JAMA Pediatrics | Original Investigation

Association of Persistent Postconcussion Symptoms With Pediatric Quality of Life

Zuzana Novak, BSc; Mary Aglipay, MSc; Nick Barrowman, PhD; Keith O. Yeates, PhD; Miriam H. Beauchamp, PhD; Jocelyn Gravel, MD; Stephen B. Freedman, MDCM; Isabelle Gagnon, PhD; Gerard Gioia, PhD; Kathy Boutis, MD, MSc; Emma Burns, MD; Andrée-Anne Ledoux, PhD; Martin H. Osmond, MD; Roger L. Zemek, MD; for the Pediatric Emergency Research Canada Predicting Persistent Postconcussive Problems in Pediatrics (PERC 5P) Concussion Team

IMPORTANCE Persistent postconcussion symptoms (PPCS) pose long-term challenges and can negatively affect patients' health-related quality of life (HRQoL). To date, no large comprehensive study has addressed the association between PPCS and HRQoL.

OBJECTIVES To determine the association between HRQoL and PPCS at 4 weeks after concussion and assess the degree of impairment of HRQoL in the subsequent 12 weeks.

DESIGN, SETTING, AND PARTICIPANTS In a prospective, multicenter cohort study (Predicting Persistent Postconcussive Problems in Pediatrics [5P]) from August 14, 2013, to September 30, 2014, children aged 5 to 18 years who presented to the emergency department within 48 hours after head injury and were considered to have an acute concussion were enrolled across 9 pediatric emergency departments within the Pediatric Emergency Research Canada Network. Persistent postconcussion symptoms were defined as 3 or more persistent symptoms on the validated Post-Concussion Symptom Inventory at 4 weeks. Linear mixed effects random coefficients models evaluated the association between PPCS and HRQoL, adjusting for potential confounders including age, sex, prior concussions, migraine, anxiety, learning disability, depression, and sleep disorder.

MAIN OUTCOMES AND MEASURES The primary outcome was HRQoL assessed with the validated Pediatric Quality of Life Inventory version 4.0 (PedsQL-4.0) at 4, 8, and 12 weeks after head injury.

RESULTS Of 2006 children enrolled (median age, 11.8 years [interquartile range, 8.9-14.6 years]; 1241 boys and 765 girls), 1667 (83.1%) completed the PedsQL-4.0 at all 3 time points. Of these 1667 children, the 510 with PPCS (30.6%) had lower total PedsQL-4.0 scores (mean, 70.0) than did those without PPCS (mean, 80.3; mean difference, −10.3; 95% CI, −9.4 to −11.2). Patients with PPCS also had significantly lower physical, emotional, social, and school PedsQL-4.0 subscores at 4, 8, and 12 weeks. Patients with PPCS had lower HRQoL than published healthy norms at 4 weeks (mean difference, 13.89; 95% CI, 11.55-16.23), 8 weeks (mean difference, 11.63; 95% CI, 9.34-13.93), and 12 weeks (mean difference, 9.38; 95% CI, 7.01-11.75; $P < .001$). Patients who recovered from concussion also had lower HRQoL than norms at 4 weeks (mean difference, 3.56; 95% CI, 1.28-5.85) and 8 weeks (mean difference, 2.75; 95% CI, 0.48-5.02; $P < .05$). School functioning PedsQL-4.0 subscores were significantly lower for all children regardless of PPCS status at all time points.

CONCLUSIONS AND RELEVANCE Children with PPCS have lower HRQoL compared with those who have recovered from concussion, yet deficits in HRQoL are pervasive across all domains and may persist for months even in children whose symptoms have resolved. Future interventional research should target the effect of concussion on HRQoL.

+ Editorial

+ Supplemental content

Author Affiliations: Author affiliations are listed at the end of this article.

Group Information: Members of the Pediatric Emergency Research Canada Predicting Persistent Postconcussive Problems in Pediatrics (PERC 5P) Concussion Team are listed at the end of this article.

Corresponding Author: Roger L. Zemek, MD, Children's Hospital of Eastern Ontario Research Institute, 401 Smyth Rd, Ottawa, ON K1H 8L1, Canada (rzemek@cheo.on.ca).

JAMA Pediatr. 2016;170(12):e162900. doi:10.1001/jamapediatrics.2016.2900
Published online October 24, 2016.

Concussion is a major public health concern in children.[1-3] Although many children recover quickly, approximately 30% experience persistent postconcussion symptoms (PPCS) for at least 1 month[4] to years after head injury, which may lead to significant functional morbidity.[5,6] *The International Statistical Classification of Diseases and Related Health Problems, Tenth Revision* defines PPCS as an increase from perceived preconcussion baseline of 3 or more concussion symptoms at 28 days following the injury.[7] Persistent postconcussion symptoms can include ongoing physical symptoms, cognitive problems, decreased mood, and behavior changes.[6] Prolonged symptoms after a concussion may detrimentally affect participation in academic and recreational activities, thereby reducing social interactions.[6,8,9] Lower educational attainment and employment status have been identified in young adults who experienced concussion as children.[10] As a result, PPCS may pose long-term challenges, thus reducing health-related quality of life (HRQoL),[6] a multidimensional concept representing one's perceived health status.

