Cognitive Behavioural Therapy to Optimize Post-Operative Recovery (COPE): A Randomized Controlled Trial

STATISTICAL ANALYSIS PLAN

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Reviewed and Approved by:		
Dr. Jason W. Busse (Principal Investigator)	*Signature:* DocuSigned by: Jason Busse 414A5700511347A	*Date:* 24-Jun-2025
Dr. Sheila Sprague (Principal Investigator)	*Signature:* DocuSigned by: Sheila Sprague 0FB2FF3A208B452...	*Date:* 24-Jun-2025

Document History

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05-May-2025	S. Sprague, J. Busse, S. Bzovsky, K. Pannozzo, N. Fleming	1.0	Initial version
24-Jun-2025	S. Sprague, J. Busse, S. Bzovsky	2.0	Minor clarifications throughout the SAP.

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LIST OF ABBREVIATIONS

aMD	Adjusted mean difference
aOR	Adjusted odds ratio
aRR	Adjusted risk ratio
BPI-SF	Brief Pain Inventory – Short Form
CBT	Cognitive behavioural therapy
CI	Confidence interval
COPE	Cognitive Behavioural Therapy to Optimize Post-Operative Fracture Recovery
HR	Hazard ratio
HRQoL	Health-related quality of life
ISS	Injury Severity Score
OR	Odds ratio
PPSP	Persistent post-surgical pain
SF-36 MSC	Short Form-36 Mental Component Summary
SF-36 PSC	Short Form-36 Physical Component Summary
SPOC	Somatic Pre-Occupation and Coping

1.0 INTRODUCTION

The purpose of this statistical analysis plan (SAP) is to outline the primary statistical analyses for the Cognitive Behavioural Therapy to Optimize Post-Operative Recovery (COPE) trial. We will adhere to the CONSORT 2010 guideline when reporting the results of COPE. The structure of this statistical analysis plan follows the Guidelines for the Content of Statistical Analysis Plans in Clinical Trials.[1] Additional SAPs will be developed for secondary analyses of trial data.

The primary objective of the COPE trial is to determine if cognitive behavioural therapy (CBT), versus usual care, reduces the prevalence of moderate to severe Persistent Post-Surgical Pain (PPSP) over 12 months post-fracture in participants with an open or closed fracture of the appendicular skeleton.

The secondary objectives of the COPE trial are to determine if CBT, versus usual care: 1) increases physical functioning over 12 months post-fracture, 2) improves mental functioning over 12 months post-fracture, 3) accelerates return to function over 12 months post-fracture, 4) reduces pain severity over 12 months post-fracture, 5) reduces pain interference over 12 months post-fracture, and 6) reduces the proportion of participants using opioid class medications at 6 and 12 months post-fracture in patients with an open or closed fracture of the appendicular skeleton.

Details on the trial design, randomization, and sample size have been published previously.[2]

2.0 TRIAL POPULATION

2.1 Patient Flow through the Trial

The number of patients screened, included, and excluded will be presented in a flow diagram **(Figure 1)**. The figure will include the number of participants who were randomly assigned to the two treatment groups. It will also include the number of participants who were subsequently deemed ineligible by the Central Adjudication Committee.

We will summarize the number of patients excluded by reason (**Table 1**) and the number of participants deemed ineligible by the Central Adjudication Committee by reason (**Table 2).** Participants deemed ineligible by the Central Adjudication Committee will not be included in any analysis, as per guidance from Fergusson et al.[3]

Figure 1 will include participant follow-up and the number of participants who were lost to follow-up, along with the reason, over the course of the trial.

2.2 Participant Demographics, Injury, and Fracture Characteristics, and Surgical and Perioperative Care Details

We will use descriptive measures to summarize participant demographics, baseline information, injury, fracture characteristics, surgical, and perioperative care details of the sample stratified by treatment group (**Tables 3 and 4**). We will use means and standard deviations (SDs) or medians and interquartile ranges (IQR) for continuous data, and categorical data will be presented as frequencies and percentages. We will examine key baseline differences between those who stopped the CBT program early and those who did not. We will not statistically test for differences

in these characteristics between treatment groups (**Section 3.2**). The potential clinical importance of any imbalance between treatment groups will be noted.

