

Predicting Wellness After Pediatric Concussion



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(RECEIVED July 31, 2018; FINAL REVISION February 25, 2019; ACCEPTED February 28, 2019)

Abstract

Objective: Concussion in children and adolescents is a prevalent problem with implications for subsequent physical, cognitive, behavioral, and psychological functioning, as well as quality of life. While these consequences warrant attention, most concussed children recover well. This study aimed to determine what pre-injury, demographic, and injury-related factors are associated with optimal outcome (“wellness”) after pediatric concussion. **Method:** A total of 311 children 6–18 years of age with concussion participated in a longitudinal, prospective cohort study. Pre-morbid conditions and acute injury variables, including post-concussive symptoms (PCS) and cognitive screening (Standardized Assessment of Concussion, SAC), were collected in the emergency department, and a neuropsychological assessment was performed at 4 and 12 weeks post-injury. Wellness, defined by the absence of PCS and cognitive inefficiency and the presence of good quality of life, was the main outcome. Stepwise logistic regression was performed using 19 predictor variables. **Results:** 41.5% and 52.2% of participants were classified as being well at 4 and 12 weeks post-injury, respectively. The final model indicated that children who were younger, who sustained sports/recreational injuries (vs. other types), who did not have a history of developmental problems, and who had better acute working memory (SAC concentration score) were significantly more likely to be well. **Conclusions:** Determining the variables associated with wellness after pediatric concussion has the potential to clarify which children are likely to show optimal recovery. Future work focusing on wellness and concussion should include appropriate control groups and document more extensively pre-injury and injury-related factors that could additionally contribute to wellness. (*JINS*, 2019, 25, 375–389)

Keywords: Traumatic brain injury, children, positive outcome, post-concussive symptoms, quality of life, neuropsychology

INTRODUCTION

Pediatric traumatic brain injury (TBI) affects a large number of children worldwide and causes a range of symptoms and

impairments that vary according to pre-morbid factors and injury severity (Dewan et al., 2016). Even the mildest form of TBI, concussion, can lead to transient and sometimes persistent physical (e.g., dizziness), cognitive (e.g., confusion), emotional (e.g., irritability), and somatic (e.g., fatigue) changes known as post-concussive symptoms (PCS) (Zemek et al., 2013). In some cases, concussion can lead to psychological problems (Emery et al., 2016) or cognitive deficits,

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though the latter often appear to be associated with pre-morbid problems (Babikian et al., 2011; Beauchamp et al., 2018). Taken together, concussion can have a deleterious effect on a person's quality of life (Fineblit et al., 2016). Research on the consequences of pediatric concussion has logically focused on identifying the negative effects of the condition and what factors are associated with poor outcome (Iverson et al., 2017; Yeates, 2010). These studies are critical to understanding the gravity of these brain injuries, identifying children most at risk for impairments, and improving the management and treatment of concussion in children. Given these potentially detrimental consequences, however, it is easy to lose sight of the fact that most children who sustain concussion ultimately recover well, with few, if any, long-term effects (Carroll et al., 2004). As such, there may be considerable value in focusing on the other face of concussion by investigating the positive outcomes and their predictors.

Course of Symptom, Cognitive, and Psychosocial Recovery

The results of a large-scale, prospective cohort study of persistent PCS (PPCS) suggested that approximately 30% of children between 5 and 18 years continue to experience symptoms 1 month after their injury (Zemek et al., 2016). Conversely, these data can be taken to highlight that 70% of children have relatively good outcome after 1 month and are on their way to full recovery. Prolonged symptom duration is increasingly being attributed to pre-morbid factors (Barlow, 2016), and substantial evidence suggests that significant cognitive and motor impairments are relatively rare and do not carry over in the mid to long term (Anderson et al., 2005; Asarnow et al., 1995; Babikian et al., 2011; Bijur & Haslum, 1995; Brooks et al., 2013; Fay et al., 1993; Hung et al., 2014; Rieger et al., 2013; Studer et al., 2014; Yeates, 2010). Using a statistically derived definition, Beauchamp and colleagues (2018) found that only about 10% of children who sustain concussion exhibit neuropsychological impairment 1 month post-injury. The same study also found that cognitive difficulties were predicted by pre-morbid factors; however, performance on acute tests of cognition also significantly predicted cognitive difficulties at 4 weeks post-concussion, and acute symptoms predicted cognitive difficulties 12 weeks after the injury, suggesting that the neuropsychological outcome in children and adolescents is not solely attributable to the presence of pre-injury problems. There is also some evidence for psychological, social, and behavioral disturbance after pediatric concussion (Catroppa et al., 2017; Taylor et al., 2015); however, at least three studies, including two systematic reviews, indicate that these problems rarely persist beyond the acute/subacute period and prognosis in these domains is generally good (Emery et al., 2016; Keightley et al., 2014; Plourde et al., 2018). Together, these findings suggest that a preponderance of children recover well from concussion.

Quality of Life after Pediatric Concussion

A disruption of one or more domains of functioning after concussion may result in an overall diminution of decrease

in children's quality of life, though the proportion of children affected is not clear. Children with PPCS reported poorer quality of life compared with those who recovered from their injury (Moran et al., 2012; Novak et al., 2016; Russell et al., 2017); however, the evidence as to whether those deemed to have recovered clinically also experience reduced quality of life is contradictory (Novak et al., 2016; Russell et al., 2017). Some data suggest that poorer quality of life is present regardless of injury severity (DeMatteo et al., 2014) and lasts between 3 and 6 months post-injury (Brown et al., 2016). However, other research suggests that most children who sustain concussion have adequate or good quality of life. For example, several studies indicated that the quality of life of children with mild TBI is not affected in the first 3 months post-injury (Petersen et al., 2008), nor up to 24 months post-injury (Rivara et al., 2011).

Wellness and Positive Outcome after TBI

In light of the overall good prognosis for a majority of children who sustain concussion, it is relevant to consider the results of a small number of studies that have looked at positive outcomes after TBI. For example, a systematic review by Sullivan and colleagues (2016) indicated that psychological resilience, generally defined as a modifiable, dynamic, and positive adaptation process in the context of significant adversity (Luthar et al., 2000; Sullivan et al., 2016), is associated with better outcome after TBI in adults (e.g., better quality of life, less fatigue and stress, fewer depressive symptoms, fewer PCS) (Losoi et al., 2015; McCauley et al., 2013; Merritt et al., 2015). The presence of other positive character strengths, such as coping, courage, and hope, has also been found to contribute to better outcomes after TBI in adults (Belanger et al., 2013; Hanks et al., 2014). Using an alternative approach to positive outcomes, Braden and colleagues (2012) examined health status, health-related self-efficacy, health-promoting behaviors, and subjective well-being in adults with moderate–severe TBI and found that the levels of these indicators are similar to those in other disability groups, suggesting that health and wellbeing can reflect optimal outcome after TBI. One study to date that has focused on resilience in pediatric concussion and found that psychological resilience (as defined by factors related to personal competence, tenacity, tolerance of negative affect, positive acceptance of change, control, and spiritual influences) was a significant predictor of PPCS in children aged 8–18 years (Durish et al., 2018).

