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## Shabeer Syed

Harris Manchester College

University of Oxford


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**Theoretically driven research project (TDRP)** **5119 words**

Early adverse childhood experiences, emotion dysregulation and subsequent risk of chronic pain in children and adolescents: a population-based birth cohort study

**Connecting narrative** **996 words**

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## Abstracts

### Critical review of the literature (CRL)

**Trauma-focused cognitive behavioural therapies for posttraumatic stress disorder among adults with multiple-incident traumas compared with single-incident traumas: a systematic review and meta-analysis**

**Objective:** Trauma-focused cognitive behavioural therapies (TF-CBT) are considered the first-line treatment for posttraumatic stress disorder (PTSD) following different traumatic experiences. Whilst there is compelling evidence for TF-CBT for PTSD following single-incident traumas, the effectiveness of TF-CBT for PTSD following multiple-incident traumas is less clear. We conducted a systematic review and meta-analysis to evaluate the pooled effects of TF-CBT for multiple-incident PTSD relative to the effects of TF-CBT for single-incident PTSD.

**Methods**: We searched 18 electronic databases between Jan 1990 and Mar 2022 for RCTs comparing any TF-CBT for PTSD among adults exposed to multiple-incident traumas (defined as intimate partner violence; IPV; child maltreatment; CM; systemic violence and combat exposures) or single-incident traumas, relative to treatment as usual (TAU). The primary outcome was PTSD symptoms as per a validated self-report or clinician administered PTSD instrument immediately post-intervention. We used random-effects meta-analyses to pool standardised mean differences (Hedges' *g*) of TF-CBT against TAU stratified by trauma types.

**Results**: We included 144 RCTs (11,949 individuals), involving three types of single-incident traumas and four types of multiple-incident traumas, including systemic violence and refugees, CM or IPV and military combat-related exposures. We found no significant differences in the pooled effect of TF-CBT against TAU in RCTs involving multiple-incident traumas (Hedges' *g*, -0.90, 95% CI -1.07, -0.73; 65 RCTs) compared with the pooled effect from RCTs involving single-incident traumas (Hedges' *g*, -0.70, 95% CI -0.85, -0.54; 67 RCTs).

Estimates remained similar when adjusting for baseline severity of PTSD symptoms, comparing specific traumas, and limiting estimates to active comparator groups. TF-CBT produced smaller treatment effects in RCTs involving multiple-incident traumas with comorbid serious mental illnesses (e.g., psychosis and personality disorders; Hedges' *g*, -0.37 95% CI -0.57, -0.17) relative to RCTs with less comorbidity.

**Conclusions**: TF-CBT showed comparable efficacy for reducing PTSD symptoms in RCTs involving repeated and sustained traumatic events as in RCTs of PTSD from single-incident traumas. However, treatment approaches varied substantially between groups of trauma types and estimates should be considered with caution. Further research is needed to evaluate the effectiveness of TF-CBT for multiple-incident PTSD related to IPV and populations across inpatient and forensic settings.

**Service improvement project (SIP)**

**Predicting length of stays, delayed discharges, and readmissions in adult psychiatric inpatient units in one NHS trust: a mixed-methods study**

**Background:** Despite repeated NHS initiatives to reduce the length of stays (LOS) of adult acute psychiatric admissions in England, the factors influencing LOS and delayed discharges are poorly understood.

**Aims:** To identify and estimate key factors that may influence LOS and delayed discharges among adult psychiatric admissions in one NHS trust using a mixed-method design of staff interviews and risk prediction models.

**Methods:** In phase one, we thematically analysed data from 17 semi-structured interviews with inpatient staff, focusing on barriers and facilitators influencing LOS. In phase two, we analysed data on 5351 acute admissions (aged 18-65 years old) from 7 adult psychiatric inpatient units in one NHS trust covering two counties (2015-2021) using adjusted multivariable regression models. The primary outcome was locally defined delayed discharges (LOS >56 days). Secondary outcomes included adjusted mean differences in LOS and readmissions within one year of discharge.

**Results:** In phase one, consistently identified barriers included a need for inpatient social workers, increased recognition of discharge barriers with shared responsibility between professions to overcome barriers, difficulties in forming consensus within clinical teams about discharge criteria for patients with complex needs, and more effective information sharing systems with community services and placement providers. Consistently reported facilitators for reducing LOS included improved gatekeeping criteria and goals upon admission with clearly assigned staff roles, and improved communication with services outside the hospital.

In phase two, the adjusted mean LOS of adult acute admissions between 2016 and 2021 was 58.4 days (95 % CI 50.9 days-65.5 days), or 54.2 days (95% CI 44.5 days-63.9 days) excluding the psychiatric intensive care unit. Of these, 27.4% (1476/5351; 95% CI 24.4%-30.4%) had a LOS above 56 days and the national average. The strongest predictors of delayed discharges and one-year readmissions were positive COVID-19 tests, older age, black ethnicity, homelessness, a diagnosis of bipolar or psychosis (affective manic type), and patients with risk concerns of self-neglect, non-compliance with care and aggression. Faster allocation of care coordinators upon admission and admission to a ward with lower bed capacity (e.g. higher bed occupancy) were associated with significantly lower LOS and reduced delays.

**Interpretation:** In this study of one NHS Trust, only one in four adult psychiatric admissions had a LOS above the national average of 51 days for adult mental health admissions. This performance could likely be further improved by early identification of homeless patients, faster allocation of care coordinators, and increased support to make risk positive discharge decisions of patients with complex needs. Interactive risk prediction models, key findings and trust specific recommendations are provided at the end (see executive summary) and available online (https://ohft.github.io/lengthofstay/).

## Theoretically driven research project (TDRP)

**Early adverse childhood experiences, emotion dysregulation and subsequent risk of chronic pain in children and adolescents: a population-based birth cohort study**

**Objectives**: Children with adverse childhood experiences (ACEs) face an increased risk of developing chronic pain (CP), yet longitudinal evidence on the factors underlying this relationship remains limited. We assessed the association between early adverse childhood experiences (ACEs) and subsequent risk of CP, and whether this relationship was mediated by emotion regulation difficulties (ERDs).

**Design and participants:** Population-based birth cohort of 179,207 mothers and children with linked electronic health records (1998-2018) from the Clinical Practice Research Datalink GOLD (primary care), Hospital Episode Statistics (secondary care), and the Office for National Statistics mortality register. We followed the cohort from 1-year before birth (mothers only) up to 16-years post-birth.

**Primary outcome:** First recorded CP in children between 7-years and 16-years post-birth, identified by an algorithm capturing recorded diagnoses of CP and continuous pain episodes.

**Main exposures:** ACEs and ERDs in children. ACEs were defined as child maltreatment, maternal intimate partner violence, maternal mental health problems, and adverse family environments recorded one year before birth (maternal records) up to three years post-birth. ERDs were defined as emotional and behavioural presentations in children between four and six complete years post-birth. We used Cox-proportional models to test the hypotheses that ACEs increase the risk of CP, and that this risk was mediated by ERDs and common non-communicable child diseases (NCDs). NCDs were hypothesised intermediate confounders and analysed as co-joint mediators with ERDs.

**Results:** During a median follow-up of 11-years, children with any ACEs or ERDs had almost a two-fold higher risk of CP between 7 and 16-years old relative to children without ACEs or ERDs. We found a consistent dose-response relationship between the number of ACEs, the number of NCDs, ERDs and increased risk of CP. ERDs in children between 4- and 6-years post-birth mediated 10% of the association between ACEs and CP (mediated proportion range: 9%-11%; $p<0.001$).

**Conclusions**: ACEs and ERDs are associated with an increased risk of CP among children presenting to primary care during early child development. ERDs may play an important causal role in the development of CP. Further longitudinal research should evaluate specific ERD-related mechanisms for early intervention in children with recurring pain.

**Critical review of the literature**

# Trauma-focused cognitive behavioural therapies for posttraumatic stress disorder among adults with multiple-incident traumas compared with single-incident traumas: a systematic review and meta-analysis

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**Doctoral student**
Shabeer Syed,[1] Trainee Clinical Psychologist
shabeer.syed@hmc.ox.ac.uk/shabeer.syed@oxfordhealth.nhs.uk

**Supervisor**
Prof Paul Salkovskis,[1] Professor of Clinical Psychology
paul.salkovskis@hmc.ox.ac.uk/paul.salkovskis@oxfordhealth.nhs.uk

**Co-authors (additional reviewers)**
Rachel Ashwick, MSc[1]
rachel.ashwick@hmc.ox.ac.uk

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Please note: this manuscript is formatted according to the Vancouver referencing style as required by the target journals. The word count has been adjusted in accordance with the University guidelines.[1]

**Affiliations**

[1] Oxford Institute of Clinical Psychology Training and Research, University of Oxford and Oxford Health NHS Foundation Trust, Warneford Hospital, Headington, Oxford, OX3 7JX.

Keywords: PTSD; multiple-incident; complex trauma; violence; child maltreatment; partner violence; neglect; trauma-focused cognitive behavioural therapy

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**Abstract**

**Objective:** Trauma-focused cognitive behavioural therapies (TF-CBT) are considered the first-line treatment for posttraumatic stress disorder (PTSD) following different traumatic experiences. Whilst there is compelling evidence for TF-CBT for PTSD following single-incident traumas, the effectiveness of TF-CBT for PTSD following multiple-incident traumas is less clear. We conducted a systematic review and meta-analysis to evaluate the pooled effects of TF-CBT for multiple-incident PTSD relative to the effects of TF-CBT for single-incident PTSD.

**Methods**: We searched 18 electronic databases between Jan 1990 and Mar 2022 for RCTs comparing any TF-CBT for PTSD among adults exposed to multiple-incident traumas (defined as intimate partner violence; IPV; child maltreatment; CM; systemic violence and combat exposures) or single-incident traumas, relative to treatment as usual (TAU). The primary outcome was PTSD symptoms as per a validated self-report or clinician administered PTSD instrument immediately post-intervention. We used random-effects meta-analyses to pool standardised mean differences (Hedges' *g*) of TF-CBT against TAU stratified by trauma types.

**Results**: We included 144 RCTs (11,949 individuals), involving three types of single-incident traumas and four types of multiple-incident traumas, including systemic violence and refugees, CM or IPV and military combat-related exposures. We found no significant differences in the pooled effect of TF-CBT against TAU in RCTs involving multiple-incident traumas (Hedges' *g*, -0.90, 95% CI -1.08, -0.73; 65 RCTs) compared with the pooled effect from RCTs involving single-incident traumas (Hedges' *g*, -0.70, 95% CI -0.85, -0.54; 67 RCTs). Estimates remained similar when adjusting for baseline severity of PTSD symptoms, comparing specific traumas, and limiting estimates to active comparator groups. TF-CBT produced smaller treatment effects in RCTs involving multiple-incident traumas with comorbid serious mental illnesses (e.g., psychosis and personality disorders; Hedges' *g*, -0.37 95% CI -0.57, -0.17) relative to RCTs with less comorbidity.

**Conclusions**: TF-CBT showed comparable efficacy for reducing PTSD symptoms in RCTs involving repeated and sustained traumatic events as in RCTs of PTSD from single-incident

traumas. However, treatment approaches varied substantially between groups of trauma types and estimates should be considered with caution. Further research is needed to evaluate the effectiveness of TF-CBT for multiple-incident PTSD related to IPV and populations across inpatient and forensic settings.

## Introduction

Trauma-focused cognitive behavioural therapies (TF-CBT) are considered the first-line treatment for posttraumatic stress disorder (PTSD) in adults,[1] with a large proportion of adults treated in larger RCTs reaching remission post-intervention (remission rates: 55%-65%).[2,3] PTSD affects between 1.3% and 8.8% of adults and accounts for 3.8% of all treatments provided by the best-documented part of the English primary care system (Improving Access to Psychological Therapies programme; IAPT).[4] Despite the compelling evidence base for TF-CBT, there are increasing concerns that treatment effects from RCTs fail to generalise into clinical practice.[5,6] TF-CBT for PTSD in IAPT, for instance, have the third worst recovery rates (41.3%) relative to twelve other treated mental health problems in 2020 (range recovery rates: 35%-65%).[4] One consistent hypothesis for these findings is that evaluated TF-CBT protocols in RCTs have mainly focused on PTSD from single discrete incidents, limiting the generalisability of treatment effects to populations with multiple-incident traumas.[5,6] Studies from national programmes like IAPT and VA, for instance, show that higher trauma frequency is associated with poorer TF-CBT outcomes.[7-12] Similarly, a recent meta-analysis of 51 RCTs on TF-CBT against treatment as usual (TAU) found that studies on PTSD related to child maltreatment (CM) showed poorer treatment outcomes than other study samples.[13] Another recent review of TF-CBT for military personnel found that between 60% and 72% of individuals still met PTSD criteria post-treatment.[14]

Multiple-incident traumas such as repeated or prolonged exposure to interpersonal violence are associated with a higher risk of PTSD and comorbidities than single-incident traumas (e.g., car accidents).[15,16] Child maltreatment (CM) or intimate partner violence (IPV), for example, are associated with higher levels of emotion regulation difficulties (e.g. self-harm, substance misuse etc.), personality disorders and psychosis,[17,18] and chronic health conditions (e.g. cardiovascular disease, chronic pain).[19-22] The recent introduction of *"complex PTSD"* as a distinct diagnosis in ICD-11 have raised further questions regarding the efficacy of TF-CBT for multiple-incident traumas. Complex PTSD consists of additional symptom clusters that often stem from multiple-incident traumas potentially requiring additional treatment components.[23-25] Some authors, therefore, argue that multiple-incident

PTSD will need a phase-based approach by focusing on emotion regulation strategies to enhance safety before addressing traumatic events.[26] This line of reasoning has also led to the commissioning of specialist NHS services and augmented TF-CBT pathways (e.g. see IAPT enhanced trauma pathway).[27,28]

Despite numerous previous meta-analyses of RCTs on the efficacy of TF-CBT for PTSD against different control conditions,[20,29,30] few or no previous meta-analyses have pooled treatment effects of TF-CBT comparing multiple-incidents versus single-incident trauma RCTs. Most meta-analyses provide estimates for specific trauma types in isolation or compare estimates by trauma categories that are difficult to interpret clinically (e.g. *other vs veteran, TF-CBT vs other etc.*).[13,20,31] Therefore, the aims of this systematic review and meta-analysis were two-fold. First, we aimed to evaluate the pooled effect of TF-CBT for PTSD among adults with multiple-incident traumas compared with the pooled effect of TF-CBT for single incident traumas. We included RCTs that evaluated TF-CBT against TAU and used meta-analyses to compare pooled treatment effects for single versus multiple-incident traumas. Second, we aimed to explore if differences in treatment effects between trauma types could be explained by other sample characteristics, including specific trauma types, comorbidity and baseline PTSD severity.

## Methods

This systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-analyses and the Meta-analysis of Observational Studies in Epidemiology guidelines.[32,33] The review protocol was published in the PROSPERO registry prior to full commencement (CRD42021287863).[34]

### Search strategy

We searched MEDLINE®, PsycINFO, EMBASE, Web of Science, AMED, CINAHL Plus, PTSDpubs, PILOTS, SciVerse Scopus, Cochrane Library, PubMed, ERIC, DARE, Global Health Archives, ProQuest Central, Web of Science, OpenGrey, Google Scholar and 20 selected journals for studies published between 01/01/1970 and 08/03/2022 (complete search strategy in appendix A2). Reference lists of eligible full-text articles were hand-searched, and

18 frequently cited authors of eligible studies were contacted for additional article recommendations.

**Study eligibility**

The guiding framework for study selections and categorisations of single-incident and multiple-incident trauma studies are summarised in Tables 1 and 2, with details provided in appendix A3. Two independent reviewers (S.S and R.A ) screened abstracts, full texts and corresponding reference lists of articles using Covidence's systematic review software.[35] Any disagreement over study inclusions between reviewers was resolved by an expert in developing psychological interventions for anxiety and trauma-related disorders (P.S).

We included RCTs with any control group (waiting list, placebo, treatment as usual and active treatment comparisons.); any sample size; published in English or Swedish; with adults meeting PTSD or acute stress disorder (ASD) criteria (2 studies),[36,37] according to a diagnostic clinical interview or validated instrument cut-off score one-month post-trauma (except for ASD); with trauma-exposed populations relating to three predefined multiple-incident traumas or two types of single-incident traumas (Table 1). Eligible studies had to explicitly reference an established TF-CBT protocol based on information processing theories of PTSD (Table 2),[38] or evidence that participants received CBT involving a trauma-focused processing component (e.g., imaginal reliving, written exposure etc.). The intervention could be delivered in any setting or format (e.g., individual, group-basis, online video conferencing).

We excluded all forms of self-help interventions, including those with therapy assistance that did not involve trauma processing (e.g. online modules with therapist email correspondence).

***Multiple-incident traumas*.** We coded studies into a multiple-incident trauma category if the treatment focus and the main study population (trauma type endorsed >60% of the sample) belonged to any of the three following pre-defined trauma types of violence: CM or IPV (family violence), asylum seekers, refugees or military combat-related exposures (war-related trauma), emergency personnel (civilian high-risk occupational groups),[39] or studies with interventions developed for treating sustained trauma (e.g. narrative exposure therapy; NET; DBT-PTSD with stabilisation phases etc.; see Table 2). Given that most people

experienced multiple traumas in a lifetime,[16,40] this inclusion criteria and definition ensured multiple-incident trauma studies focused on a clinically meaningful category of trauma types with a higher likelihood of occurring over sustained periods.[16,40] Compared with other trauma types, global surveys by WHO show that repeated exposure to interpersonal violence is associated with an elevated risk of PTSD and longer time to remission.[16,40] We assumed studies reported on the index trauma associated with the most distress and highest level of daily interference, consistent with the majority of PTSD measures and TF-CBT protocols (Table 2).[41,42]

***Single-incident traumas (comparison group).*** We included RCTs involving single-incident traumas as a combined trauma group to compare treatment effects against multiple-incident trauma studies. However, given the large volume of eligible RCTs on single-incident traumas, we included only single-incident traumas that conferred a similar risk of PTSD as the pre-defined multiple-incident traumas using estimates from WHO as a guiding framework (Table 1).[16,40,41] Eligible single-incident trauma studies included discrete interpersonal violence in adulthood, accidents, or mixed trauma (various) exposed populations (i.e., no index trauma endorsed by >60% of the sample). This approach also helped decrease between-study heterogeneity to increase the validity of pooled estimates.[43] We excluded all other trauma types.

**Table 1.** Guiding framework for selecting and coding studies of traumatic exposures, adapted from the World Health Organization Mental Health DSM-IV interviews

| |
|---|
| **Multiple-incident trauma (sustained traumatic experiences)** |
| • Intimate partner violence: Any incident of threatening behaviour, violence or abuse (psychological, physical, sexual, financial or emotional) between adults who are, or have been, intimate partners or family members. |
| • Child maltreatment: Any act of commission or omission by a parent or caregiver resulting in harm, the potential for harm or threat of harm to a child (0–12 years) or an adolescent (13–19 years), including neglect, psychological, physical, sexual and emotional abuse. |
| • War trauma/organised violence: Any incident of systemic or organised violence including witnessing atrocities, being kidnapped, tortured, having committed or omitted violence, refugees within the context of low-resource countries affected by crises and conflict. |
| • Military combat trauma: any active, veteran or civilian military personnel who experienced deployment stressors and exposure to combat by witnessing, committing or omitting acts of violence. |
| • High-risk occupational groups: first responders including police, ambulance, and fire fighters exposed to traumatic incidents on duty. |
| **Single-incident trauma (lower likelihood of sustained repeated exposures)** |

- Interpersonal violence by unknown perpetrator: any exposure to violence by an unknown perpetrator including sexual, rape and physical assaults or being mugged in the community without referring to environments or contexts with high likelihood of sustained repeated exposures (e.g. countries affected by war and conflicts, CM or IPV).

- Accidents or disasters: any exposure to an unintentional traumatic incident including automobile accident, natural disaster, toxic chemical exposure, accidentally injured/killed someone or other life-threatening accidents

**Excluded trauma categories**

- We excluded studies focusing on trauma incidents relating to life-threatening illnesses, unexpected death of loved ones or serious illness of loved ones, witnessing injury or death (excluding the above trauma types).

### Data extraction and quality assessments

Using a standardised extraction form, two reviewers independently extracted: sample characteristics (e.g., sample size, age (mean/range, years), percentage of women); intervention protocol (Table 2); follow-up time; PTSD outcome measure and cut-off score; continuous outcome measures with their variance (e.g., means, SD, confidence intervals etc); and main type of trauma exposure (event endorsed by ≥60% of the sample). If studies reported on multiple outcome measures, we prioritised the Clinician-Administered PTSD Scale for DSM-3/5 (CAPS), followed by the instrument most frequently used by other studies to increase overall homogeneity (i.e. structured clinical interview; SCID; Posttraumatic Diagnostic Scale; PDS). If the same study compared different TF-CBT protocols against TAU, we choose the TF-CBT protocol most frequently used by other studies for the primary analysis. We include other TF-CBT protocols in subgroup analyses of specific treatment protocols (e.g. narrative exposure therapy vs TAU). If studies were based on the same sample (i.e. non-independent), we extracted data from all studies and prioritised the highest quality rated study followed by the largest sample size. We requested additional information from 10 authors, 6 of whom responded within the two-month deadline and were included.

The same two reviewers evaluated studies' risk of bias following the Cochrane Handbook for Systematic Reviews of Interventions risk-of-bias tool for randomised trials v2 (ROB-2).[44] ROB-2 addresses five overall domains: random sequence generation, allocation concealment, blinding of participants, researchers and outcome assessment, and selective reporting. Studies received an overall risk-of-bias rating of *"low risk", "some concerns"* or *"high risk*" of bias, aligning with the ROB-2 guidelines. To aid with comparisons of different TF-CBT protocols, we provide details on different TF-CBT approaches for handling multiple-incident traumas as described by cited TF-CBT manuals.

**Data analysis**

***Meta-analysis of relative effects for TF-CBT.*** For each trauma group, our primary outcome was the standardised mean difference (SMD) of PTSD symptoms (CAPS-3/5) between TF-CBT and TAU post-intervention. We re-expressed SMDs using Hedges's *g* bias correction for smaller sample sizes.[45] We pooled SMDs using random or fixed-effects meta-analyses (e.g. $I^2$ <50%) when at least three studies were available for the same outcome. [46] The random-effects model was based on the DerSimonian-Laird method, accounting for the between-study heterogeneity. Aligning with Cochrane guidelines, we also applied the Hartung-Knapp method for analyses involving less than four studies, yielding more conservative estimates for smaller sample sizes.[47] We interpreted Hedges' *g* according to Cohen's guidelines (small≤ -0.20, moderate> -0.50, and large≥ -0.80). Negative estimates of Hedges' *g* indicate a superiority of TF-CBT against the comparator group.

To aid with clinical interpretation, we also re-expressed the pooled Hedges' *g* into its natural scale on the CAPS, depicting the mean reduction of symptom scores relative to controls. We defined a clinically significant reduction on the CAPS or *"reliable improvement"* as a mean reduction of at least 10 points relative to controls, consistent with previous studies (clinically defined mean reduction range in previous studies: 10-30 points).[48] We prioritised continuous outcome data over dichotomised estimates to avoid information loss, increase statistical power and avoid inflation of boundaries.[49] Where possible, we used intention-to-treat data over complete case analyses.

***Comparing sources of variations in treatment effects (multiple vs single-incident trauma).*** We examined sources of between-study heterogeneity using subgroup analyses of overall trauma types (e.g. multiple-incidents vs single-incident), specific traumas (military-related, assaults, accidents etc) sample characteristics (comorbidity, exclusion criteria) when at least three studies were available for each subgroup as per the pre-specified protocol. We used random-effects meta-regression to assess the impact of continuous measures, including publication year, mean age, percentage of women, and baseline PTSD severity using the mean CAPS score. We examined the significance of variation in treatment effects

using the $I^2$ statistic (>75%=indicates substantial heterogeneity), standard $X^2$ tests and via prediction intervals.[43]

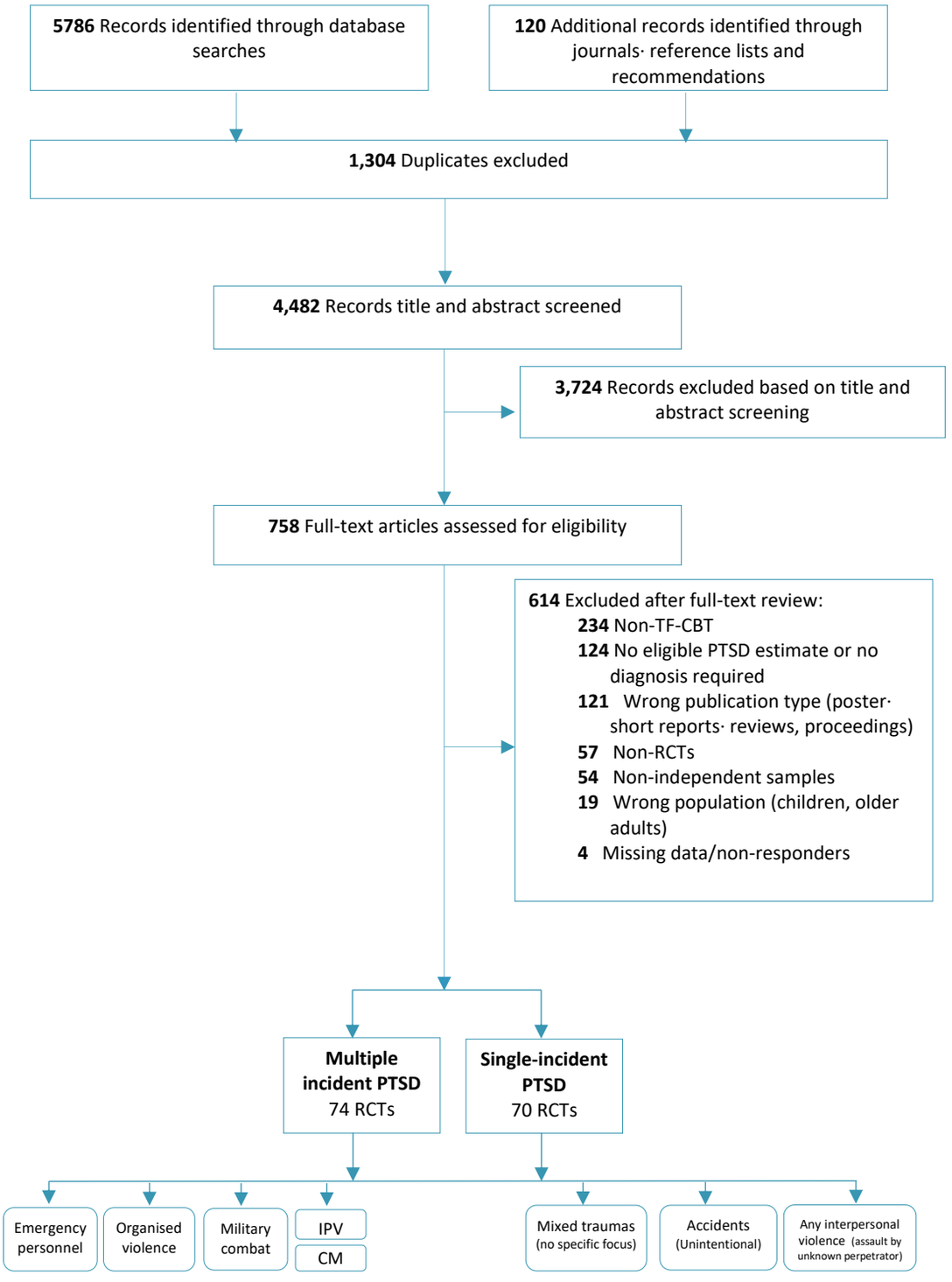
***Sensitivity analyses and publication bias.*** The influence of individual studies on pooled estimates was explored by serially omitting different studies from the overall estimates. We explored potential publication bias using funnel plots, Egger's test and Mazumdar rank correlation test for analyses with at least ten studies for the same outcome. We used R version 4.1.2 (R Foundation for Statistical Computing) and the *"meta"* package to perform all analyses.[50,51]

## Results

### Study characteristics

Key characteristics of included studies are depicted in appendix table A3. Overall, we included 144 RCTs involving seven overall groups of TF-CBT treatments (table 2), and 11,949 randomised participants (median sample: 66 participants [interquartile range participants: 34-106; range: 11-370]) from 32 different countries (figure 1). Most studies were from the USA (80 studies, 56%) followed by Germany or Netherlands (17 studies, 12%%), with a smaller proportion from Australia (7 studies, 5%) or the UK (7 studies, 5%; see supplement). Of these, we included 65 RCTs on multiple-incident traumas and 67 RCTs on single-incident traumas (including mixed traumas), comprising 132 RCTs that compared TF-CBT against TAU or minimal intervention without any psychological therapy input (e.g. medication, signposting etc). The other 12 RCTs contributed to meta-analyses comparing TF-CBT against active psychological treatments with separate estimates provided below. We provide separate estimates for single-incident trauma with and without mixed trauma studies, as a high proportion of mixed trauma studies focused on accidents (e.g. 40%-55% of samples; figure 3).

**Figure 1**. Flow diagram of the 144 selected studies for this systematic review




CM=Child maltreatment, IPV=Intimate partner violence, PTSD=Post traumatic stress disorder, TF-CBT=Trauma-focused cognitive behaviorual therapy

The use of manualised TF-CBT treatment protocols varied substantially across studies and trauma types (table 2). The most frequently evaluated treatment protocol was prolonged exposure therapy (PE; including three RCTs for virtual reality exposure and integrated substance misuse treatments), followed by 19 studies evaluating eye movement

desensitization and reprocessing (EMDR), 14 studies evaluating narrative exposure therapy (NET), 13 studies evaluating cognitive processing therapy (CPT), and 4 studies evaluating cognitive therapy for PTSD (CT-PTSD). The remaining 52 studies involved TF-CBT protocols, with less than three studies evaluating the same protocol and were grouped under non-specified TF-CBT treatments (table 2). Based on the cited treatment manuals,[48-50] PE provided the most consistent and systematic approach to PTSD symptoms relating to multiple-incident traumas, whereas CPT, CT-PTSD and EMDR provided less information and instructions to aid with systematic replication.

