This paper has been peer-reviewed and accepted for publication, but has yet to undergo copyediting and proof correction. The final published version may differ from this proof.

10. Andelic, N., Hammergren, N., Bautz-Holter, E., Sveen U., Brunborg, C., & Roe, C. (2009). Functional outcome and health-related quality of life 10 years after moderate-to-severe traumatic brain injury. Acta Neurol. Scand. 120, 16-23.
11. Forslund, M.V., Roe, C., Sigurdardottir, S., & Andelic, N. (2013). Predicting health-related quality of life 2 years after moderate-to-severe traumatic brain injury. Acta Neurol Scand. 128, 220-227.
12. Grauwmeijer, E., Heijenbrok-Kal, M.H., & Ribbers, G.M. (2014). Health-related quality of life 3 years after moderate to severe traumatic brain injury: a prospective cohort study. Arch. Phys. Med. Rehabil. 95 (7), 1268-1276.
13. Von Steinbuechel, N., Covic, A., Polinder, S., Kohlmann, T., Cepulyte, U., Poinstingl, H., ... & Formisano, R. (2016). Assessment of health-related quality of life after TBI: comparison of a disease-specific (QOLIBRI) with a generic (SF-36) instrument. Behav Neurol. 2016.
14. Thompson, H.J., Dikmen, S., & Temkin, N. (2012). Prevalence of comorbidity and its association with traumatic brain injury and outcomes in older adults. Res. Gerontol. Nurs. 5 (1), 17-24.
15. Polinder, S., Haagsma, J.A., Bonsel, G., Essink-Bot, M., Toet, H., & van Beeck, E.F. (2010). The measurement of long-term health-related quality of life after injury: comparison of EQ-5D and the health utilities index. Inj. Prev. 16, 147-153.
16. Osborn, A.J., Mathias, J.L., Fairweather-Schmidt, A.K. (2014). Depression following adult, non-penetrating traumatic brain injury: a meta-analysis examining methodological variables and sample characteristics. Neurosci. Biobehav. Rev. 47, 1-15.
17. Almeida, O.P., Hankey, G.J., Yeap, B.B., Golledge, J., & Flicker, L. (2015). Prevalence, associated factors, mood and cognitive outcomes of traumatic brain injury in later life: the health in men study (HIMS). Int. J. Geriatr. Psychiatry, *doi:* 10.1002/gps.4276.
18. Hawthorne, G., Gruen, R.L., & Kaye, A.H. (2009). Traumatic brain injury and long-term quality of life: findings from an Australian study. J. Neurotrauma 26, 1623-1633.
19. Truelle, J., Koskinen, S., Hawthorne, G., Sarajuuri, J., Formisano, R., Von Wild, K., Neugebauer, E., Wilson, L., Gibbons, H., Powell, J., Bullinger, M., Höfer, S., Maas, A., Zitnay, G., Von Steinbüchel, N., & The QOLIBRI Task Force (2010). Quality of life after

traumatic brain injury: The clinical use of the QOLIBRI, a novel disease-specific instrument. Brain Inj. 24 *(*11), 1272–1291.

