Association Between Early Participation in Physical Activity Following Acute Concussion and Persistent Postconcussive Symptoms in Children and Adolescents

Anne M. Grool, MD, PhD; Mary Aglipay, MSc; Franco Momoli, PhD; William P. Meehan III, MD; Stephen B. Freedman, MDCM, MSc; Keith Owen Yeates, PhD; Jocelyn Gravel, MD; Isabelle Gagnon, PhD; Kathy Boutis, MD; Willem Meeuwisse, MD, PhD; Nick Barrowman, PhD; Andrée-Anne Ledoux, PhD; Martin H. Osmond, MDCM; Roger Zemek, MD; for the Pediatric Emergency Research Canada (PERC) Concussion Team

IMPORTANCE Although concussion treatment guidelines advocate rest in the immediate postinjury period until symptoms resolve, no clear evidence has determined that avoiding physical activity expedites recovery.

OBJECTIVE To investigate the association between participation in physical activity within 7 days postinjury and incidence of persistent postconcussive symptoms (PPCS).

DESIGN, SETTING, AND PARTICIPANTS Prospective, multicenter cohort study (August 2013-June 2015) of 3063 children and adolescents aged 5.00-17.99 years with acute concussion from 9 Pediatric Emergency Research Canada network emergency departments (EDs).

EXPOSURES Early physical activity participation within 7 days postinjury.

MAIN OUTCOMES AND MEASURES Physical activity participation and postconcussive symptom severity were rated using standardized questionnaires in the ED and at days 7 and 28 postinjury. PPCS (≥3 new or worsening symptoms on the Post-Concussion Symptom Inventory) was assessed at 28 days postenrollment. Early physical activity and PPCS relationships were examined by unadjusted analysis, 1:1 propensity score matching, and inverse probability of treatment weighting (IPTW). Sensitivity analyses examined patients (≥3 symptoms) at day 7.

RESULTS Among 2413 participants who completed the primary outcome and exposure, (mean [SD] age, 11.77 [3.35] years; 1205 [39.3%] females), PPCS at 28 days occurred in 733 (30.4%); 1677 (69.5%) participated in early physical activity including light aerobic exercise (n = 795 [32.9%]), sport-specific exercise (n = 214 [8.9%]), noncontact drills (n = 143 [5.9%]), full-contact practice (n = 106 [4.4%]), or full competition (n = 419 [17.4%]), whereas 736 (30.5%) had no physical activity. On unadjusted analysis, early physical activity participants had lower risk of PPCS than those with no physical activity (24.6% vs 43.5%; Absolute risk difference [ARD], 18.9% [95% CI,14.7%-23.0%]). Early physical activity was associated with lower PPCS risk on propensity score matching (n = 1108 [28.7% for early physical activity vs 40.1% for no physical activity]; ARD, 11.4% [95% CI, 5.8%-16.9%]) and on inverse probability of treatment weighting analysis (n = 2099; relative risk [RR], 0.74 [95% CI, 0.65-0.84]; ARD, 9.7% [95% CI, 5.7%-13.7%]). Among only patients symptomatic at day 7 (n = 803) compared with those who reported no physical activity (n = 584; PPCS, 52.9%), PPCS rates were lower for participants of light aerobic activity (n = 494 [46.4%]; ARD, 6.5% [95% CI, 5.7%-12.5%]), moderate activity (n = 176 [38.6%]; ARD, 14.3% [95% CI, 5.9%-22.2%]), and full-contact activity (n = 133 [36.1%]; ARD, 16.8% [95% CI, 7.5%-25.5%]). No significant group difference was observed on propensity-matched analysis of this subgroup (n = 776 [47.2% vs 51.5%]; ARD, 4.4% [95% CI, −2.6% to 11.3%]).

CONCLUSIONS AND RELEVANCE Among participants aged 5 to 18 years with acute concussion, physical activity within 7 days of acute injury compared with no physical activity was associated with reduced risk of PPCS at 28 days. A well-designed randomized clinical trial is needed to determine the benefits of early physical activity following concussion.

← **Editorial** page 2491

Author Video Interview and **JAMA Report Video**

CME Quiz at jamanetworkcme.com

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

Group Information: The Pediatric Emergency Research Canada (PERC) Concussion Team members are listed at the end of this article.

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

Rest has long been considered the cornerstone of concussion management,[1] and pediatric guidelines universally recommend an initial period of cognitive and physical rest following a concussion.[1,2] Cognitive rest recommendations include modification of school attendance and mental activities.[1] Physical rest recommendations advocate avoidance of physical activity until postconcussive symptoms have resolved, endorsing gradual resumption of activities only if symptoms are not exacerbated.[1,2]

Due to limited high-quality evidence, existing physical rest guidelines are based on consensus and precautionary principles.[2,3] There is limited evidence that following these guidelines results in a positive effect on prognosis.[4,5] Although strenuous exercise in patients recovering from concussion may be deleterious and increase re-injury risk,[6] recent literature suggests that protracted rest may hamper concussion recovery,[7] leading to secondary symptoms of fatigue, depression, anxiety, and physiological deconditioning.[3,8] Increasing evidence suggests the introduction of controlled, light aerobic physical activity following pediatric concussion may be safe[9] while promoting recovery[9] by enhancing physical, psychological, and academic outcomes.[6,9,10] These preliminary findings indicate that gradual resumption of pre-injury activities could begin as soon as tolerated provided there is no increased risk of re-injury.[11]

The objective of this study was to examine the association between participation in physical activity within 7 days postinjury and the occurrence of persistent postconcussive symptoms (PPCS) following concussion in children and adolescents. It was hypothesized that early participation in physical activity would be associated with lower PPCS rates compared with no physical activity.

Methods

This research comprises a planned secondary analysis of the Predicting Persistent Postconcussive Problems in Pediatrics (5P) study,[12,13] a prospective, multicenter cohort study that recruited participants from August 2013 until June 2015 at 9 Pediatric Emergency Research Canada (PERC) network tertiary pediatric emergency departments (EDs).

Participants

This study enrolled 3063 participants aged 5.00 to 17.99 years with ED presentation for acute head injury[12,13] occurring within the preceding 48 hours, who met concussion diagnosis criteria according to the 2012 Zurich consensus statement.[1] Exclusion criteria were a Glasgow Coma Scale score of 13 or less; any abnormality on brain computed tomography or magnetic resonance imaging; neurosurgical intervention, intubation, or intensive care unit admission; multisystem injury requiring hospitalization; severe preexisting neurological developmental delay resulting in communication difficulties; intoxication; absence of trauma as the primary event; previously enrolled in this same study; insurmountable language barrier; or inability to follow-up by phone or electronic-mail. The 5P study was approved by

Key Points

Question Is participation in physical activity within 7 days following acute concussion associated with lower rates of persistent postconcussive symptoms in children and adolescents compared with conservative rest?