Additional details on the trial population have been published previously.[2]

2.3 CBT Compliance

We will report the number of participants randomized to the CBT intervention who completed the CBT modules according to the number of modules completed (0 to 7 modules). We will also look at levels of compliance by key baseline factors including the subgroup analysis factors, participant age (<60 versus ≥60), and injury severity (defined as an Injury Severity Score [ISS] greater than or equal to 9). The data will be presented as frequencies and percentages (**Tables 5 and 6**).

2.4 Outcome Completion Rates

We will report on the outcome completion rates at each follow-up visit. The data will be presented as frequencies and percentages (**Table 7**).

3.0 ANALYSIS

3.1 Analysis Methods

The primary and secondary analyses will be conducted following intention-to-treat (ITT) principles, ensuring that participants are analyzed in their originally assigned treatment groups, regardless of adherence or protocol deviations. The date on which the participant's fracture(s) occurred will be used as the starting point for all time-to-event analyses.

We will use multiple imputations to account for missing data in the analyses and minimize potential bias under the assumption that the data are missing at random (MAR). This approach will allow for the uncertainty associated with missing values to be properly accounted for, improving the robustness of statistical inferences.[4] Additionally, as we anticipate high rates of early withdrawal, we will account for this in the analyses, if needed.

3.1.1 Primary Analysis

We will use a mixed effects log-binomial model to determine the association between CBT treatment and moderate to severe PPSP (score of ≥4/10) over 12 months post-fracture. The choice of using a PPSP score of ≥4/10 for the primary analysis was based on scores of less than 4 being defined as 'mild' pain, and so less important to patients. Prevalence of moderate to severe PPSP will be our dependent variable. Only the highest PPSP score at each visit will be included for participants with multiple fractures. CBT treatment status, stratification variables (clinical site, sex, at least one open fracture versus no open fracture(s), military, veteran or first responder versus others, and greater illness beliefs [defined as Somatic Pre-Occupation and Coping [SPOC] score ≥48] versus lesser illness beliefs [SPOC score <48]), and time of assessment (continuous measure in days) will be included in the model as fixed effects, with patients entered as a random intercept. A time-by-treatment interaction term will also be added to the model, allowing the treatment effect to vary over time. If the interaction between treatment and time is significant ($p<0.05$), indicating the effect of treatment varying over time, we will report the average treatment effect across 12 months and the treatment effect for each time point of variation. If the interaction between treatment and time is not significant ($p\geq0.05$), suggesting a constant treatment effect over the study period, we will report the average treatment effect. Results will be reported using marginal

standardization as adjusted risk ratios (aRRs) with a 95% confidence interval (95% CI) and p-value (**Table 8**).

3.1.2 Secondary Analyses

1) *Health-Related Quality of Life (HRQoL):* We will use linear repeated measures mixed modeling to explore the association between: 1) CBT treatment status and Short Form-36 (SF-36) Physical Component Summary (PCS) scores over 12 months, and 2) CBT treatment status and SF-36 Mental Component Summary (MCS) scores over 12 months. The SF-36 is an established, reliable and validated health status measure.[5–7] It measures HRQoL through an 8-domain profile of functional health and well-being, physical and mental health summary measures (PCS and MCS). The SF-36 PCS and MCS are scored on a scale from 0 to 100, with 100 representing the highest level of functioning possible. SF-36 PCS and MCS scores will be included as the dependent variable in each corresponding model. CBT treatment status, stratification variables, and time of assessment (continuous measure in days) will be included in the models as fixed effects, with patients entered as a random intercept. The models will also be adjusted for baseline SF-36 PCS and MCS scores, accordingly, as well as including a time-by-treatment interaction term. If the interaction between treatment and time is significant ($p<0.05$), indicating the effect of treatment varying over time, we will report the average treatment effect across 12 months and the treatment effect for each time point of variation. If the interaction between treatment and time is not significant ($p\geq0.05$), suggesting a constant treatment effect over the study period, we will report the average treatment effect. Results will be reported using marginal standardization as adjusted mean differences (aMDs) with 95% CIs and p-values (**Table 8**).