Many of the constructs referred to in relation to the positive outcomes of brain injury (e.g., resilience, character strengths, quality of life, healthy behaviors) can be conceptualized under the broader umbrella of wellness, defined by the World Health Organization as a state of complete physical, mental, and social wellbeing, and not merely the absence of disease or infirmity (WHO, 1946). Some conceptions of wellness even go beyond the notion of minimal recovery from injury, referring to a state of optimal functioning. In this

sense, the National Wellness Institute posits that wellness is a dynamic process that strives towards individual achievement of full potential (Hettler, 1976). Applying this to the domain of TBI, Hawley and Joseph (2008) suggested that wellness may not simply be a return to *status quo*, but that recovery may actually involve going beyond pre-morbid levels of functioning.

The positive indicators of outcome, and wellness more specifically, have received limited attention in relation to TBI and are nearly absent from the pediatric TBI literature. The few studies that have documented wellness after TBI have done so in participants with more severe injuries, despite mTBI/concussion representing 90% of the TBI population and thus an important financial and societal burden. There is limited information available on the predictors of wellness after pediatric TBI, although such data could be valuable in determining which variables predict good prognosis and in identifying specific loci of intervention for improving positive outcomes in those at risk for post-concussion difficulties.

OBJECTIVES

The aim of this study was to determine what pre-existing, demographic, and injury factors are predictive of wellness after pediatric concussion. In accordance with existing notions (Bezner & Hunter, 2001; Diener, 1984; WHO, 1946), wellness is defined not only by the absence of PPCS and cognitive difficulties, but also by the presence of a subjective, global, positive indicator, namely good quality of life. A comprehensive predictive model was tested in a large sample of children and adolescents who sustained concussion and were assessed acutely in a pediatric emergency department and followed up 1 and 3 months post-injury. We hypothesized that a combination of pre-existing, demographic, and injury factors would contribute to wellness.

METHODS

Design

This was a planned substudy of a larger prospective, longitudinal, multicenter cohort study conducted among nine university-affiliated hospitals in 2013–2015 (The 5P Study). The full study protocol and details on the complete sample are provided elsewhere (Zemek et al., 2013b). Here, we summarize the methods and present the data pertaining to the participants who enrolled into the neuropsychological follow-up portion of the larger study. The neuropsychological substudy was offered in the ED at four of the nine study sites at the time of enrollment in the parent study and was conducted at 4 and 12 weeks post-injury.

Participants

Participants in the neuropsychological substudy were children ($N = 311$, aged 6–18 years, 35% female) who presented

to the EDs of four tertiary pediatric hospitals (Children's Hospital of Eastern Ontario, Toronto Sick Kids Hospital, Montreal Children's Hospital, Ste-Justine Hospital). Children were eligible to participate in the larger parent study if they were aged between 5 years and 17 years + 11 months at the time of presentation to the ED, if they sustained a concussion as defined by Zurich consensus statement (McCrorry et al., 2009), if the concussion occurred within the preceding 48 hr, and if they were proficient in English or French. The following exclusion criteria were applied at recruitment to determine eligibility: (a) Glasgow Coma Scale score <13; (b) abnormality on structural head CT or MRI (if performed clinically); (c) multisystem injury requiring hospitalization, operating room, or procedural sedation; (d) neurosurgical intervention, intubation, or ICU admission required; (e) intoxication at the time of ED presentation as per clinical judgment; (f) absence of traumatic injury as a primary event; (g) severe pre-existing neurological developmental delay resulting in communication difficulties; (h) insurmountable language barrier; (i) inability to follow up by phone or electronic mail; (j) previously enrolled in the same study (to ensure individuals who sustained another concussion during the course of the longitudinal study were not re-enrolled once they had completed follow-up).

PROCEDURE

ED Enrolment and Screening

The study was approved by the local research ethics committees of the four participating sites. Written informed consent was obtained from the participants and/or their parents prior to participation and verbal assent was obtained for all participants. The data were obtained in compliance with the Helsinki Declaration. Information and details regarding participants' demographics, past medical and developmental history, injury characteristics, and acute symptoms were collected at enrolment by a research assistant or nurse, using the validated Acute Concussion Evaluation inventory in the ED (Gioia et al., 2008). Information regarding past medical and developmental history was obtained via parent report and included questions regarding the presence or absence of a history of migraine, mood, sleep or developmental problems, such as attention-deficit hyperactivity disorder (ADHD) or learning disabilities. All data were acquired and managed in real time using the Research Electronic Data Capture (REDCap; Harris et al., 2009) application. Depending on their preferences, enrolled patients/parents completed follow-up questionnaires and surveys either electronically through REDCap or via telephone. Participants received email reminders 24 hr preceding each survey deadline; research assistants telephoned non-responders up to five times offering standardized verbal surveys.

Post-concussive Symptoms

Physical, cognitive, emotional, and sleep-related symptoms were reported acutely in the ED by parents completing the

20-item Post-Concussion Symptom Inventory (PCSI; Gioia et al., 2009; Sady et al., 2014), which included providing a baseline estimate corresponding to “pre-injury” ratings of the symptoms. The PCSI was then completed by participants at all the broader study follow-up time points (1, 2, 4, 8, and 12 weeks post-concussion), and these also included a baseline rating. Thus, PCSI delta scores were used for each time point (i.e., change in PCSI between a given time point’s baseline and the actual time point rating). The acute ED ratings (delta scores) were used as a predictor variable (i.e., PCS ratings from the ED *minus* pre-injury PCS ratings assessed in the ED), whereas the 4- (i.e., PCS ratings at 4 weeks *minus* pre-injury symptoms assessed at 4 weeks) and 12-week ratings (i.e., PCS ratings at 12 weeks *minus* pre-injury symptoms assessed at 12 weeks) were used as part of the definition for the main outcome variable (wellness).