Several studies have shed light on pediatric HRQoL following head injuries. Strong associations exist between moderate to severe traumatic brain injury (TBI) and lower HRQoL, particularly in psychosocial functioning (eg, emotional, social, and school), compared with individuals who experienced only orthopedic injuries.[11,12] A limited number of studies have addressed HRQoL in patients with mild TBI, suggesting that PPCS is associated with lower physical and psychosocial HRQoL up to 12 months after injury, as well as an increased need for educational interventions.[6,13,14] Despite these important findings, previous studies are limited by small sample sizes and lengthy intervals between concussion and enrollment into the study (introducing potential selection bias toward patients with chronic concussion). Therefore, large comprehensive studies are warranted to address the association between PPCS and HRQoL as a function of the recovery timeline.[15] Ultimately, better understanding of children's outcomes after concussion is needed to provide an improved standard of care focusing on the patient's physical, mental, and social well-being.[16]

The primary objective of this study was to determine the association between PPCS and HRQoL at 4 weeks after concussion in children aged 5 through 18 years. We hypothesized that HRQoL would be significantly lower at 4 weeks in children with PPCS than in children without PPCS. We had the following 3 secondary objectives: (1) evaluating the progression of global HRQoL and its subcomponents (physical, emotional, social, and school), (2) comparing HRQoL of both PPCS and non-PPCS groups with published healthy norms, and (3) identifying independent associations of change in overall HRQoL from 4 to 12 weeks after concussion.

Key Points

Question What is the association between persistent postconcussion symptoms and overall health-related quality-of-life (HRQoL) in children following an acute concussion?

Findings This multicenter cohort study of children aged 5 to 18 years confirmed that those with persistent postconcussion symptoms had significantly lower global as well as physical, emotional, social, and school HRQoL subscores than did those without persistent postconcussion symptoms. Furthermore, even children whose symptoms resolved quickly reported lower school HRQoL subscores compared with published healthy norms through 12 weeks after head injury.

Meaning Children with persistent postconcussion symptoms have lower HRQoL subscores compared with those who recovered from concussion, yet HRQoL deficits may persist for months even in children whose symptoms have resolved.

Methods

This was a planned secondary analysis of data from the Predicting Persistent Postconcussive Problems in Pediatrics (hereafter to be referred to as 5P) study conducted from August 14, 2013, to September 30, 2014; the protocol[17] and clinical prediction score for PPCS[4] have been previously published.

Study Population

The study uses the same inclusion and exclusion criteria as the 5P protocol.[17] Participants recruited were children aged 5 through 18 years who presented to the emergency department (ED) within 48 hours after head injury and were considered to have a concussion as defined by Zurich criteria.[18] Children were excluded if they had any of the following: Glasgow Coma Scale score of 13 or less; abnormal neuroimaging findings; a need for neurosurgical operative intervention, intubation, or intensive care; multisystem injuries requiring hospital admission, operating room, or procedural sedation; severe chronic neurologic developmental delay; or intoxication.

Study Setting

Participants were enrolled from the EDs of the following 9 Canadian pediatric hospitals within the Pediatric Emergency Research Canada Network: Izaak Walton Killam Health Centre, Halifax, Nova Scotia; Centre Hospitalier Universitaire Ste.-Justine, Montreal, Quebec; Montreal Children's Hospital, McGill University Health Centre, Montreal, Quebec; Children's Hospital of Eastern Ontario, Ottawa, Ontario; The Hospital for Sick Children, Toronto, Ontario; Children's Hospital of Western Ontario, London, Ontario; Children's Hospital of Winnipeg, Winnipeg, Manitoba; Stollery Children's Hospital, Edmonton, Alberta; and Alberta Children's Hospital, Calgary, Alberta. These EDs have a combined annual census of approximately 500 000 patient-visits. The research ethics committee at each participating institution approved the study.

Design

Recruitment

Details of patient recruitment are outlined in the published 5P protocol.[17] Briefly, children presenting to the ED with a head injury were considered to be potentially eligible for the study. Trained research assistants screened patients for eligibility; families that qualified were approached for and provided written consent in all cases and patient assent where applicable.

Standardized Assessment of Concussion

With help from research assistants, participants answered questions in electronic survey format in their first language (English or French) using a portable tablet computer. In addition to questions about patient demographics, parents completed the Acute Concussion Evaluation, a 22-item dichotomous validated tool used to objectively help diagnose concussion (as indicated by ≥1 symptoms on the Acute Concussion Evaluation).[19] Data were further collected on injury characteristics, history (prior concussion, headache, and developmental or psychiatric disorder), and presenting symptoms (physical, emotional, cognitive and sleep) through the Post-Concussion Symptom Inventory (PCSI).[20,21]

Follow-Up

Participants were contacted at 1, 2, 4, 8, and 12 weeks after head injury (eTable 1 in the Supplement) by either an automated follow-up web survey using Research Electronic Data Capture or a telephone follow-up survey. In the event that participants did not complete the electronic survey within 24 hours of receipt, a second email was sent. If there was still no response, the family was contacted by telephone for an interview. The follow-up questionnaires included the PCSI at all follow-up dates and the Pediatric Quality of Life Inventory version 4.0 (PedsQL-4.0) at 4-, 8-, and 12-week follow-up.

Outcome Measures

Pediatric Quality of Life Inventory Version 4.0

The primary outcome measure was the total score on the PedsQL-4.0, a reliable and valid measure of HRQoL in healthy children and those with acute and/or chronic health conditions.[22] Parent versions exist for children aged 2 to 18 years (in 4 age groups) and child versions exist for those 5 years or older. Patients 8 years or older completed the child PedsQL-4.0, while parents of children aged 5 through 8 years completed the parent version. Items are calculated and transformed into an overall score with a range of 0 to 100 points, with more points indicating better HRQoL. Secondary outcomes included the PedsQL-4.0 subscale scores: physical, emotional, social, and school (8, 5, 5, and 5 items, respectively). The self-report PedsQL-4.0 normative scores for a healthy child[23] are as follows: mean total, 83.9; physical, 87.7; emotional, 79.2; social, 84.9; and school, 81.3.