2) *Return to Function:* We will use Cox proportional hazards regression modeling to explore the association between: 1) CBT treatment status and returning to ≥80% of pre-injury functioning, 2) CBT treatment status and returning to full function with respect to work, 3) CBT treatment status and returning to full function with respect to leisure activities, and 4) CBT treatment status and returning to full function with respect to responsibilities around the home. These return to function components are measured using the Return to Function questionnaire, which has been used in a previous fracture trial[8] documents when participants return to work, household activities, and leisure activities without limitations, as well as when they achieve 80% of their pre-injury function. Participants will be censored at their last documented follow-up visit. The analyses will adjust for stratification variables and the results will be reported as hazard ratios (HRs) with 95% CIs and p-values (**Table 9**).

3) *Pain over Time*: We will use cumulative logit modeling to explore the association of 1) CBT treatment status and Brief Pain Inventory - Short Form (BPI-SF) Average Pain Severity scores over 12 months and 2) CBT treatment status and BPI-SF Pain Interference scores over 12 months. The BPI-SF assesses the severity of pain and its impact on function.[9] All items are rated on a 0-10 scale, with higher scores indicating greater pain severity and interference. BPI-SF Average Pain Severity and BPI-SF Pain Interference scores will be included as the dependent variable in each corresponding model. CBT treatment status, stratification variables, and time of assessment (continuous measure in

days) will be included in the models as fixed effects, with patients entered as a random intercept. The models will also be adjusted for baseline BPI-SF Average Pain Severity and BPI-SF Pain Interference scores, accordingly, as well as include a time-by-treatment interaction term. If the interaction between treatment and time is significant ($p<0.05$), indicating the effect of treatment varying over time, we will report the average treatment effect across 12 months and the treatment effect for each time point of variation. If the interaction between treatment and time is not significant ($p\geq0.05$), suggesting a constant treatment effect over the study period, we will report the average treatment effect. Results will be reported using marginal standardization as adjusted odds ratios (aORs) with 95% CIs and p-values (**Table 8**).

4) *Opioid Use*: We will use logistic regression modeling to explore the association between CBT treatment status and opioid use status. Two separate models will be created to analyze opioid use status (yes versus no) at both 6 months and 12 months. Opioid use status will be included as the dependent variable and each model will be adjusted for stratification variables. Results will be reported as ORs with 95% CIs and p-values (**Table 8**).

3.2 Subgroup Analyses

To explore for treatment effect heterogeneity on trial outcomes, we will use the same analytical approach as specified for the primary outcome above but include a treatment by subgroup interaction term in the model. If we have enough participants to conduct reliable subgroup analyses, we will report results by the prespecified subgroups, which consist of: (1) sex (indicated as male or female), (2) the presence or absence of an eligible open fracture, (3) veteran/military/first responder status (as self-reported by the participant), and (4) SPOC Scores (defined as ≥48 or <48). Towards the end of the trial, prior to unblinding, site location (Canada or the United States) was added as a subgroup in the analyses to assess its potential role as an effect modifier. Results will be reported using marginal standardization and stratified by the subgroup as aORs with 95% CIs, and the interaction p-values in a forest plot and table (**Table 10**). These analyses will be approached and reported in accordance with best practices and guidelines for subgroup analyses.[10–14] For subgroup effects that show a statistically significant test of interaction ($p\leq0.05$), we will use ICEMAN criteria to guide inferences about the credibility of our subgroup analyses.[14]

Subgroup Analyses Overview

Objective	Hypothesis
Subgroup Analysis 1	
Males versus females	CBT will be associated with a larger reduction in the prevalence of PPSP in females compared to males.
Subgroup Analysis 2	
Any open fracture versus no open fracture	CBT will be associated with a larger reduction in the prevalence of PPSP in participants with open fractures compared to participants with only closed fractures.
Subgroup Analysis 3	

Objective	Hypothesis
Military, veteran, and first responders versus other patients	CBT will be associated with a larger reduction in the prevalence of PPSP in participants who are employed by the military, veterans, or first responders.
Subgroup Analysis 4	
Higher versus lower SPOC scores	CBT will be associated with a larger reduction in the prevalence of PPSP in participants with higher versus lower SPOC scores.
Subgroup Analysis 5	
Site location (Canada versus the United States)	CBT will be associated with a larger reduction in the prevalence of PPSP in participants from sites located in Canada.

