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Protocol for a randomised clinical trial of multimodal postconcussion symptom treatment and recovery: the Concussion Essentials study

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ABSTRACT

Introduction While most children recover from a concussion shortly after injury, approximately 30% experience persistent postconcussive symptoms (pPCS) beyond 1-month postinjury. Existing research into the treatment of pPCS have evaluated unimodal approaches, despite evidence suggesting that pPCS likely represent an interaction across various symptom clusters. The primary aim of this study is to evaluate the effectiveness of a multimodal, symptom-tailored intervention to accelerate symptom recovery and increase the proportion of children with resolved symptoms at 3 months postconcussion.

Methods and analysis In this open-label, assessor-blinded, randomised clinical trial, children with concussion aged 8–18 years will be recruited from The Royal Children's Hospital (The RCH) emergency department, or referred by a clinician, within 17 days of initial injury. Based on parent ratings of their child's PCS at ~10 days postinjury, symptomatic children (≥2 symptoms at least 1-point above those endorsed preinjury) will undergo a baseline assessment at 3 weeks postinjury and randomised into either Concussion Essentials (CE, n=108), a multimodal, interdisciplinary delivered, symptom-tailored treatment involving physiotherapy, psychology and education, or usual care (UC, n=108) study arms. CE participants will receive 1 hour of intervention each week, for up to 8 weeks or until pPCS resolve. A postprogramme assessment will be conducted at 3 months postinjury for all participants. Effectiveness of the CE intervention will be determined by the proportion of participants for whom pPCS have resolved at the postprogramme assessment (primary outcome) relative to the UC group. Secondary outcome analyses will examine whether children receiving CE are more likely to demonstrate resolution of pPCS, earlier return to normal activity, higher quality of life and a lower rate of utilisation of health services, compared with the UC group.

Ethics and dissemination Ethics were approved by The RCH Human Research Ethics Committee (HREC: 37100). Parent, and for mature minors, participant consent, will be obtained prior to commencement of the trial. Study results will be disseminated at international conferences and international peer-reviewed journals.

Strengths and limitations of this study

- This study is novel in delivering and evaluating a multimodal, symptom-tailored approach to the treatment of persisting postconcussive symptoms in children and adolescents.
- This study employs gold-standard trial methodology and aims to minimise the emergence of secondary symptoms by providing individualised intervention relatively early postinjury.
- This study will provide data into the economic costs of concussion to individuals and the community with the potential to identify and reduce this cost to health systems.
- Due to the time commitment and face-to-face delivery of the intervention, it is possible that the sample will be biased towards families who are well supported and resourced, and who are geographically proximal to the study location.

Trial registration number ACTRN12617000418370; pre-results.

INTRODUCTION

A concussion is defined as a biomechanical injury to the head associated with transient postconcussive symptoms (PCS) including balance impairment, somatic and/or emotional symptoms, cognitive impairment and/or sleep wake disturbance.[1] Mild head injuries, of which concussion is a subset, account for 90% of emergency department (ED) presentations for paediatric head injury.[2 3] Global figures estimate around 33 million children sustain a concussion each year, with around 12% of these injuries presenting to EDs.[4–7] In most children PCS are short-lived, however, a subset of children (~30%)[4 8 9] experience persisting PCS (pPCS) exceeding 1 month, which pose significant

clinical and community burden.[10–13] Those at risk of pPCS are often identifiable within 2–3 weeks postinjury. Early identifiable risk factors for pPCS include demographic (eg, female sex, adolescent age), psychosocial (eg, parental mental health), preinjury (eg, psychiatric history, history of migraine, history of concussion with symptoms lasting beyond 1 week) and injury-related (eg, postacute symptoms) factors.[8 14 15] Recent findings suggest that early intervention, specifically early participation in aerobic exercise, may prevent the onset of pPCS.[16 17]