Post-Concussion Symptom Inventory

The PCSI was used to measure the persistence and severity of symptoms. The PCSI is a valid and reliable set of symptom scales for parents (20 items on a 7-point Likert scale) and children aged 5 to 7 years (13 items on a 3-point scale), 8 to 12 years (17 items on a 3-point scale), and 13 to 18 years (21 items on a 7-point scale), with excellent internal consistency and interrater agreement.[20,21] The PCSI measures symptoms in physical, cognitive, emotional, and sleep domains. Symptoms were defined as the absolute difference between the current self-reported PCSI ratings and those from before the injury. To be considered as having PPCS, patients were required to have a positive minimum 1-point change for 3 or more symptoms.[4,17]

Statistical Analysis

The primary objective of this study was to determine the association between HRQoL and PPCS at 4 weeks after concussion. Health-related quality of life was calculated using scoring instructions for the PedsQL-4.0. Descriptive statistics were used to summarize the data. Differences between patients who completed the PedsQL-4.0 and PCSI and those who did not were compared at each time point using χ^2 and Mann-Whitney tests where appropriate. Variables associated with HRQoL (total score) were identified by using parametric and nonparametric tests (*t* tests and Wilcoxon rank sum tests). For the primary outcome, linear mixed effects random coefficient models were used to evaluate the association between PPCS and HRQoL over time, adjusting for variables associated with univariate analyses or supported by observations from clinical practice. This method resulted in a model with fixed effects of PPCS, time, interaction of PPCS with time, age, sex, previous concussion, duration of previous concussion symptoms, prior treatment for headache, personal history of migraines, learning disability, anxiety, depression, and sleep disorder. The mixed effects procedure avoids listwise deletion owing to missing data. Next, the estimated marginal means at each time point were compared with the child self-report mean total score from a sample of healthy children[23] using a *z* test with correction for multiple comparisons using the Holm method. Secondary analyses examining the association between PPCS and the PedsQL-4.0 subscale scores (physical, emotional, social, school) were conducted identically. All analyses were performed using SPSS, version 21 (IBM Corp), and R, version 3.0.2 (R Project for Statistical Computing). All *P* values were 2-sided, and $P < .05$ was considered statistically significant.

Results

Of the 5229 patients screened for eligibility, 2006 children were enrolled, of which 1667 (83.1%) completed the primary outcome survey at 4 weeks (eFigure in the Supplement). Of these 1667 children, 510 (30.6%) had PPCS at 4 weeks after injury. **Table 1** describes the enrolled patients' baseline characteristics. Minimal differences were found between patients who did and did not complete the PedsQL-4.0 and PCSI (eTable 2 in the Supplement). Participants with attention-deficit disorder or attention-deficit/hyperactivity disorder were less likely to respond at 8 weeks (77% vs 84%) and 12 weeks (72% vs 78%; $P = .05$), and participants with a history of 2 or more concussions were less likely to respond at 12 weeks (72% vs 79%; $P = .04$).

For our primary outcome, at 4 weeks, children with PPCS had a significantly lower PedsQL-4.0 total score than did children without PPCS (70.0 vs 80.3; mean difference, -10.3; 95% CI, -9.4 to -11.2). Lower PedsQL-4.0 total score in the PPCS group persisted at each follow-up time point compared with the group without PPCS. The mean difference in PedsQL-4.0 total score between the groups was -8.9 (95% CI, −8.2 to −9.6) at 8 weeks and -7.4 (95% CI, −6.5 to −8.4) at 12 weeks. **Figure 1** displays the estimated marginal means from the model, as well

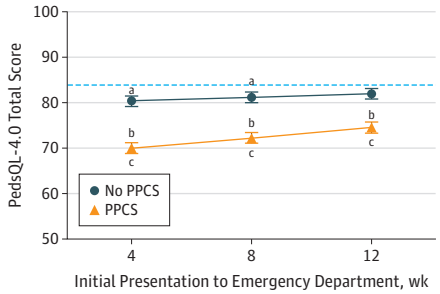
Table 1. Baseline Characteristics of Enrolled Patients

Characteristic	Value[a]
Median age (IQR), y	11.8 (8.9-14.6)
Female	765 (38.1)
Clinical features	
History	
Median time (IQR) between ED visit and head injury, h	2.8 (1.4-11.1)
Previous number of concussions	
0	1532 (76.4)
1	292 (14.6)
≥2	170 (8.5)
Migraine	242 (12.1)
ADD or ADHD	190 (9.5)
Learning disabilities	179 (8.9)
Clinical	
Loss of consciousness	239 (11.9)
Dazed and confused	971 (48.4)
Confused about events	486 (24.2)
Answers questions slowly	806 (40.2)
Forgetful of recent information	411 (20.5)
Repeats questions	270 (13.5)
No early signs of confusion or forgetfulness	726 (36.2)
Injury	
Mechanism of injury	
Sports or recreational play	1349 (67.2)
Nonsport-related injury or fall	495 (24.7)
Other	156 (7.8)

Abbreviations: ADD, attention-deficit disorder; ADHD, attention-deficit/hyperactivity disorder; ED, emergency department; IQR, interquartile range.

[a] Data are presented as number (percentage) of patients unless otherwise indicated.

Figure 1. Pediatric Quality of Life Inventory Version 4.0 (PedsQL-4.0) Total Score Between Children With and Without Persistent Postconcussion Symptoms (PPCS)



Points represent estimated marginal means from random coefficients model adjusting for PPCS, time, interaction of PPCS with time, age, sex, previous concussion, duration of previous concussion, prior treatment for headache, personal history of migraine, family history of migraine, learning disability, anxiety, depression, and sleep disorder. Error bars represent SE of the estimated marginal mean. Dashed line represents the PedsQL-4.0 mean total score for healthy children.[23]

[a] Indicates a significant difference between the group without PPCS and healthy norms described in Varni et al[23] ($P < .05$).