20. Gould, K.R., Ponsford, J.L., Johnston, L., & Schönberger, M. (2011). Relationship between psychiatric disorders and 1-year psychosical outcome following traumatic brain injury. J. Head Trauma Rehabil. 26 (1), 79-86.
21. Diaz, A.P., Schwarzbold, M.L., Thais, M.E., Hohl, A., Bertotti, M.M., Schmoeller, R., Nunes, J.C., Prediger, R., Linhares, M.N., Guarnieri, R. R., & Walz, R. (2012). Psychiatric disorders and health-related quality of life after severe traumatic brain injury: a prospective study. J. Neurotrauma 29 (6), 1029–1037.
22. Haagsma, J.A., Scholten, A.C., Andriessen, T.M., Vos, P.E., van Beeck, E.F., & Polinder, S. (2015). Impact of depression and post-traumatic stress disorder on functional outcome and health-related quality of life of patients with mild traumatic brain injury. J. Neurotrauma 32 (11), 853-862.
23. Pagulayan, K.F., Temkin, N.R., Machamer, J., & Dikmen, S.S. (2006). A longitudinal study of health-related quality of life after traumatic brain injury. Ann. Rehabil. Med. 87, 611-618.
24. Wise, E.K., Mathews-Dalton, C., Dikmen, S., Temkin, N., Machamer, J., Bell, K., & Powell, J.M. (2010). Impact of traumatic brain injury on participation in leisure activities. Am. J. Phys. Med. Rehabil. 91 (9), 1357-1362.
25. Carlozzi, N.E., Tulsky, D.S., & Kisala, P.A. (2011). Traumatic brain injury patient-reported outcome measure: identification of health-related quality of life issues relevant to individuals with traumatic brain injury. Am. J. Phys. Med. Rehabil. 92 (10), 52-60.
26. Williamson, M.L.C., Elliott, T.R., Berry, J.W., Underhill, A.T., Stavrinos, D., & Fine, P.R. (2013). Predictors of health-related quality-of-life following traumatic brain injury. Brain Inj. 27 (9), 992-999.
27. Gould, K.R., Ponsford, J.L., & Spitz, G. (2013). Association between cognitive impairments and anxiety disorders following traumatic brain injury. J. Clin. Exp. Neuropsychol. 36 (1), 1-14.
28. Neugebauer, E., Lefering, R., Bouillon, B., Bullinger, M., & Wood-Dauphinee, S. (2002). Quality of Life after Multiple Trauma. Aim and Scope of the Conference. Restor. Neurol. Neurosci., 20 (3-4), 87-92.

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This paper has been peer-reviewed and accepted for publication, but has yet to undergo copyediting and proof correction. The final published version may differ from this proof.

29. Cella, D., Yount, S., Rothrock, N., Gershon, R., Cook, K., Reeve, B., Ader, D., Fries, J.F., Bruce, B., & Rose, M. (2007). 'The patient-reported outcomes measurement information system (PROMIS)': progress of an NIH Roadmap cooperative group during its first two years. Med. Care 45 (5), 3.
30. Gershon, R., Lai, J.S., Bode, R., Choi, S., Moy, C., Bleck, T., Miller, D., Peterman, A., & Cella, D. (2012). Neuro-QOL: quality of life item banks for adults with neurological disorders: item development and calibrations based upon clinical and general population testing. Qual. Life Res. 21 (3), 475-486.
31. Cella, D., Riley, W., Stone, A., Rothrock, N., Reeve, B., Yount, S., Dagmar, A., Bode, R., Buysse, D., Choi, S., Cook, K., DeVellis, R., DeWalt, D., Fries, J.F., Gershon, R., Hahn, E.A., Lai, J.S., Pilkonis, P., Revicki, D., Rose, M., Weinfurt, K., Hays, R., & P.C. Group (2010). The patient-reported outcomes measurement information system (PROMIS) developed and tested its first wave of adult self-reported health outcome item banks: 2005-2008. J. Clin. Epidemiol. 63 (11), 1179-1194.
32. Perez, L., huang, J., Hansky, L, Nowinski, C., Victorson, D., Peterman, A., & Cella, D. (2007). Using focus groups to inform the Neuro-QOL measurement tool: exploring patient centered, health-related quality of life concepts across neurological conditions. J. Neurosci. Nurs. 39 (6), 342-353.
33. Reeve, B.B., Hays, R.D., Bjorner, J.B., Cook, K.F., Crane, P.K, Teresi, J.A., Thissen, D., Revicki, D.A., Weiss, D.J., Hambleton, R.K., Liu, H., Gershon, R., Reise, S.P.,Lai, J.S., & Cella, D. (2007). Psychometric evaluation and calibration of health-related quality of life item banks: plans for the Patient-Reported Outcomes Measurement Information System (PROMIS). Med. Care 45 (5), 22-31.
34. Polinder, S., Haagsma, J.A., van Klaveren, D., Steyerberg, E.W., & van Beeck, E.F. (2015). Health-related quality of life after TBI: a systematic review of study design, instruments, measurement properties, and outcome. Popul. Health Metr. 13 (4), 1-12.
35. Von Steinbüchel, N., Wilson, L., Gibbons, H., Hawthorne, G., Höfer, S., Schmidt, S., Bullinger, M., Maas, A., Neugebauer, E., Powell, J., von Wild, K., Zitnay, G., Bakx, W., Christensen, A., Koskinen, S., Sarajuuri, J., Formisano, R., Sasse, N., Truelle, J., & the QOLIBRI Task Force (2010a). Quality of life after brain injury (QOLIBRI): scale development and metric properties. J. Neurotrauma. 27, 1167-1185.