3.3 Sensitivity and Exploratory Analyses

We will conduct the following additional analyses to explore the robustness of our findings:

1. Assess if CBT, versus usual care, reduces the prevalence of any severity of PPSP over 12-months post-fracture (**Table 11**).

2. A sensitivity analysis limited to the primary outcome to compare those participants randomized to the CBT intervention at the primary site, defined as the site with the highest CBT compliance (**Table 11**)

3. Assess the primary outcome in only those participants randomized to the CBT intervention who fully adhered to: 1) at least three CBT modules and 2) at least six CBT modules (**Table 11**), limiting data to the primary site only, defined as the highest enrolling site.

These analyses will help determine whether greater engagement with CBT is associated with improved outcomes. The exploratory and sensitivity analyses will follow the same analysis methods as described for the primary outcome, including appropriate regression models and adjustments for stratification variables.

3.4 Harms

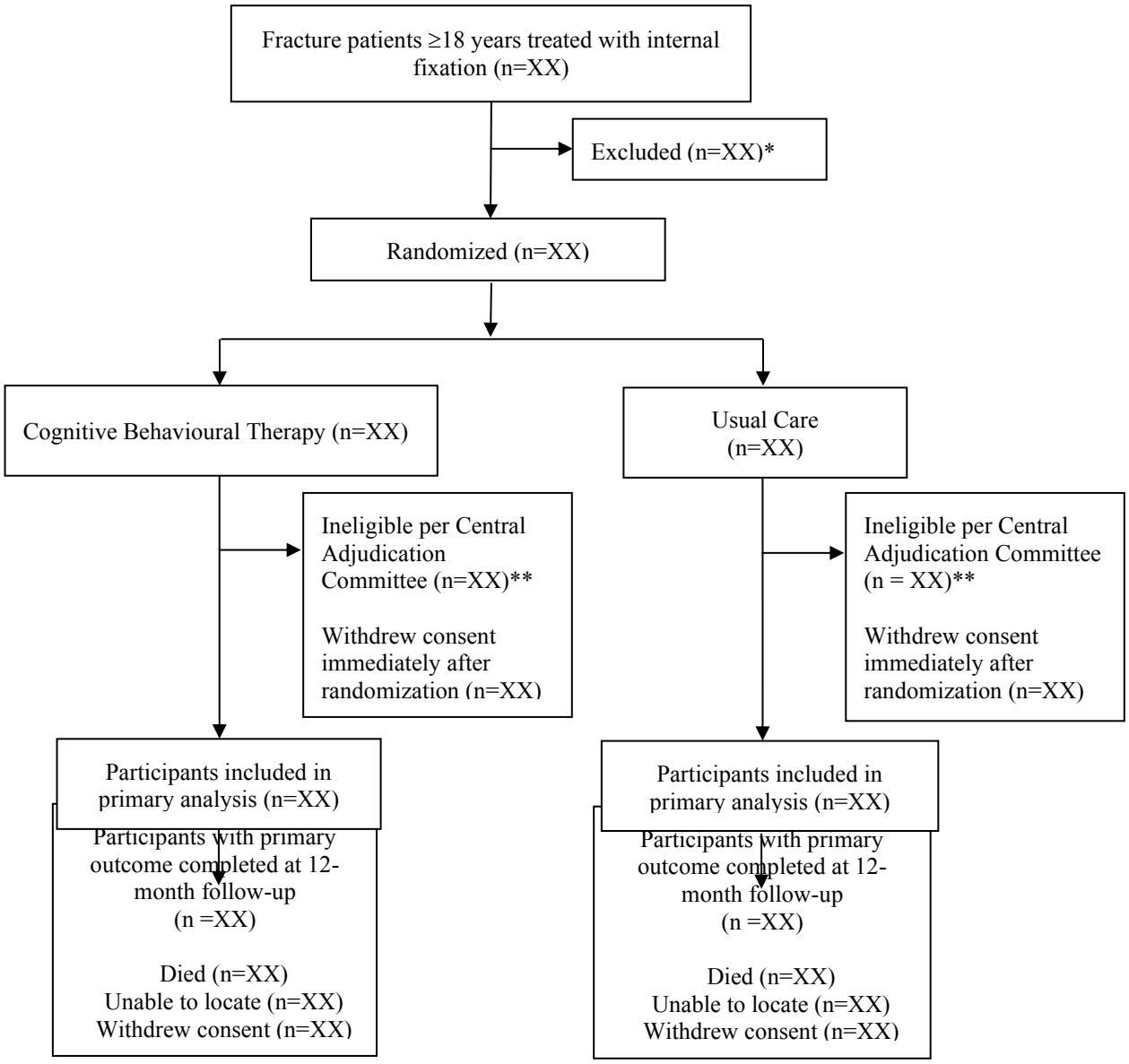
The number and percentage of patients experiencing treatment-related serious adverse events and fracture-related complications will be presented by treatment arm (**Table 12**). No formal statistical testing will be undertaken.