The presentation of pPCS, and the particular constellation of pPCS experienced by a child, is most likely the result of interactions across multiple coexisting factors (eg, headache syndromes, vestibular dysfunction, psychological symptoms).[18 19] A network analysis conceptualisation of pPCS argues that these symptoms can trigger, exacerbate and mutually reinforce each other, resulting in their interdependent co-occurrence.[20] Despite approximately 30% of children suffering pPCS,[8 21] the scientific evidence surrounding effective intervention in this population is surprisingly limited.[4 18] A recent scoping review of non-pharmacological rehabilitation interventions for concussion in children noted that there were few studies evaluating interventions for concussion in youth, that the quality of existing research was low, and that heterogeneous methodologies and intervention approaches emphasised the uncertainty in the area.[22] A few trials, mostly in adults, have taken unimodal approaches to reduce pPCS, including strict rest,[23–25] graded aerobic exercise,[16 26–29] school-based interventions,[30] family counselling[31 32] and psychoeducation.[31 32] These unimodal approaches fail to recognise the heterogeneity of PCS profiles, or interaction across PCS clusters (eg, vestibular symptoms may cause anxiety).[20] Acknowledging these limitations, a handful of recent studies have examined multimodal interventions among a paediatric population[29 33] (eg, multimodal physiotherapy,[34–36] a combination of physiotherapy treatment, visualisation/imagery techniques and education,[29 33 37–39] and collaborative care comprising of care management, cognitive–behavioural therapy (CBT) and psychopharmacological consultation[40]), with improvements observed in symptomatology. While these studies show promise in the efficacy of multimodal interventions for treatment of pPCS, they are limited by methodological issues including small sample sizes,[29 33 34 36 39] a lack of control group and/or non-randomised clinical trial (RCT) design.[29 33–38]

Very few child interventions have attempted to treat and accelerate the resolution of pPCS. Existing intervention studies are in their infancy and hindered by methodological limitations. The interacting and varied nature of pPCS, coupled with emerging evidence regarding the efficacy of multimodal treatments, calls for further examination of a methodologically rigorous integrated multimodal intervention, that is delivered by an interdisciplinary team, and tailored to the individual child's PCS profile.

Objectives

The primary objective of this study is to assess the effectiveness of a multimodal, symptom-tailored interdisciplinary-delivered intervention, Concussion Essentials (CE), versus usual care (UC), to accelerate symptom recovery and increase the proportion of children whose symptoms have resolved at 3 months postconcussion. Our secondary objectives are to determine whether, at treatment completion, children receiving CE are more likely to demonstrate: (1) resolution of pPCS, (2) earlier return to normal activity (eg, school and sports), (3) higher physical and psychological quality of life and (4) a lower rate of utilisation of health services, compared with children in the UC group.

METHODS

Patient and public involvement

The study design incorporates parent, participant and clinician feedback, obtained from a pilot investigation of this protocol and from our previous longitudinal studies.[41 42] The Standard Protocol Items: Recommendations for Interventional Trials guidelines were used in the preparation of this protocol.[43]

Study design

This study is an investigator-initiated, single-site, parallel-design, open-label, assessor-blinded RCT of standardised multimodal treatment CE versus UC, for children with pPCS. Participants will be recruited and assessed for eligibility up to 17 days postinjury (screening) and reassessed for eligibility at 3 weeks postinjury (baseline). A postprogramme assessment will occur at 3 months postinjury. The intervention will be provided to the CE group for up to 8 weeks between baseline and postprogramme assessments. See online supplemental material 1 for an example of a participant consent form utilised in the study.

Study setting

The study will be conducted at the Murdoch Children's Research Institute, and The Royal Children's Hospital (The RCH), Melbourne, Australia. Families will be recruited from The RCH ED or through community clinician referrals.

Study population

Participants

Participants recruited up to 17 days postinjury will be screened for pPCS between 10 and 17 days post injury and again at their baseline assessment. The study will recruit 216 participants with pPCS; 108 in each of the two arms, CE and UC. Participants will be randomised to the CE or UC groups if they meet all study eligibility criteria.

Concussion definition

Concussion is defined using the Concussion in Sport Group criteria.[1] Study eligibility requires a child to present with evidence of a blow to the head or impulsive force

transmitted to the head, and one or more of the following symptoms or physical signs; somatic (eg, headaches), cognitive (eg, feeling like in a fog), emotional symptoms (eg, lability), loss of consciousness, amnesia, neurological deficit, balance impairment (eg, gait unsteadiness), behavioural changes (eg, irritability), cognitive impairment (eg, slow reaction time) or sleep disturbance (eg, drowsiness).[1]

A child will be defined as suffering pPCS if their parent endorses ≥2 symptoms on the Post-Concussion Symptom Inventory Plus-Parent (PCSI(+)-P),[44] at least 1-point above those endorsed pre-injury, at their baseline assessment. The PCSI(+)-P includes all items from the PCSI-P in addition to 10 clinical questions, surveying modality specific symptoms (see online supplemental material 2). We have previously validated this cut-off score for the original PCSI and shown that it is able to accurately classify symptomatic children.[21]

Inclusion criteria

Participants will (1) be aged between 8 and 18 years, (2) have suffered a concussion up to 17 days prior to referral/screening, (3) have a Glasgow Coma Scale (GCS)[45 46] score of ≥13 at time of hospital presentation and thereafter, and (4) present with pPCS as previously defined, at their baseline assessment (3-weeks±4 days postinjury).