36. Power, M., Quinn, K., & Schmidt, S. (2005). Development of the WHOQOL-old module. Qual. Life Res. 14 (10), 2197-2214.

37. Teasdale, G., & Jennett, B. (1974). Assessment of coma and impaired consciousness: a practical scale. Lancet 304 (7872), 81-84.

38. Wilson, J.L., Pettigrew, L.E., & Teasdale, G.M. (1998). Structured interviews for the Glasgow outcome scale and the extended Glasgow outcome scale: guidelines for their use. J. Neurotrauma 15 (8), 573-585.

39. Weir, J., Steyerberg, E.W., Butcher, I., Lu, J., Lingsma, H.F., McHugh, G.S., Roozenbeek, B., Maas, A.I.R., & Murray, G.D. (2012). Does the extended Glasgow outcome scale add value to the conventional Glasgow outcome scale? J. Neurotrauma 29 (1), 53-58.

40. Zigmond, A.S., & Snaith, R.P. (1983). The hospital anxiety and depression scale. Acta Psychiatr. Scand. 67 (6), 361-370.

41. Whelan-Goodinson, R., Ponsford, J., & Schönberger, M. (2009). Validity of the hospital anxiety and depression scale to assess depression and anxiety following traumatic brain injury as compared with the structured clinical interview for DSM-IV. J Affect. Disord. 114 (1-3), 94-102.

42. Ware, J.E., & Sherbourne, C.D. (1992). The MOS 36-item short-form health survey (SF-36): I. conceptual framework and item selection. Med. Care 30, 473-483.

43. Ware, J.E., & Kosinski, M. (1996). *The SF-36 Health Survey (Version 2). Technical Note.* Health Assessment Lab: Boston, September 20.

44. Ware, J.E. (2000). SF-36 Health Survey Update. SPINE, 25 (24), 3130-3139.

45. Brazier, J. E., Harper,R., Jones,N.M.B., O'Cathain, A., Thomas, K.J., Usherwood, T., & Westlake, L. (1992). Validating the SF-36 health survey questionnaire: new outcome measure for primary care. BMJ 305, 160-164.

46. McHorney, C.A., Ware, J.E., & Raczek, A.E. (1993). The MOS 36-item short-form health survey (SF-36) II. Psychometric and clinical tests of validity in measuring physical and mental health constructs. Med. Care 31 (3), 247-263.

47. Wei, L.J., & Lachin, J.M. (1984). Two-sample asymptotically distribution-free tests for incomplete multi-variate observations. Journal of American Statistics Association 79, 653–661.