3.5 Statistical Software

All analyses will be performed using R (version 4.4.3 or newer, R Foundation for Statistical Computing, Vienna, Austria).

4.0 FIGURES AND TABLES

Figure 1: Consort Flow Chart for Trial Participants



*Please refer to Table 1 for reasons for exclusion
**Please refer to Table 2 for reasons for ineligibility per the Central Adjudication Committee

Table 1: Reasons for Exclusion*

Reasons for Exclusion	Total (n= XX patients excluded)
Patient does not have an eligible fracture, n (%)	
Patient has a concomitant injury which, in the opinion of the attending surgeon, is likely to impair function for as long as or longer than the patient's extremity fracture(s), n (%)	
Patient is facing current or impending incarceration	
Currently not experiencing any pain in the fracture region despite being fully weight bearing, n (%)	
Patient has active psychosis, n (%)	
Patient has active suicidality, n (%)	
Patient has an active substance use disorder that, in the judgement of the treating surgeon, would interfere in the patient's ability to partake in the CBT and/or the study, n (%)	
Patient does not have the cognitive ability and language skills to participate in CBT, n (%)	
Patient is already participating in or planning to start other psychological treatments (including CBT) within the duration of the study (12 months), n (%)	
Patient does not have consistent online access from a smartphone/internet-enabled device with a minimum operating system able to use the CBT provider's application, n (%)	
Anticipated problems, in the judgement of study personnel, with the patient participating in CBT intervention and/or returning for follow-up, n (%)	
Patient is not willing to participate in CBT, n (%)	
Currently enrolled in a study that does not permit co-enrolment in other trials, n (%)	
Previously enrolled in the COPE trial, n (%)	
Patient was not screened/approached within 2-12 weeks following their fracture, n (%)	
Patient's fracture was not treated operatively with internal fixation, n (%)	
Patient did not provide informed consent, n (%)	

*This table shows all response options for the data collected. In the primary manuscript, some data categories may be removed if there are no responses selected.