Exclusion criteria

Participant exclusion criteria are; unknown mechanism of injury or non-accidental injury, head injury secondary to a faint/collapse or seizure, evidence of structural brain injury on neuroimaging, multiple trauma requiring hospitalisation or cervical spine injury, pre-existing conditions such as congenital neuro-ophthalmological or vestibular dysfunction, central neurological conditions (eg, stroke, moderate to severe brain injury) or severe mental health history (eg, bipolar or psychotic disorder, recent suicidal ideation, responses on the Diagnostic and Statistical Manual of Mental Disorders Fifth Edition (DSM-5) Level 1 Cross-Cutting Symptom Measure[47]), a complex psychosocial history (eg, family violence, child protection involvement), pre-existing developmental disorders for which a child is not in mainstream school and/or requires a teacher's aide, insufficient English or inability to attend visits on campus.

Procedures

Recruitment

Participants will be recruited in-person from The RCH ED, via phone call within 48 hours of ED presentation, or via a referral network.

1. Within The RCH ED, initial screening of patients occurs in real-time through The RCH electronic medical record (EMR) database. A research assistant (RA) will screen potentially eligible patients with their treating clinician, who provides approval for study approach. RAs obtain consent in the ED using an electronic REDCap consent form. Initial assessment measures are collected in the ED.
2. RAs will retrospectively screen the ED EMR for patients presenting within the previous 48 hours, where there was no RA recruitment cover. RAs will contact these families via phone to explain the study. Interested families will be sent an electronic REDCap consent form via email.
3. The Referral Network will be provided with a referral form, via an online REDCap study database. Patients (and parents) who self-refer will be required to obtain a referral from a medical practitioner. Parents of potential participants who are referred to the study will be contacted via phone. If the child meets eligibility criteria, they will be sent electronic consent forms via REDCap.

Following consent, participants' parents complete the PCSI(+)-P (via REDCap survey) between 10 and 17 days postinjury to assess if their child remains symptomatic. Participants meeting study criteria for pPCS are invited to attend The RCH for baseline assessment.

Randomisation

RAs will consent participants into the study at the commencement of their baseline assessment. Randomisation to CE or UC will occur after the baseline assessment in a 1:1 ratio. Randomisation will be built into the study's REDCap database and will be generated by a member of the research team. To limit the potential for age and sex to disproportionately affect group outcome, participants will be stratified by age (8–10, 11–12, 13–18) and sex (male, female) prior to randomisation. The randomisation sequences will be computer-generated with variable block sizes, to reduce risk of allocation bias. The trial will be assessor-blinded, that is, RAs conducting postprogramme assessments will be blind to treatment allocation.

Screening and feedback on recovery

All participants will receive a summary report following their baseline assessment. The report will provide standardised feedback on persisting symptoms (responses to the PCSI(+)-P and PCSI(+) Self-Report (PCSI(+)-SR), mental health (parent and child psychological questionnaires), and performance on physiotherapy and cognitive assessments. The report also indicates whether follow-up medical treatment is recommended.

Programme

The main study programme is delivered up to 3 months postconcussion. Participants are randomised into one of two arms:

1. UC: Children receive routine care and complete the PCSI(+)-SR weekly. Parents complete the PCSI(+)-P, which is monitored by the study team. Parents are contacted and advised to visit their general practitioner (GP) if their child's recovery appears concerning (eg, symptoms endorsed at a high severity). There are no limitations on healthcare utilisation.

Table 1 Summary of CE individual symptom-tailored intervention modules

	CE intervention		
Week 1	► Introduction (concussion education, normalisation of symptoms, recovery trajectory, CE programme expectations) ► Generic (symptom-tailored education and strategies) ► Physiotherapy		
	Symptom-tailored treatment modules		
	Generic	**Physical**	**Psychological**
Weeks 2–8	► Return to school ► Return to physical activity ► Sleep ► Headaches ► Fatigue	► Vestibular ► Ocular motor ► Cervical spine ► Physiological	► COPE: manualised CBT (child and teen versions)

CBT, cognitive–behavioural therapy; CE, concussion essentials; COPE, creating opportunities for personal empowerment.