Acute Balance and Cognitive Screening

The Standardized Assessment of Concussion–Child Version (SAC-C) was administered in the ED as part of the Child-Sport Concussion Assessment Tool (McCrorry et al., 2013). The SAC-C is a 30-point objective assessment of acute cognition comprising four indices: orientation (4 points), immediate verbal memory (15 points), concentration (6 points), and delayed verbal recall (5 points). The modified Balance Error Scoring System (BESS), a brief static postural stability assessment tool to measure performance on double-leg stance and tandem stance conditions, was also administered in the ED.

Neuropsychological Assessment

The neuropsychological test battery performed at 4 and 12 weeks post-injury included either eight (6–7-year-olds) or nine (≥ 8 -year-olds) standardized scores (either z -, T -, or standard scores) covering intellectual functioning, attention, working memory, executive functioning, verbal memory, processing speed, and psychomotor abilities. Full details of the neuropsychological protocol are published elsewhere (Beauchamp et al., 2018).

Quality of Life

Quality of life was documented at 4 and 12 weeks post-injury using the Pediatric Quality of Life Inventory (PedsQL) (Desai et al., 2014). The generic version of the questionnaire measures the core dimensions of health in terms of physical (eight items), emotional (five items), social (five items), and school (five items) functioning, providing a total score representing a transformation of the sum of scores on a 0–100 range. Participants ≥ 8 years completed the self-report version, and a parent proxy version was used for participants 6–7 years old.

STATISTICAL ANALYSES

Definitions

Wellness

The criteria used to define wellness in the analyses were based on existing conceptualizations of wellness (Diener, 1984; WHO, 1946), which require the absence of impairment in addition to the presence of a positive outcome. Applying this to the context of concussion and to the data available for this cohort, it was defined as:

Wellness = absence of PPCS + absence of cognitive inefficiency + presence of optimal quality of life

To reflect the notion that wellness describes a state of optimal outcome, participants were classified as “less well” if any of the above criteria were unmet. For descriptive purposes, if any one of the three definition components was missing and all others were “well,” the participant’s data were not used ($N = 270$ at 4 weeks post-injury and $N = 180$ at 12 weeks post-injury). The three components were combined to represent the construct of wellness, and their respective cut-off scores were defined as follows.

Persistent Post-concussive Symptoms

PPCS was the primary outcome of the larger cohort study and was defined according to the *International Statistical Classification of Disease and Related Health Problems*, Tenth Revision (Steindel, 2010) as the persistence of at least three symptoms compared with the state of being prior to the injury. An individual symptom was defined as “a positive difference between the current PCSI minus the perceived preinjury symptom rating” (Zemek et al., 2013b). To be classified as having no PCS, at least 85% of the PCSI items had to be completed.

Cognitive Inefficiency

Cognitive inefficiency was defined based on an adaptation of the published, statistically derived Neuropsychological Impairment Rule (Beauchamp et al., 2015), which determines the presence of neuropsychological impairment based on an individual’s performance on a large battery of neuropsychological measures. To fully capture more subtle cognitive changes typical of concussion in the current cohort, a less conservative approach used by Beauchamp et al. (2018) was applied here. Thus, cognitive inefficiency was considered to be present when an individual performed 1.0 SD *below* the mean on two or more neuropsychological measures. To be classified, participants had to have completed at least six of the battery subtests.

Quality of Life

The presence of optimal quality of life was defined as a score at or above the population means reported by Varni and

colleagues (2003) for the same measure. Age-appropriate norms were used for 6–7, 8–12, and 13–18-year-olds.

Modeling Strategy

To determine the predictors of wellness following concussion, we derived a comprehensive multivariable logistic regression model that incorporated data at both follow-up time points (i.e., wellness at 4 and 12 weeks treated as repeated outcomes, represented in separate rows in the dataset). Since previous research is limited on the predictors of wellness following concussion, we elected an “exploratory” modeling strategy that enabled the consideration and testing of a broad range of candidate predictors, but also the opportunity to add flexibility to model specifications by accommodating complex (e.g. non-linear) predictor–outcome relations. To this end, the model strategy had three main components: (1) an initial *a priori* selection of candidate predictors to be assessed within the confines of the sample size, (2) multiple imputation of missing data on candidate predictors and model outcomes, and (3) implementation of a model fitting procedure that involves a conservative backward elimination step and subsequent refitting where flexible splines were incorporated in the regression.

Selection of Candidate Predictive Factors

The *a priori* selection of candidate predictive factors (i.e., independent variables) considered conceptual relevance, hypothesized associations with outcome based on study investigators’ clinical experience, and data features [e.g., variable completeness (i.e., <15% missing values), presence of meaningful score variability, no significant correlation [i.e., $r < 0.7$] with other predictor candidates]. Additional considerations ensured a sufficiently broad coverage of domains, encompassing sociodemographic factors, patient history, and injury mechanism, as well as clinical presentation (e.g., scores from the SAC and PCSI collected acutely in the ED), within the constraints of the available sample size. Specifically, our approach was to keep within an approximate 10:1 event-per-variable ratio throughout the entire modeling process. The 20 candidate variables ultimately selected included: time (4 or 12 weeks), site (four levels, reference set to the largest level; $n = 103$), age (continuous), sex (males vs. females), maximum symptom duration of previous concussion (five levels: no previous concussion to longer than 8 weeks symptom duration), personal history of migraine (yes/no), history of developmental problem (yes/no: learning disability, ADHD, other developmental problem), history of mood/sleep disorders (yes/no), duration of lost consciousness (continuous), injury mechanism (sports related vs. others), post-traumatic amnesia (yes/no), acute ED PCSI physical factor score (range 0–6), acute ED PCSI fatigue factor score (range 0–6), acute ED PCSI emotional factor score (range 0–6), acute ED PCSI cognitive factor score (range 0–6), SAC orientation score (range 0–4), SAC immediate memory score (range 0–15), SAC delayed recall score (range 0–5),

SAC concentration score (range 0–6), and BESS tandem stance score (range 0–7). Summary statistics of these variables (e.g., median, IQR, range, percentage) as well as additional descriptive variables of interest are provided in Table 1.