Findings In this prospective, multicenter cohort study of 3063 children and adolescents aged 5.00 to 17.99 years after propensity matching, the proportion with postconcussive symptoms at 28 days was 28.7% with participation in early physical activity vs 40.1% with conservative rest, a significant difference.

Meaning Participation in physical activity within 1 week after injury may benefit symptom recovery following acute concussion in children and adolescents.

ethics committees of each participating institution, and a written informed consent and assent was obtained from all participants or parents as appropriate.

Study Protocol

Trained research assistants completed standardized assessments of all patients in the ED.[12] Data were collected and managed using Research Electronic Data Capture (REDCap) tools hosted at the Children's Hospital of Eastern Ontario Research Institute.[14] Patients and parents provided information on demographics and past history (ie, prior concussion, headache, developmental or psychiatric conditions), as well as injury characteristics using the Acute Concussion Evaluation inventory,[15] a validated scale used to identify concussion in children and adolescents aged 3 to 18 years. Patients and parents quantified pre-injury and current symptoms (ie, physical, emotional, cognitive, and sleep) using the Post-Concussion Symptom Inventory (PCSI).[16] Cognitive status, physical examination, and balance assessments were completed using the Child-Sport Concussion Assessment Tool-3rd Edition (Child-SCAT3) evaluation.[1,17]

Follow-up Procedures

Enrolled patients were offered web-based survey or telephone follow-up at 7 and 28 days postenrollment.[12] Patients received email reminders 24 hours after each survey deadline; research assistants telephoned nonresponders as many as 5 times and offered verbal interviews. Surveys were parent reported for children aged 5.00 to 7.99 years and patient reported for all other participants. Current level of physical activity was self-categorized as no activity (eg, physical rest), light aerobic exercise (eg, walking, swimming, or stationary cycling), sport-specific exercise (eg, running drills in soccer or skating drills in ice hockey), noncontact training drills (eg, complex passing drills), full-contact practice (eg, normal training activities), and return to competition (eg, normal game play).[12] Early physical activity participation was defined as any level of physical activity other than no activity at 7 days postenrollment. Early physical activity subcategories were defined as no activity, light aerobic exercise, moderate exercise (sport-specific exercise or noncontact training drills), or full exercise (full-contact practice or return to competition). Questions regarding physical activity were based on Zurich

Consensus Statement on Concussion in Sport return-to-play[1] steps; these questions have not been validated.

Primary Outcome Measure

Primary outcome was the presence of PPCS, defined as at least 3 new or worsening individual symptoms compared with the preconcussion status measured at day 28 according to the validated PCSI.[12,13,18] An individual symptom was defined as a positive difference between the current minus the perceived pre-injury symptom rating as completed 28 days postenrollment.[12,13]

Statistical Analysis

Frequencies and descriptive statistics were used to summarize patient baseline characteristics for the overall sample and by early physical activity. Missing data were managed via listwise deletion (ie, participants were excluded from the analysis if any single values were missing).

The proportion of PPCS in each group was computed, along with a Wilson score 95% CI, a method for obtaining a CI for a proportion.[19] The unadjusted association between early physical activity and PPCS was estimated using the sample relative risk (RR) and the sample Absolute risk difference (ARD).

Propensity scores[20] were developed to account for potential confounding by observed baseline characteristics.[21,22] A propensity score was derived to reflect the probability of a participant having engaged in early physical activity given an observed set of baseline characteristics. Propensity score methods replace an entire set of baseline characteristics with a single composite score, and this can be accomplished with numbers of potential confounders in excess of what is possible with conventional regression methods.[23-25] Clinically relevant variables (defined a priori) and those that may be associated with early physical activity were included in the models. Continuous variables were categorized based on the Youden index[26] or through visualization using locally weighted polynomial regression (LOESS) curves. The following variables were included as predictors of early activity using multivariate logistic regression to calculate the propensity score: age group, sex, duration of prior concussion (no prior concussion or concussion with symptoms lasting <1 week vs prior concussion with symptoms lasting ≥1 week), personal history of migraines, family history of migraines, learning disability, attention-deficit/hyperactivity disorder, developmental disorder, anxiety, depression, sleep disorder, other psychiatric disorder, loss of consciousness duration (did not lose consciousness or loss of consciousness <3 minutes vs loss of consciousness ≥3 minutes), time between head injury and triage, seizure, early symptoms on the Acute Concussion Evaluation (appears dazed and confused, confused about events, answers questions slowly, repeats questions, forgetful), balance tandem stance (0-3 errors vs ≥4 errors or physically unable), sports injury, all 20 parent reported indicators of the Postconcussion Symptom Inventory,[16] and site.

To examine the outcome associated with early activity,[21] participants who did and did not engage in early physical activity were matched 1:1 in random order on the logit of the propensity scores using a greedy algorithm and nearest-neighbor approach (maximum caliper distance, 0.1) using the MatchIt package in R (R Project for Statistical Computing).[27] Equivalence between matched participants (activity vs non-activity groups) was assessed by testing for differences in covariates using χ^2 analyses and Mann-Whitney U tests where appropriate. Standardized mean differences were calculated using the R package Tableone. After obtaining a matched data set, the association between early participation in physical activity and PPCS was estimated using the sample RR and the sample ARD.

Inverse probability of treatment weighting (IPTW) was used to investigate the association of early participation in physical activity among the entire population of youth recovering from acute concussion when this population is hypothetically moved from no early activity to participation in early activity. Participants were weighted by the inverse of the probability of engaging in physical activity at day 7. The association between early participation in physical activity and PPCS was estimated using the RR obtained from log-binomial regression and the ARD obtained from identity link binomial regression. In both cases, the IPTW weights were used with a quasibinomial model to obtain robust variance estimates. To avoid convergence issues, the R package glm2 was used. Group differences were assessed by calculating IPTW proportions, weighted medians, and standardized mean differences.

Because the self-report questionnaire at day 7 does not differentiate between the timing of activity and symptoms within the first week postinjury, 2 sensitivity analyses were performed. First, the original analyses were repeated by replacing the total ED symptom load with the total score at day 7. Second, a subanalysis of only patients remaining symptomatic with at least 3 symptoms at day 7 was performed, thus excluding recovered patients and those with minimal symptomatology. A sensitivity analysis was also conducted to investigate a possible interaction between age and physical activity in the model for PPCS. A quasibinomial model with a log link included an effect for early exercise, age (as a continuous variable), and the product of these 2 variables. Two sided P values of less than 0.05 were considered statistically significant. All analyses were performed using IBM SPSS Statistics version 23 (IBM Corp) and R version 3.0.2.