2. CE: Participants receive weekly individual, clinician-delivered sessions, for up to 8 weeks, or until symptom resolution. Treatment modules include concussion education, physiotherapy and psychology, and are designed as 30 min sessions. All participants complete a 1-hour intervention session per week. This hour may be composed of two modules, or a double dose of one module. All CE participants receive education and physiotherapy modules in week 1, with treatment of physical symptoms (eg, physiotherapy) prioritised in initial intervention sessions. Specific CE modules for subsequent intervention sessions are selected weekly, based on clinician consensus (physiotherapist, psychologist, neuropsychologist) at weekly multidisciplinary team meetings, taking into account the child's previous intervention sessions and most severe symptoms. CE treatment modules are summarised in table 1. There are no limitations on additional healthcare utilisation.

Each participant will receive individualised treatment, and will progress through, or between, symptom-specific modules based on symptom expression and resolution.

Generic modules: provides strategies and education regarding commonly endorsed symptoms by children with pPCS, including management of headaches (eg, identifying triggers, strategies for headache management), fatigue (eg, manifestations of fatigue, pacing) and sleep difficulties (eg, sleep hygiene, bedtime routines, consistent sleep-wake time). Initial sessions will provide symptom-targeted education and strategies supported by handouts (see online supplemental material 3). Subsequent sessions monitor recovery in the context of CE strategies, provide revised plans or additional strategies based on symptoms or problem areas. While general guidance on return to school and sport can be provided as part of physiotherapy and psychology modules, children requiring a more detailed return to school/sport plan, specific classroom or homework management strategies, and/or liaison with teachers, will have this delivered as part of the generic module. Content is delivered by trained physiotherapists and psychologists.

Physical modules: participants endorsing physical PCS will receive treatment targeting vestibular, ocular motor and cervical symptoms, in addition to treatment supporting a graded return to aerobic exercise. Treatment will be delivered by a trained physiotherapist.

Psychological modules: participants endorsing psychological PCS (or physical PCS with physiotherapy clearance or opinion that psychological modules are appropriate) will receive a manualised CBT-based programme, COPE (Creating Opportunities for Personal Empowerment).[48 49] COPE has age appropriate child or adolescent versions and is delivered by a trained psychologist. Sessions cover topics such as the connection between thoughts, feeling and behaviour, stress and coping, and dealing with emotions in healthy ways. Participants also receive education about the link between stress, the mind and body.

Treatment cessation: Up to eight sessions are delivered to participants in the CE arm. Participants can be discharged earlier if their pPCS have resolved. pPCS resolution is determined if one or both of the following criteria are met: (1) the PCSI(+)-P is asymptomatic (ie, <2 symptoms, at least 1-point above those endorsed preinjury) and/or (2) intervention clinicians agree the participant is ready to be discharged. PCSI(+)-P ratings will be the primary criteria for discharge, with clinician judgement exercised where participant and parent subjective reports are inconsistent with PCSI(+)-P discharge criteria. Participants discharged from the intervention will be provided with a summary report to provide to their GP, which includes information about obtaining medical clearance to return to contact sport.

Programme fidelity: To optimise treatment adherence and minimise therapist drift, clinicians will receive regular supervision within discipline. Ten per cent of sessions will be video-recorded for fidelity checking by a senior clinician. Specific CE modules delivered throughout treatment will be logged to quantify PCS cluster treatment dose as well as overall treatment dose.

Symptom monitoring: During the programme period, participants and their parents will complete the PCSI(+)-P and PCSI(+)-SR weekly on REDCap's MyCap app, or via online REDCap survey. Families may cease to provide ratings on symptom resolution, or choose to continue up until the end of the programme period (3 months postinjury).

Adverse events: the study coordinator or investigator is responsible for recording all adverse events, regardless of their relationship to study intervention.

Table 2 Screening and preprogramme and postprogramme measures administered for both CE and UC arms

	SCREEN (10 days)	BASELINE (3 weeks)	POST (3 months)
Concussion diagnosis/clinical details: CRF	X		
Primary outcome: PCS Resolution*: PCSI(+)-P, PCSI(+)-SR+	X	X	X
Secondary Outcomes			
Return to normal activity		X	X
Child QoL: PedsQL (parent rated)		X	X
Health economics: CHU-9D, Medicare†, service utilisation		X	X
Generic: ASHS, CSHS, FPS, PROMIS physical activity and fatigue, FPS-R		X	X
Physical: Treadmill sub-maximal test, BESS, VOMS, DVA, HTT, CFR, MCA-DCF, SPNTT		X	X
Psychological: RCADS-25, PROMIS emotional stress & depression, SDQ		X	X
Cognitive: RAVLT, CNT, WISC-V/WAIS-IV (coding, digit span), Rey-15		X	X
Parent mental health/stress: K10, PSS		X	X