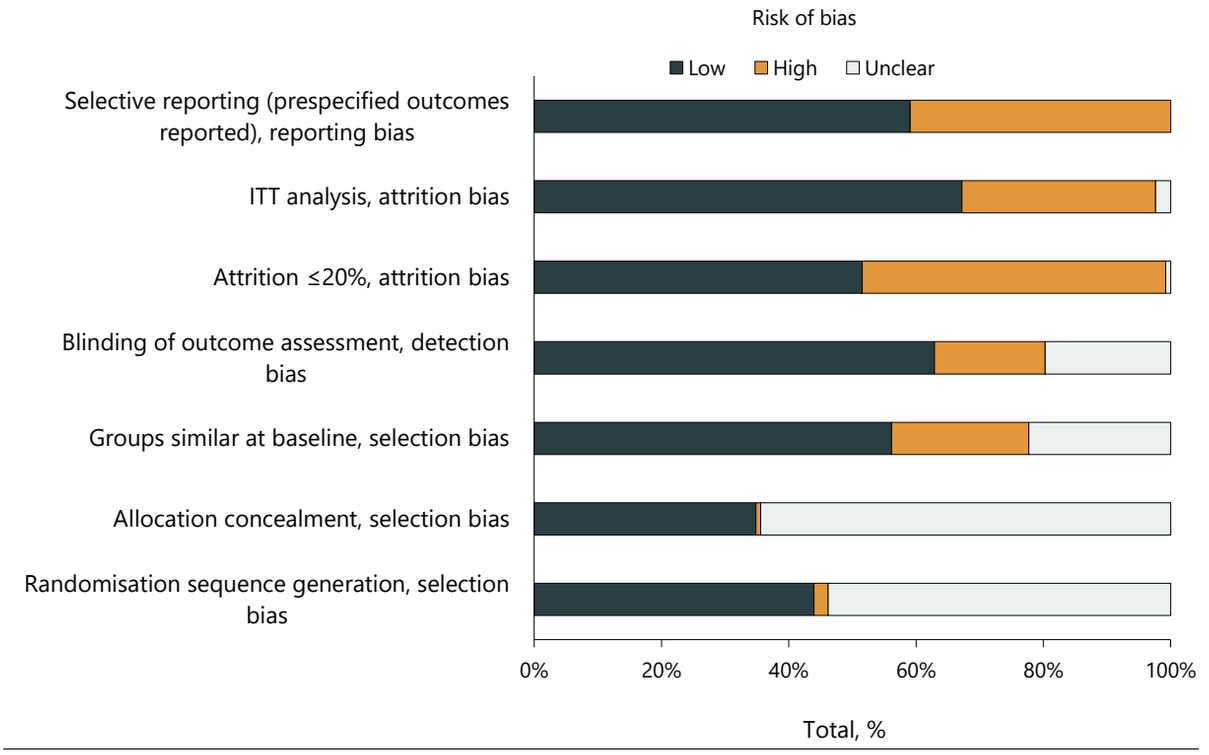
| **Table 2.** Categories of trauma-focused CBT protocols based on information processing theories[38] | **Studies** |
|---|---|
| **Prolonged exposure therapy (PE) 8-15 sessions (60-120 mins)[52]**<br>**Emotional processing theory**: Traumatic events are connected to a node in a fear network. This fear node involves a stronger behavioural and physiological response than other emotionally linked memories of similar situations. In this review, we provide separate and combined estimates for PE with or without virtual reality exposure, as treatments are informed by the same theory.<br>**Main treatment:** Introduction: psychoeducation + general coping skill (breathing technique). Main treatment: repeated exposure to the distressing memories in imagination and in-vivo for feared and avoided triggers, followed by 15-20 min of processing thoughts and feelings, emphasising reflective perspective-making *(not questioning/challenging beliefs) facilitating* "new" learned information associated with the trauma.<br>**Protocol for handling multiple traumas**: Ranking method. List and hierarchically order traumatic events in descending order of the most daily interference/distress from PTSD based on Subjective Units of Discomfort Scale (SUDS). Where possible, start with the trauma with the highest SUD. The SUDS range across anchor points: 0%, 50% and 100% distress. Avoid starting in a gradual way (i.e., less distressing trauma). Avoid moving onto another trauma until sufficient distress reduction is evident (e.g., SUDS <50%).<br>**Protocol published open access**: Yes online via U.S. Department of Veterans Affairs | 50 |
| **Dialectical Behavior Therapy for PTSD (DBT-PTSD) 45 sessions (1-year treatment)[53]**<br>**Biosocial theory.**[54]<br>**Main treatment:** A phased based treatment in three parts with seven overall components involving emotion regulation and interpersonal skills and *"exposure-based techniques to reduce fear of trauma-associated emotions"*[55]<br>**Protocol published open access:** Yes online via detailed trial protocol[53] | 2 |
| **Cognitive Processing Therapy (CPT)[56]**<br>**Social cognitive theory:** The traumatic events are linked to beliefs in conflict with old beliefs, causing a *"stuck point"* which, without challenge, maintains PTSD symptoms.<br>**Main treatment:** Identifying, challenging, and modifying unhelpful trauma-related cognitions, e.g., *"I am to blame for the abuse," "Closeness means danger."*<br>**Protocol for handling multiple traumas**: Focus on the event causing the *"most PTSD symptoms*". Then systematically challenge the most distressing *"stuck point"* until the distress is reduced.<br>**Protocol published open access**: Yes online via U.S. Department of Veterans Affairs | 17 |
| **Cognitive therapy (CT-PTSD)[57,58]**<br>**Cognitive model of PTSD**: Traumatic information is poorly integrated with other autobiographical memories in ways that leads to a current sense of threat, which is reinforced/maintained by negative beliefs and avoidance strategies linked to the trauma.<br>**Main treatment:** Modify excessively negative appraisals identified from imaginal reliving. Multiple components are used for *"updating"* hot-spots/cognitive restructuring during imaginal reliving, and strategies aimed at reducing avoidance, including stimulus discrimination for triggers; and more behavioural experiments than regular CBT.<br>**Protocol for handling multiple traumas**: Focus on updating hot-spots linked to the most distressing trauma (e.g. based on re-experiencing symptoms) OR hot-spots linked to the trauma with most significant personal meaning. If the distress still persists for similar traumas following hot-spot updating of one trauma, continue with the next trauma.<br>**Protocol published open access**: No. Some resources available via website oxcadatresources.com/manual, stating: *"The PTSD "training manual is currently being created. It will be posted here once it is complete." Accessed on 20.05.2022*) | 4 |

| | |
|---|---|
| **Narrative exposure therapy (NET)[26]**<br>**Dual representation theory of PTSD:**[38,59]Traumatic events are encoded by lower-level systems only capturing sensory information ('hot memories'), without context and details ('cold memories'), hindering proper autobiographical memory encoding. [52,57,60]<br>**Main treatment:** Work through each traumatic memory in chronological order to build a cohesive narrative (incl. positive events)<br>**Protocol for handling multiple traumas**: Therapist and client works through each trauma in chronological order to create a narrative. Ranking traumas are not recommended. *"…rank countless single events and compare different types of horror is not only formidable, we think it is inhumane.. (p 95)"*<br>**Protocol published open access**: No. Protocol available in published book by Hogrefe Publishing | 15 |
| **Eye Movement Desensitization and Reprocessing (EMDR)**<br>**Adaptive information processing theory (theory added post-hoc**): Trauma disrupts normal adaptive information processing, resulting in unprocessed information problematically held in memory networks. However, no empirically grounded theory have been put forward to inform EMDR.<br>**Main treatment:** Person is asked to observe emerging thoughts, feelings, and body reactions during "bilateral physical stimulation" (usually horizontal eye movements) without judgment.<br>**Protocol for handling multiple traumas**: Yes, "Eight phased" treatment targeting each specific event, using "building blocks three-phased approach".<br>**Protocol published open access**: No. Protocol available in published book by Guilford Press & protocol must be delivered by an "EMDR certified" therapist | 24 |
| **Other mixed TF-CBT**<br>**Information processing theories of PTSD**: If there were less than three studies using the same TF-CBT treatment protocol, studies were classed as *"other mixed-TF-CBT"*.<br>**Main treatment:** Elgible studies included cognitive behavioural therapy (CBT) involving at least one component of processing a traumatic memory in any form as guided by a therapist (e.g., imaginal reliving, written exposure etc). Some studies may cite a consistent protocol or build on a previous established protocol (e.g. PE), but with treatment showing significant deviation across studies to be classed under the same treatment group. For instance, five RCTs evaluating "other mixed TF-CBT" followed Bryant et al.'s treatment protocol for acute stress disorder. Whilst based on emotional processing theory and PE, Bryant et al.'s protocol is often shorter than PE (approx. 5x90min sessions vs. 8-15) and involves cognitive restructuring following exposure, which is not included in PE. Some studies also involved<br>**Protocol published open access**: Varied | |
| **Excluded non-TF-CBT [61,62]**<br>We excluded any psychological intervention with or without CBT that did not include processing or exposure to traumatic memories. | |

## Quality assessments

***Risk of bias.*** The intraclass correlation coefficient for the independently quality rated studies were 0.81 (95% CI 0.78-0.83), indicating good inter-rater reliability. RCTs were generally rated as high risk of bias or with concerns of bias (133 studies; 71.5%; figure 2), with a smaller proportion rated as low risk of bias 41 studies (28.5%). There was a relatively equal proportion of high risk of bias ratings among RCTs on single-incident trauma populations (48 RCTs, 68.6%; or 21 RCTs, 72.4% excluding mixed traumas) as in RCTs on multiple-incident trauma (55 RCTs, 74.3%). Most studies rated as high risk of bias did not adequately describe allocation concealment (94 RCTs, 65.2%) or did not describe using independent assessors to assess treatment adherence (87 RCTs, 60.4%). Individual ROB-2 scores for each study are given in appendix table A4.

**Figure 2.** Risk of bias assessment scores by domain




***Publication bias.*** Eggers' test and visual inspection of funnel plots (appendix A16-A17) showed evidence of publication bias for meta-analyses of both single-incident trauma and multiple-incident trauma studies for estimates involving at least ten or more studies ($p$<0.014, slope> -3.32, 0.971, rank correlation test: $p$>0.026), indicating smaller studies yielding larger estimates were more likely to be published.

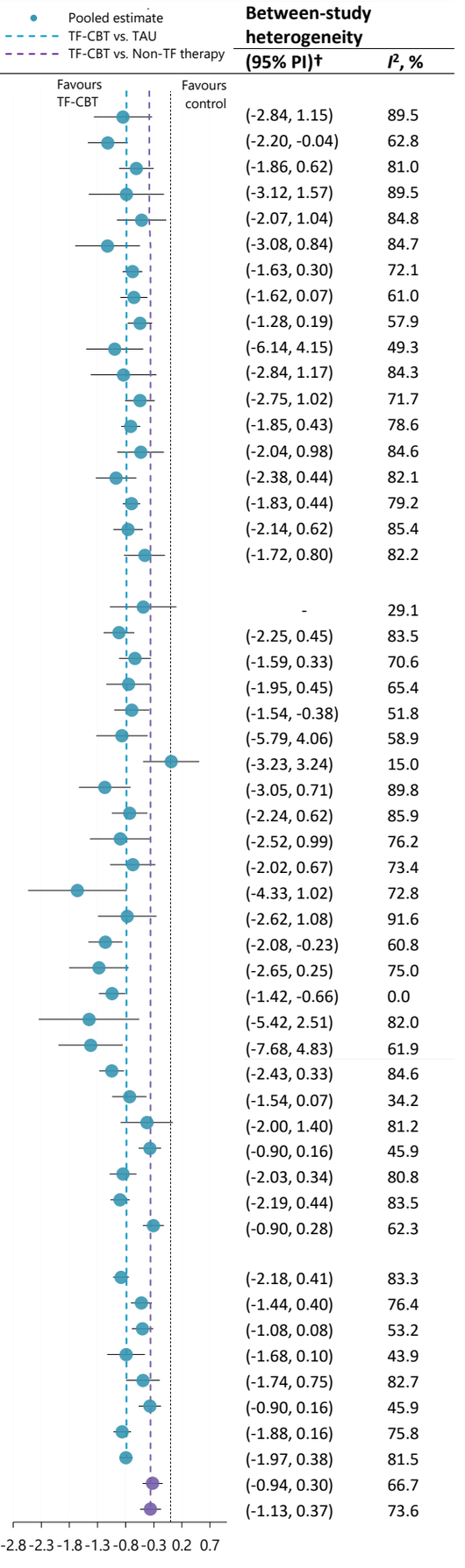
**Main analyses: TF-CBT multiple-incident traumas vs single-incident traumas**

Figure 3 presents pooled effect sizes and between-study heterogeneity by trauma type and subgroups. Figure 4 shows the individual study's mean reduction of PTSD symptom severity pre-post treatment for studies with CAPS data. Individual forest plots and funnel plots for all meta-analyses are provided in the supplementary.

Overall, a random-effects meta-analysis showed no significant differences between TF-CBT against TAU for multiple-incident traumas (Hedges' *g*, -0.90 95% CI -1.08, -0.73; *k*=65) compared with single-incident traumas (Hedges' *g*, -0.70 95% CI -0.88, -0.54; *k*=67) [*P*=0.089, *Q*=2.9 for subgroup comparisons]. When limiting the analysis to studies with CAPS data only (*k*=42), the effect size corresponded to a CAPS mean reduction of -18.6 points for multiple-incident traumas (Hedges' *g: -0.86 [-1.08; -0.64], k*=28) and a CAPS mean reduction of -20.2 points for single-incident traumas (Hedges' *g: -0.86 [-1.08; -0.65], k*=14).

**Figure 3.** Pooled standardised mean differences of TF-CBT compared to TAU, WL or minimal intervention by type of traumatic exposure, intervention and outcome

| Trauma type | TF-CBT intervention or subgroup | n | Inter/ctrl | Pooled Hedges' *g* (95% CI) | Between-study heterogeneity (95% PI)† | $I^2$, % |
|---|---|---|---|---|---|---|
| **Single-incident trauma** | | | | | | |
| Accidents | Overall | 12 | 488/418 | -0.85 (-1.37, -0.33) | (-2.84, 1.15) | 89.5 |
| | CAPS only | 8 | 213/198 | -1.08 (-1.49, -0.67) | (-2.20, -0.04) | 62.8 |
| Physical/sexual assaults | Overall | 16 | 572/471 | -0.60 (-0.92, -0.30) | (-1.86, 0.62) | 81.0 |
| | CAPS only | 6 | 185/180 | -0.78 (-1.44, -0.11) | (-3.12, 1.57) | 89.5 |
| | PE | 10 | 379/ 303 | -0.52 (-0.96, -0.08) | (-2.07, 1.04) | 84.8 |
| Sexual assault/rape | Overall (PE only) | 8 | 206/200 | -1.12 (-1.70, -0.55) | (-3.08, 0.84) | 84.7 |
| Mixed traumas (various types) | Overall | 40 | 1159/1079 | -0.68 (-0.86, -0.50) | (-1.63, 0.30) | 72.1 |
| | CAPS only | 17 | 548/510 | -0.78 (-1.01, -0.54) | (-1.62, 0.07) | 61.0 |
| | PE | 15 | 455/408 | -0.55 (-0.77, -0.33) | (-1.28, 0.19) | 57.9 |
| | CPT | 3 | 76/77 | -0.99 (-1.50, -0.49) | (-6.14, 4.15) | 49.3 |
| | EMDR | 7 | 184/164 | -0.84 (-1.42, -0.25) | (-2.84, 1.17) | 84.3 |
| | TF-CBT | 16 | 576/557 | -0.55 (-0.81, -0.28) | (-2.75, 1.02) | 71.7 |
| Comorbid conditions | Excluded all comorbidity | 56 | 1547/1391 | -0.71 (-0.88, -0.54) | (-1.85, 0.43) | 78.6 |
| | Included SUD or BPD | 11 | 382/318 | -0.53 (-0.95, -0.12) | (-2.04, 0.98) | 84.6 |
| Overall single-incident trauma (CAPS only)‡ | | 14 | 989/920 | -0.97 (-1.33, -0.61) | (-2.38, 0.44) | 82.1 |
| **Overall single-incident trauma (all measures)** | | 67 | 1929/1709 | -0.70 (-0.85, -0.54) | (-1.83, 0.44) | 79.2 |
| Single-incident trauma, excl. mixed trauma‡ | | 29 | 959/802 | -0.76 (-1.02, -0.50) | (-2.14, 0.62) | 85.4 |
| TF-CBT vs. non-TF therapy (active comparator) | | 10 | 439/388 | -0.46 (-0.83, -0.10) | (-1.72, 0.80) | 82.2 |
| **Multiple-incident traumas** | | | | | | |
| Emergency personnel | Overall | 2 | 65/67 | -0.49 (-1.08, 0.10) | - | 29.1 |
| Military combat-related | Overall | 28 | 1067/1009 | -0.92 (-1.19, -0.64) | (-2.25, 0.45) | 83.5 |
| | CAPS only | 12 | 422/370 | -0.63 (-0.92, -0.35) | (-1.59, 0.33) | 70.6 |
| | PE | 6 | 214/174 | -0.75 (-1.15, -0.35) | (-1.95, 0.45) | 65.4 |
| | PE+VRET | 9 | 253/197 | -0.69 (-1.00, -0.38) | (-1.54, -0.38) | 51.8 |
| | CPT | 3 | 112/93 | -0.87 (-1.32, -0.41) | (-5.79, 4.06) | 58.9 |
| | EMDR | 3 | 32/31 | 0.01 (-0.49, 0.51) | (-3.23, 3.24) | 15.0 |
| | TF-CBT | 15 | 758/757 | -1.17 (-1.63, -0.71) | (-3.05, 0.71) | 89.8 |
| War/organised violence | Overall | 20 | 722/647 | -0.73 (-1.05, -0.41) | (-2.24, 0.62) | 85.9 |
| | CAPS only | 6 | 172/135 | -0.76 (-1.29, -0.22) | (-2.52, 0.99) | 76.2 |
| | NET | 10 | 250/193 | -0.67 (-1.08, -0.27) | (-2.02, 0.67) | 73.4 |
| | EMDR | 3 | 62/63 | -1.66 (-2.54, -0.78) | (-4.33, 1.02) | 72.8 |
| | TF-CBT | 8 | 410/ 391 | -0.77 (-1.29, -0.25) | (-2.62, 1.08) | 91.6 |
| Child maltreatment | Overall | 10 | 285/274 | -1.16 (-1.46, -0.86) | (-2.08, -0.23) | 60.8 |
| | CAPS only | 6 | 199/197 | -1.20 (-1.64, -0.76) | (-2.65, 0.25) | 75.0 |
| | PE | 5 | 172/154 | -1.04 (-1.28, -0.81) | (-1.42, -0.66) | 0.0 |
| | TF-CBT | 5 | 84/84 | -1.45 (-2.35, -0.56) | (-5.42, 2.51) | 82.0 |
| IPV | Overall | 3 | 105/96 | -1.42 (-2.00, -0.85) | (-7.68, 4.83) | 61.9 |
| Comorbid conditions | Excluded all comorbidity | 47 | 1418/1315 | -1.05 (-1.27, -0.83) | (-2.43, 0.33) | 84.6 |
| | Included SUD | 5 | 177/122 | -0.73 (-1.04, -0.43) | (-1.54, 0.07) | 34.2 |
| | Included SUD or BPD | 6 | 296/205 | -0.42 (-0.89, 0.04) | (-2.00, 1.40) | 81.2 |
| | Psychosis & SUD or BPD | 8 | 389/414 | -0.37 (-0.57, -0.17) | (-0.90, 0.16) | 45.9 |
| Overall multiple-incident trauma (CAPS only) | | 28 | 911/812 | -0.85 (-1.09, -0.61) | (-2.03, 0.34) | 80.8 |
| **Overall multiple-incident trauma (all measures)** | | 65 | 2191/2033 | -0.90 (-1.08, -0.73) | (-2.19, 0.44) | 83.5 |
| TF-CBT vs. Non-TF therapy (active comparator) | | 17 | 704/676 | -0.31 (-0.48, -0.14) | (-0.90, 0.28) | 62.3 |
| **Overall estimates** | | | | | | |
| Comorbid conditions | Excluded all comorbidity | 105 | 3030/2773 | -0.88 (-1.02, -0.74) | (-2.18, 0.41) | 83.3 |
| | Any SUD/BPD/Psychosis | 30 | 1240/1005 | -0.52 (-0.71, -0.34) | (-1.44, 0.40) | 76.4 |
| | CAPS only (any) | 13 | 551/510 | -0.50 (-0.69, -0.31) | (-1.08, 0.08) | 53.2 |
| | Included SUD | 6 | 183/128 | -0.79 (-1.13, -0.46) | (-1.68, 0.10) | 43.9 |
| | Included SUD or BPD | 17 | 678/523 | -0.49 (-0.79, -0.19) | (-1.74, 0.75) | 82.7 |
| | Psychosis & SUD or BPD | 8 | 414/389 | -0.37 (-0.57, -0.17) | (-0.90, 0.16) | 45.9 |
| Overall estimate all studies (CAPS only) | | 56 | 1900/1732 | -0.86 (-1.02, -0.71) | (-1.88, 0.16) | 75.8 |
| Overall estimate all studies (all measures) | | 132 | 4129/3644 | -0.80 (-0.91, -0.68) | (-1.97, 0.38) | 81.5 |
| Overall TF-CBT vs Non-TF therapy (CAPS only) | | 15 | 830/779 | -0.32 (-0.50, -0.14) | (-0.94, 0.30) | 66.7 |
| Overall TF-CBT vs Non-TF therapy (all measures) | | 27 | 1325/1234 | -0.38 (-0.54, -0.21) | (-1.13, 0.37) | 73.6 |




Each circle represents the pooled Hedges' *g* (bias-corrected standardised mean difference) by trauma type and intervention type. Horizontal lines indicate 95% confidence intervals of the estimate. The dashed lines are reference lines. The blue dashed line refers to the overall estimate, and the grey dashed line indicates the zero point of no effect relative to comparators. Pooled estimates are based on random-effects meta-analyses unless otherwise specified. The dashed lines mark the estimate for no effect (e.g., 0). Individual forest plots are shown in appendix A5-A12.

*Estimates based on a fixed-effects meta-analysis due to lower between-study heterogeneity (i.e., $I^2$<50%).

†A 95% prediction interval is a measure of between-study variation and approximates where the SMD is to be expected for 95% of similar future studies

‡ Excludes studies with mixed/various traumatic events, as no specific type of event could be ascertained over other events (i.e. endorsed <60% of sample) .

Abbreviations: BPD=Borderline personality disorder; CAPS=Clinician-Administered PTSD Scale for DSM (2-5). EMDR=Eye Movement Desensitization and Reprocessing; TF-CBT=Trauma Focused Cognitive Behavioural therapy; NET=Narrative Exposure Therapy; PE=Prolonged Exposure; Hedges' *g*=corrected Cohens d/standardised mean difference; SUD=Substance misuse disorder;

The results remained non-significant when excluding mixed traumas from the single-incident trauma group; when limiting estimates to outcomes based on the CAPS only (*k*=42); when comparing groups overall risk of bias ratings; when limiting estimates to comparators of active non-trauma focused psychological therapies only (*k*=27; or when restricting estimates to studies with any levels of comorbidity (e.g. psychosis, personality disorders; substance misuse (*P*>0.44 for all between-subgroup comparisons; figure3).

By contrast, we found that the efficacy of TF-CBT varied significantly by different types of multiple and single-incident traumas including: accidents, sexual or physical assaults, mixed traumas and multiple-incidents of systemic violence and refugees, CM or IPV and military combat-related exposures (figure 3) [*P*=0.024, *Q*=16.1 for all subgroup comparisons]. However, the between-group differences of trauma types became non-significant (*P*=0.058, *Q*=10.7, *k*=89; Hedges' *g*, -0.86, 95%CI -1.01, -0.71), when excluding emergency personnel due to limited studies (*k*=2) and when excluding mixed trauma types (*k*=41).

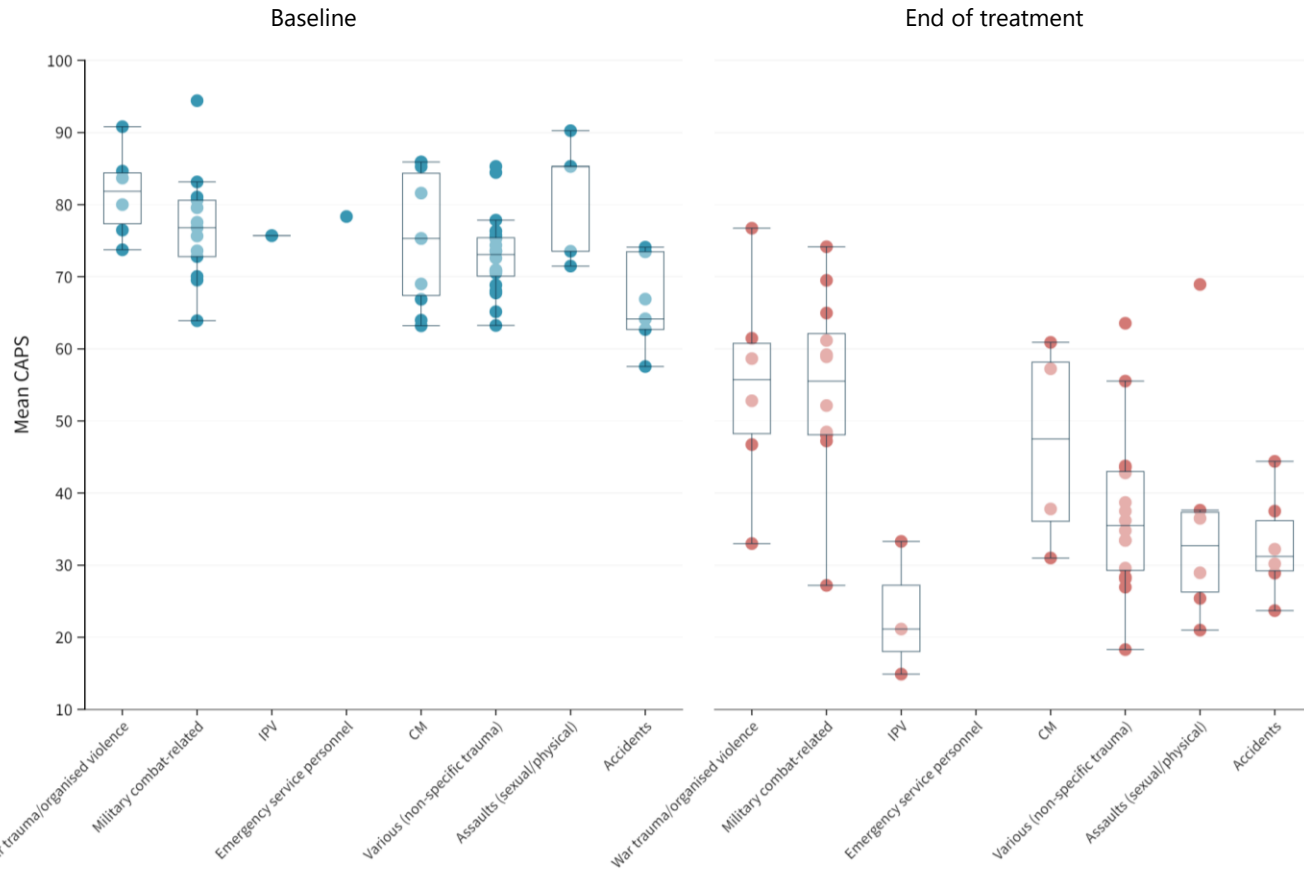
**Subgroup analyses by trauma types**

***Single-incident traumas (accidents, interpersonal violence, and mixed trauma types)***

We included 44 studies on mixed trauma-exposed populations (i.e. no single main trauma type could be distinguished from others), and 31 RCTs on single-incident traumas of interpersonal violence (physical/sexual assault), 15 RCTs for accidents. The most common TF-CBT protocol for interpersonal violence was PE. In contrast, non-specified TF-CBT (mixed protocols) were the most common for accidents and mixed trauma populations. The overall risk of bias was high in 20 RCTs (28.2%) on single-incident trauma, with the highest proportion made up of 12 mixed traumas studies (16.9%).

Compared with TAU, the pooled effect size for single-incident traumas ranged from a medium size (Hedges' *g*, -0.55, 95% CI, -0.77, -0.33) for PE in studies of mixed trauma

**Figure 4.** Box plot of studies mean PTSD symptom scores (CAPS) for the intervention group by assessment time point and trauma type




studies to a large effect size in studies on accidents with mixed TF-CBT protocols (Hedges' g, -0.91 95% CI, -1.36, -0.46). PE for sexual assaults (e.g., rape, military-related sexual assaults) showed the largest effect size (Hedges' *g,* -1.12; 95% CI, -1.70 to -0.55), relative to TAU. There were no significant differences in treatment effects between different types of single-incident traumas (*P*>0.105; *Q*=6.13), or when excluding studies with mixed traumas from the overall estimate (*P*=0.058; *Q*=5.7).

**Multiple-incident traumas (emergency personnel, military, systemic violence, CM and IPV)**

Emergency personnel. Two RCTs compared TF-CBT (NET and TF-CBT) against TAU for firefighters or disaster workers from 9/11, resulting in a small to medium pooled effect size (Hedges' *g*, -0.49 95% CI -1.08, 0.10) and small between-study heterogeneity ($I^2$=29%). Notably, one older RCT for police personnel showed a larger effect size of brief eclectic psychotherapy,[63] but provided only binary end points and were excluded from this review.

***Military-related combat trauma.*** Thirty-three RCTs evaluated TF-CBT against TAU for military-related combat exposure. Most studies focused on other mixed TF-CBT protocols aimed at US veterans (12 RCTs), followed by PE (9 RCTs including virtual reality PE) and CPT (3 RCTs). A smaller proportion of sampled studies included active-duty military personnel (6 RCTs, 19.4%). The risk of bias was high in 17 RCTs (51.2%).

The overall pooled effect size of TF-CBT for military-related trauma was large (Hedges' *g*, -0.90; 95% CI, -1.17 to -0.63), with substantial between-study heterogeneity ($I^2$ >83%). The mixed TF-CBT protocols showed the largest pooled effect size for reducing PTSD relative to TAU (Hedges' *g*, -1.17; 95% CI, -1.63 to -0.71). Three RCTs on EMDR for military-related trauma showed the smallest effect size of all evaluated TF-CBT protocols and were equally as effective as no treatment or TAU (Hedges' *g*, -0.01; 95% CI, -0.49 to 0.51).

***War-related and systemic violence.*** Of the 22 RCTs on TF-CBT for war and systemic violence-related PTSD, the most common intervention was NET (10 RCTs) followed by mixed TF-CBT protocols (8 RCTs). Most RCTs recruited (15 RCTs; 71%) from refugee camps for conflicts in the middle east or immigration centres in the country of safety. The remaining studies involved former child soldiers, torture victims and forced displacement across conflict zones in Africa. The risk of bias was high in 4 RCTs (18.2%).

The overall pooled effect size of TF-CBT was large (Hedges' *g*, -0.81; 95% CI, -1.13 to -0.49), with considerable between-study heterogeneity ($I^2$>85%). Three small RCTs comparing EMDR against waiting list or stabilisation only showed the largest effect size (Hedges' *g*, -1.66; 95% CI, -2.54 to -0.78;*P*=0.015) on self-report measures, followed by mixed TF-CBT protocols (Hedges' *g,* -0.77; 95% CI, -1.29 to -0.25, *k*=8), and NET (Hedges' *g,* -0.67; 95% CI, -1.08, -0.27, *k*=10).

***Child maltreatment (CM).*** Eleven RCTs investigated different TF-CBT interventions among adults for PTSD relating to CM, with the index trauma generally occurring below 12 years old (pooled average age: 7 years). Five RCTs used different TF-CBT protocols (including DBT-PTSD and EMDR) and four studies used PE. The risk of bias was high in 3 RCTs (27.2%).

Relative to TAU, the pooled effect size of TF-CBT for CM-related PTSD was large (Hedges' *g,* -1.21 95% CI -1.54, -0.87), with moderate to large between-study heterogeneity was ($I^2$= 63.4%).

***Intimate partner violence (IPV).*** Three RCTs compared TF-CBT against TAU for PTSD related to IPV among women in past abusive relationships. Two RCTs showed some concern of bias and were from the US evaluating cognitive trauma therapy for battered women (CTT-BW), and one recent RCT from Iran that evaluated NET showed high risk of bias. Compared with TAU, the overall pooled effect size of TF-CBT was large (Hedges' *g*, -1.42 95% CI, -2.00, -0.85), with moderate between-study heterogeneity ($I^2$=61.9%). We excluded three RCTs on non-TF CBT for PTSD relating to IPV among women in shelters ("*Helping to Overcome PTSD through Empowerment")*, as the interventions did not process trauma (e.g. exposure by any means).[64-66]

**Sensitivity analyses**

Serially excluding individual studies showed that no study impacted the overall effect size of Hedges' *g* by more than +/-0.01 or affected the between-study heterogeneity ($I^2$) by more than 0.4% (appendix A13). Meta-regressions showed a significant association between higher baseline PTSD symptom severity and decreased effect size for TF-CBT vs TAU by trauma types (appendix A14-A15). This association became non-significant when excluding eight studies on comorbid serious mental illness (psychosis, homelessness), indicating that the impact of PTSD baseline severity was likely driven by higher comorbidity samples than PTSD severity itself.

## Discussion

This systematic review and meta-analysis compared the treatment effects of TF-CBT for multiple and single-incident traumas against TAU, and the efficacy of TF-CBT for specific trauma types. It drew upon data from 144 selected RCTs involving diverse populations, settings and comparator groups. Consistent with previous meta-analyses,[20,29,30] TF-CBT showed moderate to large effect sizes for reducing PTSD symptoms relative to TAU, with no

significant differences between multiple-incident traumas and single-incident traumas. We generally found larger effects of TF-CBT for PTSD related to CM or IPV, relative to TF-CBT for single-incident traumas or military-related combat traumas**.** However, as a large proportion of included studies were of high risk of bias and treatment approaches varied significantly between trauma groups, estimates should be interpreted with caution.