[b] Indicates a significant difference between the groups with and without PPCS ($P < .05$).

[c] Indicates a significant difference between the group with PPCS and healthy norms ($P < .05$).

as the progression of PedsQL-4.0 total scores over time for the groups with and without PPCS.[23] Although both groups showed increases in PedsQL-4.0 total scores over time (β = 0.56; 95% CI, 0.43-0.70; $P < .001$), the scores for the PPCS group increased faster than did the scores for the group without PPCS from 4 to 12 weeks after concussion, as reflected in a significant interaction of PPCS with time (β = 0.36; 95% CI, 0.21-0.51; $P < .001$).

Figure 2 displays the PedsQL-4.0 subscale scores (physical, emotional, social, and school) of children with and without PPCS at 4, 8, and 12 weeks of follow-up.[23] The PPCS group scored significantly lower on all subscales compared with the group without PPCS. This finding was consistent at each follow-up point (weeks 4, 8, and 12) for all subscales (**Table 2**).[23]

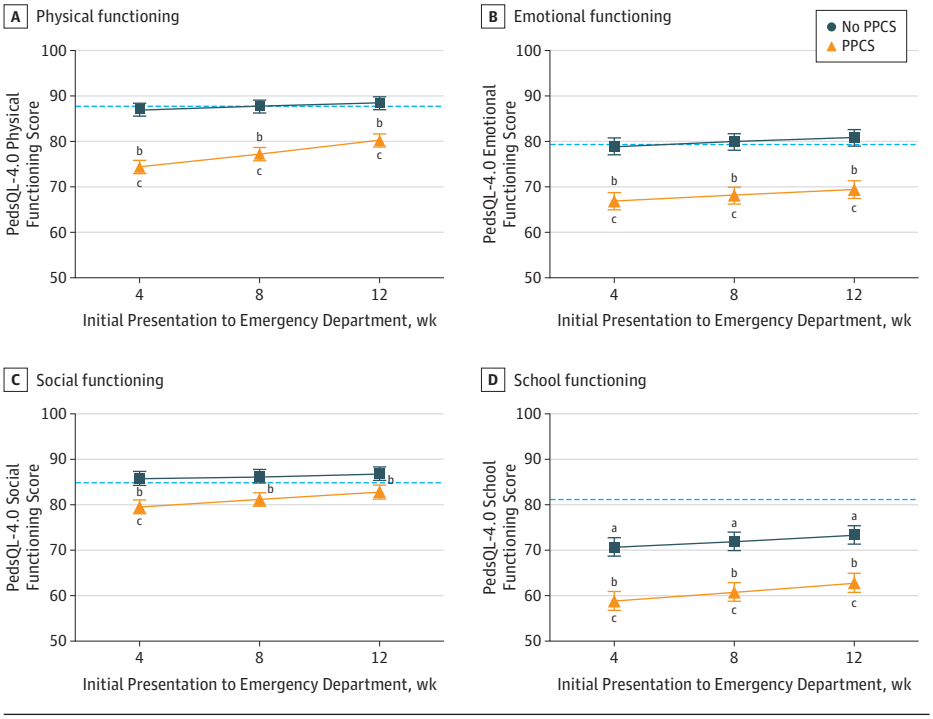
Using published healthy norms, we compared the total and subscale PedsQL-4.0 scores for all patients with concussion (both those with and without PPCS). The estimated marginal means of patients with PPCS were significantly lower than the healthy population mean of 83.9 at 4, 8, and 12 weeks (eTable 3 in the Supplement). Patients without PPCS had significantly lower estimated marginal means than the healthy population mean at weeks 4 and 8, but not at week 12 (eTable 3 in the Supplement). Compared with published norms, children with PPCS scored significantly lower than healthy children at every time point for the physical, emotional, and school subscales (eTable 3 in the Supplement). Children with PPCS scored lower on the social subscale at 4 weeks but not at 8 or 12 weeks (eTable 3 in the Supplement). In comparison, children without PPCS did not have significantly lower physical, emotional, or social scores compared with healthy children at any of the time points (eTable 3 in the Supplement). However, scores on the school subscale were significantly lower (eTable 3 in the Supplement) for children without PPCS at all time points.

Finally, we examined factors significantly associated with lower overall HRQoL. Variables associated with lower HRQoL during 3 months included female sex, previous concussion, history of migraine, learning disability, and anxiety disorder (**Table 3**).

Discussion

Children with PPCS report significantly lower overall HRQoL for up to 12 weeks after concussion when compared with children whose symptoms resolve within the first 4 weeks after injury. The detriments to HRQoL are pervasive across all domains (physical, emotional, social, and school functioning). All children with concussion (regardless of duration of symptoms after injury) have significantly lower HRQoL compared with published norms. Furthermore, even children who reported resolution of symptoms exhibited prolonged declines in HRQoL relative to healthy norms owing primarily to detriments in school functioning. However, both the HRQoL in children with and without PPCS improved over time.

Figure 2. Pediatric Quality of Life Inventory Version 4.0 (PedsQL-4.0) Subscale Scores Between Children With and Without Persistent Postconcussion Symptoms (PPCS)



A, Physical functioning subscale. B, Emotional functioning subscale. C, Social functioning subscale. D, School functioning subscale. Points represent estimated marginal means from random coefficients model. Error bars represent SE of the estimated marginal mean. Dashed line represents the PedsQL-4.0 mean total score for healthy children.[23]

[a] Indicates a significant difference between the group without PPCS and healthy norms described in Varni et al[23] ($P < .05$).

[b] Indicates a significant difference between the groups with and without PPCS ($P < .05$).