*PCS is monitored weekly.
†Optional consent for collection of Medicare and Pharmaceutical Benefits Scheme information.
ASHS, adolescent sleep hygiene scale; BESS, balance error scoring system; CE, concussion essentials; CFR, cervical flexion rotation; CHU-9D, child health utility 9D; CNT, contingency naming test; CRF, clinical report form; CSHS, child sleep hygiene scale; DVA, dynamic visual acuity; FPS-R, faces pain scale revised; HTT, head thrust test; K10, kessler psychological distress scale; MCA-DCF, motor control assessment of deep cervical flexors; PCS, postconcussive symptoms; PCSI(+)-P, postconcussive symptom inventory plus–parent; PCSI(+)-SR, postconcussive symptom inventory plus–self-report; PedsQL, paediatric quality of life inventory; PROMIS, patient-reported outcomes measurement information system; PSS, parent stress scale; RAVLT, rey auditory verbal learning test; RCADS-25, revised children's anxiety and depression scale; Rey-15, rey fifteen-item test; SDQ, strengths and difficulties questionnaire; SPNTT, smooth pursuit neck torsion test; TOMM, test of memory malingering; UC, usual care; VOMS, vestibular/ocular motor screen; WAIS-IV, wechsler adult intelligence scale–fourth edition; WISC-V, Wechsler Intelligence scale for children fifth edition.

Study outcomes

Primary outcome

The primary study outcome is proportion of participants who are fully recovered, determined as no more than 1-point increase in severity for <2 items on the PCSI(+)-P, compared with preinjury PCSI(+)-P ratings, at, or prior to, completion of the study programme.

Secondary outcomes

The secondary outcomes will be assessed at baseline and postprogramme to investigate the following: (1) pPCS across common, physical and psychological domains; (2) return to normal activity (school, sports, leisure activities), (3) physical and psychosocial quality of life and (4) health service utilisation.

Clinical diagnostic measures: Baseline results of these clinical measures will guide intervention module selection in the CE intervention. A summary of the data collected at each time point is provided in table 2.

Measures

At baseline assessment, parents and participants complete an eligibility questionnaire to determine whether the participant remains symptomatic (using the PCSI(+)-P. The questionnaire will also screen for serious mental health problems using the DSM-5 Level 1 Cross Cutting Symptom Measure[50] (parent rated for participants aged 8–11 inclusive, or self-report for participants aged 12–18 inclusive). This will be used to ensure the participant does not meet our serious mental health history exclusion criterion. Children whose symptoms have resolved or who disclose serious mental health problems will be excluded from further participation and offered medical referral if necessary.

Primary outcome measure

The PCSI(+)-P is a modified version of the PCSI-P,[51] which is a parent-report measure of PCS following concussion, with strong reliability and validity.[44] The PCSI(+)-P contains all items from the original PCSI-P, with an additional 10 key clinical questions. The PCSI(+)-P will be collected at screening (ED recruitment and between 10 and 17 days postinjury), baseline (3 weeks postinjury), weekly during the programme period and postprogramme (3 months postinjury). The PCSI(+)-SR will be completed by the participant at the same time points, however, will not contribute to the primary outcome.

Secondary outcome measures

The secondary measures will be administered at baseline and postprogramme assessments.

Return to normal activity: return to school, sports and leisure activities will be assessed via a self-report (for participants ≥13 years old) or parent survey (for participants<13 years old).

Paediatric Quality of Life (PedsQL): a measure of health-related quality of life (HRQOL).[52] The 23-item common core scale measures physical, emotional, social and school functioning. Parent and child versions will be used in this study. The PedsQL uses a 5-point Likert scale

Table 3 Common/general clinical diagnostic measures

Common/general	
Child Sleep Hygiene Scale (parent report)[58 59] Adolescent Sleep Hygiene Scale (self-report)[60 61]	Measures sleep habits on a 6-point scale (never=6, aways=1), with higher scores indicating better sleep hygiene. The measures have nine domains (eg, physiological, sleep environment, sleep stability, etc), providing mean domain scores and an overall sleep hygiene score.[60]
PROMIS Physical Activity (Paediatric Short Form v1.0)[62]	An 8-item measure of physical activity that reflects bodily movement levels (eg, how many days did you exercise or play so hard that your body got tired?). Parent proxy and child self-report versions will be completed. Responses are rated on a 5-point Likert scale (1=no days, 5=6–7 days). Responses are scored using response pattern scores or T-score conversions.
PROMIS Fatigue (Paediatric Short Form V.2.0)[63 64]	A10-item measure of the experience (frequency, duration, and intensity) and impact of fatigue on physical, mental, and social activities. Parent proxy and child self-report versions will be used in this study. Responses are rated on a 5-point Likert scale (1=never, 5=almost always). Responses are scored using response pattern scores or T-score conversions.
Faces Pain Scale Revised (FPS-R)[65]	A validated self-report measure of pain in children aged five or older. The FPS-R is numbered 0–10 with pictorial faces depicting increasing severities of pain.