Multiple Imputation

To add robustness in model fitting, we performed an initial multiple imputation of missing data for all relevant variables (i.e., all candidate predictors and outcomes with any missing values) using a chained equations approach (Little & Rubin, 2002; Moons et al., 2006; van Buuren, 2012; van Buuren et al., 2006). Through this process, “educated guesses” of missing data were generated on a variable-by-variable basis based on the interrelationships among the variables included in the imputation model. The chained equations approach affords unique univariate imputation techniques to be employed according to the type of target variable being imputed. Specifically, the predictive mean matching strategy was used for imputing missing values from numeric variables (continuous or ordinal), and logistic regression was the basis for imputing missing values for categorical variables. At the end, multiple sets of imputed data were generated to help capture the variability/uncertainty of the imputed values. To optimize imputation performance, we initially considered a comprehensive set of 169 variables collected from the parent study as potential auxiliary variables for inclusion in the imputation model. Of these, 62 were ultimately selected. As with our candidate predictors, these auxiliary variables encompassed a wide range of factors, including constituent items of various scales common in concussion research (e.g., specific items from the PCSI, PedsQL, and SAC; scores from specific neuropsychological tests and balance tests), with the key condition being that, to be selected, they must be reasonably well completed (i.e., >50% data available) among the subset of observations that had incomplete data on any variables intended for modeling (i.e., candidate predictors or model outcomes). Thus, combining outcome measures and 19 candidate predictors, a comprehensive 83-variable imputation model was derived. In accordance with the current recommendations (I.R. White et al., 2011), the imputation procedure was repeated seven times to match the percentage of patients with incomplete data (on intended model covariates or outcome) in the sample (6.8%). This created seven unique, imputed datasets available for further analysis. Notably, no imputation was performed on missing data due to non-participation. The imputed dataset was constructed based only on the eligible observations of individuals who participated at a given time point. Thus, the amount of missing data among those who did participate was only 17/287 (5.9%) at week 4 and 16/196 (8.2%) at week 12.

Model Fitting Procedure

After multiple imputations, a preliminary logistic regression model with all 19 candidate predictors was fitted for each

Table 1. Participants' demographic, pre-morbid, and clinical characteristics

	<i>n</i> usable	Range/level	Median (IQR) / <i>n</i> (%)
Age	311	6.0–18.0	11.9 (9.1, 14.2)
Sex	311	Female	109 (35.0)
Maximum symptom duration of previous concussion(s)			
No previous concussion	308	223	72.4
<1 week	308	33	10.7
1–2 weeks	308	23	7.5
3–4 weeks	308	12	3.9
5–8 weeks	308	7	2.3
>8 weeks	308	10	3.2
History of migraine	309	Yes	39 (12.6)
History of developmental problem ^a	310	Yes	48 (15.5)
History of mood/sleep disorders	310	Yes	33 (10.6)
Duration of loss of consciousness (minutes)	309	0.0–10.0	0.0 (0.0, 0.0)
Seizure ^b	311	Yes	8 (2.6)
Mechanism of injury ^c	311	Sports/recreational	198 (63.7)
		Non-sport/Fall	102 (32.8)
		MVC	7 (2.3)
		Assault	4 (1.3)
PCSI physical factor score (acute ED ratings)	307	0.0–5.5	1.6 (0.9, 2.4)
PCSI fatigue factor score (acute ED ratings)	307	0.0–6.0	2.3 (1.0, 4.0)
PCSI emotional factor score (acute ED ratings)	307	0.0–5.0	0.5 (0.0, 1.5)
PCSI cognitive factor score (acute ED ratings)	306	0.0–5.4	0.8 (0.0, 2.0)
Amnesia ^d	311	Yes	100 (32.2)
Tandem stance, no. of errors	303	0.0–10.0	3.0 (1.0, 10.0)
Double-leg stance, no. of errors ^e	304	0.0–10.0	0.0 (0.0, 1.2)
SAC orientation	306	0.0–4.0	4.0 (3.0, 4.0)
SAC immediate memory	306	0.0–15.0	14.0 (13.0, 15.0)
SAC delayed recall	306	0.0–5.0	4.0 (3.0, 5.0)
SAC concentration	304	0.0–6.0	4.0 (3.0, 5.0)

Notes: ^aIncludes developmental disorders, ADHD, and learning disabilities (e.g., dyslexia, dyscalculia). ^bThe seizure variable was excluded from modeling because there were too few cases. ^cThis was dichotomized to sports/recreational vs. other for modeling. ^dIncludes amnesia before and/or after the event, but only amnesia after the event was considered in modeling to reflect ongoing impairments in memory formation. ^eDouble-leg stance was not considered for modeling because of high correlation ($r > 0.6$) with tandem stance.

Abbreviations: ED = emergency department; IQR = interquartile range; MVC = motor vehicle collision; PCSI = Post-Concussion Symptom Inventory; SAC = Standardized Assessment of Concussion.

of the seven imputed datasets. To pool the results, parameter estimates were then averaged across all models and imputation-adjusted variance estimates were computed according to Rubin's rule (Rubin, 2004). To correct for intra-subject correlation due to clustering (i.e., repeated outcomes at different weeks may be provided by the same participant), standard errors of model parameters were further adjusted using the Huber–White method (Huber, 1967; H. White, 1980). Then, a conservative backward stepwise elimination was performed to retain the variables that contributed most to outcome prediction using a cut-off of $p > 0.25$ (for removal). The acceptable variance inflation factor for each retained covariate (<5) was verified at this step. To allow for the exploration of the nature of the predictor–outcome relationship (e.g., non-linearity), as a final step the model was refitted by incorporating flexible restricted cubic spline functions with three knots at 0.1, 0.5, and 0.9 quantiles (Harrell, 2015) for all continuous predictors that remained in the model, and the same corrections were re-applied to the estimated standard errors as above to arrive at the final

multivariable model. Interaction terms were not considered, as priority for degree-of-freedom spending was given to the testing of a more comprehensive set of individual predictors and also to exploring the potential non-linearity effects.

Contributions of individual predictors were summarized by an overall Wald chi-square statistic, which provides an indication of the relative importance of model predictors. Adjusted odds ratios and p -values were also estimated based on specific contrast hypotheses. For each continuous predictor (with associated spline terms), a multiple degree-of-freedom joint test of the predictor and associated non-linear terms was performed. Estimated adjusted odds ratios were based on a contrast of the 25th vs. 75th quantile values. For categorical predictors, a contrast of all predictor levels against the reference level was performed. Discrimination performance of the model was assessed by the c -statistic (averaged from models derived from each imputed dataset). All analyses were performed using R version 3.3.2 (rms, mice packages; R Core Team, 2016).