Results

In total, 2584 of 3063 (84.4%) patients completed the primary outcome assessment (**Figure 1**). Of these, 171 were excluded because of missing data on participation in physical activity at day 7, resulting in a cohort of 2413 patients. Baseline characteristics for the total cohort, and for participant groups with and without early physical activity are summarized in **Table 1**. Overall, 733/2413 (30.4%) patients met criteria for PPCS.

Early Participation in Physical Activity

At 7 days postenrollment, 1677 (69.5%) patients reported participating in physical activity including light aerobic exercise

(795 [32.9%]), sport-specific exercise (214 [8.9%]), noncontact training drills (143 [5.9%]), full contact practice (106 [4.4%]), or return to competition (419 [17.4%]), and 736 patients (30.5%) reported no physical activity. Of the 1677 patients who engaged in early physical activity, 523 (31.3%) were symptom free and 803 (48.0%) had at least 3 persistent or worsening postconcussive symptoms at day 7. Of those reporting engaging in no physical activity at day 7, 584 (79.5%) had at least 3 persistent or worsening postconcussive symptoms at day 7.

Bivariable Analysis

In bivariable analysis (unweighted sample), early participation in any type of physical activity compared with no physical activity was associated with lower risk of PPCS (413 [24.6%] patients vs 320 [43.5%] patients; RR, 0.75 [95% CI, 0.70-0.80]; ARD, 18.9% [95% CI, 14.7%-23.0%]). When early physical activity subcategories were distinguished, participation in light aerobic exercise (250 patients [31.4%]; RR, 0.82 [95% CI, 0.76-0.89]; ARD, 12.0% [95% CI, 7.2%-16.8%]), moderate exercise (87 patients [24.4%]; RR, 0.75 [95% CI, 0.69-0.81]; ARD, 19.1% [95% CI, 13.2%-24.6%]), and full exercise (76 patients [14.5%]; RR, 0.66 [95% CI, 0.61-0.71]; ARD, 29.0% [95% CI, 24.2%-33.5%]) were all associated with significantly lower risk of PPCS as compared with the no activity group (320 patients [43.5%]; **Table 2**).

Propensity Score-Matched Analysis

Prior to matching, median propensity to engage in physical activity in the activity group was 0.74 (interquartile range [IQR], 0.65-0.80) vs 0.66 (IQR, 0.55-0.75) in the nonactivity group. Matching resulted in 554 children and adolescents participating in early physical activity matched to 554 children not participating in activity. Because more participants reported engaging in physical activity than not, 900 who participated in physical activity were unmatched in contrast to 91 nonactivity participants. The distribution of propensity scores in the early activity and nonactivity groups are shown in before matching (**Figure 2**A) and after matching (Figure 2B). Following propensity score matching, mean (SD) propensity for early physical activity was similar for those reporting activity (0.641 [0.176]) vs no physical activity (0.627 [0.171]) and also resulted in between-group balance on baseline characteristics (Table 1). In propensity score-matched bivariable analysis (n = 1108), early participation in physical activity remained significantly associated with lower PPCS risk (n = 159 [28.7%]) vs n = 222 [40.1%]; RR, 0.84 [95% CI, 0.77-0.92]; ARD, 11.4% [95% CI, 5.8%-16.9%]).

Inverse Probability Treatment Weighting Analysis

IPTW, formed by those with complete data on exercise and all 43 covariates included in the propensity analysis, also resulted in between-group balance on baseline characteristics (Table 1; n = 2099). Figure 2C shows the weighted distribution of propensity scores in the early activity and nonactivity groups. Mean (SD) weight was 2.00 (1.52) with a range of 1.03 to 12.9. The highest values for standardized mean differences in the weighted data were 0.113 for wearing a mouth guard and

Figure 1. Flow Diagram of Participants With and Without Early Physical Activity Following Acute Concussion
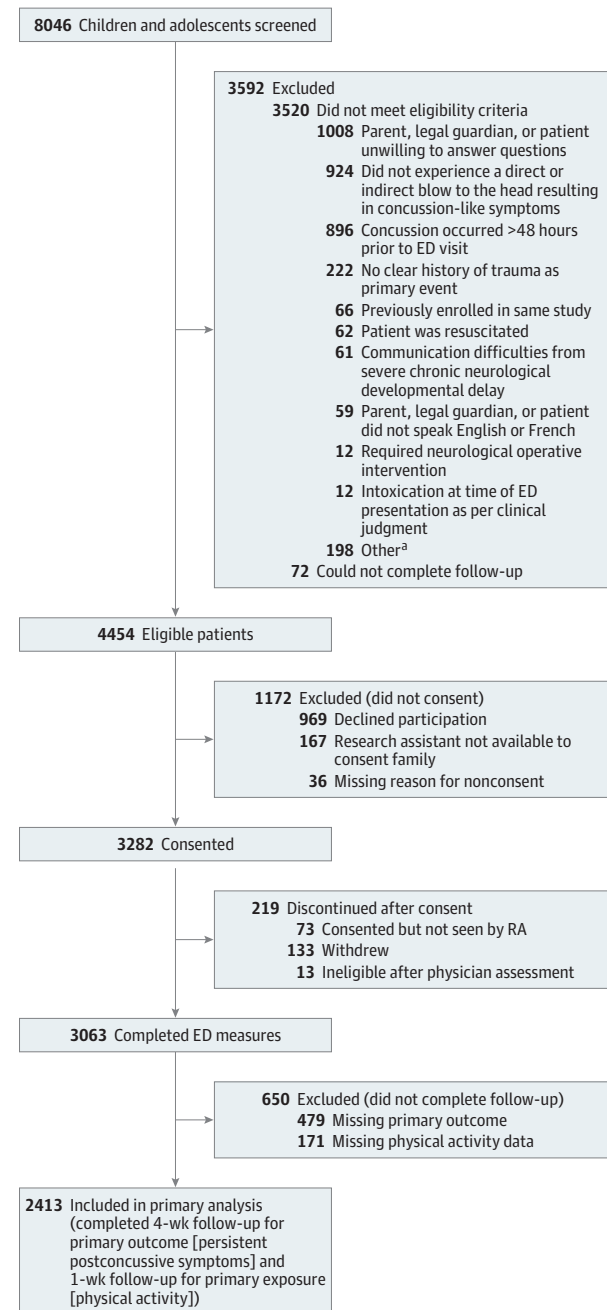
ED indicates emergency department; RA, research assistant.

[a] Includes those for whom reason was not specified or was missing data due to the fact that 1 of the 9 research ethics boards did not permit the collection of reasons for meeting exclusion criteria due to provincial regulations.