PROMIS, patient-reported outcomes measurement information system.

(0=never, 4=almost always), with items reversed scored and linearly transformed to a 0-100 scale. Higher scores indicate a higher HRQOL.

Child Health Utility 9D: a measure of HRQOL to examine quality of life from a health economics perspective (ie, calculation of quality of adjusted life years for cost utility analysis).[53 54] It is a 9-item, dimensional scale with five response options per item. It has been validated in children age 7–17 years. A higher score is indicative of poorer HRQOL.

Medicare and Pharmaceutical Benefits Scheme data: to assist with calculating the cost of concussion, participants will complete a Department of Human Services consent form to allow access to their Medicare Benefits Scheme and Pharmaceutical Benefits Scheme data. This will provide information about the community health services and prescription medicine participants use in the course of their recovery.

Access to additional care: parents will provide information on type of treatment (eg, medical, allied health, alternative/complementary therapy), frequency of treatment, additional medication, cost of lost parental employment, childcare, travel, accommodation and school absenteeism via a REDCap survey.

Clinical diagnostic measures

All clinical diagnostic measures are listed in tables 3–6. A trained physiotherapist will administer physical measures. Trained RAs will administer questionnaires and cognitive measures. Study questionnaires will be completed on an iPad.

Data management, quality and analysis

All data will be collected and stored on a REDCap database. Data management quality control procedures include the following: staff completing the baseline and post-programme assessments will be trained in all test administration; compliance with the study protocol will be assessed regularly for all documentation; staff providing interventions will require appropriate discipline training/supervision, and will be trained in all aspects of the CE modules; to optimise treatment adherence and minimise drift, a randomly selected set of 20% of sessions will be video-recorded for supervision and fidelity checking; all equipment (eg, treadmill, heart rate monitors) will be standardised and checked according to the equipment specifications by the study team; independent checks will be performed by members of the trial steering committee (TSC).

Interim analyses are not planned for this trial. There are no stopping guidelines; individual participants from both groups are monitored by physiotherapists and psychologists throughout their participation in the study. Premature closure and extension of the trial will depend on funding and the number of adverse events. The decision to close or extend the trial will be made by the principal investigator or TSC. The principal investigator and trial statistician will have access to the final trial dataset.

Statistical analysis plan

Data will be collected to meet Consolidated Standards of Reporting Trials guidelines for reporting of randomised trials. All analyses will be conducted using the intention-to-treat population where outcome data are available. The primary outcome measure, the proportion of participants who are fully recovered at completion of the study, will be evaluated using chi-square tests of independence and risk difference. Generalised linear models will be used to estimate 95% CIs, adjusting for the stratification factors used in randomisation. All other binary outcome measures will be analysed similarly. Comparison of means will be

Table 4 Physical clinical diagnostic measures

Physical	
Treadmill Submaximal Test[66]	An incremental treadmill exercise test to quantify physiological recovery. Performance is monitored by heart rate and a rating of perceived exertion.
Balance Error Scoring System (BESS)[67]	Measures static balance in three different postures (double leg stance, tandem stance, and single leg stance) on two different surfaces (firm and foam) for 20s in each stance. The BESS is validated for children aged 5–19 years.[68]
Vestibular/Occular Motor Screen[69]	Assesses vestibular and ocular motor functions via a self-report of symptom provocation after each assessment. Domains include: (1) smooth pursuit; (2) horizontal and vertical saccades; (3) convergence; (4) horizontal and vertical vestibular ocular reflex (VOR); and 5) visual motion sensitivity.
Dynamic Visual Acuity Test[70]	Determines integrity of the vestibular system. The test assesses the ability to read while the head is static and during active, assisted head rotation.
Head Thrust Test[70 71]	Assesses the angular vestibulo-ocular reflex and has been used to identify individuals with peripheral vestibular hypofunction.
Deep Neck Flexor Endurance Test[72]	Assesses the endurance of the cervical deep neck flexor muscles.
Cervical Flexion/ Rotation Test[70]	Assesses the range of the upper cervical spine motion and the presence of pain or dizziness at end range.
Smooth Pursuit Neck Torsion[70]	Measures the presence of upper cervical impairment by observing smooth pursuit of eye movements, in neutral and rotation (45° to left and 45° to the right) positions.

undertaken for continuous variables using independent samples t-tests where data are normally distributed. If data are non-normal, other generalised linear model distributions (eg, Poisson, ordinal logistic), outcome transformation (eg, logarithmic, square) or Mann-Whitney U non-parametric tests will be explored to find the best fit for the data. Ranked or Likert type scales will be analysed using cumulative ORs. Secondary and domain-specific outcomes will be compared between treatment groups.