The finding that TF-CBT is as effective for both multiple-incident trauma populations and single-incident trauma populations challenges previous assumptions that TF-CBT may not generalise to real-world settings for patients with *"complex trauma"* (defined as *"multiple, prolonged or early life trauma")*.[67] TF-CBT showed the largest effect sizes for multiple-incident traumas of family violence (e.g. CM occurring at a mean age of 7-8 years old, at a monthly rate for over 5- years),[68-74] and organised violence (e.g. torture, refugees etc.) with therapy led by laypeople.[75-80] Whilst the effect size of TF-CBT was smaller in studies with active therapy comparators groups, effects remained significant and clinically meaningful (e.g. -15 points mean reduction on the CAPS). The result also remained stable when accounting for baseline severity of PTSD symptoms across trauma types and comparator groups. Taken together, our findings contrast observations from English and US studies from national services such as IAPT or VA reporting on a "*research to practice gap*", where multiple-incident trauma has been associated with poorer PTSD outcomes.[7-12] Rather, our results emphasise that trauma types or trauma frequency are poor predictors of TF-CBT outcomes, which is consistent with the NICE recommendations to offer TF-CBT (excluding EMDR which is not recommended for certain populations) for PTSD in adults regardless of trauma type.[81]

Consistent with previous reviews,[20,29,30] the effect size was, however, smaller in specific multiple-incident trauma samples with comorbid serious mental illness compared with studies that excluded serious mental illness. The impact of comorbidity may help explain previous "*research to practice"* gaps in primary care and VA studies as people with multiple-incident PTSD (e.g. IPV or refugees) may present with competing treatment demands from

comorbidities, living circumstances and ongoing threats (e.g. current IPV). However, it is essential to recognise that most people with multiple-incident trauma and PTSD in primary care do not show the same extent of complexity as the samples included in this review (e.g. psychosis, BPD, inpatient/forensic care).[82,83] Our results, therefore, emphasise the likely importance of viewing *"complex trauma"* and *"complex needs"* as separate concepts and moderators of TF-CBT.

The moderate effect size of TF-CBT relative to active comparator groups in samples with high comorbidity is a critical finding. Presentations of multiple-incident trauma and comorbidity continue to be a barrier to receiving TF-CBT because of clinician perceptions about patients' fragility and risk (e.g., patients cannot handle processing multiple trauma-related memories, or trauma processing will increase SUD or self-harm).[84] Our findings do not support these assumptions and reinforce that patients with complex and comorbid mental health needs benefit from TF-CBT. The result partly aligns with the updated NICE guidelines (2018) that recommend offering TF-CBT for people with comorbid substance misuse and severe PTSD symptoms.

The effect size varied depending on trauma type and TF-CBT protocol type. Not all subgroup analyses by trauma type provided effect sizes of TF-CBT against active comparators or non-trauma focused therapies. Notably, the highest quality RCTs evaluating PE or CPT against non-trauma focused therapies (present centred therapy or medication management) showed marginally better and often non-significant effect sizes for military traumas among US veterans.[85-88] The relative effects of TF-CBT specific components compared with other non-trauma focused therapies for military veterans are therefore yet to be established. It is also possible that TF-CBT for other multiple-incident trauma populations (e.g. IPV) will yield different effect sizes when compared with active therapy comparator groups in larger methodologically sound RCTs.

**Limitations**

This review has important limitations. First, we used a meta-analysis that indirectly compared subgroups of coded trauma exposures (i.e. trauma types not directly compared within the same RCT), and we were unable to classify a large proportion of studies with mixed or overlapping traumas into a specific trauma category. Many coded studies for adult interpersonal traumas, for instance, may include people with multiple-incident traumas. Additionally, some RCTs in the multiple-incident trauma group evaluated different treatment protocols than RCTs in the single-incident trauma group. Some protocols, for instance, were designed specifically to account for the additional comorbidity of multiple-incident PTSD (e.g. DBT-PTSD), and treatments were less comparable with other TF-CBT protocols. The treatment effects of TF-CBT for single-incident traumas relative to multiple-incident traumas should therefore be considered with caution, as several factors not examined in the subgroup analyses may have influenced our results. Nonetheless, given the scarcity of previous relevant reviews, our findings provide a comprehensive overview of the pooled effects from theoretically similar treatments, providing a platform for more specific treatment comparators in future reviews. Also, the consistency of effect sizes among different trauma-exposed populations, combined with the statistical power from 144 RCTs to detect differences between specific traumas, suggests that these estimates are valid and merit further study. Future meta-analyses would benefit from comparing results from specific TF-CBT protocols (e.g. PE) for different traumas to minimise potential confounding from treatment variation and performance bias.

Second, most studies do not measure PTSD symptoms related to repeated, sustained traumas, as PTSD measures (e.g. CAPS) measure symptom change according to a selected index event at starting treatment. Hence, it remains unclear whether treatment effects generalise to PTSD symptoms related to other traumatic events (which may not have been examined in treatment) in multiple-incident exposed populations.

Third, we used a direct meta-analysis to compare TF-CBT relative to one comparator (e.g., TAU or active treatment), rather than a network meta-analysis that can produce efficacy estimates relative to multiple comparator groups across RCTs (e.g., TAU vs active treatment vs PE vs EMDR etc).[89] However, a comparison of different TF-CBT protocols were not the focus of this review. Given the substantial proportion of studies using mixed and unspecified TF-CBT protocols for different trauma types, it is also unlikely a simultaneous comparison of different TF-CBT protocols (e.g. mixed TF-CBT vs PE vs EMDR) would yield reliable or clinically meaningful results.[90]

Fourth, whilst the mean reduction in PTSD symptom scores were similar for multiple and single-incident PTSD related studies, multiple-incident trauma studies had generally higher symptom scores at baseline and ended treatment with higher symptom severity than studies on single-incident trauma. The pooled effect sizes are therefore not directly comparable with service relevant reports on proportions of cases reaching *"recovery"* post-treatment, as a substantial proportion of trauma-exposed populations will still meet criteria for PTSD. However, remission rates of PTSD were not the focus of our review. It is likely that such figures would vary significantly depending on the treatment dose and service context.

**Implications and future research**

Compared to all other TF-CBT interventions and study populations, interventions for family violence, including IPV and affected family members, were rare. This most likely reflects the poor consensus over TF-CBT interventions for adults with PTSD with ongoing life threats. Theoretically, TF-CBT works by reducing avoidance of trauma reminders by confronting, processing and updating trauma memories with new information that inhibit previously learned fear responses.[38,41] However, this is a challenging goal to achieve in the context of ongoing threats even under intervals of safety. We excluded three RCTs, for instance, on CBT for PTSD among women in shelters with ongoing IPV ("*Helping to Overcome PTSD through Empowerment")*, as the studies choose to not address traumas directly due to concerns of re-traumatisation.[64-66] Given the sustained and intergenerational

nature of family violence and increased risk of PTSD,[16,40] there is a pressing need to evaluate TF-CBT for people with ongoing threats such as IPV to inform clinical guidance and optimise access to treatments. Preliminary evidence of RCTs supports the efficacy of TF-CBT against TAU for multiple-incident PTSD in people with ongoing threat, including terrorist attacks in Thailand,[91] active first responders and military personnel,[63,92] children with mothers in abusive relationships and other ongoing traumas.[93,94]

There is also a need to evaluate TF-CBT's efficacy for continuous sustained trauma exposure in people with serious mental health problems (e.g. psychosis), inpatient settings and forensic settings. People with severe mental health problems are at increased risk of traumatisation from admissions,[95] restraints, seclusions, or from witnessing others self-harming or from the experience of psychosis itself. [96] Despite this, we found only a handful of studies that evaluated mixed TF-CBT for people with serious mental health problems and repeated trauma.

Finally, we found that TF-CBT showed consistent efficacy across settings for diverse types of multiple-incident traumas, suggesting treatment effects can be replicated in different clinical settings. Most published TF-CBT protocols applied the same treatment approach to single-incident PTSD as in multiple-incidents related PTSD. Yet, in practice, “complex trauma” presentations can sometimes tempt significant protocol deviation favouring broader and more skill-based components, resulting in less focus on trauma processing.[97,98] Therefore, one significant challenge to the generalisability of TF-CBT’s efficacy is to ensure clinicians feel confident in applying TF-CBT protocols for multiple-incident PTSD symptoms with appropriate training provided (e.g. see Foa for an overview on TF-CBT dissemination challenges).[97] Further dismantling studies of TF-CBT protocols should evaluate the usefulness of multiple component protocols (e.g. stabilisation) and clinician experiences to current protocols when focusing on multiple-incidents PTSD,[67] to examine if treatment delivery can be optimised further.

## Conclusions

This is the largest meta-analysis to investigate the treatment effects for TF-CBT interventions for multiple-incident PTSD, involving over 11,000 individuals across 45 countries. Despite the large between-study heterogeneity, the consistent results highlight that TF-CBT provide large effects for reducing PTSD symptoms in multi-incident exposed populations, relative to TAU. Given the consistent recommendations for improved TF-CBT approaches to multiple-incident trauma,[99] our findings underscore the importance of offering commonly available TF-CBT approaches for high-risk groups across the life course. However, estimates varied depending on TF-CBT type and outcome, with substantial heterogeneity.

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Drafting of the manuscript: All authors
Acquisition, analysis, or interpretation of data: All authors
Statistical analyses: Shabeer Syed
Critical revision of the manuscript for important intellectual content: All authors
Study supervision: Paul Salkovskis
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**Declarations of interest**
All authors have completed the ICMJE uniform disclosure form (www.icmje.org/coi_disclosure.pdf) and declare no competing interests.

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**Service improvement project**

# Predicting length of stays, delayed discharges and readmissions in adult psychiatric inpatient units in one NHS trust: a mixed-methods study

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**Doctoral student**
Shabeer Syed,[1] Trainee Clinical Psychologist
shabeer.syed@hmc.ox.ac.uk/shabeer.syed@oxfordhealth.nhs.uk

**Supervisor**
Prof Paul Salkovskis,[1] Professor of Clinical Psychology
paul.salkovskis@hmc.ox.ac.uk/paul.salkovskis@oxfordhealth.nhs.uk

**Co-authors (Oxford Health oversight)**
Angela Bird, Patient Flow Transformation lead[2]
Catherine Sage, Head of Service, Adult Mental Health Urgent Care and Social Care [3]
Dr Rob Bale, Clinical Director and Consultant Psychatrist[2]

**Co-authors (additional collaborators)**
Samantha Walden, Data Analyst
Suzanne Fisher, CRIS Academic Support and Information Analyst

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**Affiliations**

[1] Oxford Institute of Clinical Psychology Training and Research, University of Oxford and Oxford Health NHS Foundation Trust, Warneford Hospital, Headington, Oxford, OX3 7JX.

[2]Adult Directorate Management Team, Oxford Health NHS Foundation Trust

[3] Mental Health Urgent Care and Social Care, Oxfordshire BSW Mental Health Directorate, Oxford Health NHS Foundation Trust

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**Abstract**

**Background:** Despite repeated NHS initiatives to reduce the length of stays (LOS) of adult acute psychiatric admissions in England, the factors influencing LOS and delayed discharges are poorly understood.

**Aims:** To identify and estimate key factors that may influence LOS and delayed discharges among adult psychiatric admissions in one NHS trust using a mixed-method design of staff interviews and risk prediction models.

**Methods:** In phase one, we thematically analysed data from 17 semi-structured interviews with inpatient staff, focusing on barriers and facilitators influencing LOS. In phase two, we analysed data on 5351 acute admissions (aged 18-65 years old) from 7 adult psychiatric inpatient units in one NHS trust covering two counties (2015-2021) using adjusted multivariable regression models. The primary outcome was locally defined delayed discharges (LOS >56 days). Secondary outcomes included adjusted mean differences in LOS and readmissions within one year of discharge.

**Results:** In phase one, consistently identified barriers included a need for inpatient social workers, increased recognition of discharge barriers with shared responsibility between professions to overcome barriers, difficulties in forming consensus within clinical teams about discharge criteria for patients with complex needs, and more effective information sharing systems with community services and placement providers. Consistently reported facilitators for reducing LOS included improved gatekeeping criteria and goals upon admission with clearly assigned staff roles, and improved communication with services outside the hospital.

In phase two, the adjusted mean LOS of adult acute admissions between 2016 and 2021 was 58.4 days (95 % CI 50.9 days-65.5 days), or 54.2 days (95% CI 44.5 days-63.9 days) excluding the psychiatric intensive care unit. Of these, 27.4% (1476/5351; 95% CI 24.4%-30.4%) had a LOS above 56 days and the national average. The strongest predictors of delayed discharges

and one-year readmissions were positive COVID-19 tests, older age, black ethnicity, homelessness, a diagnosis of bipolar or psychosis (affective manic type), and patients with risk concerns of self-neglect, non-compliance with care and aggression. Faster allocation of care coordinators upon admission and admission to a ward with lower bed capacity (e.g. higher bed occupancy) were associated with significantly lower LOS and reduced delays.

**Interpretation:** In this study of one NHS Trust, only one in four adult psychiatric admissions had a LOS above the national average of 51 days for adult mental health admissions. This performance could likely be further improved by early identification of homeless patients, faster allocation of care coordinators, and increased support to make risk positive discharge decisions of patients with complex needs. Interactive risk prediction models, key findings and trust specific recommendations are provided at the end (see executive summary) and available online (https://ohft.github.io/lengthofstay/).

**Box 1. Lay summary**

Most hospital admissions for people with mental health problems are short-term interventions to help people stay safe during a mental health crisis. However, sometimes people end up staying longer in hospitals than needed, which can cause problems for the person and is linked to increased healthcare costs. There are, however, very few UK studies that investigate factors that are linked to longer hospital stays and delayed discharges. Most studies have looked at broader general characteristics and provided limited information to improve services. We aimed to identify factors linked to longer hospital stays and delayed discharges among adult mental health admissions in one NHS trust.

We first conducted staff interviews and analysed common themes. All staff we interviewed saw delayed discharges as a large problem in the Trust. Most staff reported difficulties with finding placements, lack of community resources and inpatient social workers, and challenges with agreeing on a shared responsibility over addressing discharge barriers. Staff identified several solutions to reduce delays, including: weekly active tracking of patients and discharge barriers to meet targets of discharge dates, actively screening patients for rehabilitation; proactive attitudes, and the need for increased community recovery pathways.

We then used routinely recorded and non-identifiable clinical records to analyse common factors contributing to longer stays and potential delays. The largest proportion of longer hospital stays occurred among patients with higher underlying needs, including patients with COVID-19, patients of black ethnicity, homeless patients and patients with risk concerns of self-neglect. The risk for readmission within one-year after discharge was also high within these patient groups. The strongest factors linked to reduced delays included faster allocation of care coordinators upon admission and higher bed occupancy. We hope findings will help improve the prioritisation of resources and support discharge planning.

## Introduction

Since the closure of the large asylums in the 1970s, acute psychiatric inpatient care in the UK has mainly focused on crisis response and stabilisation.[1] In the past, larger asylums and hospitals cared for a substantial numbers of patients who stayed in the hospital for years or even decades.[1,2] As policy shifted towards reducing institutionalisation and hospital use, services substantially reduced bed numbers, thus increasing pressure to reduce lengths of stay (LOS), favouring longer-term care in the community.[3] Whilst there has been consensus on the value of this approach, reducing LOS has not always been successful. Patients sometimes still end up staying for considerably longer than intended,[4] placing patients at higher risk of physical and psychological harm.[5] Psychiatric community services have faced significant challenges in meeting the complex needs of people who previously received longer-term inpatient care, with increased use of longer-term out of area placements.[6,7] At the same time, studies suggest hospitals managed the reduced bed numbers by increasing their thresholds for admission and decreasing the threshold for discharge.[8] Of particular note are reports which show no significant reduction in LOS for psychiatric admissions in England for the past 15-years.[8] This could be due to the current levels being optimal, or alternatively that there are systemic problems preventing further progress.

Whilst NHS trusts are monitored on different LOS metrics by different organisations (appendix B3),[9] there are currently no agreed definitions over what constitutes a longer LOS. Legally, the Mental Health Act 1983 of England and Wales (*Section 2*) defines a "short stay" in hospitals as less than 28 days (an arbitrary cut-off). Other LOS measures include delayed transfers of care (DTOC) which refers to patients occupying a bed after being deemed medically fit for discharge.[10] Oxford Health Foundation Trust (OHFT) has reported challenges in this respect. Oxfordshire as a whole is ranked eight of the ten bottom Local Authorities for the number of DTOCs days.[11,12] DTOCs can, however, only be classified once a patient is ready to leave the hospital and *"DTOC days"* do not refer to individual delays, and a smaller proportion of patients can contribute to larger proportion of DTOC days. DTOCs are heavily

influenced by external factors (e.g. waiting for social care). They do not reflect longer LOS due to internal factors (e.g. discharge decisions).[11,12] Trusts will still have a high proportion of patients who are delayed due to internal factors and stay longer than needed, but such data is not nationally reported.

In 2019, the NHS Long Term Plan set targets for all NHS trusts to reduce their average LOS of acute inpatient admissions to 32 days by 2024 (national average LOS: 47-51 days ),[13] but did not indicate how the reductions could be achieved. LOS is a complex outcome and underpinned by multiple internal and external factors that influence discharge decisions. One way of understanding LOS is, therefore, to consider the discharge decision-making process itself. Decisions are almost invariably based on subjective judgements and often driven by individuals applying various implicit criteria.[14] Such decisions are cognitively demanding tasks and subject to the views of the discharge decision-maker.[14-19] To make faster decisions, clinicians may rely on heuristics (i.e. "mental shortcuts") or intuitive rules for decision making.[20,21] According to prospect theory,[22,23] there are two main mental heuristics*: (a)* the *availability heuristic* (i.e. paying more attention to more easily recalled information), and *(b)* the *representativeness* heuristic (i.e. the similarity between the current decision and previous cases – *"I have seen this before"*). Clinicians who experience repeated risk escalations (e.g. suicide attempts) or re-admissions following early discharge may opt for more risk aversive decisions resulting in longer LOS.[24] However, a clinician with several recent positive discharge experiences may be prone to positive risk-taking and discharge the same patient earlier.[25] Heuristics are automatic and faster than conscious analytic thinking. They are influenced both by external factors outside the clinician's control (e.g. socioeconomic factors),[17,26] and internal modifiable factors within the clinician's control (e.g. challenging one's own decisions regarding discharge suitability). The best way to minimise the inappropriate application of such heuristics is to provide discharge decision-makers with evidence on key factors that influence LOS to guide less subjective discharge decisions.

Whilst older RCTs (1969-1980) are generally consistent with the assumption that there is an association between shorter LOS and improved patient outcomes (see Cochrane review on six RCTs),[27] few studies have examined specific factors that are associated with reduced LOS. UK studies on predictors of LOS are limited to small sample sizes (e.g. n=106), shorter periods (1-month),[28] or broader general non-modifiable factors (e.g. age, sex, ethnicity) with limited relevance to service intervention.[29] Meta-analyses of larger cohort studies have tended to focus on reducing readmissions,[30-32] rather than reducing unnecessarily prolonged LOS. A recent scoping review on 66 publications found various patient flow improvement tools for reducing DTOCs,[33] including improved discharge planning, tracking delays ("*Red2Green"*), case reviews and multiagency meetings.[33-36] However, the review found no study relevant to mental health, nor evidence on factors that may minimise delays and reduce LOS in adult acute psychiatric care.

The present two-phase study aimed to estimate longer LOS (including DTOCs) and examine risk factors influencing excessive LOS and readmissions across eight acute adult inpatient units in one NHS trust. First, we use qualitative semi-structured interviews to gain staff views on factors influencing discharge decisions and delays. In the second phase, we investigate risk and modifiable factors (as informed by the first phase) associated with delays, readmissions and LOS in a population-based cohort study of all adult psychiatric between 2015 and 2021. Accurate probabilistic predictions of who is likely to be delayed and how long they will be delayed will allow for timelier prioritisation of discharge planning and transitional care packages (e.g. community/social care liaison), decreasing chances of delays.

## Methods

### Design

This mixed-methods study involves two phases: (1) qualitative semi-structured interviews with key discharge decision-makers from the trust's nine adult psychiatric inpatient units,

(2) prevalence estimates and characteristics of delays in the trust, and risk prediction models of potential delays, LOS and readmissions.

**Data sources**

OHFT is the leading care provider for mental health across Oxfordshire and Buckinghamshire, England, covering a population of 1.2 million. The counties contain, on average, a slightly higher proportion of more affluent populations than the national average. The trust has eight acute units (including one psychiatric intensive care unit) and one rehabilitation unit for adult mental health patients. The units comprise 123 beds and 215 employed non-medical staff with one primary consultant psychiatrist per unit. Five units are in Oxfordshire, and three units are in Buckinghamshire (including the rehabilitation unit). The rehabilitation unit is mainly available to patients in Buckinghamshire.

***Phase one: participants for qualitative interviews.*** In purposive sampling, we defined key discharge decision-makers as the legally responsible inpatient consultant and the staff whose role focuses on coordinating admission, discharge/transfers, or inpatient staff regarding themselves as key decision-makers. We invited all consultant psychiatrists, modern matrons, and connected social workers for individual semi-structured interviews. The patient flow team had previously tried focus groups but with limited recruitment success. We recruited staff via direct emails and phone calls. Senior management and participating staff were encouraged to ask others to participate and improve response rates.

We adapted an interview schedule from a previous relevant study,[37,38] with modifications to cover items from the NICE and RCPsych guidelines of inpatient discharge standards (e.g. decision-making, barriers, facilitators, transitions; details of the structured interview can be found in appendix B2). The interview schedule was piloted with one Consultant Psychiatrist and one Trainee Clinical Psychologist and modified following feedback.

***Phase two: population-based cohort study.*** Table 1 provides an overview of definitions and data sources for outcomes, predictors and LOS calculations. Appendix eTables B3-B4 provide further information about relevant LOS metrics by different monitoring

organisations. We derived a population-based cohort of all psychiatric adult admissions in the trust (2015/01/01-26/06/2021) using anonymised electronic health records (EHRs). We extracted EHRs from the local Clinical Record Interactive Search (CRIS) system and the Hospital Episode Statistics Admitted Patient Care (HES-APC).[39] CRIS is directly linked to Oxford Health NHS Foundation Trust clinical records systems representing data for all patients in the trust. CRIS enables the extraction of most clinically entered data (anonymised), including individual-level treatment data, admission details, demographics, and mental diagnoses entered by treating clinicians using the International Classification of Diseases 10th revision (ICD-10).

HES-APC includes all hospital admission data in the trust as supplied to NHS England for billing purposes.[39] To minimise missing data, we combined CRIS and HES-APC data by data linkage using local unique patient identifiers and episode IDs, with a 99.9% match rate (Figure 1). We used patients postcodes to link Index of Multiple Deprivation 2019 data (IMD; https://imd-by-postcode.opendatacommunities.org/imd/2019).[40] The IMD is the official national metric for social deprivation, made up of a composite score of a patient's small area level deprivation derived from multiple metrics (e.g. income, employment status, crime levels etc). The IMD score can be classified into five quantiles ranging from the most deprived to the least deprived (1-5 quantiles).

We included admissions from seven adult acute wards, including one psychiatric intensive care unit (PICU). We excluded children and adolescents, older adults, rehabilitation-related and forensic admissions.

**Table 1.** Key definitions, candidate predictors and data sources

| Variable | Description or definition | Data sources |
|---|---|---|
| **Outcomes** | | |
| Length of stay (LOS) | Length of stay is calculated as the number of days between the admission start date (episode start) and the hospital spell end date (referred to as one admission) [48]. A provider spell starts when a decision has been made to admit the patient, and a consultant has taken responsibility for their care. The spell ends when the patient is transferred to another hospital, dies or is discharged. | HES-APC, CRIS |
| *Episodes and spells (admissions)* | An admission was defined as one hospital spell (combined episodes). As shown below, an episode is a single period of care under one consultant. The treatment of one patient in one hospital by one consultant is an example of an episode. A spell can contain one or several episodes (see example below). In general, a patient's entire stay in hospital (admission) is a spell, which is usually only one episode.<br>Admission to unit (start date) → Discharge from unit (end date)<br>Episode 1 (consultant A) \| Episode 2 (consultant B) \| Episode 3 (consultant C) | HES-APC, CRIS |
| Locally defined delayed discharge (LOS >56 days) | An LOS longer than 56 days, calculated as above. The 56 days cut-off is the NHS trust's benchmark to monitor potential delays, as there are currently no nationally defined cut-offs to define delays. See eTable 1 for other relevant LOS monitoring metrics by different organisations. | HES-APC, CRIS |
| Readmission within 1-year post-discharge | The length of time taken to a readmission within 1-year post-discharge. Calculated as the number of days between the first discharge date up to the first next admission date within 1-year, the study end date (2021-05-31) or 1-year mark (365 days) post-discharge, or whichever came first. | HES-APC, CRIS |
| Delayed transfer of care/discharge (DTOC) | Patients who are deemed medically fit for discharge (or transfer) but who is still occupying a bed due to non-clinical reasons. NHS trusts are required to supply monthly DTOC data to NHS England, including start date and end dates of delays. However, reliable collection of individual-level data has not yet been achieved, and the small number of observations in the OHFT trust precluded any reliable analysis in the current study. NHS trusts provide separate summary statistics (i.e. simple counts) to NHS England Monthly SitRep (MSitDT), which is most commonly used in reports. | MHSDS |
| **Candidate predictors** | | |
| Demographics | Age groups: 18-65 years old or age <50 years old (yes/no)<br>Gender: being male (yes/no)<br>Ethnicity per ONS five summary classification [49]: Black (yes/no); control group: White, Asian, Mixed, or Other | CRIS, HES-APC |
| Deprivation | Index of multiple deprivation 2019 (IMD): official ONS composite variable based on metrics of patient's postcode. IMD is divided into five quantiles ranging from most deprived (combined 1-2 quantile) to 3-5 (Most affluent; control group)<br>Homeless (no fixed abode): as recorded 1-year within the admission (yes/no) | IMD, CRIS |
| COVID-19 test positive | PCR positive confirmed test of COVID-19 as recorded during admission | CRIS |
| Seven adult acute inpatient units (A, B, C, D [PICU], E, F, G) | The trust has three female-only inpatient units, three male-only inpatient units, and one mixed-gender psychiatric intensive care unit (PICU). Two inpatient units are located in another local authority with slight differences in social care provision and discharge procedures. In sensitivity analyses, we also include data from an additional rehabilitation unit (totalling 8 units). However, the rehabilitation unit was excluded from the main analyses due to differences in treatment aims (non-acute). The PICU was included in the main analysis, as the LOS did not significantly differ from the other inpatient units and to aid with comparisons of national estimates (which includes PICU's). All analyses account for potential clustering effects by inpatient units. | CRIS, HES-APC |
| Number of previous admissions | Number of previous admissions in the study period, ranging from 0 (none/first admission) to 1, 2 or ≥3 previous admissions | CRIS, HES-APC |
| Ward capacity (% occupied beds; proxy for ward stress/business) | The number of bed days occupied per month divided by the number of bed days available in a month. E.g. For October, one inpatient unit has 20 beds, and there are 31 days in the month (20 beds x31 days)=620 days available. If the same unit was occupied for 520 days, this would result in 83.9% occupancy level (i.e. 520/620 days) or 16.1% capacity. RCPsych recommends inpatients units to maintain an 85% bed occupancy level for efficiency. | CRIS |
| Planned discharge date present (yes/no) | The inpatient consultant sets a planned discharge date or expected dates of discharge (EDD) during admission. EDDs indicate the estimated LOS required to achieve a *"minimum physiological, therapeutic and functional level"(NHS, 2021)* for a patient to be discharged. | CRIS, HES-APC |

| | | |
|---|---|---|
| | EDDs should be set no later than the first consultant post-take ward round. Given that eligible recorded eligible discharge dates were rare (present in 36.5% of admissions), we used the presence of a planned discharge date as a candidate predictor of delays (yes/no). | |
| Risk assessment (Trust specific) | Trust specific risk assessment involving 18 different risk items with three response options per item (risk identified, no risk identified, or unable to assess) and additional free-text fields. We created a summary score by totalling the number of items identified as a risk (ticked "yes"), with a maximum score of 14. See supplementary eTable 2 for descriptions of individual risk items. We did not use free-text data. | CRIS |
| Ward level observation | Ward level of observation is a categorical variable for the required staff monitoring during a patient's admission: 1. General Observation, 2. Intermittent Observation, 3. Within Eyesight, 4. Within Arm's Length. We collapsed 3 and 4 into one category (3-4), owing to the rarity of admissions requiring level "4" observations. | CRIS |
| Admission type | Emergency or planned admission | CRIS, HES-APC |
| Care coordinator assigned within 2-weeks | The number of weeks until a care coordinator was assigned. Time was measured in relation to the admission start date. We extracted data on professional roles linked to each admission. Care-coordinator roles lasting less than 2 days were classified as "none". | CRIS |
| Section 117 After Care | Section 117 After Care can be provided under specific conditions to ensure support services in the community following discharge from the hospital to avoid future admissions. We obtained all issued Section 117 for discharges (yes/no) with start dates. We did not include time spent on section 117 in the overall LOS. | CRIS |
| Primary diagnosis of mental health problem on admission | Primary ICD-10 classification of mental health problems entered on admission or a previous admission. A patient can have multiple secondary diagnoses on admission. For conflicting values between CRIS and HES-APC, we prioritised the most recent consultant entered diagnosis in CRIS. | CRIS, HES-APC |
| Any mental health problem during the study period | For categories labelled "Any", we included any diagnoses ever recorded for neurodevelopmental conditions and learning disabilities, and separately substance misuse if recorded within 2-years of admission. | CRIS, HES-APC |

**Outcomes**

There is currently no agreed national definition over what constitutes an excessive hospital stay (appendix B3). The primary outcome was a potential delayed discharge defined as an admission length longer than 56 days (table 1). The trust uses this outcome as a benchmark to monitor potential delays, as there are currently no nationally defined cut-offs for LOS to define delays. The 56 days cut-off corresponds to a mean LOS of 5 days above the national average for adult psychiatric care (47-51 days, appendix B4).[41] Secondary outcomes included the mean difference in LOS for each predictor and time-to-readmission (number of days) within one year-post discharge. We selected a one-year follow-up for readmissions, consistent with the lengths of follow-up in meta-analyses and reviews of studies on readmissions.[30,31] We did not use officially reported DTOCs as outcomes, given the small number of eligible observations (n=39).

**Candidate predictors**

All candidate predictors are shown in Table 1. We identified a reduced number of candidate predictors from the qualitative phase, NHS England's checklist for discharge

barriers, previous systematic reviews and Vincent et al.'s framework (appendix B7) on contributory factors influencing LOS in acute psychiatric care.[16,30,35,42-47]

**Data analyses**

***Thematic analyses***. Interviews were audio-recorded on a secure encrypted NHS trust device, and transferred to an encrypted NHS computer for *on-disk* management. Audio recordings were automatically processed to remove *"white noise",* followed by speech volume levelling and spectral de-noise algorithms (Adobe Audition CC 2021).

We used Dragon Anywhere (Nuance, v15) for automatic verbatim transcription, manually cross-checked and corrected for inaccuracies by the first author (S.S). The first author (S.S) is a doctoral clinical psychology student who undertook a clinical placement in the NHS Trust's CAMHS inpatient unit (Highfield) during the start of this project, with a research background in psychiatric epidemiology. We used Nvivo Pro (v 12) to manually analyse transcripts broadly based on the Braun and Clarke's six steps for thematic analyses.[50] We made several modifications to Braun and Clarke's approach to help contextualise the findings and increase the report's readability for the commissioning service. We also employed a less reflexive approach than recommended by Braun and Clarke. First, two researchers (S.S & R.A) independently coded all data and identified semantic themes at a non-interpretative level. Second, Researchers met to discuss and resolve inconsistencies. The final themes and supporting quotes were reviewed by a third researcher (P.S) for general refinements. Finally, we included frequency counts of themes to help commissioners gauge potential consistency of themes across interviewed staff. We broadly mapped themes to three stages of patient flow for acute admissions (pre-admission, treatment, discharge). Participants did not provide feedback on the analysis. One interviewed consultant (R.B) was invited as a co-author following the completion of the qualitative phase to support the remaining work.

***Descriptive statistics, prevalences and means.*** Detailed statistical methods are provided in the appendix B6 (eMethods). Briefly, we calculated adjusted average LOS using marginal prediction estimates from generalised linear regression models.[51,52] We computed adjusted

overall and annual period prevalences of delayed discharges using marginal predictions from logistic regression models. We used Poisson regression models to examine trends of delayed discharges over time, with differences between admission years expressed as incidence ratios. For all models, we accounted for clustering effects from specific hospitals by including the hospital ID as a cluster variable in the calculation of robust standard errors (SE) based on the sandwich estimator. When applicable, we adjusted models for sex, admission year, and age groups to account for uneven distributions (e.g. single sex inpatient units).