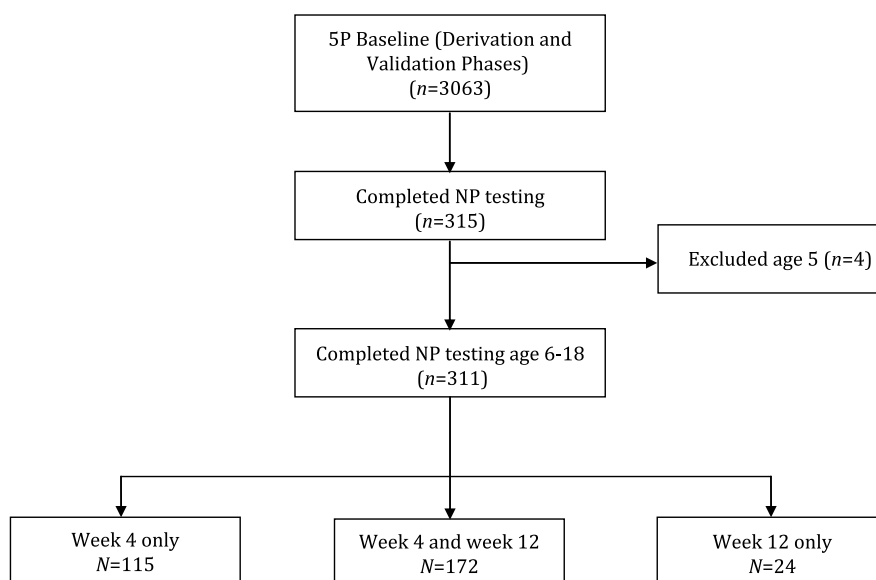


Fig. 1. Flowchart of recruitment for the main study and those enrolled in the neuropsychological follow-up in four of the study sites.

Table 2. Outcome distribution of wellness variables

Variable	Week 4 <i>n</i> usable	Level	Frequency	%	Week 12 <i>n</i> usable	Level	Frequency	%
Cognitive inefficiency	284	Yes	46	16.2	196	Yes	25	12.8
		No = well	238	83.8		No = well	171	87.2
Good quality of life	262	No	102	38.9	176	No	46	26.1
		Yes = well	160	61.1		Yes = well	130	73.9
Persistent PCS	262	Yes	103	39.3	175	Yes	56	32.0
		No = well	159	60.7		No = well	119	68.0
Wellness	270	No	158	58.5	180	No	86	47.8
		Yes = well	112	41.5		Yes = well	94	52.2

Note: Frequencies represent raw, unimputed cases.

Abbreviation: PCS = post-concussion symptoms.

RESULTS

Final Sample Characteristics

The recruitment flowchart is presented in Figure 1, and participant characteristics are described in Table 1. As reported elsewhere (Beauchamp et al., 2018), the participants enrolled in the neuropsychological follow-up tended to be slightly younger, were more likely to have had a previous concussion, had a greater prevalence of a family history of migraine, and displayed greater PCS at 4 and 12 weeks post-injury than those in the larger parent study. There was no significant difference in PCSI between children who participated in the 4-week post-injury follow-up and those who completed both the 4- and 12-week follow-up (frequency of PPCS between groups: $p = 0.776$; all PCSI factor score differences between $p = 0.14$ and 0.69). Children who completed week 4 (but not week 12) tended to be slightly older ($M = 12.35$; $SD = 3.07$ years) than those who completed both time points

($M = 11.36$; $SD = 3.08$) or only the week 12 time point ($M = 11.04$; $SD = 2.91$ years) ($p = 0.02$).

Outcome Distribution for Wellness Variables

Table 2 presents the outcome distribution for the main study variables. This table is based on unimputed data so as to describe the actual number of cases that were classified according to the wellness definition. Of the 270 participants who had completed wellness data, 112/270 (41.5%) were defined as well at 4 weeks post-injury, and the rate increased to 94/180 (52.2%) at 12 weeks post-injury (difference 10.7%; 95% CI = 2–20%). Of the 172 individuals who participated at both time points, 151 had (non-imputed) wellness outcome values at both time points. Among these 151 participants, 60 were classified as “well” at week 4, of which 13 (20%) were less well at week 12. Among the 115 subjects who participated only at week 4 (missing at week 12), 45 (39.1%)

Table 3. Correlations between the variables comprising wellness and the wellness composite

Variable	Cognitive inefficiency	QOL	PPCS	Wellness
Cognitive inefficiency	1.00	-0.10	0.02	-0.40
Quality of life	-0.10	1.00	-0.49	0.68
PPCS	0.02	-0.49	1.00	-0.72
Wellness	-0.40	0.68	-0.72	1.00

Abbreviations: PPCS = persistent post-concussion symptoms; QOL = quality of life.

Table 4. Distribution of how the three wellness components contributed to a classification of “less well” (absence of wellness) at 4 and 12 weeks post-injury

Variable	N	Week 4 (n = 158)	Week 12 (n = 86)
Category, frequency/ n (%)	244		
Cognitive inefficiency <i>only</i>		25/158 (15.8)	15/86 (17.4)
Cognitive inefficiency and low QOL		5/158 (3.2)	4/86 (4.7)
Cognitive inefficiency and low QOL and PPCS		13/158 (8.2)	4/86 (4.7)
Cognitive inefficiency and PPCS		3/158 (1.9)	2/86 (2.3)
Low QOL <i>only</i>		25/158 (15.8)	11/86 (12.8)
Low QOL and PPCS		59/158 (37.3)	27/86 (31.4)
PPCS <i>only</i>		28/158 (17.7)	23/86 (26.7)

Abbreviations: PPCS = persistent post-concussion symptoms; QOL = quality of life.

were “well” at week 4, 60 (52.2%) were less well at week 4, and 10 (8.7%) were indeterminate due to missing component score(s).

Table 3 presents the correlations between the wellness sub-criteria (cognitive inefficiency, PPCS, quality of life) and the overall wellness score, and Table 4 shows the frequency distribution for each of the wellness sub-criteria, and combinations thereof, in relation to the classification of “less well” at 4 and 12 weeks post-injury.

Wellness Prediction Model

Table 5 presents the results of the logistic regression predicting wellness, including the contribution of 13 predictor variables. The overall model was significant ($\chi^2 = 85.92$, $df = 21$, $p < 0.001$) and five variables were found to have a significant effect on the outcome (wellness): age, mechanism of injury, history of developmental problem, acute ED PCSI physical symptoms, and SAC concentration. Sex and history of mood/sleep disorders approached significance.