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48. DeLong ER, DeLong DM, Clarke-Pearson DL. Comparing the Areas under Two or More Correlated Receiver Operating Characteristic Curves: A Nonparametric Approach, Biometrics 1988;44(3):837-845
49. Lachin, J.M. (2014). Applications of the Wei-Lachin multivariate one-sided test for multiple outcomes on possibly different scales. PLoS One 9 (10), 1-14.
50. Draper, K., Ponsford, J., & Schonberger, M. (2007). Psychosocial and emotional outcomes 10 years following traumatic brain injury. J. Head Trauma Rehabil. 22, 278–287.
51. Soberg, H., Røe, C., Anke, A., Arango-Lasprilla, J.C., Skandsen, T., Sveen, U., von Steinbüchel, N., & Andelic, N. (2013). Health-related quality of life 12 months after severe traumatic brain injury: a prospective nationwide cohort study. J. Rehabil. Med. 45 (8), 785-791.
52. Hoofien, D., Gilboa, A., Vakil, E., & Donovick, P.J. (2001). Traumatic brain injury (TBI) 10-20 years later: a comprehensive outcome study of psychiatric symptomatology, cognitive abilities and psychosocial functioning. Brain Inj. 15 (3), 189-209.
53. May, M., Milders, M., Downey, B., Whyte, M., Higgins, V., Wojcik, Z., ... & O'Rourke, S. (2017). Social behavior and impairments in social cognition following traumatic brain injury. J Int Neuropsychol Soc. 23(5), 400-411.
54. McLean, A. M., Jarus, T., Hubley, A. M., & Jongbloed, L. (2014). Associations between social participation and subjective quality of life for adults with moderate to severe traumatic brain injury. Disabil Rehabil. 36(17), 1409-1418.
55. Lamontagne, M., Poncet, F., Careau, E., Sirois, M., & Boucher, N. (2013). Life habits performance of individuals with brain injury in different living environments. Brain Inj. 27 (2), 135-144.
56. McIntyre, M., Ehrlich, C., & Kendall, E. (2018). Informal care management after traumatic brain injury: perspectives on informal carer workload and capacity. Disabil Rehabil. 1-9.
57. Martin, R., Levack, W. M., & Sinnott, K. A. (2015). Life goals and social identity in people with severe acquired brain injury: An interpretative phenomenological analysis. Disabil Rehabil. 37(14), 1234-1241.

58. Maas, A. I., Menon, D. K., Steyerberg, E. W., Citerio, G., Lecky, F., Manley, G. T., ... & Sorgner, A. (2014). Collaborative european neurotrauma effectiveness research in traumatic brain injury (center-tbi) a prospective longitudinal observational study. Neurosurgery, 76(1), 67-80.

59. Dikmen, S.S., Machamer, J.E., Powell, J.M., & Temkin, N.R. (2003). Outcome 3 to 5 years after moderate to severe traumatic brain injury. Arch. Phys. Med. Rehabil. 84 (10), 1449-1457.

60. Hoofien, D., Gilboa, A., Vakil, E., & Donovick, P. J. (2001). Traumatic brain injury (TBI) 10? 20 years later: a comprehensive outcome study of psychiatric symptomatology, cognitive abilities and psychosocial functioning. Brain Inj., 15(3), 189-209.

61. Dikmen, S. S., Machamer, J. E., Powell, J. M., & Temkin, N. R. (2003). Outcome 3 to 5 years after moderate to severe traumatic brain injury. Arch Phys Med Rehabil. 84(10), 1449-1457.

62. Polinder, S., Cnossen, M. C., Real, R. G., Covic, A., Gorbunova, A., Voormolen, D. C., ... & van Steinbuechel, N. (2018). A multidimensional approach to post-concussion symptoms in mild traumatic brain injury: A focused review. Front Neurol. 9, 1113.

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Table 1. Demographic characteristics of participants (*N* = 795).

		Frequency/Statistic
Gender	*Female*	222 (27.9%)
	Male	573 (72.1%)
Age	Mean; SD (range)	39; 13.3 (17-68)
Relationship	*Partnered*	403 (50.7%)
Status	*Not Partnered*	303 (38.1%)
Education	*Primary School*	42 (5.3%)
	Secondary School & Trade or Technical	403 (50.7%)
	Certificate	173 (21.8%)
	College Diploma/Degree	88 (11.1%)
	University Degree	
Living	*At home – independently*	420 (52.8%)
Arrangement	*At home – supported*	245 (30.8%)
(missing *N* = 45)	*Nursing Home*	75 (9.4%)
Help Needed	*Yes*	306 (38.8%)
(missing *N* = 62)	*No*	427 (53.7%)
Leisure Activities	*Individual (internet +hobbies)*	425 (53.5%)
	Social (socializing + physical activities)	505 (63.5%)
	Hobbies (hobbies + music)	395 (49.7%)

Table 2. MW effect size threshold values and their interpretation, comparing Test and Comparator groups (specified for each predictor in respective tables).

MW threshold	Degree of Sensitivity	Interpretation
0.29	Large	Higher HRQOL for 'Comparator'
0.36	Medium	group
0.44	Small	Higher HRQOL for 'Comparator'
0.50	**Equal**	group
0.56	Small	Higher HRQOL for 'Comparator'
0.64	Medium	group
0.71	Large	**Equal**
		Higher HRQOL for 'Test' group
		Higher HRQOL for 'Test' group
		Higher HRQOL for 'Test' group

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Table 3. Clinical characteristics of participants (*N* = 795).