[c] Indicates a significant difference between the group with PPCS and healthy norms ($P < .05$).

Table 2. Total and Subscale Mean Differences on the PedsQL-4.0 From 4 to 12 Weeks Between the Groups With and Without PPCS

	Mean Difference (95% CI)[a]				
Week	Total	Physical	Emotional	Social	School
4	10.3 (9.4-11.2)	12.6 (11.6-13.7)	12.1 (10.6-13.5)	6.2 (5.1-7.3)	11.8 (10.3-13.3)
8	8.9 (8.2-9.6)	10.5 (9.7-11.3)	11.7 (10.6-12.8)	5.1 (4.3-5.9)	11.2 (10.0-12.4)
12	7.4 (6.5-8.4)	8.3 (7.2-9.4)	11.4 (9.8-12.9)	4.0 (2.8-5.2)	10.6 (8.9-12.3)

Abbreviations: PedsQL-4.0, Pediatric Quality of Life Inventory Version 4.0; PPCS, persistent postconcussion symptoms.

[a] The minimal clinically meaningful difference for total and subscale score point change are as follows: total score (parent, 4.50; child, 4.36), physical (parent, 6.66; child, 6.92), emotional (parent, 8.94; child, 7.79), social (parent, 8.36; child, 8.98), and school (parent, 9.12; child, 9.67).[23]

Results of our study are consistent with those of smaller studies reporting decrements in the HRQoL of children following concussion. Moran et al[13] concluded that higher initial symptom burden puts patients at risk for lasting declines in HRQoL and thus suggest that PPCS may be a target for improving HRQoL. Furthermore, Ransom et al[24] determined that symptomatic children and their parents report greater difficulties at school after concussion than their nonsymptomatic counterparts. Similarly, children who were no longer symptomatic after concussion also had school difficulties, with nearly half reporting diminished academic skills and trouble in at least 1 class during their recovery. These results are supported by our findings, which established that even asymptomatic children reported lower PedsQL-4.0 school functioning compared with healthy norms for at least 12 weeks after head injury. Our results indicate that school functioning is the last domain of HRQoL to resolve in both children with PPCS and those with concussion but without PPCS.

There are several hypotheses for the delayed effect of concussion on school functioning in children with PPCS and those without PPCS. First, our results may reflect a direct cognitive effect of concussion on pediatric HRQoL. A second hypothesis involves an epiphenomenon of the injury situation. As a student recovers from a concussion, schoolwork begins to accumulate, which may be stressful for certain children. After the student has largely recovered, completing the accumulated work takes time, and some children still feel this stress when no other symptoms are present. Therefore, their school HRQoL reports may reflect the effect of this stress. Third, our baseline school measure did not differentiate between quality of school functioning before and after the concussion. Therefore, it is possible that reports of school difficulties may be associated with those already present before the concussion.

Comparing our findings with those of other studies reporting on HRQoL among children with chronic illness provides insight into the potential effect of concussion on

Table 3. Multivariable Longitudinal Mixed Model Analysis Assessing Persistent Postconcussion Symptoms as an Association With Health-Related Quality of Life[a]

Covariate	Estimate (95% CI)	*P* Value
Age group, y		
5-7	1 [Reference]	.77
8-12	0.49 (-0.84 to 1.82)	
13-18	0.40 (-1.00 to 1.80)	
Sex		
Male	1 [Reference]	<.001[b]
Female	-2.10 (-3.10 to -1.10)	
Previous concussion		
No	1 [Reference]	.04[b]
Yes, symptoms lasted <1 wk	-0.68 (-2.32 to 0.95)	
Yes, symptoms lasted ≥1 wk	-1.93 (-3.41 to -0.45)	
Prior treatment for headache		
No	1 [Reference]	.49
Yes	-0.47 (-1.77 to 0.84)	
Personal history of migraine		
No	1 [Reference]	<.001[b]
Yes	-3.21 (-4.76 to -1.67)	
Family history of migraine		
No	1 [Reference]	.60
Yes	0.26 (-0.71 to 1.24)	
Learning disability		
No	1 [Reference]	<.001[b]
Yes	-3.95 (-5.69 to -2.22)	
Prior diagnosis of anxiety		
No	1 [Reference]	<.001[b]
Yes	-4.49 (-6.46 to -2.52)	
Sleep disorder		
No	1 [Reference]	.79
Yes	-0.49 (-4.12 to 3.14)	
Persistent symptoms		
No	1 [Reference]	<.001[b]
Yes	-11.77 (-13.10 to -10.4)	
Time (wk)	0.20 (0.13 to 0.28)	<.001[b]
Time (wk) persistent symptoms		
No persistent symptoms	1 [Reference]	<.001[b]
Persistent symptom	0.36 (0.21 to 0.51)	

[a] N = 1732 patients.

[b] *P* < .05.

HRQoL. For instance, 1 month after hematopoietic stem cell transplantation, children report a mean total PedsQL-4.0 score of 74, similar to that in our overall concussion cohort.[25] Children with PPCS reported a lower HRQoL than that reported by children with type 1 diabetes, whose PedsQL-4.0 scores are similar to those in our group without PPCS.[26] Furthermore, both children with and without PPCS scored below healthy norms on the PedsQL-4.0 school functioning subscale, which seems to be the subscale most affected by chronic health conditions.[23]

Several studies have examined independent associations with poor HRQoL after concussion. For instance, Scholten et al,[27] in a cohort of adults with mild, moderate, and severe TBI, identified female sex and medical comorbidities as the strongest associations with decreased HRQoL at 6 and 12 months after TBI. Furthermore, pediatric patients with TBI exhibited improvement in the initial 3 to 24 months after injury compared with their baseline PedsQL-4.0 results[28]; however, significant long-term HRQoL impairments remained without further improvement from 24 to 36 months.[29] Significant associations of poor functioning after pediatric mild TBI included lower parental education, Hispanic race/ethnicity, low household income, and Medicaid insurance.[30] Additional studies have found that repeated concussions may lead to greater cognitive dysfunction and neuropsychiatric conditions, which themselves can negatively affect pediatric HRQoL.[31,32] Furthermore, female sex, previous TBI, and neurologic and psychological illness were associated with PPCS in both children and adults.[33-35] Female sex and prior concussion were also identified in our study, along with migraine history, learning disability, and/or anxiety disorder as independently associated with overall HRQoL decrement in children after concussion.