Table 5. Wald chi-square statistic from model fit for logistic regression predicting wellness after pediatric concussion

Variable	χ^2	df	p
Week	2.44	1	0.119
Site	3.54	3	0.316
Age	15.43	2	<0.001
Nonlinear	0.60	1	0.438
Sex	3.72	1	0.054
History of developmental problem	5.40	1	0.020
History of mood/sleep disorders	3.85	1	0.050
Mechanism of injury	4.47	1	0.034
PCSI-P physical factor score	9.23	2	0.010
Nonlinear	3.86	1	0.050
PCSI-P emotional factor score	1.54	2	0.463
Nonlinear	0.11	1	0.745
PCSI-P cognitive factor score	4.66	2	0.097
Nonlinear	2.38	1	0.123
Amnesia	2.32	1	0.128
SAC delayed recall	1.91	2	0.386
Nonlinear	0.28	1	0.595
SAC concentration	7.55	2	0.023
Nonlinear	0.24	1	0.622
Total nonlinear	7.61	6	0.268
Total	58.92	21	<0.001

Notes: Bold implies significant predictors at $p < .05$.

Abbreviations: PCSI = Post-Concussion Symptom Inventory; SAC = Standardized Assessment of Concussion.

The resulting c -statistic was modest ($c = 0.730$), but satisfactory (i.e., >0.70).

The relations of predictor variables with wellness are illustrated in Figure 2, and the model contrasts and odds ratios are presented in Table 6. Older participants and those who reported a history of developmental problems (ADHD or learning difficulties) were less likely to be well. Those who sustained sports/recreational injuries and those who had higher scores on the SAC concentration subscale were more likely to be well. Female sex and the presence of a history of mood or sleep disorders were again just at the cut-off for significance and were associated with a greater likelihood of not meeting the wellness criteria ($p = 0.054$ and 0.050 , respectively). Although the overall Wald chi-square statistic was not significant in the previous analysis, acute ED ratings of PCSI cognitive symptoms emerged in the odd ratios as a significant predictor.

DISCUSSION

This study aimed to determine what factors are associated with the probability of being well after a childhood concussion, where “wellness” was defined as the absence of PPCS or cognitive difficulties combined with optimal quality of life at 4 and 12 weeks post-injury. Of the children who had sufficient data to determine wellness, 41.5% were considered to be well at 4 weeks, and this increased, though not significantly, to just over half the group (52.2%) at 12 weeks

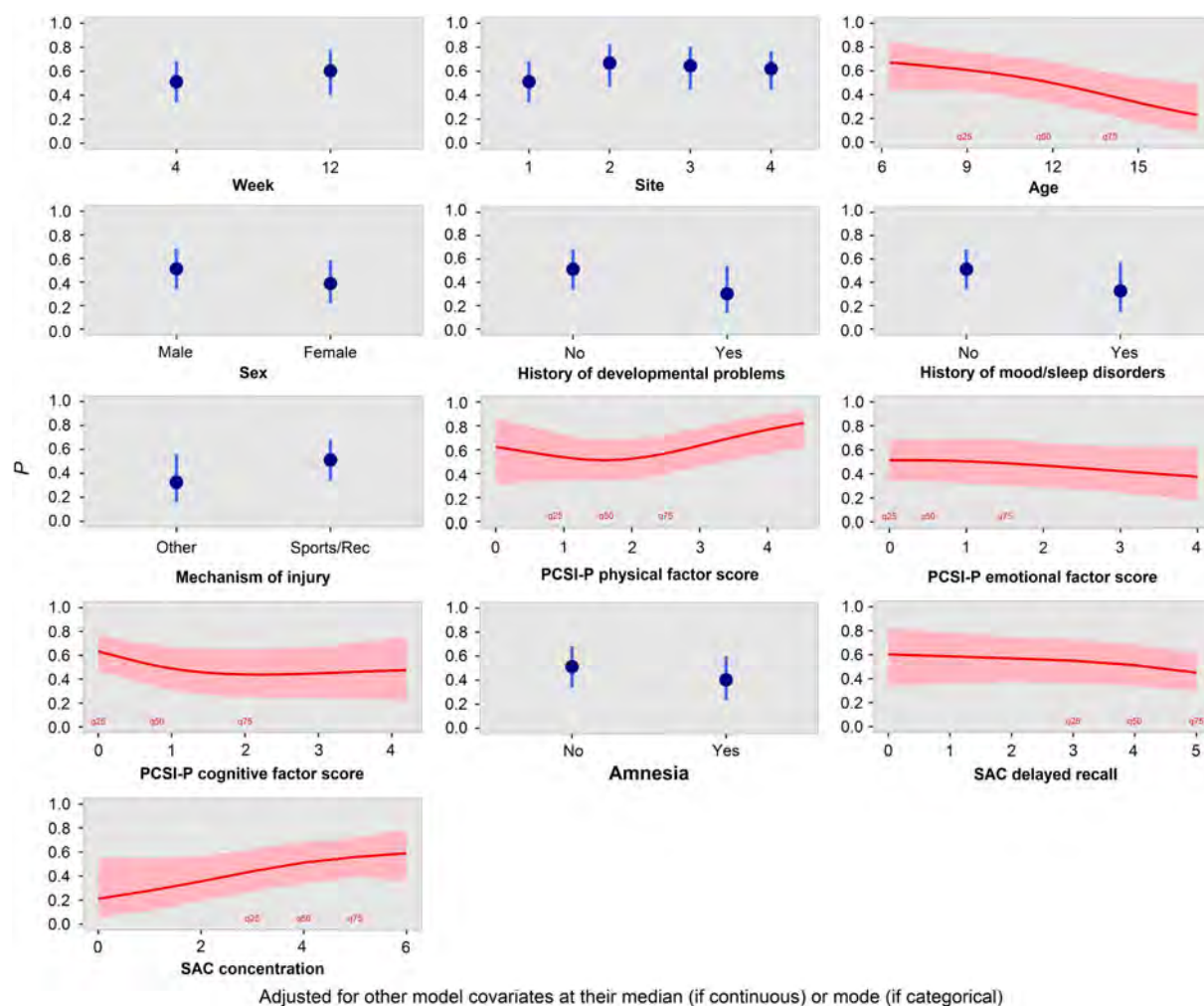


Fig. 2. Partial effect plots illustrating the relation of each predictor variable with the wellness outcome.

post-injury. The individual components of wellness (cognitive inefficiency, PPCS, quality of life) were all moderately to strongly correlated with the global outcome and, in isolation, had similar frequency distributions in children classified as less well. At both 4 and 12 weeks post-injury, the most common reason for being less well was a combination of PPCS and lower quality of life (37% and 31%). Given the paucity of research focusing on wellness after TBI and the novel approach used here, it is premature to determine whether this is a typical rate of wellness after concussion and whether it is comparable to other patient cohorts.