		Frequency
GCS	*Mild (≥ 13)*	255 (32.1%)
	Moderate(8-12)	76 (9.6%)
	Severe (< 8)	464 (58.4%)
Months Since Injury	Mean; SD	59.8 (46.5)
Major Lesion	*None*	117 (14.9%)
	Frontal	256 (32.6%)
	Posterior	162 (20.6%)
	Diffuse	250 (31.8%)
GOSE	*Good Recovery (7-8)*	219 (27.6%)
	Moderate Disability (5-6)	433 (54.5%)
	Severe Disability (3-4)	143 (17.9%)
Self-Reported Health	*Comorbidity*	440 (55.3%)
Status	*Sensory/Psychosomatic*	631(79.4%)
	complaints	363 (45.7%)
	Motor/Skeletal complaints	
HADS Anxiety Score	*Normal*	496 (62.4%)
(missing *N* = 3)	*Mild*	144 (18.1%)
	Moderate/Severe	152 (19.1%)
HADS Depression Score	*Normal*	537 (67.5%)
(missing *N* = 6)	*Mild*	120 (15.1%)
	Moderate/Severe	132 (16.6%)

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Table 4. Pearson correlation between QOLIBRI and SF-36 subscales.

QOLIBRI Subscales	Physical Problems	Emotions	Social Relat.	Daily Life/ Autonomy	Self	Cognition	*Total QOLIBRI*
SF-36 Subscales							
RP	.52	.27	.29	.44	.33	.39	.46
PF	.56	.29	.27	.50	.37	.36	.48
BP	.59	.35	.24	.36	.34	.36	.45
GH	.52	.39	.33	.46	.48	.42	.54
PCS	.63	.23	.23	.47	.34	.41	.47
RE	.43	.43	.32	.39	.41	.33	.48
MH	.45	.64	.48	.48	.58	.42	.63
SF	.52	.52	.45	.49	.52	.45	.61
VT	.49	.48	.36	.46	.57	.42	.58
MCS	.43	.62	.45	.44	.56	.40	.60

NB: all correlations $p < .01$ (two-tailed), color-coded with darker shades representing stronger relationships.

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Table 5. Mann-Whitney (MW) effect size for QOLIBRI and SF-36 subscales and combined QOLIBRI scores (multivariate, Wei-Lachin procedure). Differences in HRQOL for patients with distinct levels of independence and reliance on others.

		Living Arrangements			**Help Needed**
Comparison *Comparator(left) vs. Test (right)*		*At home - independent vs. supported*	*At home - independent vs. Nursing Home*	*At home - supported vs. Nursing Home*	*No vs. Yes*
QOLIBRI subscales	Cognition	.38*	.50	.62*	.29*
	Self	.41*	.49	.58	.33*
	Daily Life/Autonomy	.32*	.41	.61*	.26*
	Social Relationships	.43*	.45	.53	.37*
	Emotions	.42*	.42	.50	.34*
	Physical Problems	.36*	.50	.62*	.27*
Combined Wei-Lachin		.39***	.46	.58**	.31***
SF-36 subscales	RP	.35*	.49	.66*	.33*
	PF	.35*	.42	.56	.31*
	BP	.42*	.51	.61*	.36*
	GH	.40*	.46	.56	.34*
	RE	.40*	.50	.61*	.37*
	MH	.43*	.43	.50	.34*
	SF	.40*	.51	.62*	.32*
	VT	.41*	.45	.54	.35*
Combined Wei-Lachin		.39***	.47	.58**	.34***

NB: significance level †$p_{Combined\ Wei\text{-}Lachin} < .10$,* $p_{Combined\ Wei\text{-}Lachin} < .05$, ** $p_{Combined\ Wei\text{-}Lachin} < .01$, $p_{Combined\ Wei\text{-}Lachin}$ ***< .001, and for subscales *$p < .001$, color-coded with darker shades representing larger effect sizes.