The study has several strengths that contribute to the validity of our results. First, to our knowledge, this is the largest prospective multicenter study to date examining the effect of pediatric concussion on HRQoL. We collected a large sample from a geographically diverse population from pediatric hospitals across Canada, with participants being included despite preexisting behavioral, learning, or psychological problems. By excluding patients presenting more than 48 hours after head injury, we ensured that our results are applicable to any child presenting for acute concussion assessment and not biased toward those presenting with persisting symptoms. Our data are bolstered by the standardization of training for all research staff. Furthermore, we used validated outcome variables and achieved excellent follow-up rates.

This study has several potential limitations. First, we did not include a control group, and thus we are unable to directly attribute PPCS and its effect on HRQoL to concussion. However, we did compare our results with published normative data. Second, we used only self-report for assessing both PPCS and HRQoL in the group 8 years or older, introducing shared rater variance. However, parent-child agreement regarding PPCS and HRQoL is only moderate, so using different raters might underestimate the association of PPCS with HRQoL.[19,36] Moreover, as we included only children with concussions who presented to the ED within 48 hours of their injury, our results may not be generalizable to those presenting with delayed-onset symptoms, those not seeking care, or seeking care outside the ED (as only few children with concussion may seek ED care).[37] Patients in the ED may be primed to have lower HRQoL and/or higher risk of PPCS, but since we did not collect baseline PedsQL-4.0 assessments, we were unable to assess their HRQoL before injury. This fact, plus our nontrial study design, precluded our ability to determine causality. Future research should examine if PPCS leads to poor HRQoL or vice versa, with subsequent interventions targeting the root cause.

Conclusions

Children with PPCS had significantly lower total, physical, emotional, social, and school quality of life that persisted for at least 12 weeks after concussion than did children with no PPCS. Overall, both patients with and without PPCS with concussion report declines in overall and school quality of life relative to healthy norms.[23] Finally, the following independent associations with HRQoL decrement in children after concussion were identified: female sex, having a previous concussion, history of migraine, learning disability, or anxiety disorder. Results from our study provide insight into the psychosocial burden of pediatric concussion and may help identify patients and families requiring extra support or guidance regarding management of expectations and coping mechanisms after concussion. Finally, our results will help guide future interventions to reduce the effect of concussion on HRQoL.

Knowledge translation and mobilization is an important next step to ensure that parents, teachers, school administrators, and educational boards are aware of the effect of concussion on children's HRQoL in school. Health care professionals should identify patients and families at higher risk for PPCS and decreased HRQoL.

ARTICLE INFORMATION

Accepted for Publication: July 28, 2016.

Published Online: October 24, 2016. doi:10.1001/jamapediatrics.2016.2900

Author Affiliations: Faculty of Medicine, University of Ottawa, Ottawa, Ontario, Canada (Novak); Children's Hospital of Eastern Ontario Research Institute, Ottawa, Ontario, Canada (Aglipay, Barrowman, Ledoux, Osmond, Zemek); Department of Psychology, Alberta Children's Hospital Research Institute, University of Calgary, Calgary, Alberta, Canada (Yeates); Hotchkiss Brain Institute, University of Calgary, Calgary, Alberta, Canada (Yeates); Ste.-Justine Research Centre, University of Montreal, Montreal, Quebec, Canada (Beauchamp, Gravel); Department of Psychology, University of Montreal, Montreal, Quebec, Canada (Beauchamp); Department of Pediatrics, Hospital Ste.-Justine, Montreal, Quebec, Canada (Gravel); Department of Pediatrics, Alberta Children's Hospital, Calgary, Alberta, Canada (Freedman); Department of Pediatrics, Montreal Children's Hospital, McGill University Health Centre, Montreal, Quebec, Canada (Gagnon); School of Physical and Occupational Therapy, McGill University, Montreal, Quebec, Canada (Gagnon); Department of Neuropsychology, Children's National Health System, George Washington University School of Medicine, Rockville, Maryland (Gioia); Department of Pediatrics, Hospital for Sick Children, Toronto, Ontario, Canada (Boutis); Department of Pediatrics, Izaak Walton Killam Health Centre, Halifax, Nova Scotia, Canada (Burns); Department of Pediatrics, Children's Hospital of Eastern Ontario, University of Ottawa, Ottawa, Ontario, Canada (Osmond, Zemek).

Author Contributions: Dr Zemek had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: Aglipay, Gravel, Freedman, Gagnon, Gioia, Boutis, Burns, Osmond, Zemek.
Acquisition, analysis, or interpretation of data: Novak, Aglipay, Barrowman, Yeates, Beauchamp, Gravel, Freedman, Gagnon, Gioia, Boutis, Burns, Ledoux, Zemek.
Drafting of the manuscript: Novak, Aglipay, Boutis, Zemek.
Critical revision of the manuscript for important intellectual content: Novak, Aglipay, Barrowman, Yeates, Beauchamp, Gravel, Freedman, Gagnon, Gioia, Burns, Ledoux, Osmond, Zemek.
Statistical analysis: Aglipay, Barrowman.
Administrative, technical, or material support: Gravel, Freedman, Gioia, Ledoux, Zemek.
Study supervision: Beauchamp, Gravel, Freedman, Gagnon, Boutis, Zemek.