0.101 for wearing a helmet; all other baseline variables had standardized mean difference values of less than 0.1. PPCS remained significantly less likely in the early physical activity group in IPTW log-binomial regression analysis compared with the no physical activity group (RR, 0.74 [95% CI, 0.65-0.84]; ARD, 9.7% [95% CI, 5.7%-13.7%]).

Table 1. Baseline Characteristics Total Sample, Unweighted Sample, Propensity Score–Matched Sample, and Inverse Probability of Treatment-Weighted Sample

Characteristic	Physical Activity at 7 Days, No. (%)										
	Total (N = 3063)	Unweighted Sample (n = 2413)			Propensity 1:1 Matching (n = 1108)			IPTW (n = 2099)[a,b]		
		No (n = 736)	Yes (n = 1677)	Standardized Mean Difference	No (n = 554)	Yes (n = 554)	Standardized Mean Difference	No (n = 645)	Yes (n = 1454)	Standardized Mean Difference
Age, y[c]										
5-7	534 (17.4)	73 (9.9)	343 (20.5)		69 (12.5)	79 (14.3)		352.5 (16.9)	379.4 (18.0)	
8-12	1282 (41.9)	268 (36.4)	762 (45.4)	0.434	226 (40.8)	232 (41.9)	0.068	935.9 (44.8)	906.1 (43.1)	0.040
13-18	1247 (40.7)	395 (53.7)	572 (34.1)		259 (46.8)	243 (43.9)		798.5 (38.3)	818.5 (38.9)	
Female sex[c]	1205 (39.3)	350 (47.6)	605 (36.1)	0.234	237 (42.8)	243 (43.9)	0.022	822.4 (39.4)	822.5 (39.1)	0.007
Time between head injury and triage, median (SD), h[c]	8.7 (11.8)	10.3 (12.8)	8.0 (11.0)	0.197	9.5 (12.1)	9.6 (12.1)	0.004	9.0 (11.7)	8.8 (11.6)	0.011
Previous concussion lasting ≥1 wk[c]	390 (12.8)	139 (19.0)	164 (9.8)	0.262	86 (15.5)	73 (13.2)	0.067	243.7 (11.7)	248.4 (11.8)	0.004
Personal migraine history	392 (12.9)	103 (14.1)	198 (11.9)	0.066	69 (12.5)	82 (14.8)	0.068	246.2 (11.8)	245.9 (11.7)	0.003
Family history of migraine[c]	1436 (48.2)	345 (48.3)	808 (49.2)	0.019	263 (47.5)	264 (47.7)	0.004	1000.2 (47.9)	1021.3 (48.5)	0.012
Learning disabilities[c]	243 (8.0)	53 (7.2)	124 (7.4)	0.007	42 (7.6)	42 (7.6)	<0.001	144.3 (6.9)	158.2 (7.5)	0.023
ADD or ADHD[c]	268 (8.7)	56 (7.7)	137 (8.2)	0.02	42 (7.6)	44 (7.9)	0.013	139.6 (6.7)	161.7 (7.7)	0.039
Other developmental disorder[c]	122 (4.0)	34 (4.6)	47 (2.8)	0.096	21 (3.8)	20 (3.6)	0.01	73.0 (3.5)	69.6 (3.3)	0.01
Anxiety[c]	237 (7.7)	85 (11.6)	111 (6.6)	0.173	54 (9.7)	47 (8.5)	0.044	160.5 (7.7)	170.0 (8.1)	0.014
Depression[c]	87 (2.9)	26 (3.5)	40 (2.4)	0.067	18 (3.2)	16 (2.9)	0.021	51.3 (2.5)	49.8 (2.4)	0.006
Sleep disorders[c]	62 (2.0)	22 (3.0)	27 (1.6)	0.092	15 (2.7)	13 (2.3)	0.023	45.7 (2.2)	51.4 (2.4)	0.017
Other psychiatric disorder[c]	32 (1.1)	9 (1.2)	17 (1.0)	0.019	5 (0.9)	2 (0.4)	0.068	15.1 (0.7)	17.3 (0.8)	0.011
Loss of consciousness duration, mean (SD)[c]										
Did not lose consciousness	2317 (76.0)	552 (75.0)	1274 (76.1)		427 (77.1)	420 (75.8)		1592.9 (76.3)	1603.2 (76.2)	
Lost consciousness, min				0.042			0.058			0.041
<3	395 (13.0)	101 (13.7)	206 (12.3)		71 (12.8)	68 (12.3)		275.3 (13.2)	257.8 (12.3)	
≥3	337 (11.1)	83 (11.3)	194 (11.6)		56 (10.1)	66 (11.9)		218.7 (10.5)	242.9 (11.5)	
Seizure[c]	57 (1.9)	13 (1.8)	32 (1.9)	0.011	11 (2.0)	5 (0.9)	0.091	40.8 (2.0)	40.1 (1.9)	0.003

(continued)

Table 1. Baseline Characteristics Total Sample, Unweighted Sample, Propensity Score-Matched Sample, and Inverse Probability of Treatment-Weighted Sample (continued)