Table 2: Reasons for Exclusion after Blinded Central Adjudication Committee Review*

Reasons for Exclusion	Number of Patients Excluded Following Adjudication	
	CBT (n= XX adjudicated as ineligible)	Usual Care (n= XX adjudicated as ineligible)
Fragility fracture (a fall from a standing height or less, that results in a fracture) as their only extremity fracture treated with internal fixation, n (%)		
Stress fracture as their only extremity fracture treated with internal fixation, n (%)		
Patient has a concomitant injury which, in the opinion of the attending surgeon, is likely to impair function for as long as or longer than the patient's extremity fracture(s), n (%)		
Patient is facing current or impending incarceration		
Currently not experiencing any pain in the fracture region despite being fully weight bearing, n (%)		
Patient has active psychosis, n (%)		
Patient has active suicidality, n (%)		
Patient has an active substance use disorder that, in the judgement of the treating surgeon, would interfere in the patient's ability to partake in the CBT and/or the study, n (%)		
Patient does not have the cognitive ability and language skills to participate in CBT, n (%)		
Patient is already participating in or planning to start other psychological treatments (including CBT) within the duration of the study (12 months), n (%)		
Patient does not have consistent online access from a smartphone/internet-enabled device with a minimum operating system able to use the CBT provider's application, n (%)		
Anticipated problems, in the judgement of study personnel, with the patient participating in CBT intervention and/or returning for follow-up, n (%)		
Patient is not willing to participate in CBT, n (%)		
Currently enrolled in a study that does not permit co-enrolment in other trials, n (%)		
Previously enrolled in the COPE trial, n (%)		
Patient was not screened/approached within 2-12 weeks following their fracture, n (%)		
Patient's fracture was not treated operatively with internal fixation, n (%)		
Patient did not provide informed consent, n (%)		
Patient is under 18 years of age, n (%)		
Another reason to exclude the patient (must be approved by the Methods Centre), n (%)		

*This table shows all response options for the data collected. In the primary manuscript, some data categories may be removed if there are no responses selected.

Table 3: Baseline characteristics*

	CBT (n= XX)	Usual Care (n= XX)
Age in years, mean (SD)		
Sex, n (%) Female Male Did not want to disclose		
Body mass index in kg/m^2, n (%) Underweight (BMI < 18.5) Normal weight (18.5 – 24.9) Overweight (25 – 29.9) Obese (BMI ≥ 30) Did not want to disclose		
Race or ethnicity, n (%) White South Asian East Asian Southeast Asian Middle Eastern People of African and/or Caribbean Descent Indigenous Latinx Multiethnic Background Did not want to disclose		
Latin or Hispanic origin, n (%)		
Employment prior to injury, n (%)		
First responder, n (%) Police officer Firefighter Emergency medical technician Paramedic Search and rescue personnel		
Military employment history, n (%) Active duty Reserve/Guard Veteran/Retiree Civilian		
Highest level of education completed, n (%) 8th grade or less 9th to 12th grade, no diploma General education diploma or high school graduate Some college, no degree Associates degree (2-year degree) Bachelors/college degree Some graduate work, no degree Graduate degree Professional degree Did not want to disclose		
Current smoker, n (%)		

	CBT (n= XX)	Usual Care (n= XX)
Functional Comorbidity Index, mean (SD)		
Receiving other mental health support, n (%)** Counselling Support group Other		
Receiving medication for mental health support, n (%)** Antidepressant medications Antipsychotic medications Mood stabilizers Psychostimulants, stimulants Anxiolytics Central nervous system depressants Substance abuse medications Cognitive enhancers Other		
Taking pain medication in the past two weeks, n (%)* * Acetaminophen (e.g., Tylenol) Opioids (e.g., oxycodone, Dilaudid) NSAIDs (e.g., ibuprofen, Aleve, naproxen) GABA Analogue (e.g., Neurontin, Lyrica) Benzodiazepines (e.g., diazepam) Cannabis Other		
Baseline SPOC Score*** Low (<48) Moderate/high (≥48)		

*This table shows all response options for the data collected. In the primary manuscript, some data categories may be collapsed as appropriate or presented in a supplementary appendix.
**Some participants specified more than one type of mental health support/medication.
***SPOC: Somatic Pre-Occupation and Coping