Conflict of Interest Disclosures: Dr Gioia reported being the author of the Postconcussion Symptom Inventory (PCSI); the PCSI is freely available and he receives no financial benefit for its use. No other conflicts were reported.

Funding/Support: This study was supported by operating grant TM1 127047 from the Canadian Institutes of Health Research and grant 126197 from the Canadian Institutes of Health Research–Ontario Neurotrauma Foundation Mild Traumatic Brain Injury Team. Preliminary work was funded by planning grant MRP 119829 from the Canadian Institutes of Health Research.

Role of the Funder/Sponsor: The funding sources had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Group Information: The Pediatric Emergency Research Canada Predicting Persistent Postconcussive Problems in Pediatrics (PERC 5P) Concussion Team includes Candice McGahern, BA (Children's Hospital of Eastern Ontario Research Institute, Ottawa, Ontario, Canada); Gurinder Sangha, MD (Department of Pediatrics, Children's Hospital of Western Ontario, Western University, London, Ontario, Canada); Darcy Beer, MD (Department of Pediatrics, Manitoba Children's Hospital, Winnipeg, Manitoba, Canada); William Craig, MDCM (Department of Pediatrics, Stollery Children's Hospital, Edmonton, Alberta, Canada); Ken J. Farion, MD (Department of Pediatrics, Children's Hospital of Eastern Ontario, University of Ottawa, Ottawa, Canada); Angelo Mikrogianakis, MD (Department of Pediatrics, Alberta Children's Hospital, Calgary, Alberta, Canada); Karen Barlow, MD (Department of Pediatrics and Clinical Neurosciences, Alberta's Children's Hospital, University of Calgary, Calgary, Canada); Alexander S. Dubrovsky, MDCM, MSc (Department of Pediatrics, Montreal Children's Hospital, McGill University Health Center, Montreal, Quebec, Canada); Willem Meeuwisse, MD, PhD (Sport Injury Prevention Research Centre, Faculty of Kinesiology, University of Calgary, Calgary, Canada); William P. Meehan III, MD (Sports Concussion Clinic, Boston Children's Hospital, Boston, Massachusetts); Yael Kamil, BSc (Children's Hospital of Eastern Ontario Research Institute, Ottawa, Canada); Anne M. Grool, MD, PhD, MSc (Children's Hospital of Eastern Ontario Research Institute, Ottawa, Canada); Blaine Hoshizaki, PhD (Department of Kinesiology, University of Ottawa, Ottawa, Canada); Peter Anderson, PhD (Department of Psychology, Children's Hospital of Eastern Ontario, Ottawa, Canada); Brian L. Brooks, PhD (Alberta Children's Hospital Research Institute, University of Calgary, Calgary, Canada); Michael Vassilyadi, MDCM, MSc (Department of Neurosurgery, Children's Hospital of Eastern Ontario, Canada); Terry Klassen, MD (Department of Pediatrics, Manitoba Children's Hospital, Winnipeg, Canada); Michelle Keightley, PhD (Bloorview Research Institute, Holland Bloorview Kids Rehabilitation Hospital, Toronto, Ontario, Canada); Lawrence Richer, MD (Department of Neurology, Stollery Children's Hospital, Edmonton, Canada); and Carol DeMatteo, MSc (School of Rehabilitation Science, McMaster University, Hamilton, Ontario, Canada).

REFERENCES

1. Macpherson A, Fridman L, Scolnik M, Corallo A, Guttmann A. A population-based study of paediatric emergency department and office visits for concussions from 2003 to 2010. *Paediatr Child Health*. 2014;19(10):543-546.

2. Moran LM, Taylor HG, Rusin J, et al. Quality of life in pediatric mild traumatic brain injury and its relationship to postconcussive symptoms. *J Pediatr Psychol*. 2012;37(7):736-744.

3. Zemek RL, Farion KJ, Sampson M, McGahern C. Prognosticators of persistent symptoms following pediatric concussion: a systematic review. *JAMA Pediatr*. 2013;167(3):259-265.

4. Zemek R, Barrowman N, Freedman SB, et al. Clinical risk score for persistent postconcussion symptoms among children with acute concussion in the ED. *JAMA*. 2016;315(10):1014-1025.

5. Taylor HG, Orchinik LJ, Minich N, et al. Symptoms of persistent behavior problems in children with mild traumatic brain injury. *J Head Trauma Rehabil*. 2015;30(5):302-310.

6. Yeates KO, Kaizar E, Rusin J, et al. Reliable change in postconcussive symptoms and its functional consequences among children with mild traumatic brain injury. *Arch Pediatr Adolesc Med*. 2012;166(7):615-622.

7. World Health Organization. *International Statistical Classification of Diseases, 10th Revision*. Geneva, Switzerland: World Health Organization; 1992.

8. Carroll L, Rosner D. *The Concussion Crisis: Anatomy of a Silent Epidemic*. New York, NY: Simon & Schuster; 2011.

9. Scorza KA, Raleigh MF, O'Connor FG. Current concepts in concussion: evaluation and management. *Am Fam Physician*. 2012;85(2):123-132.

10. Anderson V, Brown S, Newitt H, Hoile H. Educational, vocational, psychosocial, and quality-of-life outcomes for adult survivors of childhood traumatic brain injury. *J Head Trauma Rehabil*. 2009;24(5):303-312.

11. Stancin T, Drotar D, Taylor HG, Yeates KO, Wade SL, Minich NM. Health-related quality of life of children and adolescents after traumatic brain injury. *Pediatrics*. 2002;109(2):E34.