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Table 6. Mann-Whitney (MW) effect size for QOLIBRI and SF-36 subscales and combined QOLIBRI scores (multivariate, Wei-Lachin procedure). Differences in HRQOL for patients with distinct levels of participation in leisure activities.

		Leisure Activities		
Comparison *Comparator(left) vs. Test (right)*		*Individual (internet, hobbies) Yes vs. No*	*Social (socializing, physical act. Yes vs. No*	*Hobbies/music Yes vs. No*
QOLIBRI subscales	Cognition	.41*	.41*	.44*
	Self	.43*	.35*	.44*
	Daily Life/Autonomy	.38*	.34*	.44*
	Social Relationships	.42*	.40*	.47
	Emotions	.42*	.38*	.46
	Physical Problems	.43*	.34*	.44
Combined Wei-Lachin		.41***	.37***	.45**
SF-36 subscales	RP	.45	.38*	.46
	PF	.42*	.35*	.47
	BP	.47	.39*	.48
	GH	.46	.35*	.46
	RE	.48	.41*	.47
	MH	.66*	.35*	.44
	SF	.43*	.38*	.46
	VT	.44	.35*	.45
Combined Wei-Lachin		.44*	.37***	.46*

NB: significance level †$p_{Combined\ Wei\text{-}Lachin} < .10$,* $p_{Combined\ Wei\text{-}Lachin} < .05$, ** $p_{Combined\ Wei\text{-}Lachin} < .01$, $p_{Combined\ Wei\text{-}Lachin}$ ***< .001, and for subscales *$p < .001$, color-coded with darker shades representing larger effect sizes.

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Table 7. Mann-Whitney (MW) effect size for QOLIBRI and SF-36 subscales and combined QOLIBRI scores (multivariate, Wei-Lachin procedure). Differences in HRQOL for patients with distinct levels of health and functioning.

		Self-Reported Health Status		
Comparison *Comparator(left) vs. Test (right)*		*Comorbidity: No vs. Yes*	*Sensory/Psychosomatic complaints: No vs. Yes*	*No Motor/Skeletal complaints: No vs. Yes*
QOLIBRI subscales	Cognition	.39*	.33*	.36*
	Self	.37*	.29*	.35*
	Daily Life/Autonomy	.41*	.31*	.32*
	Social Relationships	.44*	.36*	.38*
	Emotions	.43*	.30*	.38*
	Physical Problems	.34*	.24*	.23*
Combined Wei-Lachin		.40***	.31***	.34***
SF-36 subscales	RP	.40*	.37*	.32*
	PF	.40*	.33*	.21*
	BP	.30*	.32*	.32*
	GH	.33*	.29*	.33*
	RE	.44	.35*	.38*
	MH	.46	.49	.41*
	SF	.41*	.32*	.36*
	VT	.39*	.28*	.36*
Combined Wei-Lachin		.39***	.32***	.34***
		GOSE Score		
Comparison *Comparator(left) vs. Test (right)*		*Good recovery vs. Moderate disability*	*Moderate disability vs. Severe disability*	*Good recovery vs. Severe disability*
QOLIBRI	Cognition	.32*	.45	.27*

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subscales	Self	.34*	.43	.29*
	Daily Life/Autonomy	.33*	.39*	.18*
	Social Relationships	.42*	.39*	.30*
	Emotions	.37*	.48	.34*
	Physical Problems	.27*	.43	.22*
Combined Wei-Lachin		.33***	.43***	.26***
SF-36 subscales	RP	.34*	.46	.30*
	PF	.31*	.36*	.19*
	BP	.33*	.52	.34*
	GH	.36*	.44	.29*
	RE	.37*	.47	.34*
	MH	.43*	.42	.35*
	SF	.34*	.47	.30*
	VT	.39*	.44	.33*
Combined Wei-Lachin		.36***	.45**	.30***

NB: significance level †$p_{Combined\ Wei\text{-}Lachin} < .10$,* $p_{Combined\ Wei\text{-}Lachin} < .05$, ** $p_{Combined\ Wei\text{-}Lachin} < .01$, $p_{Combined\ Wei\text{-}Lachin}$ ***< .001, and for subscales *$p < .001$, color-coded with darker shades representing larger effect sizes.