Table 4: Injury Details and Fracture Characteristics*

	CBT (n= XX)	Usual Care (n= XX)
Mechanism of injury, n (%) Motor vehicle accident Fall Direct trauma (penetrating) Direct trauma (blunt) Crush injury Twist injury Blast injury Ballistic injury Spontaneous		
Work-related injury, n (%)		
Injury severity score, mean (SD)		
American Society of Anesthesiologists (ASA) physical class, n (%) Class I or II Class III or higher		
Days from injury to admission, mean (SD)		
Duration of hospital stay (days), mean (SD)		
Fracture type, n (%) Open Closed Both		
Number of included fractures per patient, n (%) 1 2 3 4 5 or more		
Location of fracture, n (%) Upper extremity Lower extremity Both		
AO/OTA classification, n (%) 11 A-C 12 A-C 13 A-C 14 A-C 15 A-C 2R1 A-C 2R2 A-C 2R3 A-C 2U1 A-C 2U2 A-C 2U3 A-C 31 A-C	N=XX fractures	N=XX fractures

32 A-C 33 A-C 34 A-C 41 A-C 42 A-C 43 A-C 4F1 A-C 4F2 A-C 4F3 A-C 44 A-C 61 A-C 62 A-C 71 A-C 72 A-C 73 A-C 74 A-C 75 A-C 76 A-C 77 A-C 78 A-C 79 A-C 81 A-C 82 A-C 83 A-C 84 A-C 85 A-C 86 A-C 87 A-C 88 A-C 89 A-C		
Severe soft tissue injury for closed fractures, n (%) Extensive skin contusion or crush injury Severe damage to underlying muscle Compartment syndrome Degloving	N=XX closed fractures	N=XX closed fractures
Type of internal fixation, n (%) Intramedullary nail Plate(s) and adjacent screws Screw(s) alone K-wire(s) Cerclage Other	N=XX fractures	N=XX fractures

*This table shows all response options for the data collected. In the primary manuscript, some data categories may be collapsed as appropriate or presented in a supplementary appendix.

Table 5: CBT Compliance (n=XX)

	Number of CBT Modules Completed							
	None	**1**	**2**	**3**	**4**	**5**	**6**	**7**
All Participants Randomized to CBT								
Sex								
Male, n (%)								
Female, n (%)								
Fracture Type								
Any open fracture, n (%)								
No open fracture, n (%)								
Background/Employment								
Military, veteran, and first responder, n (%)								
Not a veteran, first responder or employed by the military, n (%)								
SPOC Score								
Low (<48), n (%)								
Moderate/high (≥48), n (%)								
Site Location								
Canada, n (%)								
United States, n (%)								
Age								
<60, n (%)								
≥60, n (%)								
Injury Severity Score								
<9, n (%)								
≥9, n (%)								

Table 6: CBT Compliance (Condensed to Categories) (n=XX)

	Number of CBT Modules Completed			
	None	**1-3**	**4-6**	**7**
All Participants Randomized to CBT, n (%)				
Sex				
Male, n (%)				
Female, n (%)				
Fracture Type				
Any open fracture, n (%)				
No open fracture, n (%)				
Background/Employment				
Military, veteran, and first responder, n (%)				
Not a veteran, first responder or employed by the military, n (%)				
SPOC Score				
Low (<48), n (%)				
Moderate/high (≥48), n (%)				
Site Location				
Canada, n (%)				
United States, n (%)				
Age				
<60, n (%)				
≥60, n (%)				
Injury Severity Score				
<9, n (%)				
≥9, n (%)				

Table 7: Outcome Completion Rates at Follow-up Visits (N=XX total sample size)

Outcome	3 months	6 months	9 months	12 months
PPSP Form, n (%)				
SF-36 Form, n (%)				
Return to Function Form, n (%)				
BPI-SF Form, n (%)				
Opioid Class Medication Question, n (%)				

Table 8: Impact of CBT versus Usual Care on Primary and Secondary Outcomes

Outcome	**CBT (n= XX)**	**Usual Care (n= XX)**	**Estimate** (95% CI)**	**p-value**
Primary Outcome				
Moderate to Severe (≥4/10) PPSP, n (%)				
Secondary Outcomes				
SF-36 PCS, mean (SD)				
SF-36 MCS, mean (SD)				
BPI-SF Average Pain Severity Score, mean (SD)				
BPI-SF Pain Interference Score, mean (SD)				
Taking an opioid class medication, n (%)				

**Estimates are presented as an adjusted risk ratio for the primary outcome, as adjusted odds ratios for the BPI-SF outcomes, as an odds ratio for the opioid use outcome, and as adjusted mean differences for the remainder of the secondary outcomes.