Sample size estimation

Our study findings[14 21] and review of the literature indicate that spontaneous recovery occurs in ~60%–70% of children by 4 weeks postinjury. Thus ~30%–40% of children have pPCS and these rates are stable to 3 months postinjury.[8 55] Taking these figures, we predict that the UC arm will have ~60%–70% spontaneous recovery rate to 3 months, with ~30%–40% of children remaining symptomatic. To attain a clinically significant, cost-effective impact, we aim to halve that rate of symptomatic children in the CE arm, that is, a recovery rate of ~80% at treatment completion. With a 90% power and 5% error level, we require a total sample of 172, with two equal groups of 86. Based on our previous research, we expect a 20% lost to follow-up, and will therefore aim to recruit 216

Table 5 Psychological clinical diagnostic measures

Psychological	
Revised Children's Anxiety and Depression Scale-Child, Short Version (RCADS-25)[73]	A 25-item, self-report questionnaire (8–18 years) which incorporates items from the original RCADS subscales for separation anxiety, social phobia, generalised anxiety, panic disorder, obsessive-compulsive disorder and major depressive disorder into an Anxiety Total scale, and retains the original Depression Total scale. Items are rated on a 4-point Likert-scale (0=never, 3=always).
PROMIS Emotional Distress-Depression[74]	A 14-item measure of negative mood, views of self, social cognition, decreased positive affect and engagement. Parent proxy and self-report versions will be used in this study.
Strengths and Difficulties Questionnaire[75]	A 25-item emotional and behavioural screen, compromising 5 scales of 5 items each: emotional symptoms, conduct problems, hyperactivity/inattention, peer relationship problems, and prosocial behaviour. Parent proxy and self-report versions will be used in this study.
Parent mental health/stress	
Kessler Psychological Distress Scale[76]	A 10-item self-report measure assessing parent mental health or psychological distress.
Parent Stress Scale[77]	Measures levels of stress experienced by parents. It is an 18-item self-report measure, representing positive and negative themes of parenthood. Responses are on a 5-point scale (strongly disagree to strongly agree).

PROMIS, patient-reported outcomes measurement information system.

Table 6 Cognitive clinical diagnostic measures

Cognitive	
Rey Auditory Verbal Learning Task[78 79]	15-item list learning task. Recall is tested over five trials, and delayed recall at 20 to 30 min, standardised for use in children 7 years and older.
WISC-V and WAIS-IV Digit Span and Coding[80 81]	Used to assess working memory and information processing speed, respectively. Subtest versions from the Wechsler Intelligence Scale for Children, Fifth Edition (WISC-V) will be used for 8–16 years participants, and versions from the Wechsler Adult Intelligence Scale, Fourth Edition (WAIS-IV) will be used for 17–18 years participants.
Contingency Naming Test[82]	Assesses aspects of executive function, including processing speed, reactive flexibility, and inhibitory attention. It contains four tasks of increasing complexity, with age norms for children 7 years and older.
Rey 15-Item Test[83 84]	Provides an assessment of symptom validity or feigned memory impairment. The stimulus consist of a 3×5 matrix of meaningful symbols, which are to be drawn from memory following a 10s exposure. A recognition trial involves identifying the 15 stimuli out of 15 targets and 15 foils.

participants. With data on 86 per group, we will have 90% power to find a difference of ~0.4 SD on the secondary outcome measures, and ~23% absolute difference between groups in the percentage who return to preinjury levels of school/sport participation.

Study oversight

The TSC will provide oversight on trial progress, data quality, study violations and adverse events. The TSC will include the principal investigator, research coordinator, independent psychologist and independent medical doctor. The trial management committee (TMC) will be responsible for the study design, maintenance of the study, ongoing monitoring of staff and participants, and writing study publications. The TMC will include the principal investigator, research coordinator and statistician. The data safety monitoring board (DSMB) will be responsible for safeguarding the interests of trial participants by assessing the safety of the interventions during the trial, and the general progress of the trial. The DSMB will meet every 12 months. Their responsibility will be exercised by providing recommendations about continuing, modifying or stopping the trial. They may also formulate recommendations relating to the selection, recruitment, retention of participants; participant management; improving adherence to protocol; and the procedures for data management and quality control, to enhance trial integrity. The DSMB will include an independent chair (medical doctor), independent clinical expert in concussion, and a second independent statistician. The DSMB will be advisory to the investigator and TSC. The investigator holds ultimate responsibility for decisions regarding the trial. The trial's DSMB charter can be obtained from the study team on request.