Characteristic	Total (N = 3063)	Unweighted Sample (n = 2413)			Propensity 1:1 Matching (n = 1108)			IPTW (n = 2099)[a,b]		
		No (n = 736)	Yes (n = 1677)	Standardized Mean Difference	No (n = 554)	Yes (n = 554)	Standardized Mean Difference	No (n = 645)	Yes (n = 1454)	Standardized Mean Difference
ACE[c]										
Appears dazed and confused	1504 (49.1)	425 (57.7)	773 (46.1)	0.235	312 (56.3)	290 (52.3)	0.08	1029.6 (49.3)	1058.3 (50.3)	0.019
Confused about events	755 (24.6)	211 (28.7)	387 (23.1)	0.128	151 (27.3)	135 (24.4)	0.066	491.6 (23.6)	520.7 (24.7)	0.028
Answers questions slowly	1253 (40.9)	353 (48.0)	618 (36.9)	0.226	254 (45.8)	237 (42.8)	0.062	859.3 (41.2)	844.8 (40.2)	0.021
Repeats questions	418 (13.6)	120 (16.3)	207 (12.3)	0.113	88 (15.9)	69 (12.5)	0.098	296.7 (14.2)	288.1 (13.7)	0.015
Forgetful	643 (21.0)	184 (25.0)	319 (19.0)	0.145	132 (23.8)	122 (22.0)	0.043	445.7 (21.4)	441.6 (21.0)	0.009
Sports injury[c]	2071 (67.6)	539 (73.2)	1119 (66.8)	0.141	400 (72.2)	394 (71.1)	0.024	1441.6 (69.1)	1452.9 (69.1)	0.001
Balance tandem stance[c]	1206 (40.6)	304 (42.0)	650 (39.7)	0.047	223 (40.3)	217 (39.2)	0.022	835.7 (40.0)	826.8 (39.3)	0.015
Mechanism of injury										
Sports and recreational play	2071 (67.6)	539 (73.2)	1119 (66.8)		400 (72.2)	394 (71.1)		1441.6 (69.1)	1452.9 (69.1)	
Non-sports-related injury and fall	741 (24.2)	139 (18.9)	429 (25.6)		108 (19.5)	129 (23.3)		453.2 (21.7)	501.0 (23.8)	
Motor vehicle collision	55 (1.8)	18 (2.4)	28 (1.7)	0.183	13 (2.3)	9 (1.6)	0.164	51.1 (2.4)	30.7 (1.5)	0.123
Assault	39 (1.3)	11 (1.5)	17 (1.0)		11 (2.0)	3 (0.5)		39.5 (1.9)	17.7 (0.8)	
Other	143 (4.7)	29 (3.9)	82 (4.9)		22 (4.0)	19 (3.4)		101.5 (4.9)	101.6 (4.8)	
Helmet use[c]	779 (37.6)	217 (40.3)	407 (36.4)	0.08	164 (41.0)	145 (36.8)	0.086	605.1 (42.0)	538.4 (37.1)	0.101
Mouth guard use[c]	448 (21.7)	134 (24.9)	222 (19.9)	0.12	104 (26.1)	87 (22.2)	0.091	368.3 (25.6)	302.1 (20.9)	0.113
Parent report indicators of PPCS[c,d]										
Headache	2517 (86.8)	638 (90.4)	1359 (84.9)	0.166	497 (89.7)	495 (89.4)	0.012	1844.5 (88.4)	1829.5 (87.0)	0.044
Nausea	1702 (58.8)	442 (62.6)	904 (56.6)	0.123	338 (61.0)	336 (60.6)	0.007	1241.9 (59.5)	1225.5 (58.2)	0.026
Balance problems	1265 (43.7)	363 (51.4)	660 (41.3)	0.203	278 (50.2)	262 (47.3)	0.058	934.0 (44.8)	936.2 (44.5)	0.005
Dizziness	2032 (70.2)	540 (76.5)	1069 (66.9)	0.214	413 (74.5)	411 (74.2)	0.008	1463.9 (70.2)	1471.9 (70.0)	0.004
Drowsiness	2127 (73.4)	531 (75.2)	1142 (71.5)	0.085	411 (74.2)	397 (71.7)	0.057	1557.0 (74.6)	1546.3 (73.5)	0.025
Increased sleeping	1007 (34.8)	264 (37.4)	536 (33.6)	0.081	196 (35.4)	180 (32.5)	0.061	763.5 (36.6)	737.8 (35.1)	0.032
Sensitivity to light	1136 (39.2)	326 (46.2)	578 (36.2)	0.206	242 (43.7)	236 (42.6)	0.022	839.1 (40.2)	828.9 (39.4)	0.017
Sensitivity to noise	1033 (35.7)	316 (44.8)	496 (31.0)	0.286	234 (42.2)	234 (42.2)	<0.001	754.5 (36.2)	757.8 (36.0)	0.003
Irritability	778 (26.9)	211 (29.9)	391 (24.5)	0.122	156 (28.2)	148 (26.7)	0.032	553.3 (26.5)	551.3 (26.2)	0.007
Sadness	1152 (39.8)	260 (36.8)	643 (40.2)	0.07	210 (37.9)	201 (36.3)	0.034	807.1 (38.7)	813.8 (38.7)	<0.001

(continued)

Table 1. Baseline Characteristics Total Sample, Unweighted Sample, Propensity Score–Matched Sample, and Inverse Probability of Treatment-Weighted Sample (continued)

Physical Activity at 7 Days, No. (%)

Characteristic	Total (N = 3063)	Unweighted Sample No (n = 736)	Unweighted Sample Yes (n = 1677)	Unweighted Standardized Mean Difference	Propensity 1:1 Matching (n = 1108) No (n = 554)	Propensity 1:1 Matching Yes (n = 554)	Propensity Standardized Mean Difference	IPTW (n = 2099)[a,b] No (n = 645)	IPTW Yes (n = 1454)	IPTW Standardized Mean Difference
Nervousness	720 (24.9)	167 (23.7)	397 (24.8)	0.028	126 (22.7)	121 (21.8)	0.022	486.8 (23.3)	505.6 (24.0)	0.017
Acts more emotional	1153 (39.8)	260 (36.9)	648 (40.5)	0.074	211 (38.1)	195 (35.2)	0.06	850.8 (40.8)	832.2 (39.6)	0.025
Seems mentally foggy	1546 (53.5)	434 (61.5)	792 (49.7)	0.239	326 (58.8)	316 (57.0)	0.037	1129.4 (54.1)	1129.3 (53.7)	0.009
Poor concentration	1075 (37.2)	322 (45.7)	529 (33.1)	0.259	230 (41.5)	214 (38.6)	0.059	782.7 (37.5)	778.3 (37.0)	0.011
Forgetfulness	866 (29.9)	247 (35.0)	440 (27.5)	0.163	177 (31.9)	178 (32.1)	0.004	629.3 (30.2)	621.9 (29.6)	0.013
Visual problems	979 (33.8)	273 (38.7)	511 (32.0)	0.141	203 (36.6)	196 (35.4)	0.026	706.5 (33.9)	713.9 (33.9)	0.002
Increased fatigue	2160 (74.6)	567 (80.4)	1141 (71.4)	0.213	432 (78.0)	424 (76.5)	0.034	1574.6 (75.5)	1563.8 (74.3)	0.026
Confusion with directions or tasks	682 (23.6)	205 (29.2)	319 (19.9)	0.215	147 (26.5)	135 (24.4)	0.05	459.0 (22.0)	470.5 (22.4)	0.009
Clumsy movement	790 (27.3)	210 (29.8)	416 (26.0)	0.084	160 (28.9)	162 (29.2)	0.008	566.6 (27.2)	570.8 (27.1)	<0.001
Slower response to questions	1363 (47.1)	371 (52.6)	693 (43.4)	0.186	283 (51.1)	273 (49.3)	0.036	988.4 (47.4)	990.7 (47.1)	0.005
Site[c]				0.508			0.096			0.047
1		78 (10.6)	227 (13.5)		61 (11.0)	59 (10.6)		246.1 (11.8)	268.1 (12.7)	
2		144 (19.6)	376 (22.4)		106 (19.1)	121 (21.8)		431.3 (20.7)	416.6 (19.8)	
3		35 (4.8)	121 (7.2)		32 (5.8)	31 (5.6)		133.8 (6.4)	147.1 (7.0)	
4		72 (9.8)	206 (12.3)		43 (7.8)	48 (8.7)		201.1 (9.6)	198.8 (9.4)	
5		112 (15.2)	88 (5.2)		71 (12.8)	61 (11.0)		185.9 (8.9)	180.9 (8.6)	
6		54 (7.3)	156 (9.3)		47 (8.5)	45 (8.1)		197.4 (9.5)	191.1 (9.1)	
7		144 (19.6)	153 (9.1)		108 (19.5)	100 (18.1)		285.1 (13.7)	293.7 (14.0)	
8		49 (6.7)	200 (11.9)		43 (7.8)	43 (7.8)		218.2 (10.5)	226.3 (10.8)	
9		48 (6.5)	150 (8.9)		43 (7.8)	46 (8.3)		187.9 (9.0)	181.3 (8.6)	