***Risk prediction model.*** We fitted individual and multivariable logistic regression models to identify risk and modifiable factors associated with potential delayed discharges (LOS >56 days). To identify the most statistically significant predictors, we estimated individual predictors relative effects of delays using 10-fold cross-validated penalised regularised logistic regression models. We applied the least absolute shrinkage selection operator (LASSO) for variable selection.[53] The smallest derived lambda from the cross-validated model were used to select a cut-off for inclusion (i.e. the smallest value for which all coefficients are zero/not important).

We used separate Cox-proportional hazard models to examine the association between predictor variables and time to readmission within 1-year post-discharge. Where possible, we adjusted all models for age, sex, admission year and hospital of discharge for potential clustering effects as described above.[54]

***Missing data.*** We assumed data were missing at random and imputed missing data in R with the MICE package, with 20 imputations and 20 iterations. We pooled estimates using Rubin's rule fitted separately for each analysis.[55] We considered all tests as two-tailed and p-values less than 0.05 as statistically significant. We completed all analyses using Stata 17 and R (version 4.1.1) with the tidyverse, mice, epitable, lsmeans, glmnet and survival packages (complete list: github.com/shabeer-syed).

***Governance***. Study approval was granted as a priority service improvement project by the NHS trust's quality improvement clinical audit team. We did not require ethical approval for staff interviews or for analysing local anonymised patient data from HES-APC and CRIS owned by the NHS trust.[56]

## Results

### Phase 1: Staff interviews

Figure 1 provides a flow chart of the staff interview recruitment. In total, 8 consultants, 7 social workers, 1 modern matron and 1 senior nurse were interviewed, representing 17 staff involved in discharge decisions across all adult psychiatric inpatients units between May 2021 and July 2021 (2 consultants declined, response rate: 78%). We found no new emerging themes after ten participants. We completed the remaining scheduled interviews for confirmation. We identified five overall themes of interlinked factors contributing to longer LOS and delayed discharges, with sub-themes categorised into discharge barriers and facilitators (Figure 2; Tables 2-3). Illustrative case examples of delayed discharges from interviews and case note reviews are provided in appendix B8.

**Figure 1**. Participant recruitment semi-structured interviews

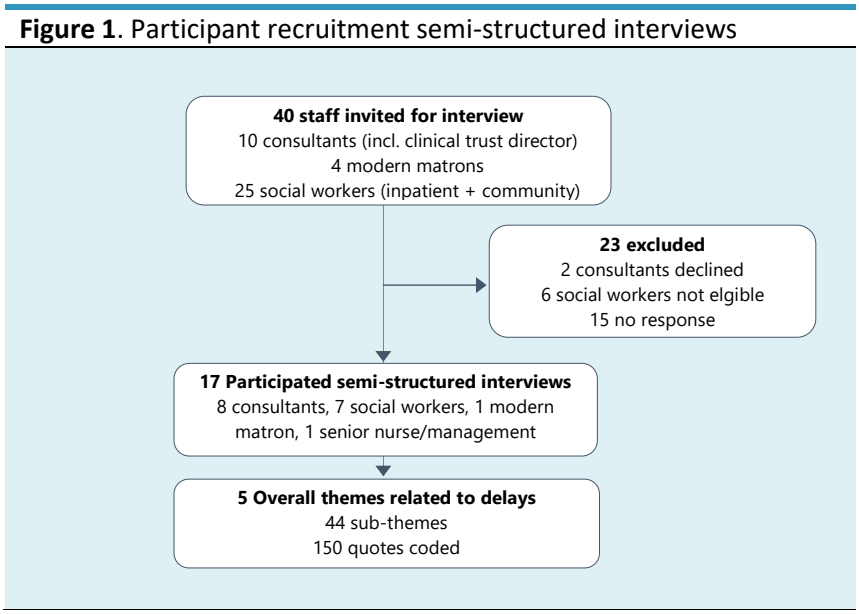
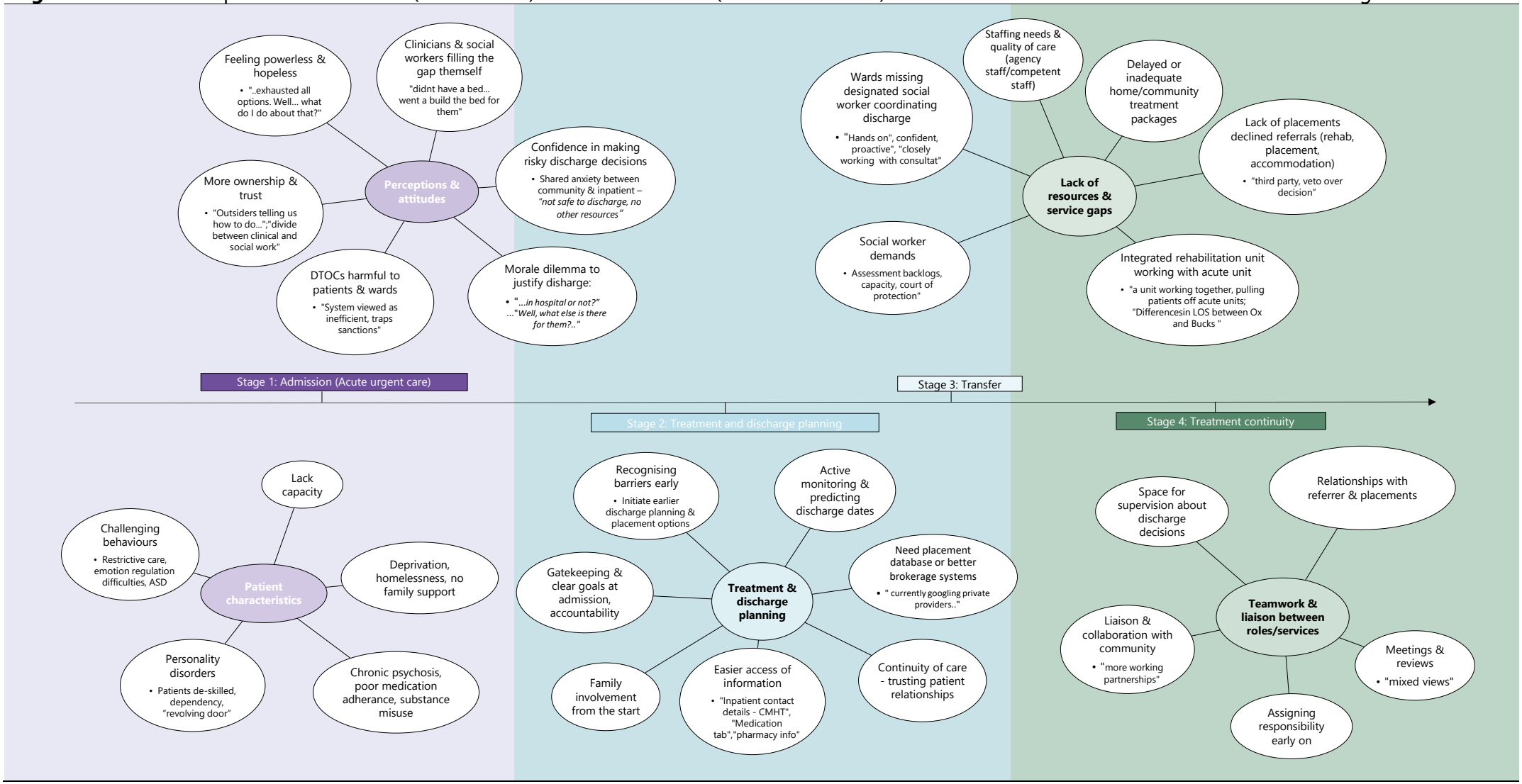


**Figure 2.** Thematic map of the five themes (centre circle) and 18 subthemes (connected circles) for staff views on barriers and facilitators of discharge



**Theme 1-2: Resource needs and patient characteristics**

***Barriers: No available placements for patients with complex needs and hard to engage groups.*** A larger proportion of staff attributed barriers of earlier discharge to external systemic factors and a lack of resources. The most frequently endorsed external barrier was rejections from local placement providers. The most frequent internal barrier was missing a designated inpatient social worker to coordinate transfers. Seven consultants mentioned going longer periods without a specific inpatient social worker and community care coordinators. Delayed patients were often described as lacking capacity (with poor medication adherence), "chronically" psychotic, homeless, with comorbid substance misuse and unable to obtain housing or suitable care packages. COVID-19 particularly impacted this patient group, and staff reported seeing an influx of homeless people being admitted. The reason suggested for this was loneliness and reduced community care, as government restrictions had frozen many face-to-face care relationships provided by the community teams (e.g. care coordinators visits etc.).

Notably, the NHS trust also went through organisational changes during the study period that may have contributed to many endorsed external barriers. Examples include an increase in significant hospital incidents during 2015, changes in the Trust directorate in 2018, changes in ward consultants and other key staff, community investments and increased vacancy factors.

***Internal facilitators.*** There was a high variation in suggested solutions. Frequently endorsed internal facilitators included early recognition of discharge barriers (e.g. housing issues). However, three consultants disagreed with the idea that patients were *"drifting"* on wards and felt active monitoring tools failed to address the root causes of delays such as lacking community resources. Instead, they emphasised the need for better databases to find suitable placements/discharge destinations. One consultant said, *"…literally, the social workers will just have to Google Rehab places and making referrals…"*. Three social workers and two consultants highlighted a positive impact from "tracking" patients via monitoring

(e.g. *Red2Green*). Staff reported "*tracking*" helped challenge their own decisions over patients discharge readiness and prioritise resources for potential delays. Social workers reported using the monitoring tool to identify potential discharge barriers to prioritise scarce staff resources and as a platform to share treatment progress. Consultants found weekly reviews and monitoring helpful to action and assign MDT responsibilities.

Many participants emphasised the need to prevent admissions or maintain treatment gains post-discharge rather than focusing on delayed discharges. Almost everyone endorsed the need for more placements, *"resourced"* home-treatment teams and emergency accommodations (e.g. for discharge transition).

**Themes 3-5: Staff attitudes and perceptions, treatment planning and teamwork to reduce longer LOS.**

***Barriers: Hopelessness, shared anxiety towards discharge ("safe uncertainty"), staff dynamics.*** Efforts to reduce delays were often accompanied by mixed feelings of anxiety and hopelessness towards reducing longer LOS. Time spent in meetings, reviews, or screening patients to reduce delays typically left staff feeling agitated and exhausted when not associated with a positive outcome (e.g. finding a placement). Four participants described situations where the hospital ended up as a "safe vehicle" to "dump" patients whilst finding alternative placements following placement breakdowns but then becoming stranded in hospitals.

Most staff reported that differences in views between professions and frameworks could sometimes fuel difficult dynamics on the wards and within linked services. Staff reported that these *"clashes"* could sometimes reduce collaboration and *"push back dynamics"* between the professions. The main endorsed differences between professions related to determining *"discharge readiness"* and treatment needs before discharge. From a clinical perspective, knowing patients had come from a previous placement breakdown or were a "readmission" often meant clinicians judged external factors more critical in determining a patient's discharge readiness (e.g. "where is the person discharged to"). The most preferred

discharge destination was a home treatment team with staff support, but this was often a scarce non-existing resource and short-term solution. Some clinicians also reported stepping back from discharge planning to maximise inpatient treatment, hoping to increase chances of placement acceptance by improving patients mental state (e.g. refined medication reviews/treatment plans).

From a social worker perspective, however, staff reflected that this pattern could result in discharge barriers being perceived as *"social care to-do lists"* that could not be achieved within their scarce resource market. Some social workers described the clinical team as sometimes wanting a *"perfect discharge"* with unrealistic expectations of what social care could achieve. Medical staff explained they at times felt pressured by social care stepping in questioning the validity of the clinical decisions, negatively impacting on perceived trust between professions.

***Facilitators.*** A frequently endorsed facilitator included having a proactive confident inpatient social worker in close working relationships with the clinical team to coordinate placements and complete assessments. The role often involved rapid assessments, balancing demands against a resource-scarce social care market (e.g. council, housing, placement providers etc.) and liaison with community services. Closer working with designated social workers also helped bring medical and social care professionals together, as they otherwise operated in different spaces. Both clinical and social care staff emphasised that these relationships need to be built on having a shared understanding of goals, increased collaborations, and trust that both parties were doing their best within the restrictions of their role (e.g. available resources). Similarly, community care coordinators reported the importance of flexibility and effective collaboration with the inpatient unit (staff/patients) and placement providers. Here, facilitators for collaboration included improved gatekeeping involving standardised consensus criteria and clear deliverables at admission for discharge, with hospital treatment aims that could not be better met by other services (e.g. housing, medication adherence). Other suggestions included increased

support for consultants and community workers in positive risk-taking of complex cases (e.g. housing issues, impending family complaints).

**Table 2.** Key themes of barriers and facilitators to minimise delays from 17 staff interviews

| Barriers | Facilitators |
|---|---|
| **Trust and organisational level** | |
| 14 Lack of appropriate placements, declined referrals (housing ,rehab, placements) - *"No one wants them, so we have to keep them"* | 9 Increase temporary transitional packages (e.g. emergency housing) & Oxford need integrated rehabilitation unit working with acute unit – *"Bucks Rehab ward pulling patients off acute"* |
| | 5 Continuity of care – pre-post admission patient relationships |
| 10 General inpatient and community staffing needs, lacking competence, no continuity of care (e.g. rotating agency staff) | 6 Predicting discharge dates communicated for community discharge planning: "Social care want to use money they still have left for people with the most need; community needs to know discharge date" |
| 8 Delayed or inadequate community treatment (e.g. no home treatment, medication care packages) | 6 Develop flexible placement relationships & working partnerships |
| 5 Lack of greater organisational understanding ("placement providers"): blocked fluidity=knock-on effects for everyone | 4 Agreeing on consensus standards and criteria for appropriate admission/discharge |
| **Ward and managerial level** | |
| 13 Missing inpatient social workers to coordinate transfer | 13 Allocate one minimum designated proactive care coordinator per ward (hands, confident, proactive) |
| 10 High social worker demands (community/inpatient) assessment backlogs | 13 Recognising discharge barriers early to prioritise lengthy processes (housing, placement, benefits, court of protection) |
| | 8 Gate keeping & clear deliverables at admission (X,Y achieved=discharge) |
| 4 Monitoring/meetings about potential DTOCs without positive outcomes; *"We're screening into the void… everyone knows"* | 6 Active monitoring/tracking & helps focus "ready for discharge" |
| | 2 Make reviews smarter – set weekly - cut-off – Automated populated fixed fields on Red2Green + optional columns for each ward |
| 5 Lacking placement database and brokerage systems - *"just googling it….. you know.. which are third party."* | 5 Collate current knowledge & build a "placement database" of previous successful placement details |
| **Professional level** | |
| 11 Shared anxieties between community and wards *"not safe to discharge"* – community overloaded vs. realistic expectations | 8 Shared goals understanding & multiagency meetings (balanced risk decisions) |
| | 5 Promoting attitudes towards mutual trust and leeway between inpatient and community |
| | 6 Take initiative for regular check-ins meetings |
| 7 No assigned responsibility – Avoidance - "No one wants it.. complexity=more work" | 7 Assigning responsibilities early on |
| 5 Miscommunication – No clear channel *"20-mins tasks that doesn't get through… can cause weeks delays"* | 4 Easier access of information and contact details of inpatient staff (ward manager, who's on shift); |
| | 1 Make a specific tab for medication reviews on carenote (reduce waste time) |
| 6 Feeling, powerless and hopeless – *"social workers exhausted all options…. what do I do about that?"* | 8 Ownership of improvement tools and power to change |
| | 4 Space for regular supervision & training |
| 5 External pressure - "Outsiders telling us" | 4 Challenge placement rejections |
| 5 Split between clinical and social work | 7 Clinicians and social workers proactively working flexibly in the same space – sharing responsibility, not adhering to strict criteria |
| **Patient characteristics (increasing risk of delays)** | |
| 10 Deprivation, homelessness, no family support | |
| 8 Psychosis + drug use + poor medication adherence | |
| 7 Patients de-skilled, dependency, "revolving door", personality disorder | |
| 5 Challenging behaviours, emotion regulation difficulties, ASD | |

Numbers for each row (n) shows how many times staff endorsed this theme according to thematic analysis.

**Table 3.** Key themes and illustrative quotes

**Lack of resources & Teamwork and liaison between roles and services**

| Barriers | | Facilitators | |
|---|---|---|---|
| Staffing needs and quality of care (agency staff/competent staff) | "...I mean writing a protocol, a "red2green" schedule, doing the reviews, or building an entire system - that's all right. But, if you haven't got enough staff with the skill set to deliver it, then no matter how good I am operationalising it, the rest of it is just never going to work...." — Consultant 1<br>"They say "Oh, get the care coordinator to do it". The care-coordinator don't have the skills nor the knowledge of the system to say... It's a highly specialist role and unless somebody is delivering on that, then you get amateurs doing it slowly and badly..."—Consultant 4 | Space for supervision & teaching | "I suppose a level of good supervisions is important. To be perfectly honest, whilst speaking now.. there wasn't anybody else to do it." — Social worker 1<br>"The first set of tools is having some effective clinical training and being trained adequately to do the job.... Secondly, to provide space for people to think about their decisions, and thirdly, to support people in making those decisions" — Consultant 1" |
| Lack of continuity of care | "...for instance.. it's about us having locum CPN's who rotate often they cannot develop a relationship with patients.. I have a patient now who lost their second care coordinator, which is probably one of the factors that led to their collapse." —Consultant 8 | Continuity of care - trusting patient relationships | "Yeah. I think that continuity is crucial. I would travel 1.5 hour to see them, and they wouldn't talk to me. So I'd be there for 10-15 mins, get a bit of a handover from staff and then drive back home...but that was probably necessary, because she remembers those appointments...That has been the foundation for us to work together to get to the point where we're discharging her to home." —Social worker 6<br>"And also, I think, historically, care coordinators thought "Oh brilliant, there are on [WARD NAME], I don't need to worry about them for a couple of years", because they're going to be there for ages. Whereas now the messages, you need to be involved all the way long, and we're proactively thinking about their discharge from the moment they get to us really.."<br>"...But when senior social workers get involved, and there are housing options available, things can move very quickly, you feel the difference..."—Participant 3<br>"...the care coordination is key, because some patients, you know, when you see who they're allocated, you're really pleased ,you think, "Oh brilliant, this is going to go well, they're going to be proactive, we're going to work together, they're going to be on the case". And then there's other people, you think "Oh, this is going to be..", and it's not trying to be personal. It's just some people's skill set is not there. |
| Wards missing designated social worker coordinating transfers | "We went through a year without a social worker, which is just awful, with people cross covering. But we've now got a ward social worker who works really hard..."—Participant 2<br>"I think also, social workers who are usually involved in this task. They have a very big caseload. Sometimes we don't have social workers. At the moment we don't have one. And we haven't for a while.." — Consultant 3 | Allocate one designated proactive care-coordinator (hands confident, proactive, challenging) | "I'll be linking in, I'll be challenging the decision if I think it needs to be challenged. If not... I would say "*that's a fair cuppa, we will look somewhere else.*" I think it needs that proactive kind of work..." —Social worker 4<br>"....because they rejected the person. So I was.. *"hang on a minute, why have you rejected him? Can we look at this and address it before you send out your rejection letter?* Okay, when we look at this, because some of this information is incorrect..." —Social worker 4 |
| Lack of placements, housing, declined referrals (rehab, placement, accommodation) | "You get a string of declined referrals from rehab units or specialist accommodations etc. Which are... you know, third party. But we can't find anywhere to take the patients, so we have to keep them..."—Consultant 2"<br>"That's parts of the issue... where they're referred to commissioned housing and turned away because they're saying they "*can't meet their needs, because they're too complex*"—Social worker 4 | Flexible placement relationships | "I think what tends to happen is... housing provider say's "*no, there's just lots of thresholds that needs to be met for us to accept them*", but what they're actually saying, "*we can't meet their needs*". But there still is these pressures for them to take them and they're kind of pushed into the corner. So I think there needs to be more collaborative working.."—Social worker 5<br>"Well, I've built up a good relationship with the housing providers over many months, they are flexible they understand the challenges, and that relationship has really improved over the past year, they are really willing to sit down and relook at things..."— Social worker 6 |
| Delayed or inadequate community treatment | "You have the option of using the crisis resolution and home treatment services as "a bridge", which is occasionally clinically a good solution, but often a very poor solution, because this is a short-term team, with changing staff, no overall care plan or resources..." —Consultant 2 | Integrated rehabilitation unit working with acute unit & transitional or maintained housing | "The reason we were able to take Oxford overflow was the brilliant service we got from the Rehab unit. So, they actively took, or came looking for people who were not acutely unwell but needed sorting out for discharge ..." —Consultant 6<br>"....we need services that are more robust in working with people to help them maintain tenancies rather than going in and out of services. I know there's been piloted a housing first mode, and I'm really excited about to see how that work." —Social worker 6 |
| Need placement database or better brokerage systems | "When the local response has been inappropriate... literally, the social workers will just have to Google it to find those Rehab places and making referrals... just from what they find on the internet." — Consultant 2 | Placement database or better brokerage systems | "We need a more structured resource for finding placements, a database, or intelligence system that helps us put our patients into the appropriate Rehab services." — Consultant 2<br>"...like I said, we haven't got any brokerage... there's no easy way to access the community of beds.... So that delays finding the appropriate accommodation" — Social worker 5 |
| Social worker demands & assessment backlogs | "...any delay in the last six months, it's largely been waiting for better lives assessments... being processed, and then funding agreed for either | Recognising discharge barriers to prioritise | "it's about identifying the barriers straightaway. As soon as that person has come in, making contact, checking *"where did you live before you came in? Are you homeless?"* as a recent example... the day that they were admitted, I |

| | | | |
|---|---|---|---|
| | supported living or a care package. I think the social workers are quite overloaded with all these assessments..." —Consultant 4 | | found out that the family were trying to give up their tenancy to make them yet again homeless. But because I've noticed it quite quickly, we managed to put to that on halt."—Social worker 2 |
| Monitoring & screening into the void without outcomes | "I think our DTOCs patients have been stuck on the ward, with full knowledge of everyone involved, and no amounts of monitoring that... will solve the problem.. You don't really need stopwatch on that, as long as you have some active MDT monitoring, weekly or fortnightly meeting where you talk about how close people are to step down towards discharging, then that's fine. It's a problem of doing something about them...without having 20 meetings to talk about that you don't know where they are going to be put...."—Consultant 2 | Active monitoring & predicting estimated discharge dates | "I think there is a place for working out or projecting how somebody is going to be, because very often is that *"they're back again, and they've done what they did four times previously, they're going to be in..."*—Consultant 2<br>"Using this tracking... we've massively reduced our length of stay, we hit our target early, we're below the national average now for length of stay. It really focused us a lot, and we have a weekly meeting where we go through every patient in detail with the social workers..."—Consultant 6<br>"...you can have all sorts of clever electronic wizardry to help you...But for me, it's about people continuing to ask the question, "why am I different? Why am I an outlier?" Why when we admit from exactly the same catchment area, why do I have twice as long the length of stay or whatever it might be. It varies all the time. And is about having that ongoing professional curiosity..."—Consultant 1 |
| **Treatment and discharge planning** | | | |
| Shared anxiety between community and wards "not safe to discharge" | "Because sometimes the people that get delayed get unrecognisably better while they wait. So, I'm a little bit... my line of "*do they need to be in hospital or not?*" I feel morally must be determined by "*Well, what else is there for them?*"... —consultant 6<br><br>"...lots of anxiety around discharge because of either escalation of violence or drug use, or whatever else it might be. It's also the issue of people being held because being refused housing as well, that's another big one. the community team and its consultant, but also the ward did share that anxiety. — Social worker 2<br><br>"....I suppose if you've got nervous community workers, and they feel that this person is not ready for discharge, and thinking it's going to increase my caseload more, and worried how we can manage it in the community.." — Social worker 3 | Gate keeping & clear deliverables at admission | "The community gets tired and exhausted and worried about risk, and patients are presenting to every bit of the system, and the whole world say "*they've got to be admitted!*". It's very hard for one alone inpatient team to say "*no*", and then to say after three or seven days, *"no, they need to be discharged now....* So, a set of expectations at admission, and clarity as to what needs to be achieved for that person to be ready for discharge. The people pushing the patient in at that point should be saying.. "*why they're coming in and what needs to be achieved for them to be able to be supported in the community*?" we need to be pragmatic, let's move onto to something that is deliverable..."—Consultant 1 |
| | | Shared goals understanding & multiagency meetings | "...We set up a meeting with everybody involved including the community consultant and the ward consultant, and we said "*this is an ongoing risk, we can't keep them admitted forever. However, we need to try and mitigate that risk [tried stabbing another resident] and how can we can manage it...* So we it was more that we worked together...". — Social worker 2<br>"...I did a lot of work with the inpatient team, also the community consultant to try and pull together an agreement about the risk and a shared understanding of the risks, and agreement that its justifiable to do this positive risk taking and discharged home rather than to a high support setting." — Social worker 4 |
| | | Family involvement from the start | "I suppose the carers support and support for families is really important, because some of our patients do either go back and live on their own with quite a bit of family support, or they go back to a family home. Yeah, so that's important. So psychoeducation, and also support" —Consultant 6 |
| Overloaded, lack of responsibility | "Nobody wants to assess capacity. So, it gets bounced about...we have arguments to and from who's going to do this capacity assessment. It delays it being done, then eventually it's done. But it could take up to 4-5 weeks sometimes... as we sometimes think when the case is complex a clinician should be doing it, because we're going to stand up in the court protection..."— Social worker 5 | Assigning responsibility | "...the things is that we have accountability... So yeah, we are just identifying *"This is what needs doing, has it been done? has it been completed? If it hasn't been completed, then, when is it going to be completed and who is going to complete it?* And just making people accountable for duties and roles..." —Modern matron 3<br>"I think there needs to be an identified person to take the lead and ensure things have been happening, and which means doesn't people just assume the wards doing this, and community are doing that." — Social worker 5 |
| Miscommunication | "....That's a really hard one. Because it's, it's not great. It's not great. We do have these joint emails. But like I say that has failed...."— Social worker 5 | Regular check ins meetings | "Yeah, I mean, the handovers in the mornings are really helpful... And then every week we have an inpatient social work meeting where we look at specifically the social care barriers, and then we raise it and flag it if there's any potential.." —Inpatient social worker 6 |
| Easier access of information | "So the chap over here, has about 1032 documents on his care notes!? And they've lived most of their life in other people's hospitals elsewhere in England, and as many of them have. So I think there's something about accessing the information we need to make swift decisions, that's about carenotes, and it's about an absence of pharmacist input..." —consultant 6 | Easier access of information | "....we do not have a medication "History tab", you must go through unbelievable numbers of notes.." —Consultant 6<br>"Yeah, the little things like knowing who to contact details not having to actually search or what's the phone number for this? Or who do I need to speak to, who's the unit manager, who's working today who, you know.." —Social worker 5 |
| **Perceptions and attitudes** | | | |
| Split between clinical and social work | "...there's a real conflict for us social workers working within a medical model, we could argue in lots of cases that the Mental Health Act is being used inappropriately to address people's social issues, as opposed to the mental health diagnosis...." —Social worker 5<br><br>"what I'm saying is the clinical staff on the unit is in agreement. And the cases where there's been a debate ...it's been with the social work side of the trust. I'm not even sure sometimes if they should step in, but they do, we | Mutual trust and leeway | "...So I think working in a respectful way with the units acknowledging the stresses they are under the difficulties that they face, then hopefully them understanding that I'm doing my very best to find solutions for the discharge and work with me in facilitating that process, rather than a sort of blinkered "she's well enough to leave now, what are you doing about it?!" which might be the case if they don't have trust that I'm doing what I can to make things happen as quickly as possible." —Social worker 6 |

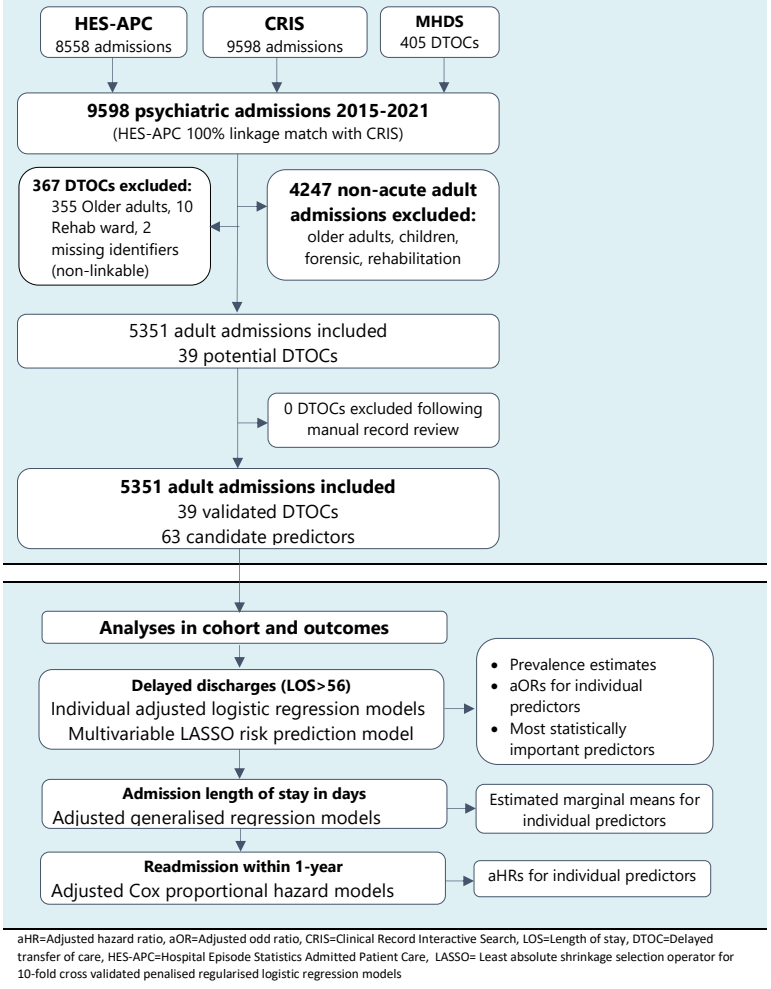
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|---|---|---|---|
| | can be put under massive pressure. We already know we need to get people out."—Consultant 6<br>"Interestingly, people very rarely mark people as "*Red*" they very rarely consider somebody doesn't need to be in hospital, no matter how long their length of stay. The *"barriers"* column became a bit of a "social work to do list". So it was interesting that the barrier never really sat with the rest of the clinical team… it became very much this is what the social workers need to do…." — Participant 3 | | |
| "Siloed thinking" – lack of understanding Fluidity blocked – knock on effects | "….a need for greater understanding, not this siloed thinking . So if you delay taking on this patient, who could be referred to your service, and you're doing it to protect your service, rather than fitting it in with an overall greater organisational need …you know, we're all NHS employees. And you should be working for the greater good, whereas some people seem to still think it's their five to fiefdom to do this… Now in some of these cases fluidity gets blocked. You have to go for a hike is power game, you have to be able to say, "if you don't do this", "I don't do this…"—Consultant 3 | Clinicians and social workers proactively working flexibly – work criteria | "They were a very hands on social worker, very bright, good clinician… The patient didn't have a bed. They'd been sleeping on the sofa without a freezer. They had a broken boiler, and there was mould on the walls…took quite a while to get people to come out and do it all… So instead, the care coordinator went and built their bed for them." —Consultant 6<br>"…strengths in Bucks was how proactive the consultants were, but it was based on a huge gap in the in the provision of other professionals. I mean, we were able to do it, but partly because we knew the system very well, but it shouldn't be like that." —Consultant 2<br>"..we do this on a one-by-one basis, but if there's people who just don't like their Depo much, and they community is trying to an avoid an admission, we often say *"bring them up to the assessment hub, we'll do it!"* All the nurses will go down to [Building], because they'll take it from the inpatient nurses that they trust." —Consultant 6 |
| Feeling, powerless and hopeless - exhausted all options | "…you can feel relatively powerless as a consultant in all of this.. because if you've got a patient that needs secure supported accommodation. And you know…I don't have a long list of those places, nor is it my job to find one. What am I going to do about it? And social workers tell me that they have exhausted a list of all options. Well… what do I do about that?" —Consultant 2<br>"…working on cases, you encountered the barriers, but you don't really have time or the power to do much about it, apart from thinking about how you might work differently on a case next time to see whether you can circumvent some barriers…"—Social worker 4 | Ownership of tools and power | "…we designed this ourselves. Whereas if somebody were talking to us about [another project] we were like… "*we don't really need it, we've got our own system".* But I think that's the difference, isn't it… And you would know, as a Psychologist?! when something being imposed from outside… versus something we've owned ourself. You can get all sorts of emails saying, *"you've got to do this.. and that*", and you don't even know why you're being asked to do it. Whereas with this, we make it work for us…"—Consultant 8 |
| **Patient characteristics** | | | |
| Deprivation, housing, lack of family support, language barriers | "…people are better treated at home with their own people. A lot of my patients have no family, no friends, or an elderly parent that can't begin to do it, or a sister somewhere… you could have somebody at home that's quite ill, if there is day-care and if they can access the psychotherapy and somewhere for them to go… Because for some of my patients, they're so lonely and they're left alone literally with the voices." —Consultant 6 | | |
| Psychosis + drug use | "The most common ones, I think, are the chronically psychotic patient who can't be placed anywhere because of their risk"—Consultant 1<br>"And then there are people on the other end of that spectrum, who may or may not have a psychotic illness, or probably have had, but have a bit of poly substance misuse thrown in and criminality, and they have lost all of their housing rights. And then they're trying to get anyone to agree housing is near end of impossible."—Consultant 2 | | |
| Patients de-skilled, dependency, "revolving door", personality disorder | "Personality disorder patients, who shouldn't really be admitted in first place, certainly not for long periods of time. And then, by the time they've been in hospital for long periods of time, they're so risky to themselves, and so de-skilled, institutionalised…that nowhere else will take them. But, you can't discharge them somewhere independent because they can't cope anymore."—Consultant 1<br>"…then immediately that individual becomes in the sick role, and they relinquish all responsibility for managing their mental illness, and actually within as a social work team tasked with finding this individual suitable accommodation, and the toeing and throwing, and the lack of family support it's never ending.." —Social worker 6 | | |
| Challenging behaviour, emotion regulation difficulties, ASD | "…challenge for us, is when we're presented with those challenging behaviours, and they're always the ones that there are arguments about…complaints from families about…And it's usually because the clinicians will all say its "all right", but the outside world can't make sense of "how on earth you can discharge somebody who's constantly trying to harm themselves".. Well that's cause we cant treat it in this setting, you make them worse, basically"—Consultant 2 | | |

## Phase 2: Cohort study on adult acute psychiatric admissions

### Cohort characteristics

Table 4 and Figure 3 shows the key characteristics of the included acute adult psychiatric admissions between January 2015 and April 2021. We included all 5351 working age adult admissions (median age, 39 years [interquartile range: 28-51; range, 15-93 years]; 49.7% female; Table 1). The most common primary diagnoses for admission were any form of psychosis (2105, 39.3%), bipolar (834, 15.6%) and personality disorders (720, 13.5%). The most frequent health comorbidities were diabetes, asthma, and hypertension. Six patients died, and 32 patients tested positive for COVID-19 whilst in the hospital during the study period.