12. Erickson SJ, Montague EQ, Gerstle MA. Health-related quality of life in children with moderate-to-severe traumatic brain injury. *Dev Neurorehabil*. 2010;13(3):175-181.

13. Moran LM, Taylor HG, Rusin J, et al. Quality of life in pediatric mild traumatic brain injury and its relationship to postconcussive symptoms. *J Pediatr Psychol*. 2012;37(7):736-744.

14. Grubenhoff JA, Deakyne SJ, Brou L, Bajaj L, Comstock RD, Kirkwood MW. Acute concussion symptom severity and delayed symptom resolution. *Pediatrics*. 2014;134(1):54-62.

15. Rivara FP. Concussion: time to start paying attention. *Arch Pediatr Adolesc Med*. 2012;166(7):666-667.

16. Pieper P, Garvan C. Health-related quality-of-life in the first year following a childhood concussion. *Brain Inj*. 2014;28(1):105-113.

17. Zemek R, Osmond MH, Barrowman N; Pediatric Emergency Research Canada (PERC) Concussion Team. Predicting and preventing postconcussive problems in paediatrics (5P) study: protocol for a prospective multicentre clinical prediction rule derivation study in children with concussion [published correction appears in *BMJ Open*. 2013;3(8):e003550corr1]. *BMJ Open*. 2013;3(8):1-10.

18. McCrory P, Meeuwisse WH, Aubry M, et al. Consensus statement on concussion in sport: the 4th International Conference on Concussion in Sport held in Zurich, November 2012. *Br J Sports Med*. 2013;47(5):250-258.

19. Gioia GA, Collins M, Isquith PK. Improving identification and diagnosis of mild traumatic brain injury with evidence: psychometric support for the Acute Concussion Evaluation. *J Head Trauma Rehabil*. 2008;23(4):230-242.

20. Gioia GA, Isquith PK, Schneider JC, Vaughan CG. New approaches to assessment and monitoring of concussion in children. *Top Lang Disord*. 2009;29(3):266-281. doi:10.1097/TLD.0b013e3181b5322b

21. Sady MD, Vaughan CG, Gioia GA. Psychometric characteristics of the Postconcussion Symptom Inventory in children and adolescents. *Arch Clin Neuropsychol*. 2014;29(4):348-363.

22. Desai AD, Zhou C, Stanford S, Haaland W, Varni JW, Mangione-Smith RM. Validity and responsiveness of the Pediatric Quality Of Life Inventory (PedsQL) 4.0 generic core scales in the pediatric inpatient setting. *JAMA Pediatr*. 2014;168(12):1114-1121.

23. Varni JW, Burwinkle TM, Seid M, Skarr D. The PedsQL 4.0 as a pediatric population health measure: feasibility, reliability, and validity. *Ambul Pediatr*. 2003;3(6):329-341.

24. Ransom DM, Vaughan CG, Pratson L, Sady MD, McGill CA, Gioia GA. Academic effects of concussion in children and adolescents. *Pediatrics*. 2015;135(6):1043-1050.

25. Rodgers C, Wills-Bagnato P, Sloane R, Hockenberry M. Health-related quality of life among children and adolescents during hematopoietic stem cell transplant recovery. *J Pediatr Oncol Nurs*. 2015;32(5):329-336.

26. Naughton MJ, Yi-Frazier JP, Morgan TM, et al; SEARCH for Diabetes in Youth Study Group. Longitudinal associations between sex, diabetes self-care, and health-related quality of life among youth with type 1 or type 2 diabetes mellitus. *J Pediatr*. 2014;164(6):1376-1383.e1.

27. Scholten AC, Haagsma JA, Andriessen TMJC, et al. 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*. 2015;46(4):616-624.

28. Rivara FP, Koepsell TD, Wang J, et al. Disability 3, 12, and 24 months after traumatic brain injury among children and adolescents. *Pediatrics*. 2011;128(5):e1129-e1138.

29. Rivara FP, Vavilala MS, Durbin D, et al. Persistence of disability 24 to 36 months after pediatric traumatic brain injury: a cohort study. *J Neurotrauma*. 2012;29(15):2499-2504.

30. Zonfrillo MR, Durbin DR, Koepsell TD, et al. Prevalence of and risk factors for poor functioning after isolated mild traumatic brain injury in children. *J Neurotrauma*. 2014;31(8):722-727.

31. Gaetz M, Goodman D, Weinberg H. Electrophysiological evidence for the cumulative effects of concussion. *Brain Inj*. 2000;14(12):1077-1088.

32. Gronwall D, Wrightson P. Cumulative effect of concussion. *Lancet*. 1975;2(7943):995-997.

33. Carroll LJ, Cassidy JD, Peloso PM, et al. Prognosis for mild traumatic brain injury: results of the WHO Collaborating Centre Task Force on Mild Traumatic Brain Injury. *J Rehabil Med*. 2004;(43 suppl):84-105.

34. McCauley SR, Boake C, Levin HS, Contant CF, Song JX. Postconcussional disorder following mild to moderate traumatic brain injury: anxiety, depression, and social support as risk factors and comorbidities. *J Clin Exp Neuropsychol*. 2001;23(6):792-808.

35. Taylor HG, Dietrich A, Nuss K, et al. Post-concussive symptoms in children with mild traumatic brain injury. *Neuropsychology*. 2010;24(2):148-159.

36. Upton P, Lawford J, Eiser C. Parent-child agreement across child health-related quality of life instruments: a review of the literature. *Qual Life Res*. 2008;17(6):895-913.

37. Arbogast KB, Curry AE, Pfeiffer MR, et al. Point of health care entry for youth with concussion within a large pediatric care network. *JAMA Pediatr*. 2016;170(7):e160294.