Table 9: Impact of CBT versus Usual Care on Return to Pre-Injury Function, Work, and Activities

Function Category	Hazard Ratio (95% CI)	p-value
≥80% of Pre-injury Functioning, n (%) CBT vs. No CBT		
Work*, n (%) CBT vs. No CBT		
Leisure Activities, n (%) CBT vs. No CBT		
Responsibilities around the Home, n (%) CBT vs. No CBT		

*Unemployed participants were excluded from analyses

Table 10: Impact of CBT versus Usual Care on Moderate to Severe PPSP in Different Subgroups

Subgroup	CBT (n= XX)	Usual Care (n= XX)	Adjusted Risk Ratio (95% CI)	Interaction p-value
Sex				
Male				
Female				
Fracture Type				
Any open fracture, n (%)				
No open fracture, n (%)				
Background/Employment				
Military, veteran, and first responder				
Not a veteran, first responder or employed by the military				
SPOC Score				
Low (<48)				
Moderate/high (≥48)				
Site Location				
Canada				
United States				

Table 11: Sensitivity and Exploratory Analyses

Outcome	**CBT (n= XX)**	**Usual Care (n= XX)**	**Adjusted Risk Ratio (95% CI)**	**p-value**
Exploratory Outcome – Any Severity of PPSP				
PPSP Severity, n (%) *Any severity (≥1/10)*				
Primary Outcome - Participants randomized to the CBT intervention at the primary site				
PPSP Severity, n (%) Moderate to Severe (≥4/10)				
Primary Outcome – Adherence to at least three CBT modules at the primary site				
PPSP Severity, n (%) Moderate to Severe (≥4/10)				
Primary Outcome – Adherence to at least six CBT modules at the primary site				
PPSP Severity, n (%) Moderate to Severe (≥4/10)				

Table 12: Treatment-Related Serious Adverse Events and Fracture-Related Complications*

Category	CBT (n= XX)	Usual Care (n= XX)
Serious adverse event, n (%)		
Fracture-related complication, n (%)		
Wound healing problem		
Compartment syndrome		
Superficial infection		
Deep/Organ/Space infection		
Delayed union		
Nonunion		
Malunion		
Implant failure/breakage		
Dislocation/instability		
Heterotopic ossification		
Osteolysis		
Avascular necrosis		
Pain (not otherwise covered)		
Other		

*This table shows all response options for the data collected. In the primary manuscript, some data categories may be collapsed as appropriate or presented in a supplementary appendix.

SUPPLEMENTARY TABLES

Table S1: Open Fracture Characteristics

	CBT (n= XX open fractures)	Usual Care (n= XX open fractures)
Gustilo classification, n (%) I II IIIA IIIB IIIC		
Skin, n (%) Laceration with edges that approximate Laceration with edges that do not approximate Laceration associated with extensive degloving		
Muscle, n (%) No appreciable muscle necrosis, some muscle injury with intact muscle function Loss of muscle but the muscle remains functional, some localized necrosis in the zone of injury that requires excision, intact muscle-tendon unit Dead muscle, loss of muscle function, partial or complete compartment excision, complete disruption of a muscle-tendon unit, muscle defect does not reapproximate		
Arterial, n (%) No major vessel disruption Vessel injury without distal ischemia Vessel injury with distal ischemia		
Contamination, n (%) None or minimal contamination Surface contamination (not ground in) Contaminant embedded in bone or deep soft tissues or high risk environmental conditions (barnyard, fecal, dirty water, etc.)		
Bone, n (%) None Bone missing or devascularized bone fragments, but still some contact between proximal and distal fragments Segmental bone loss		

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