Abbreviations: ACE, acute concussion evaluation; ADD, attention-deficit disorder; ADHD, attention deficit/hyperactivity disorder; IPTW, inverse probability of treatment weighting; PPCS, persistent postconcussive symptoms.

[a] Proportions and medians are weighted using IPTW.

[b] The IPTW sample only includes those with complete data on exercise and all 43 covariates included in the propensity analysis.

[c] Variables included in the propensity score.

[d] Indicators are based on patient complaint, parental observation of the patient, or a combination of both.

Sensitivity Analyses

When the total ED symptom score was replaced with the total score at day 7, only the association in the unweighted sample remained significant with similar magnitude and directionality as in the primary analyses (bivariable analyses RR, 0.75 [95% CI, 0.70-0.80]; **Table 3**).

In the second sensitivity analysis, the analytical sample was limited to children and adolescents with at least 3 symptoms at day 7 (n = 1387). Despite current guidelines strongly advocating physical rest until the patient is asymptomatic, 584 of 1387 (57.9%) participants engaged in some form of physical activity (ie, were nonadherent with current recommendations). Although the directionality of the association remained similar, the propensity score-matched analysis and IPTW analysis no longer reached statistical significance (bivariable analysis RR, 0.83 [95% CI, 0.74-0.92]; propensity score-matched RR, 0.92 [95% CI, 0.80-1.05]; IPTW RR, 0.92 [95% CI, 0.82-1.04]; Table 3). When early physical activity subcategories were distinguished within this symptomatic cohort, children and adolescents who participated in physical activity had lower risk of PPCS (light aerobic exercise absolute risk, 46.4% [RR, 0.88 {95% CI, 0.78-0.99}; ARD, 6.6% {95% CI, 0.6%-12.5%}]; moderate exercise absolute risk, 38.6% [RR, 0.77 {95% CI, 0.66-0.89}; ARD, 14.3% {95% CI, 5.9%-22.2%}]; and full exercise absolute risk, 36.1% [RR, 0.74 {95% CI, 0.63-0.86}; ARD, 16.8% {95% CI, 7.5%-25.5%}]) compared with the no activity group (absolute risk, 52.9%). Finally, there was no

statistically significant interaction between age and physical activity in an unadjusted model for PPCS; for each additional year of age, RR increased by a factor of 1.01 (95% CI, 0.97-1.05; *P* = .52).

Discussion

In this prospective cohort study, 69.5% of children and adolescents participated in physical activity within 7 days following an acute concussion—primarily with light aerobic exercise. The resumption of physical activity within 7 days postconcussion was associated with a lower risk of PPCS as compared with no physical activity. This finding was consistent across analytic approaches and intensity of exercise.

Evidence about the importance of physical activity in childhood for maintaining physical and cognitive health is unequivocal.[29] Physical activity is considered an effective method for improving cognitive function and brain health.[30] Compared with other conditions in which the latest insights regarding the benefits of early physical rehabilitation have been adopted, including stroke,[31] the field of pediatric concussion lags behind.[2] Overwhelming evidence supports the overall benefits of physical activity in youth [32] including better body composition,[33] skeletal health,[34] and cardiorespiratory fitness, as well as improvement of depression, anxiety, self-concept,[35] cognitive performance, and academic achievement.[36,37]

Table 2. Summary of Results of the Primary Analysis

Type Analysis	No. (Absolute Risk, %)		Absolute Risk Difference, % (95% CI)	Relative Risk (95%CI)
	Physical Activity	No Physical Activity		
Unweighted sample	1677 (24.6)	736 (43.5)	18.9 (14.7-23.0)	0.75 (0.70-0.80)
Light activity vs none (subgroup 1)	795 (31.4)	736 (43.5)	12.0 (7.2-16.8)	0.82 (0.76-0.89)
Moderate activity vs none (subgroup 2)	357 (24.4)	736 (43.5)	19.1 (13.2-24.6)	0.75 (0.69-0.81)
Full-contact activity vs none (subgroup 3)	525 (14.5)	736 (43.5)	29.0 (24.2-33.5)	0.66 (0.61-0.71)
Matched	554 (28.7)	554 (40.1)	11.4 (5.8-16.9)	0.84 (0.77-0.92)
Inverse probability of treatment weighting	1454	645	9.7 (5.7-13.5)	0.74 (0.65-0.84)

Figure 2. Distribution of Propensity Scores in the Physical Activity Group and the Rest Group
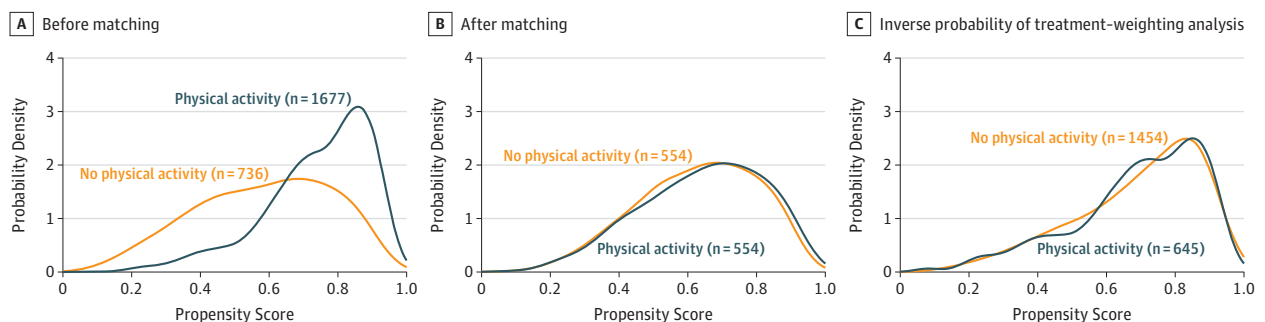
Inverse probability of treatment-weighting analysis includes only those patients with complete data on physical activity and all 43 covariates included in the propensity analysis. For intervals along the x-axis, the area under the probability density curve represents the probability of those propensity scores. Smoothing was via the kernel density estimate.[28]