**Figure 3**. Development of cohort study for adult acute psychiatric admissions between 2015 and 2021




aHR=Adjusted hazard ratio, aOR=Adjusted odd ratio, CRIS=Clinical Record Interactive Search, LOS=Length of stay, DTOC=Delayed transfer of care, HES-APC=Hospital Episode Statistics Admitted Patient Care, LASSO= Least absolute shrinkage selection operator for 10-fold cross validated penalised regularised logistic regression models

**Table 4.** Cohort characteristics of adult acute psychiatric admissions (2015-2021) by length of stay (LOS)in days

| | Overall, n=5351 | LOS in days | | | | |
|---|---|---|---|---|---|---|
| | | 1-7 days, n=1151 (21.5%) | 8-32 days, n=2056 (38.4%) | 33-55 days, n=668 (12.5%) | 56-90 days, n=471 (8.8%) | >90 days, n=1005, (18.8%) |
| **Length of stay days Mean (SD)** | 65.3 (136) | 3.83 (2.03) | 18.5 (7.07) | 43.0 (7.05) | 71.4 (9.82) | 243 (240) |
| **Length of stay days (range)** | 25.0 (1-2030) | 4.0 | 18.0 | 42.0 | 69.0 | 164 |
| **Readmission within 1-years** | 845 (15.8) | 186 (16.2) | 276 (13.4) | 120 (18.0) | 79 (16.8) | 184 (18.3) |
| **Time difference, estimated discharge date and actual discharge** | | | | | | |
| <1 month | 874 (16.3) | 242 (21.0) | 502 (24.4) | 35 (5.2) | 28 (5.9) | 67 (6.7) |
| >1 month | 527 (9.8) | 1 (0.1) | 64 (3.1) | 147 (22.0) | 95 (20.2) | 220 (21.9) |
| Median (range) | 26.0 (0-1400) | 6.00 (0-32) | 21.0 [0-184) | 42.0 (0-411) | 62.0 (0-184) | 106 (0-1400) |
| Missing | 3891 (72.7) | 897 (77.9) | 1467 (71.4) | 477 (71.4) | 345 (73.2) | 705 (70.1) |
| **Sex** | | | | | | |
| Male | 2693 (50.3) | 522 (45.4) | 1035 (50.3) | 346 (51.8) | 244 (51.8) | 546 (54.3) |
| Female | 2658 (49.7) | 629 (54.6) | 1021 (49.7) | 322 (48.2) | 227 (48.2) | 459 (45.7) |
| **Ages** | | | | | | |
| 18-30 | 1684 (31.5) | 488 (42.4) | 610 (29.7) | 183 (27.4) | 141 (29.9) | 262 (26.1) |
| 31-45 | 1663 (31.1) | 372 (32.3) | 653 (31.8) | 193 (28.9) | 136 (28.9) | 309 (30.7) |
| 46-55 | 1207 (22.6) | 201 (17.5) | 504 (24.5) | 164 (24.6) | 99 (21.0) | 239 (23.8) |
| 56-<65 | 797 (14.9) | 90 (7.8) | 289 (14.1) | 128 (19.2) | 95 (20.2) | 195 (19.4) |
| **Ethnicity** | | | | | | |
| White | 3439 (64.3) | 717 (62.3) | 1274 (62.0) | 457 (68.4) | 322 (68.4) | 669 (66.6) |
| Asian or Asian British | 323 (6.0) | 39 (3.4) | 129 (6.3) | 40 (6.0) | 32 (6.8) | 83 (8.3) |
| Black or Black British | 217 (4.1) | 22 (1.9) | 86 (4.2) | 21 (3.1) | 18 (3.8) | 70 (7.0) |
| Mixed | 317 (5.9) | 75 (6.5) | 117 (5.7) | 36 (5.4) | 27 (5.7) | 62 (6.2) |
| Other | 229 (4.3) | 43 (3.7) | 83 (4.0) | 33 (4.9) | 18 (3.8) | 52 (5.2) |
| Missing | 826 (15.4) | 255 (22.2) | 367 (17.9) | 81 (12.1) | 54 (11.5) | 69 (6.9) |
| **Index of multiple deprivation** | | | | | | |
| 1 (Most deprived) | 333 (6.2) | 64 (5.6) | 117 (5.7) | 53 (7.9) | 34 (7.2) | 65 (6.5) |
| 2 | 878 (16.4) | 167 (14.5) | 302 (14.7) | 102 (15.3) | 85 (18.0) | 222 (22.1) |
| 3 | 1052 (19.7) | 239 (20.8) | 388 (18.9) | 130 (19.5) | 88 (18.7) | 207 (20.6) |
| 4 | 1251 (23.4) | 285 (24.8) | 503 (24.5) | 156 (23.4) | 99 (21.0) | 208 (20.7) |
| 5 (Most affluent) | 1638 (30.6) | 355 (30.8) | 669 (32.5) | 212 (31.7) | 148 (31.4) | 254 (25.3) |
| Missing | 199 (3.7) | 41 (3.6) | 77 (3.7) | 15 (2.2) | 17 (3.6) | 49 (4.9) |
| **Section 117 After Care discharge** | 940 (17.6) | 30 (2.6) | 137 (6.7) | 190 (28.4) | 195 (41.4) | 388 (38.6) |
| **Homeless (incl. no fixed abode)** | 185 (3.5) | 29 (2.5) | 61 (3.0) | 21 (3.1) | 18 (3.8) | 56 (5.6) |
| **Positive COVID-19 in hospital** | 32 (0.6) | 2 (0.2) | 8 (0.4) | 2 (0.3) | 3 (0.6) | 17 (1.7) |
| **Ward of discharge** | | | | | | |
| AMHB Sapphire Ward (male) | 1046 (19.5) | 277 (24.1) | 397 (19.3) | 103 (15.4) | 80 (17.0) | 189 (18.8) |
| AMHB Ruby Ward (female) | 978 (18.3) | 283 (24.6) | 390 (19.0) | 84 (12.6) | 81 (17.2) | 140 (13.9) |
| AMHO Allen Ward (female) | 793 (14.8) | 140 (12.2) | 327 (15.9) | 127 (19.0) | 74 (15.7) | 125 (12.4) |
| AMHO Wintle (female) | 618 (11.5) | 164 (14.2) | 210 (10.2) | 64 (9.6) | 48 (10.2) | 132 (13.1) |
| AMHO Phoenix (male) | 562 (10.5) | 97 (8.4) | 216 (10.5) | 88 (13.2) | 47 (10.0) | 114 (11.3) |
| AMHO Vaughan Thomas (male) | 578 (10.8) | 85 (7.4) | 213 (10.4) | 87 (13.0) | 72 (15.3) | 121 (12.0) |
| AMHO Ashurst PICU (mixed gender) | 433 (8.1) | 53 (4.6) | 170 (8.3) | 56 (8.4) | 42 (8.9) | 112 (11.1) |
| Missing | 343 (6.4) | 52 (4.5) | 133 (6.5) | 59 (8.8) | 27 (5.7) | 72 (7.2) |
| **Ward level observation** | | | | | | |
| 1. General observation | 2331 (43.6) | 422 (36.7) | 1032 (50.2) | 349 (52.2) | 199 (42.3) | 329 (32.7) |
| 2. Intermittent observation | 558 (10.4) | 189 (16.4) | 206 (10.0) | 54 (8.1) | 41 (8.7) | 68 (6.8) |
| 3-4. Within eyesight | 389 (7.3) | 135 (11.7) | 114 (5.5) | 38 (5.7) | 25 (5.3) | 77 (7.7) |
| Missing or not assigned | 2073 (38.7) | 405 (35.2) | 704 (34.2) | 227 (34.0) | 206 (43.7) | 531 (52.8) |
| **No. previous admissions** | | | | | | |
| First admission | 2469 (46.1) | 603 (52.4) | 966 (47.0) | 291 (43.6) | 197 (41.8) | 412 (41.0) |
| 1 | 1220 (22.8) | 215 (18.7) | 457 (22.2) | 171 (25.6) | 118 (25.1) | 259 (25.8) |
| 2 | 656 (12.3) | 117 (10.2) | 261 (12.7) | 84 (12.6) | 59 (12.5) | 135 (13.4) |
| ≥3 admissions | 1006 (18.8) | 216 (18.8) | 372 (18.1) | 122 (18.3) | 97 (20.6) | 199 (19.8) |
| **Mental health problem (primary diagnosis)*** | | | | | | |
| Psychosis | 2105 (39.3) | 224 (19.5) | 754 (36.7) | 257 (38.5) | 225 (47.8) | 645 (64.2) |
| Bipolar | 834 (15.6) | 85 (7.4) | 345 (16.8) | 171 (25.6) | 96 (20.4) | 137 (13.6) |
| Personality disorder | 720 (13.5) | 341 (29.6) | 256 (12.5) | 50 (7.5) | 22 (4.7) | 51 (5.1) |
| Depression | 625 (11.7) | 131 (11.4) | 281 (13.7) | 90 (13.5) | 57 (12.1) | 66 (6.6) |
| Drug misuse | 307 (5.7) | 114 (9.9) | 137 (6.7) | 24 (3.6) | 12 (2.5) | 20 (2.0) |
| Any substance misuse | 1881 (35.2) | 461 (40.1) | 707 (34.4) | 211 (31.6) | 161 (34.2) | 341 (33.9) |
| Mental health problem NOS | 220 (4.1) | 70 (6.1) | 91 (4.4) | 21 (3.1) | 16 (3.4) | 22 (2.2) |
| Trauma- and stressor-related disorders | 218 (4.1) | 101 (8.8) | 86 (4.2) | 14 (2.1) | 10 (2.1) | 7 (0.7) |
| Anxiety disorders | 117 (2.2) | 43 (3.7) | 42 (2.0) | 15 (2.2) | 3 (0.6) | 14 (1.4) |
| Neurodevelopmental conditions | 240 (4.5) | 78 (6.8) | 87 (4.2) | 29 (4.3) | 18 (3.8) | 28 (2.8) |
| Autism spectrum disorder | 209 (3.9) | 63 (5.5) | 79 (3.8) | 22 (3.3) | 17 (3.6) | 28 (2.8) |

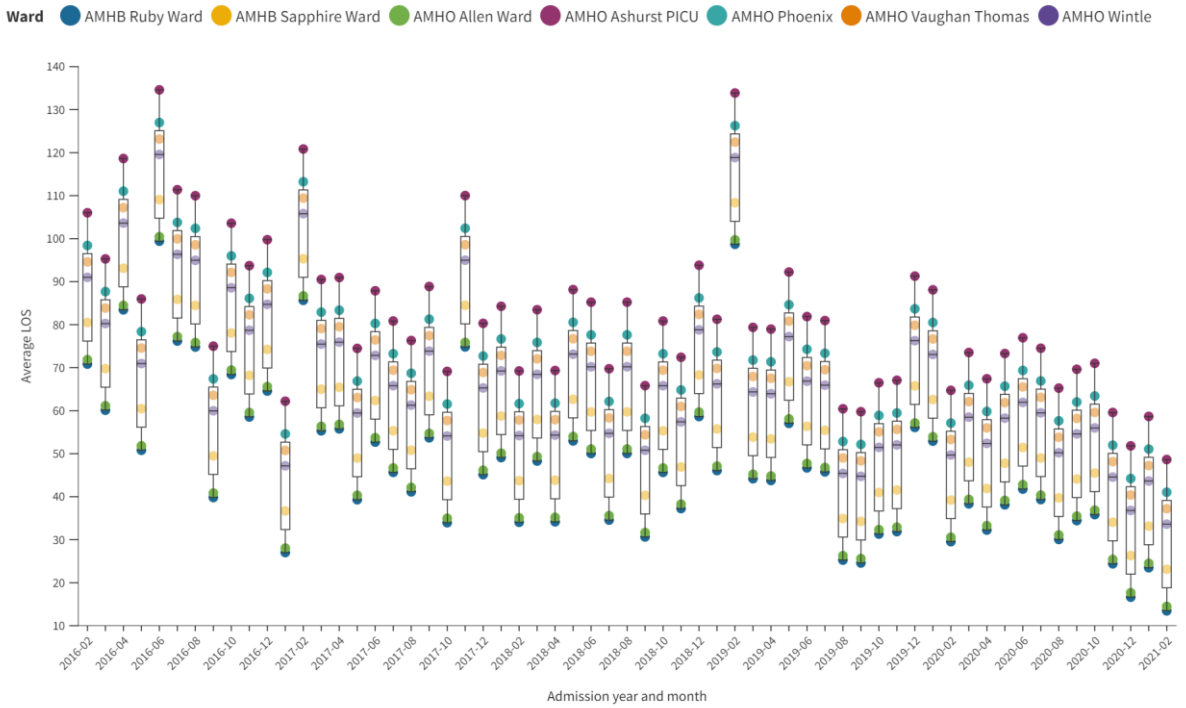
| | | | | | | |
|---|---|---|---|---|---|---|
| Any learning/intellectual disability | 85 (1.6) | 31 (2.7) | 22 (1.1) | 9 (1.3) | 11 (2.3) | 12 (1.2) |
| Eating disorders | 57 (1.1) | 10 (0.9) | 13 (0.6) | 9 (1.3) | 6 (1.3) | 19 (1.9) |
| Dementia | 29 (0.5) | 2 (0.2) | 4 (0.2) | 1 (0.1) | 12 (2.5) | 10 (1.0) |
| Missing (primary diagnosis) | 6 (0.1) | 4 (0.3) | 1 (0.0) | 0 | 1 (0.2) | 0 |
| **Risk identified by individual assessment items** | | | | | | |
| Self-neglect | 2796 (52.3) | 491 (42.7) | 999 (48.6) | 363 (54.3) | 284 (60.3) | 659 (65.6) |
| Violence and aggression | 2534 (47.4) | 396 (34.4) | 890 (43.3) | 323 (48.4) | 270 (57.3) | 655 (65.2) |
| Disengagement/non-compliance with care | 2523 (47.2) | 393 (34.1) | 904 (44.0) | 306 (45.8) | 274 (58.2) | 646 (64.3) |
| Physical health/falls | 2277 (42.6) | 391 (34.0) | 841 (40.9) | 304 (45.5) | 240 (51.0) | 501 (49.9) |
| Absconding/escaping/wandering | 1439 (26.9) | 263 (22.8) | 492 (23.9) | 179 (26.8) | 152 (32.3) | 353 (35.1) |
| Damage to property | 889 (16.6) | 130 (11.3) | 293 (14.3) | 123 (18.4) | 96 (20.4) | 247 (24.6) |
| Self-harm | 2459 (46.0) | 583 (50.7) | 944 (45.9) | 305 (45.7) | 191 (40.6) | 436 (43.4) |
| Suicide | 2807 (52.5) | 647 (56.2) | 1089 (53.0) | 361 (54.0) | 239 (50.7) | 471 (46.9) |
| Fire-setting | 383 (7.2) | 68 (5.9) | 106 (5.2) | 48 (7.2) | 41 (8.7) | 120 (11.9) |
| Misuse of medication | 1939 (36.2) | 430 (37.4) | 721 (35.1) | 246 (36.8) | 179 (38.0) | 363 (36.1) |
| Alcohol and substance misuse | 2098 (39.2) | 462 (40.1) | 786 (38.2) | 241 (36.1) | 187 (39.7) | 422 (42.0) |
| Accidental harm (outside the home) | 1250 (23.4) | 237 (20.6) | 486 (23.6) | 161 (24.1) | 114 (24.2) | 252 (25.1) |
| Sexual offending | 290 (5.4) | 39 (3.4) | 79 (3.8) | 47 (7.0) | 36 (7.6) | 89 (8.9) |
| Risk to children, or child at risk from adult/others | 657 (12.3) | 148 (12.9) | 249 (12.1) | 83 (12.4) | 51 (10.8) | 126 (12.5) |
| Risk from others | 2027 (37.9) | 372 (32.3) | 700 (34.0) | 255 (38.2) | 194 (41.2) | 506 (50.3) |
| Specific risks to others | 1521 (28.4) | 235 (20.4) | 522 (25.4) | 193 (28.9) | 166 (35.2) | 405 (40.3) |
| Multi-agency public protection arrangements | 124 (2.3) | 22 (1.9) | 47 (2.3) | 13 (1.9) | 14 (3.0) | 28 (2.8) |
| Unlawful restrictions/DoLS | 60 (1.1) | 9 (0.8) | 18 (0.9) | 7 (1.0) | 8 (1.7) | 18 (1.8) |
| **Admission year** | | | | | | |
| 2016 | 1339 (25.0) | 209 (18.2) | 516 (25.1) | 164 (24.6) | 140 (29.7) | 310 (30.8) |
| 2017 | 1025 (19.2) | 242 (21.0) | 388 (18.9) | 123 (18.4) | 80 (17.0) | 192 (19.1) |
| 2018 | 982 (18.4) | 220 (19.1) | 355 (17.3) | 132 (19.8) | 92 (19.5) | 183 (18.2) |
| 2019 | 1005 (18.8) | 249 (21.6) | 380 (18.5) | 126 (18.9) | 74 (15.7) | 176 (17.5) |
| 2021 | 1000 (18.7) | 231 (20.1) | 417 (20.3) | 123 (18.4) | 85 (18.0) | 144 (14.3) |

Missing data were for 21.1% (n=1128) for all individual risk items and ranged from 21.1% (overall) to 14.4% by categories of LOS (i.e. <8 days to >90 days)

## Length of stays (LOS)

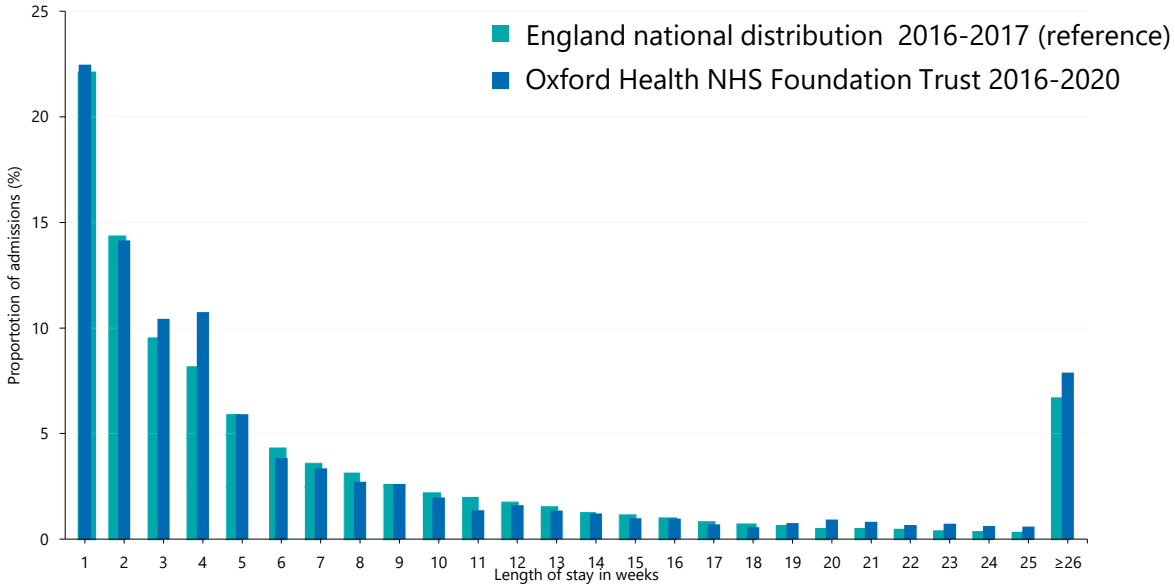
Figure 4 shows the average LOS by inpatient unit in the Trust between 2016 and 2021. The median LOS for adult acute admissions was 25 days (adjusted mean: 58.4 days [55.1 days, including day admissions]), interquartile range: 9-64 days; full-range: 1-1514 days). When excluding the PICU, the median LOS was 23 days (interquartile range: 8-59 days; full-range: 1-1514 days) and the adjusted mean LOS was 54.2 days (95% CI 44.5 days-63.9 days). Estimates were slightly higher than the national average of adult admissions during the same period (2015-2021), ranging from 47-51 days (range median: 19-20 days; appendix B4). However, the mean difference compared with the national average was not statistically significantly different ($p$>0.15). The number of discharges per weeks of stay in the trust were also similar to the national distribution (Figure 5).[8] Relative to admissions in 2016, the average LOS in the Trust decreased from 83.5 days (95% CI 75.3-91.7 days) to 57.2 days (95% CI 49.8-64.6 days) in 2020 (January, pre-COVID) with a consistent trend over time (Figure 4).

**Figure 4.** Box plot showing average length of stay (days) by ward and admission month over time (2016-2021)




See interactive version online. For each admission month between February 2016 and 2021, each coloured point shows the average length of stay (LOS). The boxplot shows the median and IQR, with whiskers extending (up to) 1·5 times the IQR above the upper quartile and below the lower quartile.

**Figure 5.** Comparison between OHFT and national admissions (2016-2017) in the distribution of LOS (weeks)

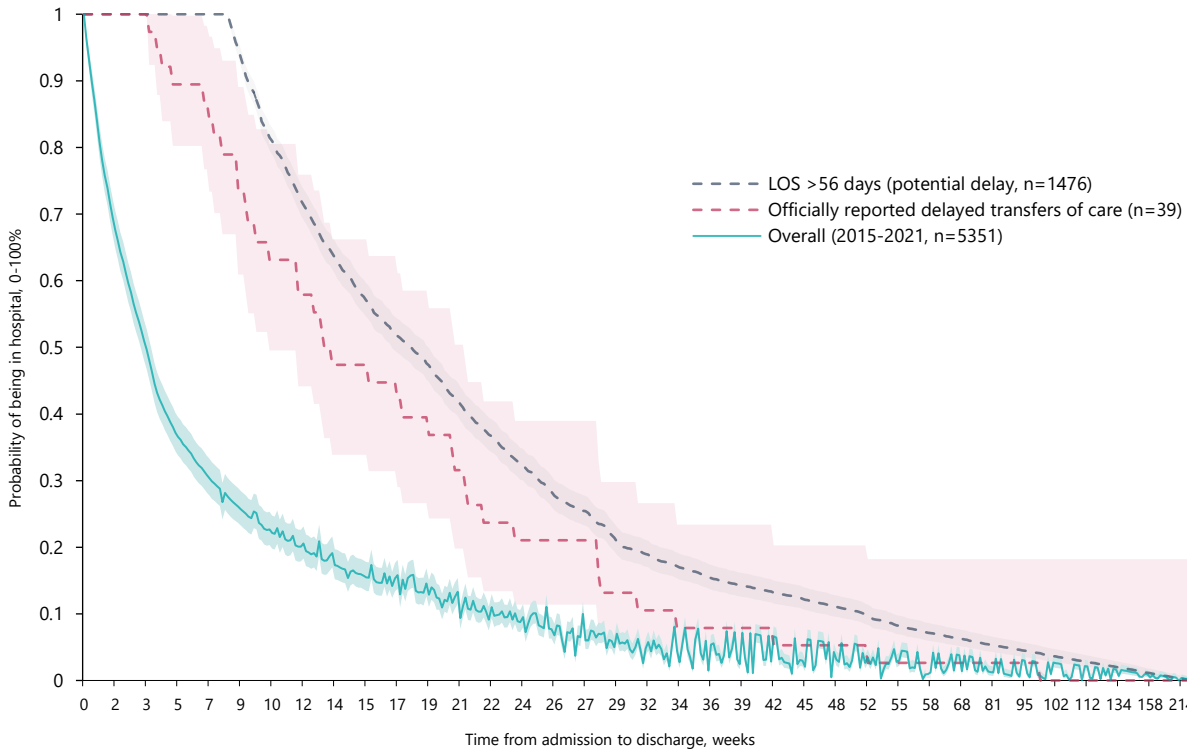



The comparator source is adapted from Wyatt et al.[8] using data from HES-APC 2016-2017. See also eTable 2 in the supplementary.

**Delayed discharges (LOS >56 days)**

Figure 6 shows the adjusted probability of staying in hospital over time for the overall cohort, delayed patients and DTOCs. A total of 1476 admissions were classified as delayed discharges (LOS >56 days), resulting in an overall period prevalence of 27.4% (1476/5351; 95% CI 24.4%-30.4%), or 28.6% (1270/4424; 95% CI 26.2%-31.0%) when excluding any time after COVID-19 started. In models adjusted for age, sex and COVID-19, the incidence of delayed discharges decreased by 6%, from 1.013 in 2016 to 1.069 per 100 000 people in 2019 (adjusted incidence rate ratio: 9.73, 95% CI 9.64–9.81; appendix B6). This overall decline was consistent across admission years. Among the 1476 potential delayed patients, the median length of stay was 127 days or 4-months (IQR, 81-196 days). Delays were higher for males compared to female patients and for older patients. There were 39 officially recorded DTOCs in the MHSDS (e.g. clinically ready to leave but held due to non-clinical factors). Among the DTOC patients, 30 (79.0%) had a LOS longer than 56 days.

**Figure 6.** Probability distribution of LOS (weeks) by potential delays and DTOCs in OHFT




The figure shows Kaplan Meier curves for the averaged adjusted probability of staying in hospital between 2015-2021 by week since admission and risk groups (delayed discharge or DTOC). Estimates are adjusted for gender and clustering effects from specific wards.

**Risk prediction model: predictors of delayed discharges (LOS >56 days)**

We identified 63 candidate predictors of delayed discharges and readmissions from staff interviews and previous reviews. Figure 5 shows individual risk estimates of predictors including adjusted odds ratios (aOR) of delayed discharges, adjusted hazard ratios (aHR) for the risk of readmissions within 1-year, and adjusted mean LOS.

All candidate predictors entered into a risk prediction model of delayed discharges (LOS >56 days; penalised logistic regression model, LASSO). The model retained 36 significant predictors (16 risk factors and 17 protective factors; appendix B9). The strongest risk factors of delayed discharges were patients placed on 117 Section after care (aOR=6.07, 95% CI 4.08-9.02), testing positive for COVID-19 (4.11, 95%CI 1.37-12.34), a diagnosis of dementia (2.78, 95% CI 1.50-5.18), psychosis (3.01, 95% CI 2.62-3.45) or bipolar (2.52, 95%CI 1.80-3.51), or risk concerns about non-compliance with care (2.56, 95% CI 2.06-3.18) or self-neglect (2.53, 95% CI 2.15-2.97). Delayed discharges were also significantly more likely to occur among patients with black ethnicity (2.10, 95% CI 1.61-2.75), homeless patients (1.79, 95% CI 1.31-2.46), and more deprived patients (1.42, 95% CI 1.31-1.55), relative to patients with no delays. We found significant differences between types of psychotic diagnosis (eTable 6), with 60% of all patients with a psychotic diagnosis relating to *"Manic", "Catatonic",* or *"Hebephrenic"* staying longer than 56 days (aOR=3.86, 95% CI 2.58-5.79).

The strongest predictors of reduced delays were patients with risk concerns to children or at-risk children at home (aOR=0.35, 95% CI 0.26-0.45), patients with assigned care coordinators within two weeks of admission (0.61, 95% CI 0.49-0.77), admissions with intermittent level of observations (0.57, 95% CI 0.39-0.81) relative to other ward level observations, admissions to a ward with lower bed capacity in the same month (0.98, 95% CI 0.98-0.98). Patients with a primary diagnosis of personality disorder (0.26 , 95% CI 0.20-0.32), trauma and stress-related disorders (e.g. PTSD; 0.20, 95% CI 0.12-0.32), and drug misuse (0.46, 95% CI 0.38-0.57) were also significantly less likely to be delayed than patients with other conditions.