Various factors related to pre-morbid status, demographics, and injury were predictive of wellness. In particular, younger children (in the 6–8-year range) were more likely to be considered well after injury than older children. This is in keeping with other studies and reviews suggesting that age is associated with outcome after mild TBI. This body of evidence generally indicates that older children have an increased risk of PPCS (Babcock et al., 2013; Field et al., 2003; Iverson et al., 2017; Scopaz & Hatzenbuehler, 2013; Zemek et al., 2013a, 2016), although some studies suggest that this effect may be related to mechanisms of injury in

different age groups (e.g., adolescents more likely to be involved in more severe mechanisms) or to measurement bias (e.g., adolescents better able to recognize and report symptoms). The wellness indicators used here combined three outcome domains (symptoms, cognition, quality of life), which may be differentially associated with age, making the results difficult to compare with previous work. Nonetheless, the current findings suggest that when these three domains are considered together, among children aged 6–18 years, younger children with concussion are more likely to be well 1 and 3 months post-injury.

The absence of pre-injury problems (mainly learning disabilities and ADHD, but also mood and sleep disorders) also emerged as a significant predictor of being well. This result aligns with previous work highlighting the significance of pre-morbid problems in neuropsychological prognosis after concussion (Babikian et al., 2013; Beauchamp et al., 2018; see also Goreth & Palokas, 2018). A direct association between diagnosis of a learning disability (Balazs et al., 2016; Waber et al., 2019) or ADHD (Klassen et al., 2004; Lee et al., 2019; Varni & Burwinkle, 2006) and reduced quality of life has also been reported. Thus, participants with these

Table 6. Adjusted odds ratios for wellness predictor variables

Contrast	<i>b</i>	SE	Lower	Upper	<i>z</i>	<i>p</i>	OR	Lower	Upper
Week 12:4	0.36	0.23	-0.09	0.82	1.56	0.119	1.44	0.91	2.28
Site 2:1	0.65	0.46	-0.26	1.56	1.41	0.159	1.92	0.78	4.75
Site 3:1	0.55	0.35	-0.14	1.23	1.56	0.119	1.73	0.87	3.44
Site 4:1	0.44	0.34	-0.22	1.10	1.31	0.189	1.55	0.80	2.99
Age 14.01:8.91	-0.90	0.23	-1.35	-0.45	-3.90	<0.001	0.41	0.26	0.64
Sex male:female	0.51	0.26	-0.01	1.03	1.93	0.054	1.66	0.99	2.79
Hx developmental problem yes:no	-0.89	0.38	-1.63	-0.14	-2.32	0.020	0.41	0.20	0.87
Hx mood/sleep disorders yes:no	-0.78	0.40	-1.55	-0.00	-1.96	0.050	0.46	0.21	1.00
Mechanism of injury	0.78	0.37	0.06	1.49	2.12	0.034	2.17	1.06	4.45
PCSI-P physical 2.50:0.875	0.10	0.29	-0.46	0.66	0.33	0.739	1.10	0.63	1.93
PCSI-P emotional 1.5:0	-0.10	0.36	-0.80	0.61	-0.27	0.788	0.91	0.45	1.83
PCSI-P cognitive 2:0	-0.79	0.37	-1.51	-0.07	-2.15	0.031	0.45	0.22	0.93
Amnesia yes:no	-0.44	0.29	-1.01	0.13	-1.52	0.128	0.64	0.36	1.14
SAC delayed recall 5:3	-0.40	0.32	-1.04	0.23	-1.24	0.216	0.67	0.35	1.26
SAC concentration 5:3	0.48	0.21	0.07	0.88	2.30	0.022	1.61	1.07	2.42

Notes: Bold indicates significant predictors at $p < .05$. Range is 75th vs. 25th quantiles for continuous/ordinal variables.

Abbreviations: Hx = history; OR = odds ratio; PCSI = Post-Concussion Symptom Inventory; SAC = Standardized Assessment of Concussion; SE = standard error.

pre-injury diagnoses may have experienced poorer quality of life and thus an increased likelihood of not meeting the criteria for wellness even before their injury, and this could either have been maintained or compounded by concussion through a double-hazard effect. However, it is not possible to objectively ascertain whether quality of life was lower in some participants before they sustained their injury, as the design did not include a pre-injury (retrospective) measure of this domain. Notably, a history of learning disability, ADHD, or other developmental disorders did not emerge as a predictor in this sample when PCS was studied in isolation (Zemek et al., 2016), suggesting that this particular predictor is especially relevant to cognitive functioning or quality of life.

Children who scored higher on the SAC concentration subtest were more likely to be well after concussion. This test of working memory assesses performance based on backward digit span and recitation of the months of the year in reverse order. To our knowledge, only two other studies (Beauchamp et al., 2018; O'Neill et al., 2015) have focused on the predictive utility of this measure in concussion, despite its inclusion in the widely used Sports Concussion Assessment Tool (Davis et al., 2017). A previous study in the same sample found that the SAC immediate memory and concentration subtests were predictive of better neuropsychological performance at 4 and 12 weeks post-injury (Beauchamp et al., 2018). The current findings suggest that intact acute working memory may be especially useful in foretelling wellness after pediatric concussion, although these findings need to be replicated in independent samples. Future work could also look into identifying a level or cut-off for the SAC concentration subtest that could provide clinicians with a marker for prognosis and thereby facilitate referral for follow-up.

Past work focusing on the negative effects of concussion have shown an effect of sex as a risk factor for poor outcome, with female sex predicting overall risk of concussion and

increased PCS, for example (McNally et al., 2013; Scopaz & Hatzenbuehler, 2013; Zemek et al., 2016). The findings of the current study were inconclusive in regard to the association between sex and wellness, though the results did align in the expected direction; males were more likely to be designated as being well when symptoms, cognition, and quality of life were considered jointly.

Despite it being used as a common measure of PCS after concussion (McCauley et al., 2012), no components of the acute ED ratings of PCSI unambiguously emerged as being especially useful in predicting wellness. The PCSI physical factor score, which taps into symptoms such as dizziness, balance problems, sensory sensitivity, and nausea, was initially identified as a predictor based on the Wald chi-square statistic, but the relation was not in the expected direction (greater presence of physical symptoms predicted wellness). The exploration of the partial effect plots indicated that most participants in the sample fell in the 0–2.5 range, which showed little effect. The estimated effects of acute ED ratings of PCSI physical scores at more extreme ranges (e.g., >3.5) were based on fewer participants, suggesting that the results were driven by a few influential scores. The PCSI physical factor score was no longer predictive when the adjusted odds ratios were considered. The exploration of the partial effect plot for the PCSI cognitive factor score, which taps into symptoms of impaired concentration, memory, and speed of processing, showed a borderline effect in the 25–75 percentile range and the results were in the expected direction (fewer cognitive symptoms associated with being well); however, there was no strong evidence for an overall effect, given that the Wald chi-square statistic was not significant ($p = .09$), and thus the effect of this variable may only be modest at best.