Table 3. Summary of Sensitivity Analysis 1 and 2

Type Analysis	No. (Absolute Risk, %)		Absolute Risk Difference (95% CI)	Relative Risk (95% CI)
	Physical Activity	No Physical Activity		
Sensitivity analysis 1				
Unweighted sample	1667 (30.4)	736 (69.6)	18.9 (14.7 to 23.0)	0.75 (0.70 to 0.80)
Matched	519 (39.1)	519 (38.3)	−0.77 (−6.7 to 5.1)	1.01 (0.92 to 1.11)
IPTW			−0.041 (−4.1 to 4.0)	1.00 (0.88 to 1.14)
Sensitivity analysis 2				
Unweighted sample	803 (43.0)	584 (52.9)	9.9 (4.6 to 15.2)	0.83 (0.74 to 0.92)
Subgroup 1 (light activity vs none)	494 (46.4)	584 (52.9)	6.6 (0.6 to 12.5)	0.88 (0.78 to 0.99)
Subgroup 2 (moderate activity vs none)	176 (38.6)	584 (52.9)	14.3 (5.9 to 22.2)	0.77 (0.66 to 0.89)
Subgroup 3 (full exercise vs none)	133 (36.1)	584 (52.9)	16.8 (7.5 to 25.5)	0.74 (0.63 to 0.86)
Matched	388 (47.2)	388 (51.5)	4.4 (−2.6 to 11.3)	0.92 (0.80 to 1.05)
IPTW	687	507	4.0 (−1.7 to 9.7)	0.92 (0.82 to 1.04)

Abbreviation: IPTW, inverse probability of treatment weighting.

Preliminary studies in concussed adolescents found that participants engaging in moderate levels of activity reported lower symptom levels and superior neurocognitive performance compared with those with physical rest, although the optimal timing for re-introducing physical activity remains undetermined.[6,11] Available evidence suggests that gradual resumption of physical activity should begin as soon as tolerated following an acute concussion,[3,11] with the exception of activities likely to increase the risk of re-injury.[6,9,11] Rest exceeding 3 days postinjury was similarly or less effective than treatment regimens allowing for earlier participation in physical activity following a concussion[11,38]; if prolonged, rest may predispose to secondary symptoms of fatigue, reactive depression, physiological deconditioning, and delayed recovery.[7,8] Also in symptomatic adolescents, pilot evidence suggests that gradual resumption of aerobic physical activities results in superior symptom recovery from concussion compared with complete rest.[9,10]

A proposed mechanism by which exercise may improve recovery is through the promotion of neuroplasticity mechanisms and from possible effects on cardioregulatory mechanisms, possibly leading to improved cerebral blood flow.[39] This is of particular importance in pediatric concussion, since autoregulatory dysfunction and abnormal cerebral blood flow regulation have been associated with PPCS in school-aged children.[40,41] Controlled aerobic exercise may improve recovery by restoring normal cerebral blood flow regulation[10] with the rate of symptom improvement relating directly to the exercise intensity achieved.[10] Conversely, physical inactivity may predispose patients to PPCS through an activity restriction cascade model; it has been theorized that the psychological consequences of removal from life-validating activities, combined with physical deconditioning, may contribute to the development of PPCS after mild traumatic brain injury in youth.[3]

The results of this study should be considered in the context of study limitations. Because of the observational design, the authors cannot account for unmeasured confounding due to factors that may have been associated with physical activity shortly after concussion, nor can causation be determined. Although potential confounding by observed baseline characteristics was accounted for by conducting a propensity analysis,[20] unmeasured confounders and intermediaries may have influenced the results. Because the lowest odds of PPCS were observed in children participating in full exercise at day 7, children who simply felt better may have started physical activity earlier and subsequently resumed full competition despite still having symptoms. This possibility was examined through sensitivity analyses in which 1-week symptoms replaced ED symptoms and the inclusion of only those children with 3 or more symptoms at day 7. Given the limitation of possible confounding variables, a well-designed and adequately powered randomized clinical trial is needed to confirm the benefits of early return to physical activity.

Second, physical activity was rated via self-report questionnaires. Although direct measures of physical activity have greater precision, no single criterion standard exists and self-rated measures remain the most common and feasible method of measuring physical activity in large settings due to their practicality, low cost, low participant burden, and general acceptance.[42]

Third, because objective data on physical activity (eg, actigraphy) was not collected, information regarding duration and frequency of physical activity is limited; uncertainty remains as to whether exercise intensity exacerbates symptoms and how total activity load may be associated with PPCS risk.

Fourth, it is possible that patients who did not resume physical activity may have participated in more cognitive activity and therefore may have been potentially more symptomatic. Measuring cognitive rest is challenging because it is poorly defined across the literature and difficult to objectively measure. Since objective cognitive activity data were not collected, conclusions regarding the benefit or detriment of cognitive rest were unattainable.

Fifth, because all participants received care as usual by treating physicians, rest and activity recommendations likely varied across sites and clinicians both in the ED and subsequent follow-up.

Sixth, the influence of interim activity (eg, participation in physical activities between days 7 and 28 postenrollment) was not considered.

Divergence from conservative rest recommendations following pediatric concussion toward early active physical rehabilitation would be a new approach in concussion management, potentially affecting the well-being of millions of children and families worldwide. Early physical activity could mitigate the undesired effects of physical and mental deconditioning associated with prolonged rest. Regardless of potential benefit, caution in the immediate postinjury period is prudent; participation in activities that might introduce risk for collision (eg, resumption of contact sports) or falls (eg, skiing, skating, bicycling) should remain prohibited until clearance by a health professional to reduce the risk for a potentially more serious second concussion during a period of increased vulnerability. To be noted, results of this study do not infer any evidence of benefit or harm in association with return to practice or play.

Conclusions

Among children and adolescents aged 5 to 18 years with acute concussion, participation in physical activity within 7 days of acute injury compared with no physical activity was associated with lower risk of PPCS at 28 days. A well-designed randomized clinical trial is needed to determine the benefits of early physical activity following concussion.

REFERENCES

1. McCrory P, Meeuwisse WH, Aubry M, et al. Consensus statement on concussion in sport. *Br J Sports Med*. 2013;47(5):250-258.

2. Zemek R, Duval S, Dematteo C. *Guidelines for Diagnosing and Managing Pediatric Concussion*. Toronto, Canada: Ontario Neurotrauma Foundation; 2014.

3. DiFazio M, Silverberg ND, Kirkwood MW, Bernier R, Iverson GL. Prolonged activity restriction after concussion. *Clin Pediatr (Phila)*. 2016;55(5):443-451.