**Risk prediction model: time to readmission one-year post-discharge**

We found that patients with COVID-19 (2.48, 95% CI 1.60-3.84), patients with risk concerns regarding self-neglect (2.26, 95% CI 1.89-2.72) or non-compliance with care (1.70, 95% CI 1.43-2.03), patients who were homeless (aHZ=1.62, 95% CI 1.23-2.15), patients with an overall longer LOS (1.35, 95% CI 1.15-1.58), and the most deprived patients (1.29, 95% CI 1.13-1.48) were more likely to be readmitted within 1-year post-discharge, relative to patients without any of these conditions. Patients diagnosed with a personality disorder (aHZ=1.91, 95% CI 1.62-2.26) or substance misuse (aHZ=1.92, 95% CI 1.71-2.16) were also significantly more likely to be readmitted within 1-year post-discharge than patients without any of these conditions

**Comparison of clinician predicted LOS vs actual LOS**

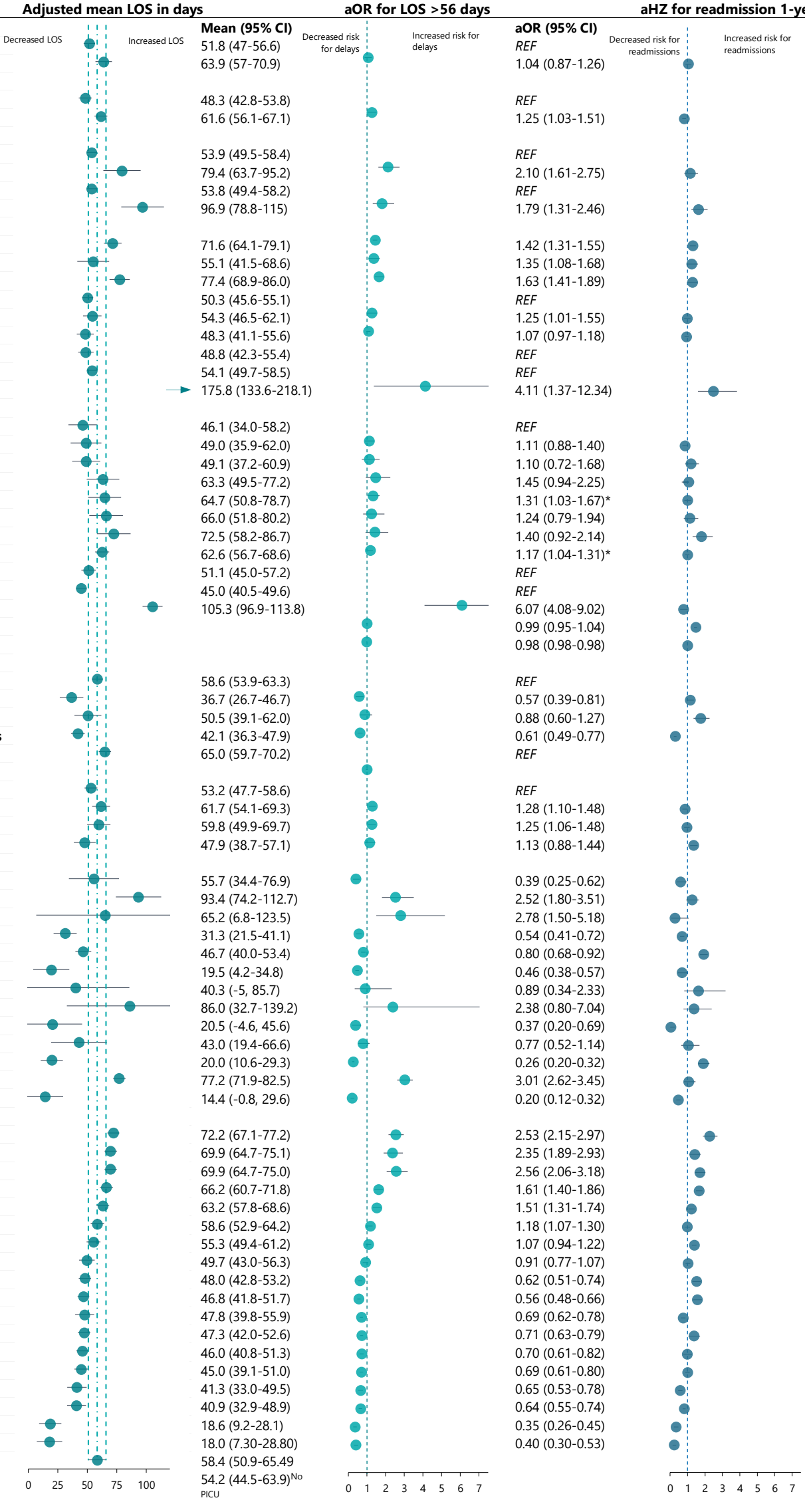
Of the 1460 (27.3%) admissions with an estimated date for discharge (EDD), 54.6% had a predicted consultant discharge date within 1-week of the actual discharge, 28.2% stayed between 1-week and 1-month longer than predicted, and 17.2% stayed longer than 1-month than predicted; none had a shorter stay. The median difference between predicted and actual discharge dates were +5 days (mean difference: 34 days, interquartile range: 0-21 days; full-range 0-1469 days). The substantial proportion of missing EDD precluded any reliable analysis beyond descriptive figures.

**Sensitivity analyses**

All risk prediction estimates remained stable after excluding the PICU and admission follow COVID-19. The average LOS decreased slightly for each predictor following exclusion of the PICU.

**Figure 5.** Adjusted estimates for the mean length of stay, delayed discharges, readmissions within one year by characteristics

| Characteristics | Mean (95% CI) | aOR (95% CI) | aHZ (95% CI) |
|---|---|---|---|
| **Older age** | | | |
| <50 years old | 51.8 (47-56.6) | *REF* | *REF* |
| > 50 years | 63.9 (57-70.9) | 1.04 (0.87-1.26) | 1.04 (0.89-1.22) |
| **Gender** | | | |
| Female | 48.3 (42.8-53.8) | *REF* | *REF* |
| Being male | 61.6 (56.1-67.1) | 1.25 (1.03-1.51) | 0.80 (0.70-0.92) |
| **Ethnicity** | | | |
| White and all other ethnicities | 53.9 (49.5-58.4) | *REF* | *REF* |
| Black | 79.4 (63.7-95.2) | 2.10 (1.61-2.75) | 1.15 (0.82-1.60) |
| **Having a home** | 53.8 (49.4-58.2) | *REF* | *REF* |
| **Homeless/no fixed abode** | 96.9 (78.8-115) | 1.79 (1.31-2.46) | 1.62 (1.23-2.15) |
| **Index of multiple deprivation (IMD)** | | | |
| 1-2 (Most deprived) | 71.6 (64.1-79.1) | 1.42 (1.31-1.55) | 1.29 (1.13-1.48) |
| *1* | 55.1 (41.5-68.6) | 1.35 (1.08-1.68) | 1.23 (0.95-1.60) |
| *2* | 77.4 (68.9-86.0) | 1.63 (1.41-1.89) | 1.27 (1.02-1.58) |
| 3-5 (More affluent) | 50.3 (45.6-55.1) | *REF* | *REF* |
| *3* | 54.3 (46.5-62.1) | 1.25 (1.01-1.55) | 0.97 (0.80-1.17) |
| *4* | 48.3 (41.1-55.6) | 1.07 (0.97-1.18) | 0.94 (0.83-1.07) |
| 5 (Most affluent) | 48.8 (42.3-55.4) | *REF* | *REF* |
| **Negative/no COVID-19 recorded** | 54.1 (49.7-58.5) | *REF* | *REF* |
| **COVID-19 test positive** | 175.8 (133.6-218.1) | 4.11 (1.37-12.34) | 2.48 (1.6-3.84) |
| **Ward/inpatient unit** (adjusting for social deprivation) | | | |
| AMHB Ruby Ward (female) | 46.1 (34.0-58.2) | *REF* | *REF* |
| AMHO Allen Ward (female) | 49.0 (35.9-62.0) | 1.11 (0.88-1.40) | 0.85 (0.71-1.04) |
| AMHB Sapphire Ward (male) | 49.1 (37.2-60.9) | 1.10 (0.72-1.68) | 1.20 (0.87-1.65) |
| AMHO Vaughan Thomas (male) | 63.3 (49.5-77.2) | 1.45 (0.94-2.25) | 1.07 (0.68-0.75) |
| AMHO Wintle (female) | 64.7 (50.8-78.7) | 1.31 (1.03-1.67)* | 1.00 (0.82-1.21) |
| AMHO Phoenix (male) | 66.0 (51.8-80.2) | 1.24 (0.79-1.94) | 1.13 (0.79-1.62) |
| Ward D (PICU mixed gender) | 72.5 (58.2-86.7) | 1.40 (0.92-2.14) | 1.78 (1.29-2.45) |
| AMHO Oxfordshire county (excluding PICU) | 62.6 (56.7-68.6) | 1.17 (1.04-1.31)* | 0.99 (0.88-1.12) |
| AMHB Buckinghamshire county | 51.1 (45.0-57.2) | *REF* | |
| **No Section 117** | 45.0 (40.5-49.6) | *REF* | *REF* |
| **On Section 117 after care** | 105.3 (96.9-113.8) | 6.07 (4.08-9.02) | 0.77 (0.58-1.02) |
| **Number of previous admissions** | | 0.99 (0.95-1.04) | 1.46 (1.38-1.55) |
| **Ward capacity (% occupied beds)** | | 0.98 (0.98-0.98) | 1.00 (0.99-1.00) |
| **Ward level observation** | | | |
| 1. General Observation | 58.6 (53.9-63.3) | *REF* | *REF* |
| 2. Intermittent Observation | 36.7 (26.7-46.7) | 0.57 (0.39-0.81) | 1.14 (0.95-1.37) |
| 3. Within Eyesight - Within Arm's Length | 50.5 (39.1-62.0) | 0.88 (0.60-1.27) | 1.75 (1.35-2.26) |
| **Faster allocation of care coordinator, within 2-weeks** | 42.1 (36.3-47.9) | 0.61 (0.49-0.77) | 0.28 (0.21-0.37) |
| **Later allocated care coordinator,** >2-weeks post-admission | 65.0 (59.7-70.2) | *REF* | *REF* |
| **No. Previous admissions /LOS for 1-readmissions*** | | | |
| First admission/ <7 days LOS | 53.2 (47.7-58.6) | *REF* | *REF* |
| Second admission / 8-21 days LOS | 61.7 (54.1-69.3) | 1.28 (1.10-1.48) | 0.84 (0.71-1.00) |
| Third admission / 22-56 days LOS | 59.8 (49.9-69.7) | 1.25 (1.06-1.48) | 0.95 (0.81-1.13) |
| Fourth or more admission / >56 days LOS | 47.9 (38.7-57.1) | 1.13 (0.88-1.44) | 1.35 (1.15-1.58) |
| **Primary diagnosis mental health problem** | | | *REF* |
| Anxiety disorders | 55.7 (34.4-76.9) | 0.39 (0.25-0.62) | 0.60 (0.37-0.96) |
| Bipolar | 93.4 (74.2-112.7) | 2.52 (1.80-3.51) | 1.24 (0.93-1.66) |
| Dementia | 65.2 (6.8-123.5) | 2.78 (1.50-5.18) | 0.27 (0.07-1.07) |
| Depression | 31.3 (21.5-41.1) | 0.54 (0.41-0.72) | 0.69 (0.57-0.82) |
| Substance misuse | 46.7 (40.0-53.4) | 0.80 (0.68-0.92) | 1.92 (1.71-2.16) |
| Drug misuse | 19.5 (4.2-34.8) | 0.46 (0.38-0.57) | 0.68 (0.45-1.03) |
| Eating disorders | 40.3 (-5, 85.7) | 0.89 (0.34-2.33) | 1.61 (0.81-3.18) |
| Learning/Intellectual disability | 86.0 (32.7-139.2) | 2.38 (0.80-7.04) | 1.36 (0.77-2.39) |
| Mental health problem NOS | 20.5 (-4.6, 45.6) | 0.37 (0.20-0.69) | 0.04 (0.01-0.27) |
| Neurodevelopmental disorder | 43.0 (19.4-66.6) | 0.77 (0.52-1.14) | 1.04 (0.64-1.69) |
| Personality disorder | 20.0 (10.6-29.3) | 0.26 (0.20-0.32) | 1.91 (1.62-2.26) |
| Psychosis | 77.2 (71.9-82.5) | 3.01 (2.62-3.45) | 1.07 (0.79-1.46) |
| Trauma- and stressor-related disorders | 14.4 (-0.8, 29.6) | 0.20 (0.12-0.32) | 0.46 (0.36-0.60) |
| **Risk assessment individual items (yes/no)** | | | |
| Self-neglect | 72.2 (67.1-77.2) | 2.53 (2.15-2.97) | 2.26 (1.89-2.72) |
| Violence and aggression | 69.9 (64.7-75.1) | 2.35 (1.89-2.93) | 1.40 (1.11-1.75) |
| Disengagement/non-compliance with care | 69.9 (64.7-75.0) | 2.56 (2.06-3.18) | 1.70 (1.43-2.03) |
| Physical health/falls | 66.2 (60.7-71.8) | 1.61 (1.40-1.86) | 1.66 (1.49-1.86) |
| Risk from others | 63.2 (57.8-68.6) | 1.51 (1.31-1.74) | 1.22 (1.05-1.41) |
| Specific risks to others | 58.6 (52.9-64.2) | 1.18 (1.07-1.30) | 0.98 (0.84-1.14) |
| Absconding/escaping/wandering | 55.3 (49.4-61.2) | 1.07 (0.94-1.22) | 1.38 (1.25-1.52) |
| Damage to property | 49.7 (43.0-56.3) | 0.91 (0.77-1.07) | 1.01 (0.89-1.16) |
| Self-harm | 48.0 (42.8-53.2) | 0.62 (0.51-0.74) | 1.50 (1.28-1.76) |
| Suicide | 46.8 (41.8-51.7) | 0.56 (0.48-0.66) | 1.56 (1.32-1.83) |
| Fire-setting | 47.8 (39.8-55.9) | 0.69 (0.62-0.78) | 0.74 (0.62-0.89) |
| Misuse of medication | 47.3 (42.0-52.6) | 0.71 (0.63-0.79) | 1.35 (1.06-1.72) |
| Alcohol and substance misuse | 46.0 (40.8-51.3) | 0.70 (0.61-0.82) | 0.98 (0.76-1.27) |
| Accidental harm (outside the home) | 45.0 (39.1-51.0) | 0.69 (0.61-0.80) | 0.99 (0.88-1.13) |
| Sexual offending | 41.3 (33.0-49.5) | 0.65 (0.53-0.78) | 0.58 (0.47-0.71) |
| Risk to children, or child at risk from adult/others | 40.9 (32.9-48.9) | 0.64 (0.55-0.74) | 0.80 (0.72-0.89) |
| Multi-agency public protection arrangements | 18.6 (9.2-28.1) | 0.35 (0.26-0.45) | 0.33 (0.22-0.48) |
| Unlawful restrictions/DoLS | 18.0 (7.30-28.80) | 0.40 (0.30-0.53) | 0.23 (0.15-0.35) |
| **Overall Mean LOS/reference** | 58.4 (50.9-65.49 | | |
| | 54.2 (44.5-63.9)[No PICU] | | |




Means are estimated marginal means for length of stay (LOS). All estimates are adjusted for age, sex, positive COVID-19 tests and admission year and potential clustering effects by inpatient unit. For differences between inpatient units, Sapphire ward had on average the shortest length of stay (figure 4) and functioned as the reference group. Estimates for inpatient units were also adjusted for patient's level of deprivation (index of multiple deprivation). CI=95% confidence interval, LOS=Length of stay in days, aHZ= Adjusted Hazard Ratio, aOR=Adjusted Odds Ratio.
*Predictors differ depending on outcome. For outcomes relating to mean adjusted LOS and ORs of delayed discharges (left & middle figure), predictors refer to the number of previous admissions. For readmissions (right figure), the predictor is a categorical variable referring to different length of stays in days of the initial admission.

## Discussion

We used a large sample of staff interviews and a population-based cohort study to identify factors that may influence longer LOS and risk of readmissions for acute adult psychiatric admissions. We achieved a high response rate of social care and clinical staff from eight inpatient units across two counties with different inpatient and community procedures. Overall, we found that 1 in 5 admissions meet the criteria for delayed discharges based on the local definition (LOS >56 days). Qualitative themes and quantitative findings were generally consistent. The most common predictors of longer LOS were older age, higher social deprivation, risks of self-neglect and non-compliance with care, dementia, psychosis and bipolar related-admissions, and black ethnicity. Staff interviews highlighted a need for inpatient social workers, increased recognition of discharge barriers with shared responsibility between professions, and more effective information sharing systems with community services and placement providers.

The findings that longer stays occur more often among socially deprived patients, older patients and patients with black ethnicity are not new and reflect findings from early RCTs in the 1980s.[57] Longer stays were more common among psychotic disorders and affective disorders than other mental disorders, such as personality disorders and substance misuse. Overall, these results are consistent with a larger UK study on mixed psychiatric admissions (n=133,156-231,998),[58] general health-related emergency department visits,[59] and smaller studies from Germany and Switzerland (n range: 738-2939).[60-62] It is likely that these interlinked patient characteristics reflect admissions with higher underlying multimorbidity and social care needs, which requires involvement from multiple systems to facilitate discharge. Hospitals are also likely to have seen an influx of this patient group in recent years and since COVID-19. Restrictions posed by the pandemic, for instance, meant many patients lost face-to-face contacts by community services, impacting continuity and adherence of care.[63] Additional increases in LOS among more socially deprived patients

may also stem from the Homelessness Reduction Act 2017, as hospitals now have a legal responsibility to liaise accommodation arrangements before discharge.[64]

Whilst the results emphasise the importance of external factors for reducing LOS, several modifiable internal factors were associated with reduced LOS. Faster allocation of social care coordinators upon admission were linked to significantly reduced delayed discharges and readmissions. The need for increased inpatient social workers was also the most frequently endorsed facilitator in staff interviews. Other significant predictors for reduced LOS were admissions during a month of higher bed occupancy, with wards discharging patients faster than wards or during months with lower bed occupancy. This finding broadly aligns with *Roemer's Law* stating that "*Hospital beds that are built tend to be used"*, which predicts that increased bed availability results in increased bed use "*as hospitals have resources to do so"*.[8,65]

Aligning with a Cochrane review (2014),[66] and previous studies,[67] we found that longer LOS was associated with increased risk of readmissions one-year post-discharge after adjustments for socioeconomic factors, psychiatric diagnosis and ward clusters. The findings are inconsistent with the longstanding position that shorter LOS compromises patient care and increase readmissions (e.g. the *"revolving door*" phenomena).[68-70] Faster emergency readmissions are often postulated to indicate patients are discharged too early with inadequate time to stabilise symptoms.[69,70] However, readmissions occurring later may reflect inadequate community care to maintain patients' conditions following discharge (e.g. medication adherence).[71] Our findings may indicate that patient groups with a higher risk of self-neglect and poorer compliance with care are significantly more likely to be re-admitted within one-year independent of their LOS. The increased risk in this group, regardless of LOS, suggests a lack of adequate care packages and suitable placements to maintain their care in the community (e.g. medication adherence).[72] The generally reduced risk of readmissions among patients with shorter LOS (adjusting for other factors)

emphasises the importance of clinical teams to continue monitoring and challenge patient's discharge readiness.

**Limitations**

This study has several limitations, and findings must be interpreted with caution. First, there is no national consensus definition over what constitutes a "delayed discharge". We used a locally defined primary outcome using an arbitrary cut-off for LOS based on local convention. This definition, however, will classify many patients as "potential delays" regardless of underlying need and their necessary LOS. A considerable proportion of patients will require an LOS beyond 56 days, and the definition should be considered with caution to prevent promoting trends of too early and unsafe discharges. We therefor also included two additional outcomes based on continuous LOS measures and readmissions, producing similar significant predictors.

Second, data were limited to one trust in England. Although demographic characteristics of population served were similar to national reports, findings may not be generalisable to other NHS trusts in the country with a different socioeconomic profile.

Third, estimating LOS for psychiatric admissions is challenging, as mental health admissions have the most overlapping episodes across health care data in England (e.g. when one admission includes multiple episodes). We followed the recommendations from NHS England and previous studies,[39,73] suggesting findings may be comparable with other estimates.

**Implications**

***NHS Trust level***. The shared view from all staff on the need for increased community care resources (e.g. placements) and closer liaison with placement providers and community teams align with current NICE guidelines.[38] Many highlighted interventions therefore relied on increasing resources (e.g. inpatient social workers) and broader systemic factors (e.g. lack of placement providers). Given its location, recruitment and retention of staff in the Trust is a longstanding issue, resulting in problems in the provision

of community mental health teams. The Trust has consistently exceeded the ceiling for agency staff spending over the past years.[74] Countywide, the Trust also lack fully functioning crisis resolution and intensive home treatment services (CRHT). Increasing CRHTs and crisis pathways in the community should therefore be of high priority in the Trust and align with the priorities set out by the NHS Longer-term plan (2019).[13]

***Practice and individual level.*** Other important themes emphasised the importance of recognising discharge barriers on admission (e.g. homelessness, no clear admission goal etc.) and improving staff dynamics towards decision-making (admission/discharge) and teamwork between services and professions. Staff alluded to a divide between the social care professions and the clinical team. Facilitators included closer and proactive working between consultants and inpatient social workers. The COVID-19 pandemic has provided an opportunity to improve the cost-effectiveness of different mental health interventions. Central to this opportunity is the willingness to rethink conventional approaches to systems planning. Staff attitudes and perceptions are, for example, directly modifiable factors with available interventions (e.g. awareness-raising, education, reflective MDT practice across professions, physically closer working etc), which may indirectly impact broader factors such as staffing levels (e.g. staff satisfaction). Other modifiable factors included improving goals upon admission/gatekeeping and a consensus statement for discharge criteria for patients with complex needs (e.g. self-neglect, non-adherence medication combined with other conditions) to help assign estimated LOS and discharge pathways on admission (see Table 2).

***Research***. Our findings indicated a positive impact of faster care coordinator allocations, which fits within the Transitional Discharge Model (TDM). TDM focus on increasing continuity of care relationships when transitioning from or to a hospital (see also NICE NG53 1.1.6, 1.3.1, 2021). Findings from one RCT in the USA showed an average of 116 days reduction in LOS from introducing TDM compared to hospitals without the TDM.[75] Similarly, a systematic review (limited to four controlled studies) of transitional

interventions to reduce psychiatric readmissions highlighted the positive impact of pre-discharge planning and bridging interventions (e.g. patient flow coordinator, in/out-patient communication).[76] Digital technologies are likely to facilitate increased availability for care coordinators in the community to liaise with patients and inpatient staff to support increased continuity of care. However, there are challenges with using remote technologies to develop relationships, and adaptions or a mix with face-to-face visits may be helpful.

Further research is needed to examine if the current findings generalise across other NHS trusts. There is also a need to move from using retrospective data to test real-time risk prediction of potential delays upon admission (i.e. built into clinical IT systems, perhaps using machine learning) to help connected services (e.g. social care) to plan and prioritise scant resources for discharge. As part of the NHS longer-term plan, the government has released £750,000 to focus on predicting LOS using automated risk scores for integration into EHRs.[78] This funding, however, applies to all health care sectors. Psychiatric admissions LOS are likely to differ from other specialties, so separate risk prediction models should be developed for mental health with local flexibility. Finally, despite the potential benefits of predicting delays, mental health-specific studies, including local audits, are needed to examine the impact of different solutions to prevent delays once identified. Systematic reviews repeatedly reveal that suggested solutions (e.g. discharge planning, monitoring tools) are developed based on small local studies in mixed populations, with little relevance to mental health.[79]

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**Author contributions**
Concept: Shabeer Syed, Angela Bird, Catherine Sage, Paul Salkovskis, Rob Bale
Design: Shabeer Syed, Angela Bird, Catherine Sage, Paul Salkovskis, Rob Bale
Drafting of the manuscript: All authors
Acquisition, analysis, or interpretation of data: All authors
Statistical analyses: Shabeer Syed
Critical revision of the manuscript for important intellectual content: All authors
Study supervision: Paul Salkovskis
Full data access: Shabeer Syed, Paul Salkovskis

**Declarations of interest**
All authors have completed the ICMJE uniform disclosure form (www.icmje.org/coi_disclosure.pdf) and declare no competing interests.

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Oxford Health
NHS Foundation Trust

# Improving patient flow for adult mental health admissions

## A mixed methods study on length of stays, delayed discharges, and readmissions

Patient Flow Transformation Team, Mental Health Urgent Care and Social Care, Oxford Health NHS Foundation Trust 2021







Oxford Health NHS Foundation Trust

# Executive summary & recommendations

## Background

Longer hospital stays can have profound effects on patients' health and development. Over the past 40 years, there has been a significant reduction of inpatient mental health beds, with increasing pressure on services to reduce lengths of stay (LOS). Whilst there has been consensus on this approach, reducing LOS has not always been successful. Reports reveal that no significant reduction of LOS for psychiatric admissions have happened in the NHS over the past 15 years. This could be due to the current occupancy levels and LOS being optimal, or due to systemic problems preventing further progress. The extent to which clinical and service factors can impact LOS is also not well understood.

This research was commissioned by the Mental Health Urgent Care and Social Care Team at Oxford Health NHS Foundation Trust to inform local interventions to reduce delayed discharges of adult psychiatric admissions.

## Aims

The research was conducted in two study phases to seek answers on:

- What do clinicians and social workers think about delayed discharges (e.g. do we have a problem)?
- What do staff think are the barriers and facilitators to preventing delayed discharges?
- How many delayed transfers of care in the Trust are adult acute admissions (2016-2021)?
- How many patients have spent more than 56 days in hospital (locally defined *"delayed discharge"*/national average: 51 days)?
- Which patient, clinical and service level factors influence LOS in OHFT's adult inpatient units?

## Methods

We completed:

- A thematic analysis of 17 semi-structured interviews with in-patient/community staff (Oxfordshire & Buckinghamshire), focusing on learning experiences of barriers and facilitators to early discharge.
- A statistical risk prediction model to identify significant factors that influence LOS, potential delays and readmissions. Estimates are based on 5351 admissions in the OHFTs seven adult acute in-patient units (2015-2021).

## Key findings

The summaries below contain key findings and corresponding recommendations. A graphical risk calculator is also available online: https://ohft.github.io/lengthofstay/

### Phase 1: Staff interviews

All staff we interviewed saw delayed discharges and transfers of care as a large problem in the Trust. Clinicians and social workers provided recent case examples of delayed discharges in the past month.

We found a large variation in how staff defined *"delays"*. Some staff focused solely on DTOCs, and others focused on longer hospital stays in general. None of the staff could confirm how and where DTOCs or delays were reported. The data management team reported difficulties in consistency and data quality.

For themes relating to external barriers, all staff reported difficulties with finding placements, lack of community resources and the impact of COVID-19. For internal barriers, staff identified themes relating to (1) a lack of shared responsibility between the clinical, social and community teams in identifying and addressing discharge barriers (team and interprofessional dynamics); (2) staffing issues (e.g. missing

inpatient social workers); (3) uncertainty and concerns towards discharging patients with complex needs.

Many of the staff reported facilitators are provided in the recommendations section. Interviews showed evidence of extraordinary achievements by staff who came together during the immense pressure of COVID-19 to reduce delays and LOS. Some examples included: weekly active tracking of patients and discharge barriers to meet targets of discharge dates, and nurses actively screening patients on the acute ward for rehabilitation (e.g. *Opal Ward*); proactive inpatient social workers overcoming discharge barriers by going the extra mile (e.g. *a social worker on Phoenix Ward went and built a bed for a patient who could not be discharged due to safety/housing regulations*); and a general desire among staff to improve and reduce delayed discharges (e.g. *early identification of discharge barriers, Red2Green, joined up MDT meetings between services etc*).

### Phase 2: Analysis of admission data

Between 2016 and 2021, the average LOS of adult acute admissions in OHFT ranged from 54.2 to 58.4 days (~2 months, median: 23-25 days). In contrast to staff interviews and previous reports, we found that the Trust performance of LOS are consistent with the national average at 47-51 days, with reductions in the LOS since 2016. The LOS was on average 11 days shorter for admissions in Buckinghamshire compared with Oxford wards. This difference may partly be explained by the rehabilitation ward in Buckinghamshire, whereas Oxford does not have a rehabilitation ward or a recovery pathway.

Most recorded DTOCs on a patient level (i.e. not summary measures) were older adults. Of the 367 officially recorded DTOCs, we could only identify 39 adult admissions (10% of all DTOCs).

The largest proportion of longer hospital stays occurred among patients with higher underlying needs, including patients with COVID-19, patients of black ethnicity, 50–65-year-olds, homeless patients, patients more frequently identified at risk of self-neglect or non-compliance with care (e.g. medication adherence), and specific psychotic and bipolar related-admissions. The risk for readmission within one-year post-discharge was also high within these patient groups.

The strongest factors linked to reduced delays included faster allocation of care coordinators upon admission and higher bed occupancy. These findings remained stable after adjusting for positive cases of COVID-19, admission year, patient's level of deprivation and mental health diagnosis.

### Recommendations

**Positively reward and recognise the hard work and achievements of in-patient, community and social work staff.**

Despite several local initiatives in the Trust, most staff described feeling hopeless and powerless in their attempts to reduce delays. Increased attempts to highlight the positive impact of local efforts towards reducing delays (e.g. ward specific case examples) are likely to motivate further efforts.

**Strengthen definitions and data collection on delayed discharges and discharge barriers.**

The identified challenges with definitions and reporting of delayed discharges impact on being able to measure performance across wards and on OHFT's ranking across different health and safety measures. We recommend strengthening data collection systems on delayed discharges to increase reliability and reduce *"waste"* of staffing resources. Common barriers to discharge (*e.g. homelessness, awaiting assessments*) are routinely recorded on Carenotes. This data can be linked to *Red2Green*, with flexibility for staff to cross-check accuracy.

**Agree on a consensus statement and shared goals discharge readiness.**

Implement a consensus statement with criteria for discharge/admission goals of patients with higher

underlying social and psychiatric needs, where differences in opinion are likely to be high. Unified and clear goals are likely to facilitate stronger working alliances and faster discharge. Qualitative themes showed differences between social workers and consultants toward discharge readiness. Smaller differences between wards were also observed.

**Ensure adequate inpatient social workers on wards to facilitate care coordination of discharges from hospital.**

Having an assigned care coordinator within two weeks of admission was the strongest predictor for faster discharge and one of the most frequently endorsed themes for improvement areas by staff. Allocate or ringfence newly released funding by the government[1] to ensure adequate staffing levels of social workers.

**Collate a placement database based on past placement providers to help staff identify suitable placements faster.**

Social workers and clinicians spend a significant amount of time identifying suitable placements and making referrals. This process could be streamlined by collating a database of previous placements, contracts and discharge destinations (e.g. the CRIS team could work with social workers to build a database using previous data).

**Commission crisis resolution home treatment teams and emergency housing providers**

Patients who spent the longest time in hospital and had the highest risk of faster readmission with one-year post-discharge were homeless, more deprived, had psychosis, and identified risks relating to self-neglect, non-compliance with care and aggression. These findings highlight a potential gap of suitable placement providers that can maintain treatment gains in the community following discharge. Allocated funding[1] could prioritise commissioning 'step-down' 24-hour supported accommodations to support transition with daily activities, health and care assessments.

**Facilitate staff support for team cohesion**

Whilst a large driver of staffing levels relates to longstanding wider systemic issues in Oxfordshire (staff retention, salary, housing prices etc.), qualitative themes point to underlying cultural issues on wards. The most frequently endorsed facilitators were working on team dynamics to build trust and define shared goals between professions.

**Increase digital solutions to help community staff and placement providers liaise with hospitals.**

COVID-19 has taught us the importance of using technology to overcome communication and information sharing barriers. Despite this, staff reported that significant time was taken up organising assessments, repeating requests for information from ward teams (or vice versa), or sourcing care agencies. Increasing the use of digital consultations on wards could allow external services to conduct assessments faster. Staff also endorsed a common platform for communicating discharge dates, contact details, and schedules earlier (e.g. staff rotas).

**Smaller significant differences between counties but not between wards**

Some qualitative themes related to significant differences between wards in LOS. We found no evidence for an overall significant difference between specific acute wards (excluding Ashurst PICU and Opal ward). However, significantly shorter LOS was observed in Buckinghamshire overall, relative to Oxfordshire. All estimates are adjusted for patients' gender, social deprivation, admission year and any positive covid tests.


## Acknowledgement

This report and research would not have been possible without the invaluable contributions of the social workers, consultant psychiatrists and modern matrons connected to the eight adult inpatient units in Oxford Health Foundation Trust NHS. We also acknowledge the support of the Performance and Information team, CRIS and the Oxford Healthcare Improvement team, patients and their families.