Finally, mechanism of injury emerged as a significant predictor of wellness. Individuals who sustained sports or recreational injuries were more likely to be well than those who

sustained other types of injuries (mainly falls, motor vehicle collision [MVC], and assault). Seiger and colleagues (2015) similarly found that youth aged 13–21 years who sustained concussion during sports (football and soccer) had shorter recovery periods and better visual memory and motor speed scores on the Immediate Post Concussion Assessment Tool (Lovell et al., 2005) than those who sustained concussion due to MVC. They suggest that this effect may be due to increased pressure on athletes to return to play, but highlight that true cognitive differences may also be present and that the unique mechanisms associated with MVC (e.g., higher velocity, different forces) may play a role in the severity of the injury. In an earlier study conducted in adults with mild TBI, Hanlon and colleagues (1999) also found that participants with sports-related injuries generally fared better on neuropsychological tests than those who sustained injury through assault, falls, or MVC.

The current findings contribute to a growing body of work that supports the value of examining indicators of positive outcome to better understand TBI. While the concept of wellness lacks a consensual definition, the breadth of the work so far in TBI suggests that positive outcomes can range from specific constructs such as resilience (Losoi et al., 2015; McCauley et al., 2013), character traits (Hanks et al., 2014), and positive psychological growth (Hawley & Joseph, 2008), to broader themes such as healthy behaviors (Braden et al., 2012) or quality of life (Di Battista et al., 2012), and that more work is needed to understand how these factors combine and evolve to influence recovery. The definition of wellness used here was based on a straightforward conceptualization combining the absence of impairment with a single indicator of suitable functioning and was applied only to the outcome of concussion. Future work could broaden this definition to other spheres of functioning (e.g., occupational, physical, social, intellectual, spiritual, emotional) and could contribute to the empirical validation of resiliency models for TBI (see, e.g., Nalder et al., 2018).

Strengths and Limitations

A strength of the study is its longitudinal nature and the analytic approach used, which allowed the investigation of the evolution of wellness across time. Of note, however, only a subset of participants was truly followed over time with complete data at all time points. The statistical model included a range of variables chosen via a rigorous approach. The *c*-statistic, however, was relatively modest, suggesting that other significant predictors are yet to be identified.

The proposed definition of wellness is useful in that it combines three domains of functioning that are relevant to concussion: symptoms, cognition, and quality of life. However, because these domains inherently rely on different measurement approaches (self-report, parent report, neuropsychological testing), this introduces possible measurement biases that are age-related. For example, the neuropsychological testing may provide a more accurate reflection of a

child's status in the younger age group than the use of self- or parent report of PCS or quality of life at the same age. Related to the issue of measurement bias, evidence suggests that self and parent proxy ratings on questionnaires, such as those used here, show only limited agreement (Balazs et al., 2016; Sady et al., 2014). The PCSI was completed by different raters in the ED (parent) and at follow-up (participant). Additionally, we did not collect data on the identity of the raters (mothers vs. fathers) in the ED. This procedure may have introduced rater-related biases.

While the sample is one of the largest for which neuropsychological outcomes of concussion have been systematically tested, the sample is characterized by a selection bias, because participants could choose to opt in or out of the neuropsychological substudy. The presence of PPCS in this subgroup was somewhat higher than that in the larger study sample (39% vs. 30–33%), suggesting that the children in the neuropsychology substudy had greater symptom burden and may therefore have been less likely to be classified as well compared to the broader population of children with concussion. Another limitation of the sample is the absence of a control group. It is possible that the demographic predictors of wellness would be the same in an uninjured population of children.

It is possible that a pre-morbid history of cognitive problems and SAC test scores are related. That is, the participants presenting with pre-morbid learning disabilities or ADHD may have performed more poorly on the SAC regardless of their concussion. Children with pre-existing cognitive or psychological difficulties appear to constitute a particular subset of the concussion population that may require specific attention, given the possibility that concussion may compound their difficulties (Beauchamp et al., 2018; Iverson et al., 2017; Plourde et al., 2018). Information on pre-morbid cognitive problems was limited in this study to parent report and was not verified quantitatively or through medical reports, which may have introduced inconsistencies in diagnoses and reporting. Related to this, pre-injury functioning was not taken into account for the quality-of-life criterion, which was only based on current ratings relative to normative standards.

CONCLUSIONS

The findings of the study indicate that younger age, absence of pre-morbid cognitive/developmental problems, sports/recreational injuries, and better acute working memory are associated with a greater probability of wellness after pediatric concussion. The advantage of using wellness to characterize recovery after concussion is that the construct takes into account multiple factors. Accordingly, a status of optimal functioning is more difficult to attain using this definition, but may better reflect an individual's overall perception of recovery in everyday life. The current approach is not meant to minimize the significant and worrisome impact that concussion may have on child development, but rather to

emphasize the value of focusing on the large proportion of children who do recover well from their injuries, to inform future research and clinical practice, ultimately leading to better management, treatment, and recovery. Future research should include comparison groups and should further examine the psychological reactions to injury that might influence outcome, as well as document more extensively pre-injury functioning where possible. These additional steps are necessary to pave the way for identifying intervention targets that promote optimal, positive outcomes.

ACKNOWLEDGMENTS

Brian Brooks receives royalties from the sale of the book, *Pediatric Forensic Neuropsychology* (2012, Oxford University Press), and three pediatric neuropsychological tests [Child and Adolescent Memory Profile (ChAMP; Sherman and Brooks, 2015; PAR Inc.), Memory Validity Profile (MVP; Sherman and Brooks, 2015; PAR Inc.), and Multidimensional Everyday Memory Ratings for Youth (MEMRY; Sherman and Brooks, 2017; PAR Inc.)]. Keith Yeates is supported by the University of Calgary Robert and Irene Ward Chair in Pediatric Brain Injury. He receives royalties for book sales from Guilford Press and Cambridge University Press, and occasionally serves as a paid expert in forensic cases. Miriam Beauchamp receives royalties for book sales from Guilford Press. This study was supported by project funding from the Canadian Institutes of Health Research (R.Z. 293380) and by a Fonds de la Recherche en Santé du Québec salary awards to M.H.B. We would like to acknowledge the input and contributions of the entire 5P Study team, with particular thanks to the coordinators and assistants at the neuropsychology substudy sites and to Mary Aglipay for initial assistance with the statistical analyses.

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