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Table 8. Mann-Whitney (MW) effect size for QOLIBRI and SF-36 subscales and combined QOLIBRI scores (multivariate, Wei-Lachin procedure). Differences in HRQOL for patients with distinct levels of depression and/or anxiety.

		HADS Anxiety Score		
Comparison *Comparator(left) vs. Test (right)*		*Normal vs. Mild*	*Mild vs. Moderate/Severe*	*Normal vs. Moderate/Severe*
QOLIBRI subscales	Cognition	.29*	.43	.23*
	Self	.28*	.41*	.23*
	Daily Life/Autonomy	.30*	.44	.27*
	Social Relationships	.34*	.44	.29*
	Emotions	.22*	.34*	.15*
	Physical Problems	.33*	.30*	.19*
Combined Wei-Lachin		.29***	.39***	.23***
SF-36 subscales	RP	.35*	.44	.29*
	PF	.41*	.38*	.30*
	BP	.40*	.35*	.26*
	GH	.33*	.39*	.24*
	RE	.28*	.42	.21*
	MH	.20*	.30*	.11*
	SF	.24*	.37*	.18*
	VT	.32*	.36*	.22*
Combined Wei-Lachin		.32***	.37***	.23***
		HADS Depression Score		
Comparison *Comparator(left) vs. Test (right)*		*Normal vs. Mild*	*Mild vs. Moderate/Severe*	*Normal vs. Moderate/Severe*
QOLIBRI	Cognition	.31*	.40*	.23*

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subscales	Self	.24*	.34*	.16*
	Daily Life/Autonomy	.28*	.34*	.19*
	Social Relationships	.32*	.34*	.19*
	Emotions	.26*	.41	.20*
	Physical Problems	.29**	.42	.24*
Combined Wei-Lachin		.28***	.37***	.20***
SF-36 subscales	RP	.39*	.37*	.29*
	PF	.34*	.41	.28*
	BP	.38*	.43	.33*
	GH	.26*	.39*	.21*
	RE	.31*	.42	.25*
	MH	.21*	.32*	.13*
	SF	.30*	.31*	.17*
	VT	.25**	.33*	.14*
Combined Wei-Lachin		.30***	.37***	.23***

NB: significance level †$p_{Combined\ Wei\text{-}Lachin} < .10$,* $p_{Combined\ Wei\text{-}Lachin} < .05$, ** $p_{Combined\ Wei\text{-}Lachin} < .01$, $p_{Combined\ Wei\text{-}Lachin}$ ***< .001, and for subscales *$p < .001$, color-coded with darker shades representing larger effect sizes.

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Table 9. Meta-level analysis for direct comparisons of disease-specific vs. general HRQoL instruments in 19 subdomains (distinct patient level contrasts) for QOLIBRI Total vs. SF-36 PCS and QOLIBRI Total vs. SF-36 MCS.

Meta-level Comparison				
Domains	*Subdomains contrasts*	*Comparison*	*p-value*	*Valid N*
Living arrangements	Independently vs. Supported by family	QOLIBRI PCS vs. MCS	0.6443 0.0078	784/ 460
	Independently vs. Nursing home	QOLIBRI PCS vs. MCS	0.8877 0.5964	784/ 146
	Supported by family vs. Nursing home	QOLIBRI PCS vs. MCS	0.5432 0.1291	460/ 146
Help needed	1 area vs. 2 areas	QOLIBRI PCS vs. MCS	0.0625 0.0004	797/ 580
Activities	Individual activities (vs. none)	QOLIBRI PCS vs. MCS	0.0444 0.0086	803/ 507
	Social activities (vs. none)	QOLIBRI PCS vs. MCS	0.6731 0.1020	947/ 355
	Hobbies (vs. none)	QOLIBRI PCS vs. MCS	0.2294 0.3178	740/ 568
Comorbidity	(none vs.) Comorbidities	QOLIBRI PCS vs. MCS	0.0055 0.0000	558/ 824
	(none vs.) Memory/Psychosomatic	QOLIBRI PCS vs. MCS	0.0490 0.0628	258/1186
	(none vs.) Motor/Skeleton	QOLIBRI PCS vs. MCS	0.0014 0.0000	704/ 692
HADS Anxiety	Normal vs. Mild	QOLIBRI PCS vs. MCS	0.0000 0.5176	938/ 268
	Normal vs. Moderate/Severe	QOLIBRI PCS vs. MCS	0.0000 0.4488	938/ 286