[1] C0894 Mental health winter 2021 discharge funding supporting-guidance, ref 001559

**Figure 2.** Thematic map of the five themes (centre circle) and 18 subthemes (connected circles) for staff views on barriers and facilitators of discharge

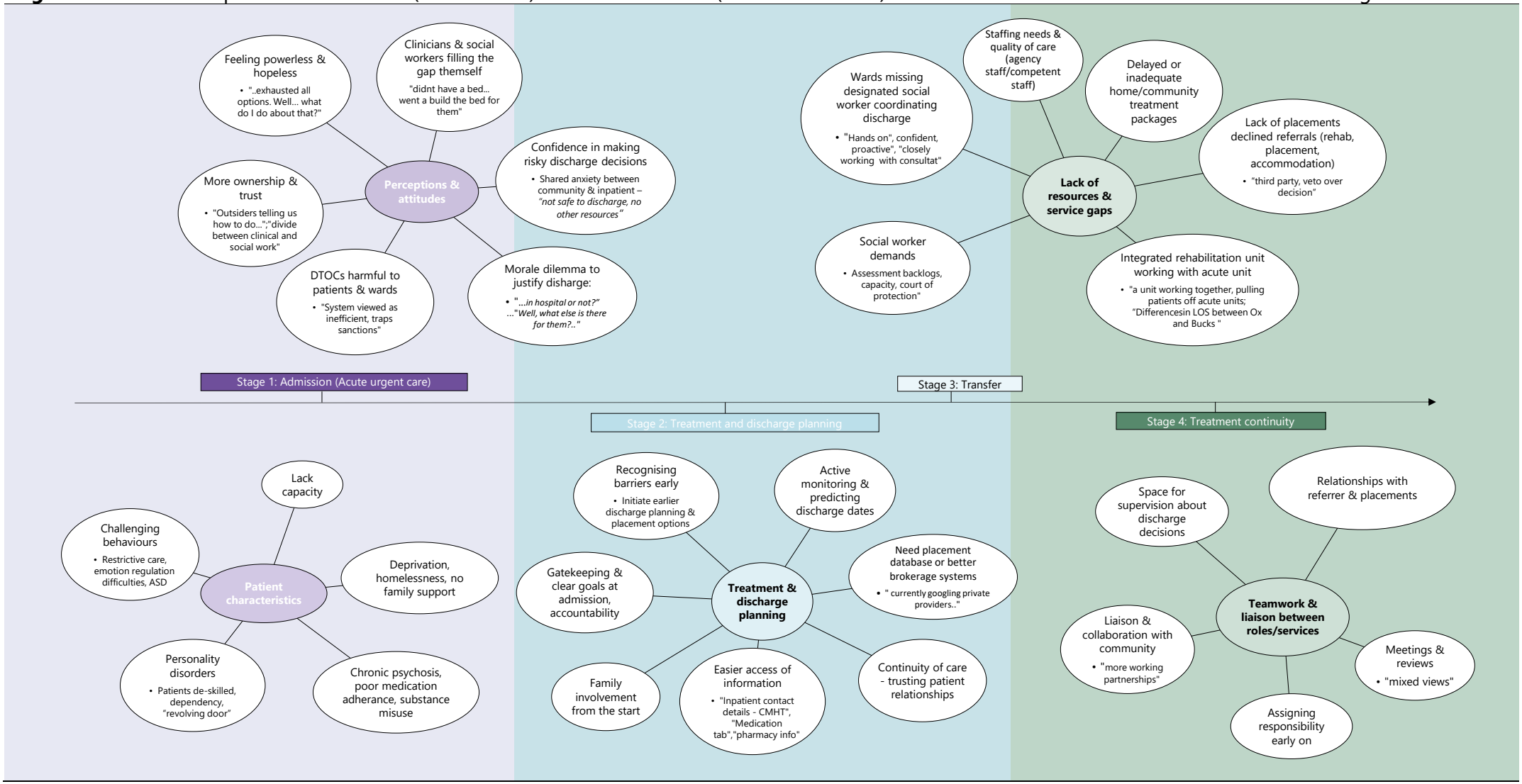
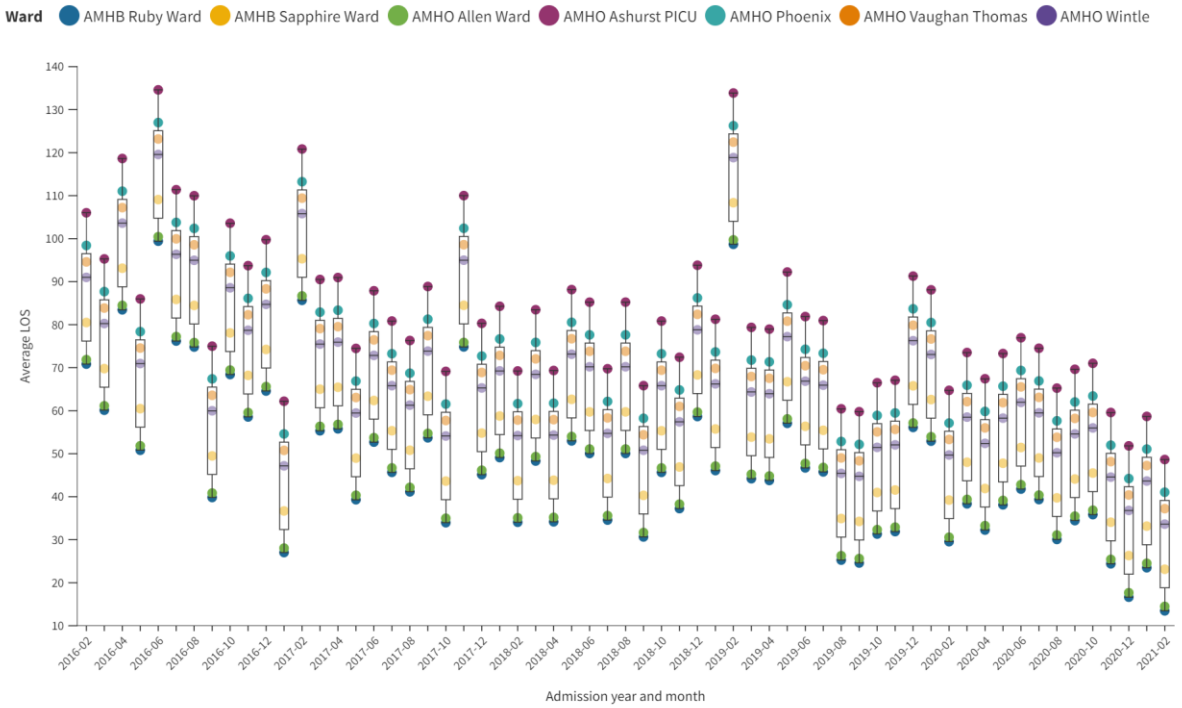
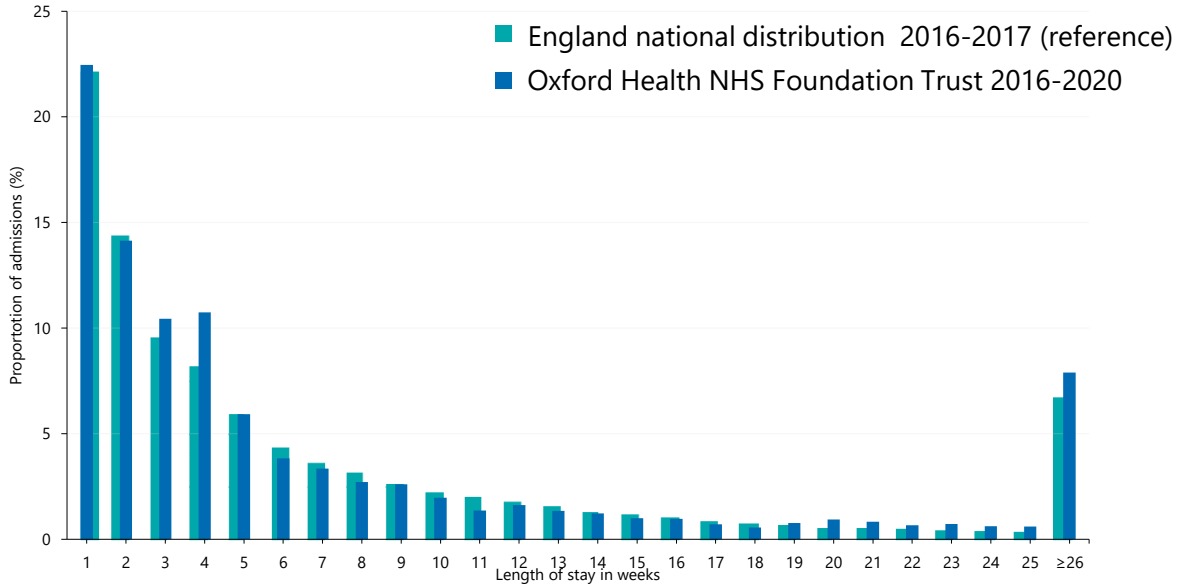


**Figure 4.** Box plot showing average length of stay (days) by ward and admission month over time (2016-2021)




See interactive version online. For each admission month between February 2016 and 2021, each coloured point shows the average length of stay (LOS) per ward. The boxes show the median and interquartile ranges, with whiskers extending (up to) 1·5 times the IQR above the upper quartile and below the lower quartile.

**Figure 5.** Comparison between OHFT and national admissions (2016-2017) in the distribution of LOS (weeks)




The comparator source is adapted from RCPsych commissioned report by Wyatt et al.[8] using the same data source for national estimates (HES-APC 2016-2017). See also eTable 2 in the supplementary.

**Theoretically driven research project**

# Early adverse childhood experiences, emotion dysregulation and subsequent risk of chronic pain in children and adolescents: a population-based birth cohort study

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**Doctoral student**
Shabeer Syed,[1,2] Trainee Clinical Psychologist

shabeer.syed@hmc.ox.ac.uk/shabeer.syed@oxfordhealth.nhs.uk

**Supervisors**
Dr Louise Johns,[1] Consultant Academic Clinical Psychologist
louise.johns@psych.ox.ac.uk

Prof Ruth Gilbert,[2,3] Professor of Clinical Epidemiology
r.gilbert@ucl.ac.uk

**Co-authors**
Dr Matthew Jay,[2] Research Fellow in Epidemiology/Statistics
matthew.jay.15@ucl.ac.uk

Dr Richard F Howard,[4,5] Consultant in Anaesthesia and Pain Medicine
r.howard@ucl.ac.uk



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Please note: this manuscript is formatted according to the Vancouver referencing system as required by the target journals. The word count has been adjusted in accordance with University guidelines.[1]


**Affiliations**

[1] Oxford Institute of Clinical Psychology Training and Research, University of Oxford & Oxford Health NHS Foundation Trust, Warneford Hospital, Headington, Oxford, OX3 7JX

[2] Population, Policy and Practice Research and Teaching Department, University College London Great Ormond Street, Institute of Child Health, 30 Guilford Street, London, WC1N 1EH, UK

[3] Institute of Health Informatics and Health Data Research UK, University College London, 222 Euston Road, NW1 2DA London, UK

[4] Department of Anaesthesia & Pain Medicine, Great Ormond Street Hospital for Children NHS Foundation Trust, Great Ormond Street, London WC1N 3JH

[5] Paediatric Pain Research Group, University College London Great Ormond Street, Institute of Child Health, 30 Guilford Street, London, WC1N 1EH, UK


**Word count:** 5119 (excl. tables, figures, abstract) | **Tables**: 2 | **Figures**: 6 | **Supplement**: 1

**Abstract**

**Objectives**: Children with adverse childhood experiences (ACEs) face an increased risk of developing chronic pain (CP), yet longitudinal evidence on the factors underlying this relationship remains limited. We assessed the association between early adverse childhood experiences (ACEs) and subsequent risk of CP, and whether this relationship was mediated by emotion regulation difficulties (ERDs).

**Design and participants:** Population-based birth cohort of 179,207 mothers and children with linked electronic health records (1998-2018) from the Clinical Practice Research Datalink GOLD (primary care), Hospital Episode Statistics (secondary care), and the Office for National Statistics mortality register. We followed the cohort from 1-year before birth (mothers only) up to 16-years post-birth.

**Primary outcome:** First recorded CP in children between 7-years and 16-years post-birth, identified by an algorithm capturing recorded diagnoses of CP and continuous pain episodes.

**Main exposures:** ACEs and ERDs in children. ACEs were defined as child maltreatment, maternal intimate partner violence, maternal mental health problems, and adverse family environments recorded one year before birth (maternal records) up to three years post-birth. ERDs were defined as emotional and behavioural presentations in children between four and six complete years post-birth. We used Cox-proportional models to test the hypotheses that ACEs increase the risk of CP, and that this risk was mediated by ERDs and common non-communicable child diseases (NCDs). NCDs were hypothesised intermediate confounders and analysed as co-joint mediators with ERDs.

**Results:** During a median follow-up of 11-years, children with any ACEs or ERDs had almost a two-fold higher risk of CP between 7 and 16-years old relative to children without ACEs or ERDs. We found a consistent dose-response relationship between the number of ACEs, the number of NCDs, ERDs and increased risk of CP. ERDs in children between 4- and 6-years

post-birth mediated 10% of the association between ACEs and CP (mediated proportion range: 9%-11%; $p<0.001$).

**Conclusions**: ACEs and ERDs are associated with an increased risk of CP among children presenting to primary care during early child development. ERDs may play an important causal role in the development of CP. Further longitudinal research should evaluate specific ERD-related mechanisms for early intervention in children with recurring pain.

## Introduction

Chronic pain (CP) is the fourth leading cause of disability among children and adolescents between 10 years and 24 years old.[1] CP affects approximately 21%-26% of children between 13 and 18 years old in the US.[2-4] The World Health Organisation (WHO) and the International Association for the Study of Pain Taskforce define pain as an unpleasant sensory and emotional experience resembling potential or threatened tissue damage.[5] CP is defined as pain persisting longer than three months or longer than the expected recovery time,[6] including unexplained pain persistence and pain from underlying health conditions (e.g., juvenile arthritis).[7] Children with CP often go extended periods without any treatment, face recurrent disbeliefs about their pain,[8] and have an increased risk of mental health problems, substance misuse,[9] and suicide.[10] Despite these health risks, the contributing factors to CP in children remain poorly understood.[11] There are currently no NICE recommended treatments for children with CP.[12] The few psychological treatments for CP among children show no long-term benefits relative to treatment as usual.[13] Reliable longitudinal studies on the biopsychosocial pathways of CP are urgently needed to inform early psychological interventions for children with CP and to prevent CP from persisting into adulthood.[11,14]

CP is a complex biopsychosocial condition that frequently co-occurs with different mental and physical health problems in children.[2,3,15] Whilst multiple possible mechanisms help explain this co-occurrence, one consistent hypothesis is that adverse childhood experiences (ACEs) predispose children to emotion regulation difficulties (ERDs), negatively influencing how children cope with future pain and distress (see figure 1).[16,17] ACEs may include child maltreatment (CM), exposure to maternal intimate partner violence (mIPV), adverse family environments (AFE) and maternal mental health problems (mMHPs), which can cause significant biopsychosocial harm to children's development.[17,18] ERDs refer to ongoing failures to re-appraise, re-direct attention or behaviourally modify one's emotional state.[19-23] ERDs affect approximately 9.5% of children between 3 and 11 years old in the UK,[24,25] and often emerge throughout childhood as a hypothesised precursor of different mental health

problems and recurring pain.[16,25-27]

**Figure 1.** Asmundson *et al*. (2009)[28] biopsychosocial shared vulnerability model (modified) for mechanisms of CP in children

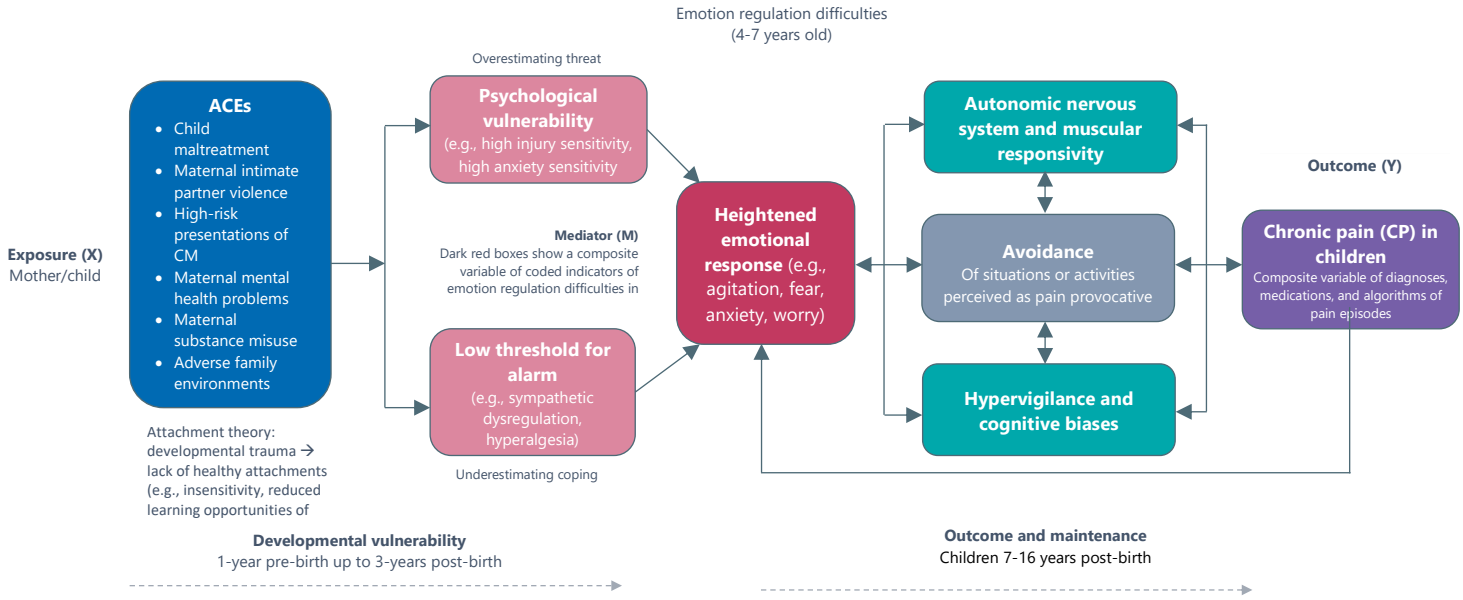



**Figure 1.** Shows a conceptual diagram of a modified version of Asmundson *et al's* shared vulnerability model of chronic pain based on its co-occurrence with anxiety and trauma-related disorders in adults. To aid with the study aims and analyses, the figure integrates a modified causal diagram with the causal factor (X), mediator (M) and outcome (Y) represented along the horizontal axis. The model postulates that children with ACEs (blue box) face an increased risk of developing heightened emotional and physiological reactivity from prolonged stress and lack of protective factors (e.g., healthy parental modelling experiences, emotional validation, secure attachments). Over time, this interaction leads to a maintained cycle of emotion dysregulation (red boxes), where children cope by attending to threat (cognitive biases/hypervigilance) and avoid pain provoking and distressing situations, fearing they will cause further distress. However, this avoidance pattern increases children's underlying anxiety and stress, reinforcing their emotional reactivity and muscular responsivity to pain. Avoidance also prevents new learning of more balanced threat perceptions and more effective emotion regulation, which maintains the pain (purple). CP does not need to be preceded by an injury.

According to Asmundson *et al.'s* shared vulnerability model of CP and mental health problems (figure 1), repeated exposure to ACEs leads to an overactivated sympathetic nervous system and elevated emotional reactivity that maintains ERDs and pain via three pathways. First, without protective factors, children with ACEs are more likely to develop insecure attachments from reduced caregiving responses of emotional validation (e.g., *"my pain matters"*) and reduced experiences of healthy parental modelling of emotion regulation.[28-30] Second, to cope, children may develop cognitive biases toward threats, learn to suppress emotions, and avoid situations they fear will cause further distress.[31,32] Finally, traumatic stress may also negatively disrupt children's nociceptive development, impacting pain processing mechanisms.[33] Over time, however, this interaction of biopsychosocial factors prevents new learning of balanced threat appraisals (e.g. *"my pain is seen", "I can cope"*), creating a maintenance cycle of ERDs and any subsequent CP.[10,11,34-38] ERDs may

therefore act as a shared potential psychological mediator of pain persistence and co-occurring health problems in children exposed to ACEs.[28,39-44]

Although cross-sectional and experimental studies support a potential shared vulnerability model of CP,[45,46] longitudinal evidence from childhood remains limited. Existing data on ACEs from childhood are primarily based on retrospective cross-sectional reports in adults, prone to reverse causality and recall bias.[47-50] A recent meta-analysis of 37 studies on the effects of multiple ACEs on poor health outcomes found 11 cohort studies,[51] all with ACE data based on retrospective self-reports and with the youngest study participant aged ≥15 years at baseline.[52] Pain specific studies in children are predominately based on smaller school samples, with limited follow-up and lack of clinically relevant measures of pain or ERDs.[11] A large systematic review in 2016 found eight longitudinal studies on psychosocial predictors of pain in children.[53] Of these, no study applied clinical cut-off criteria to ascertain outcomes of CP or psychological difficulties,[54-58] and only two studies provided follow-up longer than 24 months.[59-61]

Linked electronic health records (EHRs) of mothers and children provide a rich data source of prospectively recorded clinically relevant information on ACEs, ERDs and pain-related presentations from birth into adolescence.[62-64] Children routinely attend primary care for surveillance and vaccinations from 6-8 weeks to 4-6 years post-birth.[65,66] Taking advantage of linked EHRs from mothers and children presenting to primary care and hospitals, we conducted a population-based birth cohort study in two phases. In phase one, we developed clinically relevant indicators to estimate the prevalence of CP stratified by ACEs, ERDs and five commonly co-occurring non-communicable child health diseases (NCDs). We then longitudinally examined the effect of ACEs, NCDs, and ERDs on children's subsequent risk of CP. Based on the shared vulnerability model (figure 1), we hypothesised that ACEs measured between one year pre-birth (mothers only) and three years post-birth would increase the risk of CP in children between 7 and 16-years post-birth. We hypothesised that the risk of CP would increase in a dose-response manner dependent on the presence of ERDs measured between 4 and 6 complete years post-birth (<7$^{th}$ birthday),

dependent on the presence of NCDs, or based on the number or types of ACEs. In phase two, we conducted a mediation analysis based on the counterfactual framework,[67] to test the hypothesis that ERDs would partially mediate the risk of ACEs on subsequent CP. We stratified all analyses by child sex.

## Methods

We derived a population-based birth-cohort study of linked mothers and children using the mother-baby link (MBL) in the Clinical Practice Research Datalink GOLD (CPRD) via the CALIBER platform.[68] CPRD GOLD contains anonymised primary care health records from approximately 6% of the UK population and is nationally representative of age, gender, ethnicity, and BMI.[69] CPRD provides primary care diagnoses, prescriptions, maternity and referral records through the Read coding scheme. The data are recorded during care or opportunistically by GPs, health visitors or nurses.[69] Mothers and children are linked with high validity using GP practice-specific household IDs and maternity records.[70-72] There is no validated method to link paternal records in CPRD.

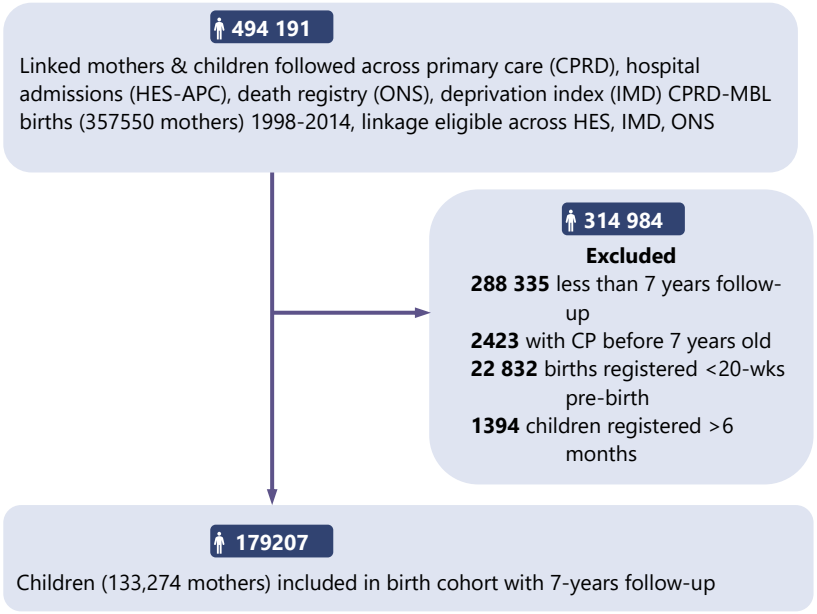
The MBL was linked to the Hospital Episodes Statistics Admitted Patient Care (HES-APC; secondary care), the 2015 edition of the Index of Multiple Deprivation (IMD-2015) and mortality data from the Office for National Statistics (ONS). HES-APC contains data on all NHS funded hospital admissions in England, with diagnoses provided via ICD-10 codes and operating procedure codes (OPCS-4). Coded records in CPRD and HES-APC show high positive predictive values for identifying mental and physical health problems,[73,74] and ACEs.[75,76] The IMD-2015 is the official composite score of deprivation in England for smaller areas (average 1500 households per area) derived from seven domains, ranging from average income to crime rates of the area. Mothers and children were assigned an IMD quantile (1=least deprived to 5=most deprived area) based on their postcode within six months of birth. ONS includes cause-specific mortality data from mandatory registered death certificates. This study was approved by the MHRA (UK) Research Data Governance process *[RDG protocol. 20_000261],* including approval under section 251 of the National Health Service Act 2006.

## Birth cohort

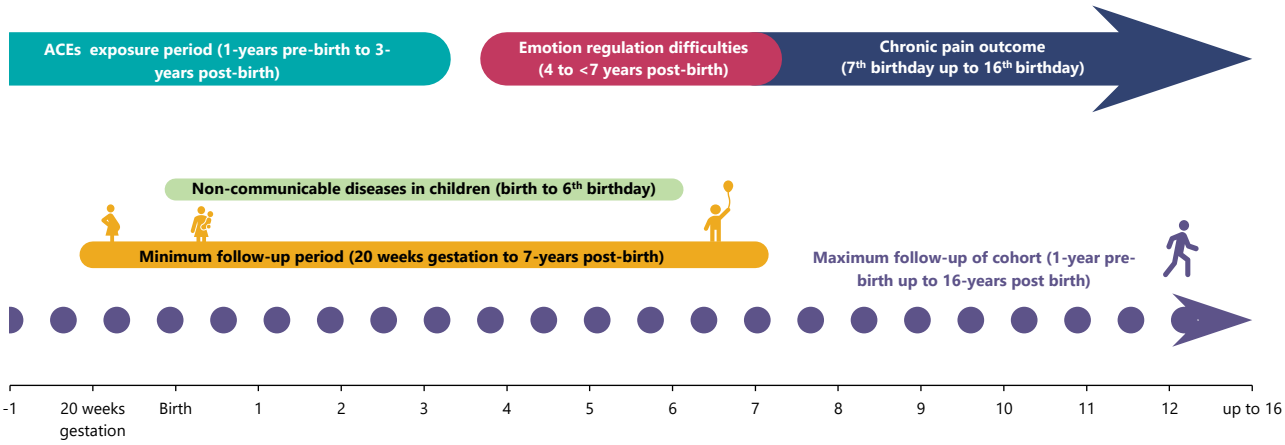
Figure 2A shows the birth cohort selection, and figure 2B depicts exposure periods for studied indicators and measures. We selected children born between 1 April 1998 and 1 April 2011 who registered with a CPRD general practice within 6-months of birth and had a minimum of 7-years follow-up post-birth with a CPRD pratice. Mothers had to register with the CPRD pratice before 20-weeks of gestation, allowing essential pregnancy or birth covariates to be obtained.[77] To ensure ACEs and ERDs occurred before the first incidence of CP, we excluded children with a CP indicator before age 7 (n=2423 children).

**Figure 2**. Flow chart of birth cohort selection and exposure periods

**A.** Flow chart of birth cohort selection




**B.** Follow-up time and different exposure periods of measures



We followed children and mothers from one year before birth (mothers only) until they transferred out of the CPRD practice, the practice's last data collection date, death, the end of the study period (27 June 2018) or children's 16th birthday, whichever came first.

**Primary outcome of chronic pain (CP; 7-16 years post-birth)**

The primary outcome was the first recorded CP in children between 7 and 16-years old. We defined CP using a developed hierarchical algorithm, prioritising any first specific diagnosis of CP, specialist pain clinic referrals, or prescriptions for higher potency pain analgesics lasting longer than three months (e.g., morphine) recorded via Read codes (GP data) or ICD-10 codes (hospital admissions).[78] The algorithm then identified CP cases using a broader code list of candidate CP indicators, drug prescriptions (e.g., adjuvant co-analgesics, weak opioids) and continuous pain episodes.[79] The code list of CP indicators was reviewed by a clinical expert (RH; Consultant in Anaesthesia and Pain Medicine for children; appendix C3), and systematically tested for relevance based on their consistent risk association with the specific CP diagnoses (i.e. acting as an internal reference standard; see appendix C2-C5).

Continuous pain episodes were defined as two or more pain recordings with a minimum of 90 days apart and a maximum of 300 days apart. We adapted this time interval from a previous validation study identifying CP in EHRs of children and adults.[80] The event date of the first pain-related recording defined the start of the episode. We classified pain types based on the most frequently recorded pain symptoms within 1-year of the index recording, including abdominal pain, joint pain (incl. arthritis/osteoarthritis), chest or breast pain, back pain, cervicalgia, or other musculoskeletal pain.

**ACEs (between 1-year pre-birth and 3-years post-birth)**

We ascertained ACEs from the child or the maternal record between one year pre-birth and three years post-birth (≤3rd birthday). We used previously validated algorithms to classify clinically relevant ACEs, including CM, mIPV, MSM, mMHPs and AFE (e.g. clinically relevant household challenges), consistent with the original ACE study.[81,82] We have reported the theoretical framework, definitions, algorithms and code lists elsewhere and online (https://acesinehrs.com/).[76]

**ERDs (4-7 years post-birth)**

As specific mental health problems are rarely diagnosed in children under 8-years old,[83] we defined ERDs as any first coded indicator of a potential anxiety disorder, post-traumatic stress disorder, depressive disorder or neurodevelopmental condition recorded via Read (GP data) or ICD-10 codes between 4 and 7-years post-birth (<7$^{th}$ birthday).[84] We developed an algorithm to ensure indicators represented clinically relevant ERDs following the same procedures described above for CP (appendix C4). Here, we compiled a broader code list of candidate ERD indicators, hierarchically classified by first prioritising diagnostic codes, emotional problems and self-harm indicators (internal reference standard of ERDs). These prioritised presentations were considered most reactive and least effective in providing long-term emotional relief (e.g., self-harm etc.),[85] hypothesised to represent a cumulation of previously failed emotion regulation strategies.[86,87] We included broader indicators of ERDs (e.g., symptoms) based on their consistent risk association with the internal ERD reference standard (appendix C4). We included potential neurodevelopmental conditions in the primary ERD indicator, given their potential association with ACEs (e.g., maternal substance misuse during pregnancy linked to Autism),[88,89] and high prevalence among children with ERDs and CP.[90] For the sensitivity analysis, we created a separate ERD indicator which excluded neurodevelopmental conditions.

**Covariates and confounders**

In phase one, we included covariates on maternal IMD (social deprivation), non-communicable diseases in children (NCDs) classified according to the global burden of disease (GBD) hierarchy (see appendix C8),[91,92] birth year and GP region. We limited NCDs to the five most common conditions in children measured between birth up to their sixth birthday, including chronic respiratory diseases, neoplasms, neurological disorders (excluding neurodevelopmental conditions), diabetes and kidney diseases, cardiovascular diseases and others (see appendix C8 for an exhaustive list).[91,92] We stratified all estimates by sex, as biological differences exist in pain classifications for girls (e.g., pelvic pain, menstruation cycle etc.) compared with boys.[93,94]

In phase two, we conducted a mediation analysis using the counterfactual framework of causal inference.[95] This approach aims to break down the total effect estimate into a controlled direct effect (CDE) and a pure indirect effect (PIE) by controlling for alternative causal pathways of CP in the analysis. The CDE is the effect of ACEs on CP when ERDs are "fixed" at the same level across all variables (i.e. how much of the effect on CP is due to ACEs). The PIE is the effect of ACEs on CP that act via ERDs (i.e. how much of ACEs effect on CP is attributable to ERDs).