4. Cancelliere C, Hincapié CA, Keightley M, et al. Systematic review of prognosis and return to play after sport concussion. *Arch Phys Med Rehabil*. 2014;95(3)(suppl):S210-S229.

5. Schneider KJ, Iverson GL, Emery CA, McCrory P, Herring SA, Meeuwisse WH. The effects of rest and treatment following sport-related concussion. *Br J Sports Med*. 2013;47(5):304-307.

6. Majerske CW, Mihalik JP, Ren D, et al. Concussion in sports. *J Athl Train*. 2008;43(3):265-274.

7. Thomas DG, Apps JN, Hoffmann RG, McCrea M, Hammeke T. Benefits of strict rest after acute concussion. *Pediatrics*. 2015;135(2):213-223.

8. Willer B, Leddy JJ. Management of concussion and post-concussion syndrome. *Curr Treat Options Neurol*. 2006;8(5):415-426.

9. Gagnon I, Grilli L, Friedman D, Iverson GL. A pilot study of active rehabilitation for adolescents who are slow to recover from sport-related concussion. *Scand J Med Sci Sports*. 2016;26(3):299-306.

10. Leddy JJ, Kozlowski K, Donnelly JP, Pendergast DR, Epstein LH, Willer B. A preliminary study of subsymptom threshold exercise training for refractory post-concussion syndrome. *Clin J Sport Med*. 2010;20(1):21-27.

11. Silverberg ND, Iverson GL. Is rest after concussion "the best medicine?". *J Head Trauma Rehabil*. 2013;28(4):250-259.

12. Zemek R, Osmond MH, Barrowman N, et al. Predicting and preventing postconcussive problems in paediatrics (5P) study. *BMJ Open*. 2013; 3(8):e003550.

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

14. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)—a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform*. 2009;42(2):377-381.

15. Gioia GA, Collins M, Isquith PK. Improving identification and diagnosis of mild traumatic brain injury with evidence. *J Head Trauma Rehabil*. 2008; 23(4):230-242.

16. 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.

17. McCrory P, Meeuwisse WH, Aubry M, et al. Child SCAT3. *Br J Sports Med*. 2013;47(5):263-266.

18. Steindel SJ. International classification of diseases, 10th edition, clinical modification and procedure coding system: descriptive overview of the next generation HIPAA code sets. *J Am Med Inform Assoc*. 2010;17(3):274-282.

19. Newcombe RG. Two-sided confidence intervals for the single proportion: comparison of seven methods. *Stat Med*. 1998;17(8):857-872.

20. Haukoos JS, Lewis RJ. The propensity score. *JAMA*. 2015;314(15):1637-1638.

21. Austin PC. An introduction to propensity score methods for reducing the effects of confounding in observational studies. *Multivariate Behav Res*. 2011; 46(3):399-424.

22. Kurth T, Walker AM, Glynn RJ, et al. Results of multivariable logistic regression, propensity matching, propensity adjustment, and propensity-based weighting under conditions of nonuniform effect. *Am J Epidemiol*. 2006;163(3): 262-270.

23. Brookhart MA, Schneeweiss S, Rothman KJ, Glynn RJ, Avorn J, Stürmer T. Variable selection for propensity score models. *Am J Epidemiol*. 2006;163 (12):1149-1156.

24. Rosenbaum P, Rubin D. The central role of the propensity score in observational studies for causal effects. *Biometrika*. 1983;70(1):41-55. doi:10.1093 /biomet/70.1.41

25. Williamson EJ, Forbes A. Introduction to propensity scores. *Respirology*. 2014;19(5):625-635.

26. Youden WJ. Index for rating diagnostic tests. *Cancer*. 1950;3(1):32-35.

27. Rosenbaum P, Rubin D. Constructing a control group using multivariate matched sampling methods that incorporate the propensity score. *Am Stat*. 1985;39:33-38. doi:10.1017 /CBO9780511810725.019

28. Scott D. *Multivariate Density Estimation: Theory, Practice and Visualization. Wiley Series in Probability and Mathematical Statistics*. New York, NY: John Wiley & Sons; 1992.

29. Khan NA, Hillman CH. The relation of childhood physical activity and aerobic fitness to brain function and cognition. *Pediatr Exerc Sci*. 2014;26 (2):138-146.

30. Hillman CH, Erickson KI, Kramer AF. Be smart, exercise your heart. *Nat Rev Neurosci*. 2008;9(1): 58-65.

31. Veerbeek JM, van Wegen E, van Peppen R, et al. What is the evidence for physical therapy poststroke? *PLoS One*. 2014;9(2):e87987.

32. Longmuir PE, Colley RC, Wherley VA, Tremblay MS. Canadian Society for Exercise Physiology position stand: benefit and risk for promoting childhood physical activity. *Appl Physiol Nutr Metab*. 2014;39(11):1271-1279.

33. Rush E, Simmons D. Physical activity in children. *Med Sport Sci*. 2014;60:113-121.

34. McKay HA, Petit MA, Schutz RW, Prior JC, Barr SI, Khan KM. Augmented trochanteric bone mineral density after modified physical education classes. *J Pediatr*. 2000;136(2):156-162.

35. Annesi JJ. Correlations of depression and total mood disturbance with physical activity and self-concept in preadolescents enrolled in an after-school exercise program. *Psychol Rep*. 2005; 96(3 Pt 2):891-898.

36. Howie EK, Pate RR. Physical activity and academic achievement in children. *J Sport Health Sci*. 2012;1(3):160-169. doi:10.1016/j.jshs.2012.09.003

37. Chaddock-Heyman L, Hillman CH, Cohen NJ, Kramer AF III. The importance of physical activity and aerobic fitness for cognitive control and memory in children. *Monogr Soc Res Child Dev*. 2014;79(4):25-50.

38. Moor HM, Eisenhauer RC, Killian KD, et al. The relationship between adherence behaviors and recovery time in adolescents after a sports-related concussion. *Int J Sports Phys Ther*. 2015;10(2): 225-233.

39. Perrey S. Promoting motor function by exercising the brain. *Brain Sci*. 2013;3(1):101-122.

40. Farquhar WB, Greaney JL. Autonomic exercise physiology in health and disease. *Auton Neurosci*. 2015;188:1-2.

41. Leddy JJ, Kozlowski K, Fung M, Pendergast DR, Willer B. Regulatory and autoregulatory physiological dysfunction as a primary characteristic of post concussion syndrome. *NeuroRehabilitation*. 2007;22(3):199-205.

42. Adamo KB, Prince SA, Tricco AC, Connor-Gorber S, Tremblay M. A comparison of indirect versus direct measures for assessing physical activity in the pediatric population. *Int J Pediatr Obes*. 2009;4(1):2-27.