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	Mild vs. Moderate/Severe	QOLIBRI vs.	PCS MCS	0.3694 0.9854	268/ 286
HADS Depression	Normal vs. Mild	QOLIBRI vs.	PCS MCS	0.0000 0.6694	1006/ 228
	Normal vs. Moderate/Severe	QOLIBRI vs.	PCS MCS	0.0000 0.8344	1006/ 252
	Mild vs. Moderate/Severe	QOLIBRI vs.	PCS MCS	0.0822 0.9117	228/ 252
GOSE	Good vs. Moderate	QOLIBRI vs.	PCS MCS	0.9589 0.0000	367/ 823
	Good vs. Severe	QOLIBRI vs.	PCS MCS	0.7816 0.0002	367/ 245
	Moderate vs. Severe	QOLIBRI vs.	PCS MCS	0.4633 0.1385	823/ 245

NB: results were adjusted for multiplicity by Bonferroni corrections (alpha-adjusted level = 0.00132). Single P-values below this benchmark are marked gray.

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Differences in Health-Related Quality of Life after Traumatic Brain Injury between varying Patient Groups: Sensitivity of a Disease Specific (QOLIBRI) and a Generic (SF-36) Instrument. (DOI: 10.1089/neu.2019.6627)

This paper has been peer-reviewed and accepted for publication, but has yet to undergo copyediting and proof correction. The final published version may differ from this proof.

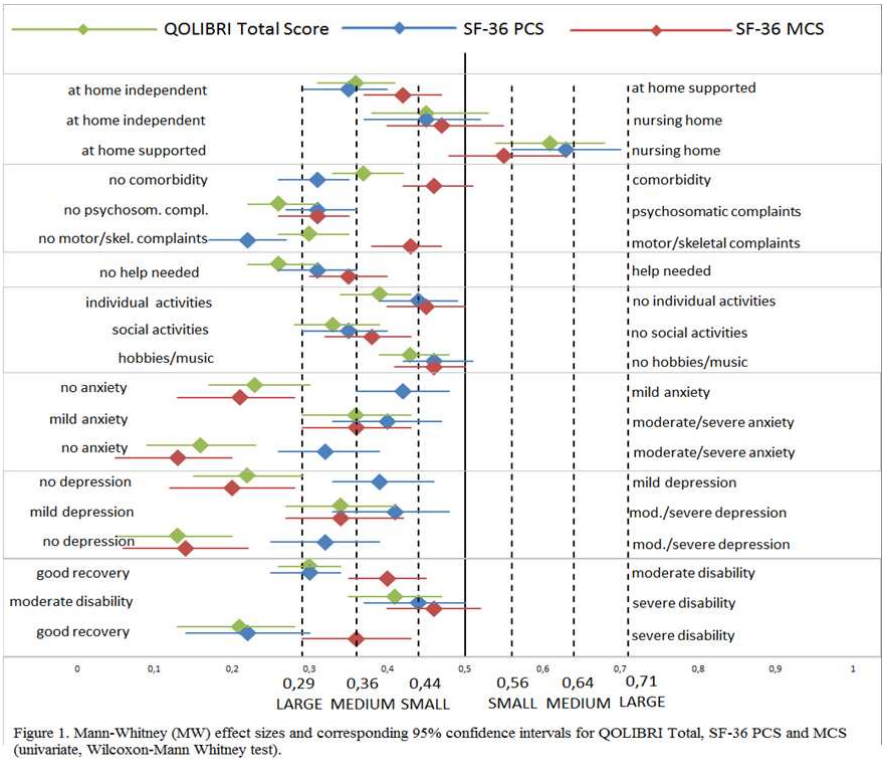

Figure 1. Mann-Whitney (MW) effect sizes and corresponding 95% confidence intervals for QOLIBRI Total, SF-36 PCS and MCS (univariate, Wilcoxon-Mann Whitney test).

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