Ethics and dissemination

Ethical approval was obtained through The RCH Human Research Ethics Committee (HREC: 37100). The RCH ethics committee will approve all protocol modifications. Participant confidentiality is strictly held in trust by the participating investigators, research staff and sponsoring institution. RAs obtain (1) electronic consent from parents for screening and recruitment and (2) informed written consent from parents for all participants at the start of the baseline assessment. Written consent is also obtained from participants aged 13 years and older at baseline, who are considered mature minors. The study poses little to no risk to participants and their families. Participation in the study is voluntary and does not interfere with typical care patients receive in the ED or in the community. Clinicians provide clinical treatment as part of the intervention and, if necessary, participants are referred for additional clinical care at the completion of their involvement in the study. Participants can withdraw consent at any time. Results from this study will be disseminated at regional and international conferences and in peer-reviewed journals. Findings may also result in changes to hospital or community policies and procedures regarding clinical concussion management. Authorship eligibility will be consistent with International Committee of Medical Journal Editors guidelines.

DISCUSSION

The overarching goal of this study is to improve the recovery rate and outcomes for children and adolescents following concussion by taking a precision medicine approach, which bases intervention components on the individual's PCS profile. Further, it uses treatment approaches that are appropriate for children and youth and are currently well established in clinical practice, but whose efficacy have not been clinically trialled. By targeting intervention relatively early postconcussion, we aim to minimise the emergence of secondary symptoms, often related to mental health, which can exacerbate and reinforce persisting problems.[20] The study will employ gold standard trial methodology and use up-to-date technology to minimise participant burden. It will also incorporate both parent and child perspectives of recovery.

Methodological considerations

Variations in the definition and severity of pPCS

Our study uses the PCSI(+), which contains all original items of the PCSI, for which we have previously validated

a pPCS cut-off score.[21] This cut-off is more stringent than those published elsewhere,[21] and therefore our study may include participants who are not considered to have pPCS by other studies or measures. We account for variations in symptom severity by providing symptom monitoring for both treatment groups, and terminating CE intervention when symptoms have resolved.

Multimodal intervention

Our team has designed a multimodal rehabilitation intervention comprising of education, physiotherapy and psychology modules. Given the multimodal approach adopted in our study, the efficacy of the individual modules comprising our intervention will be difficult to ascertain.

Bias in recruitment

Participation in the study requires participants to attend baseline and postprogramme assessments that can each last up to 3 hours, while the CE group will have hour-long weekly intervention sessions. Consenting participants will be aware that 50% of the group will not be receiving active treatment as part of the study. Our previous longitudinal studies[41 42] have seen many eligible participants express interest in participating, but decline due to the significant time commitment. It is possible that we may recruit a biased sample (eg, families with only one parent in full-time employment, greater family support, higher socioeconomic status, geographical proximity to The RCH). To limit this bias, families are offered afternoon/evening appointments, the option of alternate off-site locations and videoconferencing for education and psychology modules.

Open-label assessor-blinded design

There is a risk of bias associated with the open-label design of the trial. Factors such as external treatment, natural recovery, and placebo effects cannot be excluded as contributing to participant pPCS recovery. There are a number of procedures in place to ensure postprogramme assessors remain blinded to group allocation, including assessor training and education and reminders provided to families and children in an age appropriate manner.

Significance and outlook

By using a sample and definition of concussion that is not sport specific, the findings are generalisable to a broad population of children. Furthermore, concussions may be downplayed or overlooked by parents and children. A study of high school footballers found that up to 50% of concussions went unreported, mainly due to unawareness of the seriousness of the injury, a desire to immediately return to play, and lack of awareness of concussion.[56] Premature return to normal activity can heighten the risk of further injury, including repeat concussion.[57] The current study will promote psychoeducation on concussion and graded return to aerobic activity, and encourage participants to monitor symptoms which may be nonspecific and which they may not otherwise readily associate with the concussion.

Our findings will help to determine whether a weekly multimodal treatment approach can improve pPCS outcome, and reduce the economic impact of child concussion, both at an individual and population level. Overall, the completion of this study may be translated into improvements in the clinical management of concussion in hospitals, the community or dedicated concussion clinic.

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