We used a *"joint mediator"* approach to decompose the direct and indirect effects of ACEs as described by VanderWeele *et al*.[95] Causal inference requires adjustment for all known confounders (*see appendix C9 and* VanderWeele *et al*., for a complete list of assumptions).[67,95,96] However, as described by De Stavola *et al*.,[97] adjustments for exposure-induced mediator-outcome confounders (herein termed "*intermediate confounders"*) are often unrealistic within life course epidemiology given the myriad factors that contribute to health conditions during child development.[97] As shown in the simplified causal directed acyclic graph below (figure 3), ACEs may be causally linked to multiple different health conditions (i.e. NCDs acting as intermediate confounders), which may affect both ERDs and CP, violating the causal assumption of no "*intermediate confounders".*

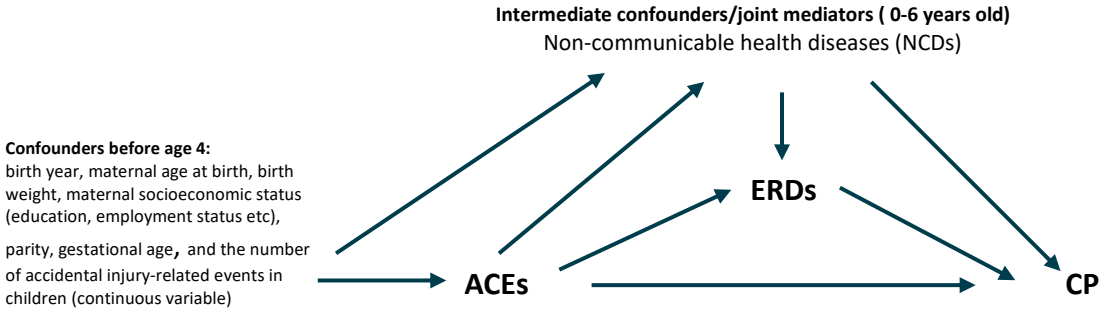



**Figure 3.** Simplified* causal directed acyclic diagram
**Does not show all interrelationships between confounding variables under each heading*

To statistically circumvent the *"no intermediate confounder"* causal assumption, we adopted the strategies by VanderWeele *et al*.,[95] treating ERDs and NCDs as joint mediators of ACEs whilst adjusting for baseline cofounders (appendix C9). This approach also mirrors

NICE practice guidelines that children should receive joint interventions (i.e. mediators) for co-occurring NCDs and ERDs.[98] Baseline confounders included (figure 3): maternal age, birth weight, maternal IMD, parity, gestational age, birth year and the number of accidental injury-related events in children as per Herbert *et al*. (continuous variable).[99] Intermediate confounders included any of the above GBD classified NCDs.

**Statistical analyses**

***Development of indicators.*** We used a data-driven machine learning variable selection approach to expand the CP and the ERD indicators, respectively, with broader identified candidate indicators (see appendix C2).[100] For each indicator, the machine learning model, automatically selects clinically relevant indicators with the highest predictive values of the internal reference standard.[100]

***Inverse probability weighting for censoring.*** To account for potential selection bias by excluding children who could not be followed up to their 7$^{th}$ birthday, we modelled all estimates using inverse probability weights (IPWs; appendix C6).[101,102] We calculated the IPWs using a logit regression model based on the probability of being censored before 7-years post-birth using predictors and auxiliary variables described by Abel *et al*.[103] (appendix C10).

***Phase one: prevalences and associations between ACEs, ERDs, NCDs and CP.*** We plotted cumulative incidence curves of first recorded CP by ACE, NCDs and ERDs, relative to unexposed children using age as the timescale. To compute period prevalences of ACEs, ERDs and CP within respective exposure periods, we used logistic regression models with IPWs (adjusted for birth year and clustering of siblings). We then examined the association between ACEs (including number/types of ACEs) and CP, and separately ERDs and CP using Cox-proportional hazard models with IPWs adjusted for birth year and GP region. We used robust sandwich estimators to account for the clustering of multiple children per mother. To examine if CP was associated with expected social and health risk factors, we repeated the analysis to examine the association between maternal deprivation, the five selected NCDs and CP.[91,92] We checked the cox-proportional hazards assumption using Schoenfeld's

residuals, log-log plots of Kaplan-Meier estimates of the survival function and the link test.[104]

***Phase two: mediation analysis****.* To assess potential mediation*,* we decomposed the overall effect of ACEs on CP in the presence of ERDs as a mediator with NCDs using the four-way decomposition method as recommended by VanderWeele *et al*.[105] This decomposition examines the causal effect via four pathways: the controlled direct effect (*"neither due to mediation or interaction"*), reference interaction ("*due to interaction only"*), mediated interaction ("*due to mediated interaction"*) and pure indirect effect (*"due to mediation only*"). We used the *"med4way"* package in Stata 16 to conduct the mediation analysis,[106,107] using Cox proportional hazards models and weighted logistic regression models with IPWs adjusted for the hypothesised confounders. We computed 95% percentile confidence intervals using bootstrapping (repeated 1000 times). The *"med4way"* package automatically calculates the proportion of excess risk from each decomposition to aid with clinical relevance.[108]

***Sensitivity analyses.*** To test the robustness of our estimates and explore potential selection bias, we compared estimates from phase one with results from cox-proportional hazard models in the complete linkable birth cohort before exclusions. We also repeated the mediation analysis on ERDs, excluding any neurodevelopmental conditions.

***Missing data.*** We imputed missing values under the missing at random assumption for covariates on parity, gestational age, birth weight, and deprivation (IMD) obtained during pregnancy or up to one year before birth (table 1). Predictors in the model included ACEs, ERDs, CP and birth characteristics (table 1). We used the MICE package in R to create 25 imputed datasets (25 iterations for each imputation) and pooled estimates using Rubin's rules.

## Results

Table 1 summarises child and maternal cohort characteristics by ACEs and CP. We included 179,207 children of 133,274 mothers (312,481 patients; 400 GP practices), followed from 1-year pre-birth up to 16-years post-birth (range follow-up: 7 years to 16

years; median: 11.1 years [IQR: 8.9-14.01]; figure 1). The adjusted and weighted period prevalence for any ACEs between 1-year before birth and 3-years post-birth was 41.9% (95% CI 41.7%-42.2%; 77,357/179,207), with similar estimates for boys (42.2%; 39,971/92,026) and girls (41.6%; 37,386/87181).

**Table 1.** Cohort characteristics by adverse childhood experiences (ACEs) and chronic pain (CP; n=179,207)

| | No ACEs (n=101,850) | | Any ACE (n=77,357; 41.9%) | | |
|---|---|---|---|---|---|
| | **No CP (n=96,478; 53.8%)** | **CP (n=5372; 5.2%)** | **No CP (n=72,369; 40.4%)** | **CP (n=4988; 6.4%)** | **Total (n=179,207)** |
| **Gender** | | | | | |
| Male | 49767 (51.6%) | 2288 (42.6%) | 37835 (52.3%) | 2136 (42.8%) | 92026 (51.4%) |
| Female | 46711 (48.4%) | 3084 (57.4%) | 34534 (47.7%) | 2852 (57.2%) | 87181 (48.6%) |
| **Maternal ethnicity** | | | | | |
| White | 82247 (85.2%) | 4558 (84.8%) | 64513 (89.1%) | 4440 (89.0%) | 155758 (86.9%) |
| Asian | 5043 (5.2%) | 340 (6.3%) | 2932 (4.1%) | 245 (4.9%) | 8560 (4.8%) |
| Black | 2401 (2.5%) | 117 (2.2%) | 1691 (2.3%) | 95 (1.9%) | 4304 (2.4%) |
| Other | 1247 (1.3%) | 54 (1.0%) | 614 (0.8%) | 54 (1.1%) | 1969 (1.1%) |
| Mixed | 637 (0.7%) | 30 (0.6%) | 587 (0.8%) | 30 (0.6%) | 1284 (0.7%) |
| *Missing data* | 4903 (5.1%) | 273 (5.1%) | 2032 (2.8%) | 124 (2.5%) | 7332 (4.1%) |
| **Maternal socioeconomic status quintile*** | | | | | |
| 1 (least deprived) | 28100 (29.1%) | 1599 (29.8%) | 15938 (22.0%) | 1115 (22.4%) | 46752 (26.1%) |
| 2 | 21946 (22.7%) | 1197 (22.3%) | 13814 (19.1%) | 1005 (20.1%) | 37962 (21.2%) |
| 3 | 18253 (18.9%) | 996 (18.5%) | 14007 (19.4%) | 988 (19.8%) | 34244 (19.1%) |
| 4 | 15364 (15.9%) | 872 (16.2%) | 14259 (19.7%) | 963 (19.3%) | 31458 (17.6%) |
| 5 (most deprived) | 12769 (13.2%) | 705 (13.1%) | 14293 (19.8%) | 916 (18.4%) | 28683 (16.0%) |
| *Missing data* | 46 (0.0%) | 3 (0.1%) | 58 (0.1%) | 1 (0.0%) | 108 (0.1%) |
| **Region of England, GP practice** | | | | | |
| London | 14769 (15.3%) | 729 (13.6%) | 8845 (12.2%) | 505 (10.1%) | 24848 (13.9%) |
| Northeast, West, Yorkshire | 19729 (20.4%) | 1049 (19.5%) | 16139 (22.3%) | 1100 (22.1%) | 38017 (21.2%) |
| East/West Midlands | 12090 (12.5%) | 699 (13.0%) | 10514 (14.5%) | 732 (14.7%) | 24035 (13.4%) |
| East England | 11596 (12.0%) | 705 (13.1%) | 7602 (10.5%) | 667 (13.4%) | 20570 (11.5%) |
| Southeast/West/Central | 38294 (39.7%) | 2190 (40.8%) | 29269 (40.4%) | 1984 (39.8%) | 71737 (40.0%) |
| **Type of ACEs (non-exclusive)** | | | | | |
| AFE | - | - | 38452 (53.1%) | 2598 (52.1%) | 41050 (22.9%) |
| MSM | - | - | 6388 (8.8%) | 328 (6.6%) | 6716 (3.7%) |
| mIPV | - | - | 1290 (1.8%) | 89 (1.8%) | 1379 (0.8%) |
| CM | - | - | 3960 (5.5%) | 261 (5.2%) | 4727 (2.6%) |
| Any CM or mIPV | - | - | 5110 (7.1%) | 351 (7.0%) | 6138 (3.4%) |
| mMHPs | - | - | 47141 (65.1%) | 3550 (71.2%) | 50691 (28.3%) |
| **Number of different ACEs (exclusive)** | | | | | |
| 1 | - | - | 52290 (72.3%) | 3468 (69.5%) | 55758 (31.1%) |
| 2 | - | - | 17142 (23.7%) | 1325 (26.6%) | 18467 (10.3%) |
| ≥3 | - | - | 2937 (4.1%) | 195 (3.9%) | 3132 (1.7%) |
| **Child health comorbidities (GBD classification scheme)*** | | | | | |
| Any GBD | 9027 (9.4%) | 698 (13.0%) | 8869 (12.3%) | 970 (19.4%) | 19564 (10.9%) |
| Chronic respiratory diseases | 8050 (8.3%) | 630 (11.7%) | 7875 (10.9%) | 853 (17.1%) | 17408 (9.7%) |
| Other | 606 (0.6%) | 62 (1.2%) | 648 (0.9%) | 63 (1.3%) | 1379 (0.8%) |
| Congenital anomaly* | 3661 (3.8%) | 234 (4.4%) | 3353 (4.6%) | 324 (6.5%) | 7572 (4.2%) |
| Neurological disorders† | 331 (0.3%) | 28 (0.5%) | 364 (0.5%) | 49 (1.0%) | 772 (0.4%) |
| Diabetes and kidney diseases | 352 (0.4%) | 24 (0.4%) | 324 (0.4%) | 36 (0.7%) | 736 (0.4%) |
| Cardiovascular diseases | 230 (0.2%) | 22 (0.4%) | 269 (0.4%) | 44 (0.9%) | 565 (0.3%) |
| **Any CP by location/type** | | | | | 10360 (4.4%) |
| Abdominal pain | - | 1133 (21.1%) | - | 1109 (22.2%) | 3572 (2.0%) |
| Joint pain (incl. arthritis/osteoarthritis) | - | 826 (15.4%) | - | 728 (14.6%) | 2556 (1.4%) |

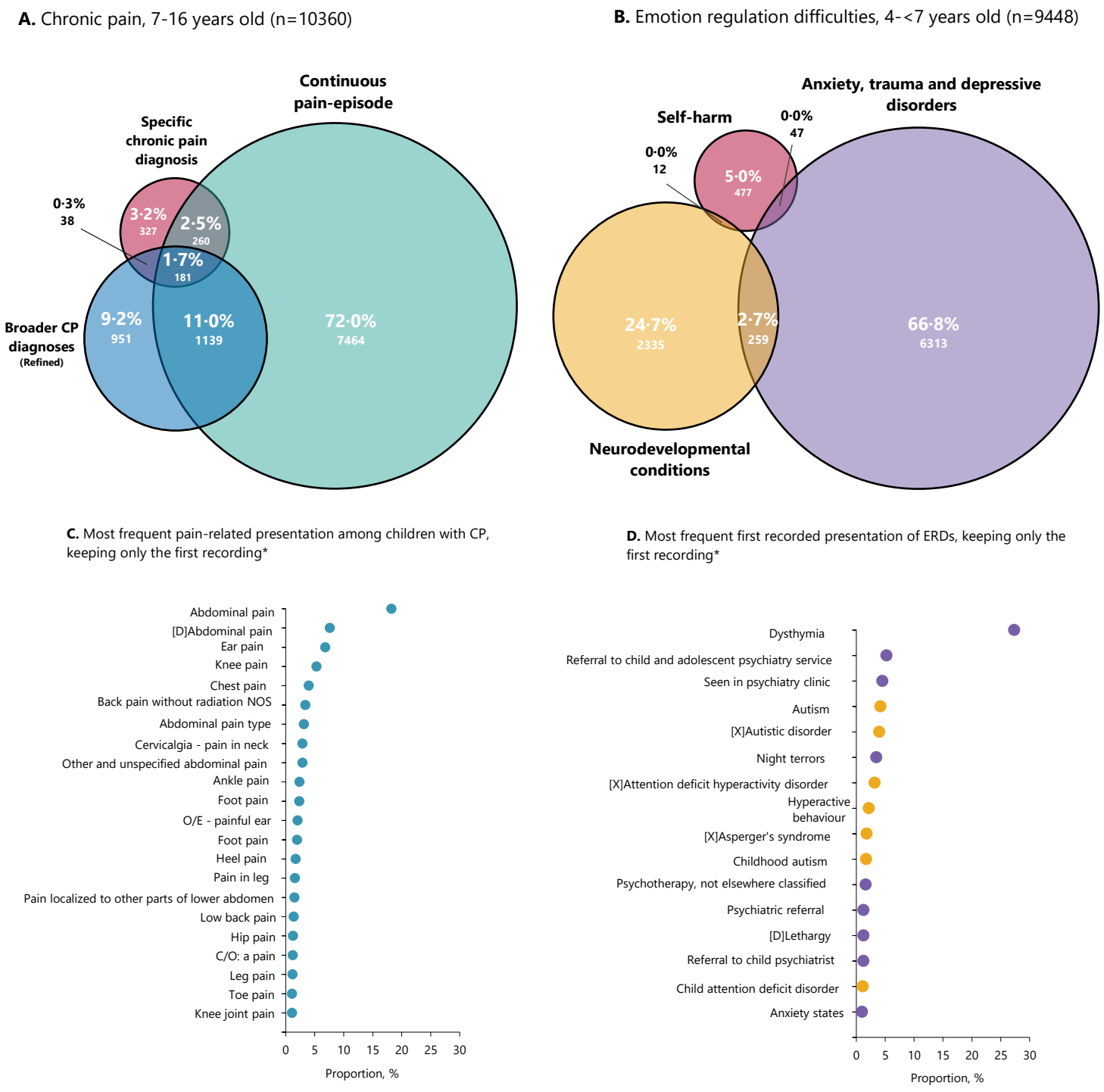
| | | | | | |
|---|---|---|---|---|---|
| Unspecified pain | - | 257 (4.8%) | - | 237 (4.8%) | 624 (0.3%) |
| Musculoskeletal, all others | - | 536 (10.0%) | - | 557 (11.2%) | 1916 (1.1%) |
| Any back pain | - | 206 (3.8%) | - | 201 (4.0%) | 547 (0.3%) |
| Chest or breast | - | 121 (2.3%) | - | 119 (2.4%) | 417 (0.2%) |
| Cervicalgia | - | 43 (0.8%) | - | 45 (0.9%) | 118 (0.1%) |
| **Available follow-up post-birth** | | | | | |
| <12 years | 51502 (53.4%) | 2804 (52.2%) | 42922 (59.3%) | 2829 (56.7%) | 29240 (16.3%) |
| ≥12 years | 44976 (46.6%) | 2568 (47.8%) | 29447 (40.7%) | 2159 (43.3%) | 149967 (83.7%) |
| **Birth characteristics** | | | | | |
| **Maternal age at birth, years*** | | | | | |
| <20 | 2172 (2.3%) | 113 (2.1%) | 3620 (5.0%) | 242 (4.9%) | 6147 (3.4%) |
| 20-30 | 31668 (32.8%) | 1866 (34.7%) | 29837 (41.2%) | 2090 (41.9%) | 65461 (36.5%) |
| 30-40 | 57528 (59.6%) | 3130 (58.3%) | 35762 (49.4%) | 2434 (48.8%) | 98854 (55.2%) |
| ≥40 | 5110 (5.3%) | 263 (4.9%) | 3150 (4.4%) | 222 (4.5%) | 8745 (4.9%) |
| **Multiple pregnancy*** | | | | | |
| Singleton | 86951 (90.1%) | 4778 (88.9%) | 66434 (91.8%) | 4518 (90.6%) | 162681 (90.8%) |
| Multiple (twins etc)* | 2491 (2.6%) | 113 (2.1%) | 1928 (2.7%) | 119 (2.4%) | 4561 (2.5%) |
| *Missing data* | 7036 (7.3%) | 481 (9.0%) | 4007 (5.5%) | 351 (7.0%) | 11875 (6.6%) |
| **Gestational age, weeks*** | | | | | |
| ≥37 | 65212 (67.6%) | 3528 (65.7%) | 51369 (71.0%) | 3418 (68.5%) | 123527 (68.9%) |
| <37 | 5002 (5.2%) | 262 (4.9%) | 4561 (6.3%) | 332 (6.7%) | 10157 (5.7%) |
| *Missing* | 26264 (27.2%) | 1582 (29.4%) | 16439 (22.7%) | 1238 (24.8%) | 45523 (25.4%) |
| **Birthweight, g*** | | | | | |
| ≥3500 | 33272 (34.5%) | 1730 (32.2%) | 24688 (34.1%) | 1597 (32.0%) | 61287 (34.2%) |
| 2500-3499 | 37298 (38.7%) | 2087 (38.8%) | 30373 (42.0%) | 2110 (42.3%) | 71868 (40.1%) |
| <2500* | 4301 (4.5%) | 253 (4.7%) | 4182 (5.8%) | 319 (6.4%) | 9055 (5.1%) |
| Missing | 21607 (22.4%) | 1302 (24.2%) | 13126 (18.1%) | 962 (19.3%) | 36997 (20.6%) |
| **Parity*** | | | | | |
| 0 | 36687 (38.0%) | 1993 (37.1%) | 27244 (37.6%) | 1814 (36.4%) | 67738 (37.8%) |
| 0-3 | 49483 (51.3%) | 2519 (46.9%) | 37916 (52.4%) | 2483 (49.8%) | 92401 (51.6%) |
| ≥4* | 3382 (3.5%) | 175 (3.3%) | 3512 (4.9%) | 173 (3.5%) | 7242 (4.0%) |
| *Missing data* | 6926 (7.2%) | 685 (12.8%) | 3697 (5.1%) | 518 (10.4%) | 11826 (6.6%) |
| **Birth years*** | | | | | |
| 1998-2005 | 66809 (69.2%) | 4705 (87.6%) | 47499 (65.6%) | 4325 (86.7%) | 123338 (68.8%) |
| 2006-2011 | 29669 (30.8%) | 667 (12.4%) | 24870 (34.4%) | 663 (13.3%) | 55869 (31.2%) |

*Denotes co-variates included in the multiple imputation model. Abbreviations: ACE=Adverse childhood experience, AFE=Adverse family environments, CM=Child maltreatment, CI=Confidence interval, ERDs=Emotion regulation difficulties (depression, anxiety, emotion, self-harm related and neurodevelopmental conditions), GBD scheme=Global burden of disease study grouping of diseases and disorders, HZ=Hazard ratio, IQR=Interquartile range , mIPV=Maternal intimate partner violence, mMHPs=Maternal mental health problems, MSM=Maternal substance misuse

### Prevalence estimates of CP and ERDs

Figures 4A-D show the developed CP and ERDs by the overlap of underlying presentations and frequently recorded codes. Figures 5A to 5E show the cumulative incidence of first CP by the number of ACEs and ERDs. The adjusted weighted period prevalence for any CP among children between 7 and 16-years old was 4.4% (95% CI 4.3-4.5%; 10,360/179,207). The period prevalence of CP was slightly higher for girls (5.1%, 95% CI 4.3%-4.5%; 5936/87,181) than for boys (3.7%, 3.6%-3.9%; 4424/92,026). The average age at first CP diagnosis was 11.1 years old (median: 10.9 years, [IQR: 9.0-13.2 years], range: 7.0-15.9 years), with no differences between girls and boys. Most children with CP were identified via continuous-pain episodes (83%), whereas 806 children (7.8%) were identified

**Figure 4.** Venn diagram showing overlap of different indicators for CP and ERD




*The y-axis represents specific coding terms of the clinical code assigned to the child's health care record in the GP data (Read codes) or hospital admission (ICD-10 codes) during .

via specific CP diagnoses (reference standard; figure 5A). Children with CP had, on average, 9.5 unique pain-related GP or hospital recordings. In contrast, children without a CP indicator had, on average, one pain-related recording (median: 2 pain visits). Abdominal

pain was the most common recorded pain type (34.5%; 3572/10,360), followed by joint pains (24.5%; 2556/10,360). Notably, about 1 in 3 children (31.2%; 55,924/179,207) had any pain-related recording between 7 and 16-years old.

The adjusted weighted period prevalence of ERDs in children between 4 and 7 years old was 5.4% (95% CI: 5.3%-5.5%; 9448/179,207). The period prevalence of ERDs was slightly higher for boys (6.7%, 6.6%-6.9%; 6075/92,026) than for girls (3.9%, 3.8-4.0%; 3373/87,181). The average age at the first record of ERDs was 5.4 years old (median: 5.4 years, [IQR: 4.6-6.2 years], range: 4-7 years old). The ERD indicator comprised mainly anxiety, trauma-related or depressive disorders (66.8%), followed by NCDs (24.7%; figure 4B).

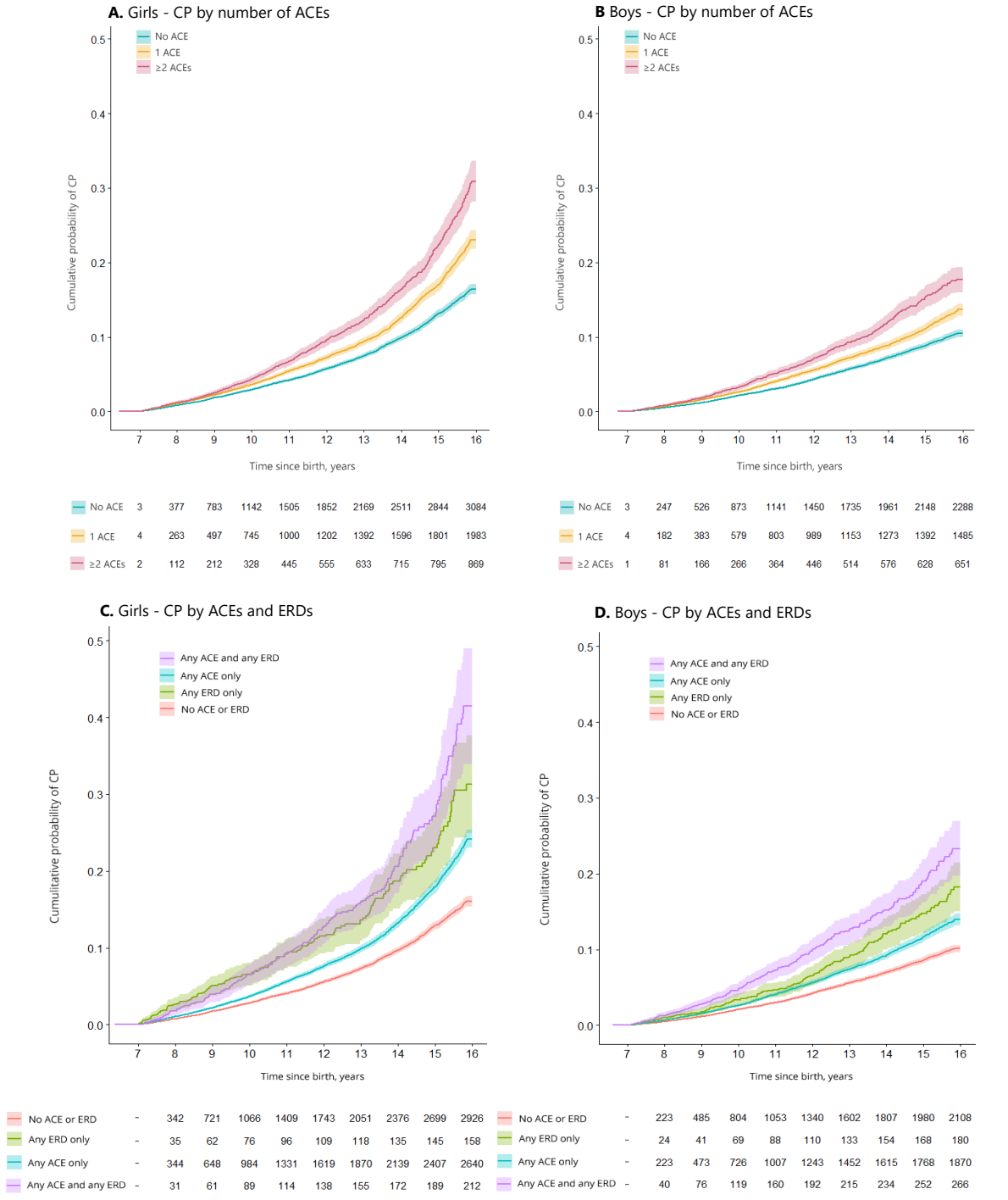
**Association between ACEs, ERDs and risk factors of CP**

Figures 5A-D show the cumulative incidence of CP by ACEs and ERDs (cumulative incidence of CP by NCDs shown in appendix C11), delineating that the highest incidence of first CP occurred between ages 14 and 16 years. Figure 6 displays CP's adjusted and weighted hazard ratios (aHZ) by ACEs, ERDs and risk factors stratified by child's sex. Overall, children with ACEs had a significantly higher risk of developing CP over time than children without

ACEs. Estimates were marginally higher for girls (aHZ: 1.39, 95% CI: 1.31-1.51; figure 6) than boys (1.33, 1.24-1.42). We found a consistent dose-response relationship between the number of ACEs and the risk of CP. For instance, girls with one ACE had an aHZ of 1.28 (1.20-1.35), whereas girls with four or more ACEs had an aHZ of 2.02 (1.37-2.97; boys aHZ: 1.99, 1.31-3.00), relative to girls with no ACEs. Girls and boys with any ERDs had a significantly higher risk of developing CP than children without ERDs (range aHZ: 1.92-1.77).

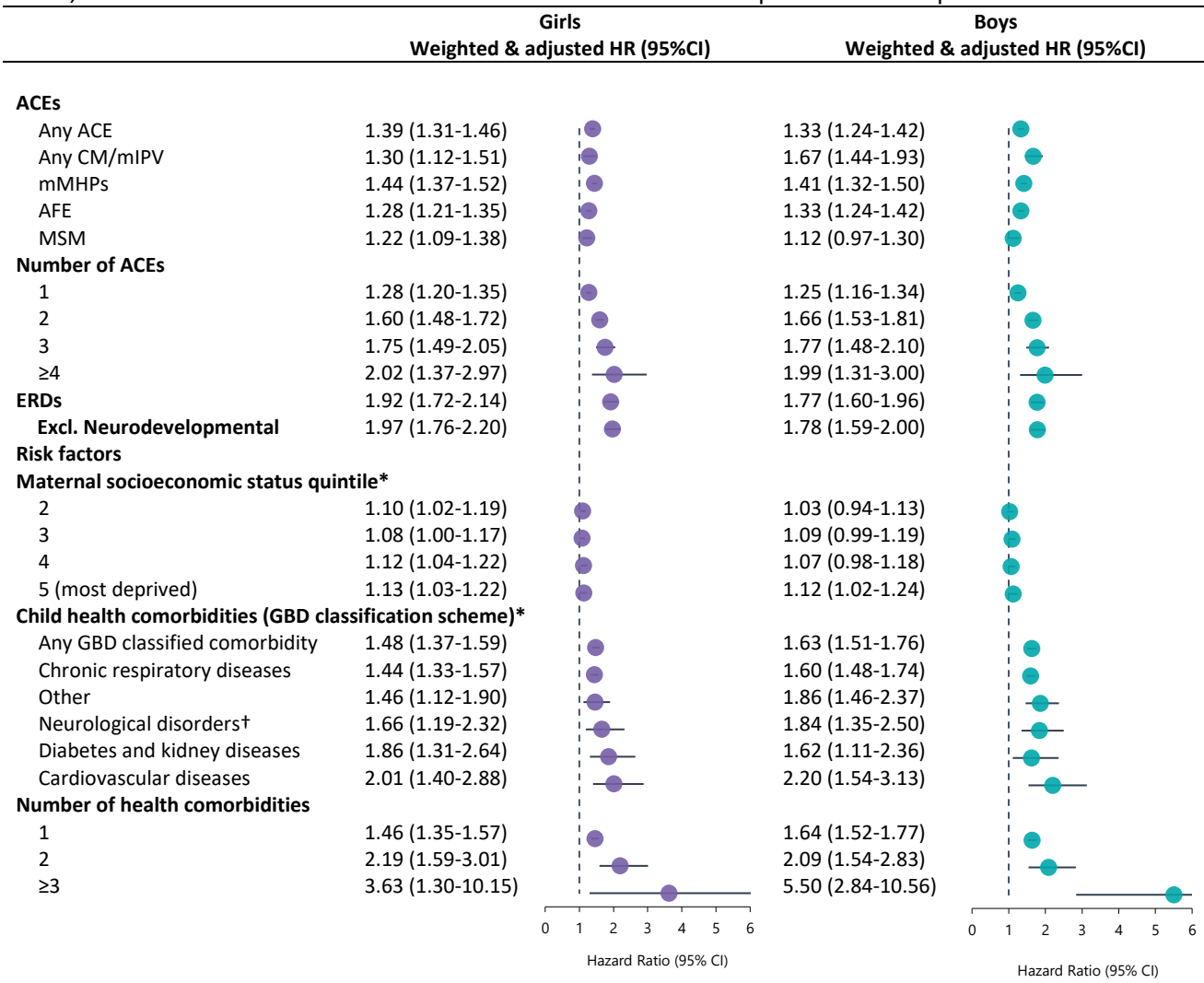
All of the six examined social and health risk factors for CP showed a significant association with CP, with similar estimates for boys and girls. The aHZ ranged from 5.50 (2.84-10.56) for boys with three or more diagnosed non-communicable diseases to 1.12 (1.02-1.24) for boys belonging to the most socially deprived quantile.

**Figure 5.** Cumulative probability of chronic pain by ACEs, number of ACEs and ERDs by sex




Small cell counts at baseline (<7 observations) in Figures 5C-5D have been censored (i.e. "-") as required by the Office for National Statistics disclosure control procedures.

**Figure 6**. Adjusted and weighted hazard ratios of chronic pain in children between 7 and 16-years old by ACEs, ERDs and common non-communicable health conditions compared with unexposed children




Risks of CP in children between 7 and 16-years old. Circles represents adjusted and weighted hazard ratios (HR). Horizontal lines represents the 95% confidence interval. HRs are adjusted for children's birth year and region. Weights are based on the inverse probability for loss-to-follow-up at 7-years post-birth using maternal age, region, number of non-birth-related hospital admissions, IMD, number of days enrolled with practice before birth, ACEs and CP as predictors. We accounted for clustering effects of siblings in the calculation of the robust standard errors based on the sandwich estimator. Abbreviations: ACE=Adverse childhood experience, AFE=Adverse family environments, CM=Child maltreatment, CI=Confidence interval, ERDs=Emotions regulation difficulties (anxiety, emotion, depressive and self-harm presentations), HZ=Hazard ratio, mIPV=Maternal intimate partner violence, mMHPs=Maternal mental health problems, MSM=Maternal substance misuse.

## Mediation analysis

The four-way decomposition analysis is shown in table 2. The four-way decomposition provides four estimates (i.e. controlled direct effect, reference interaction, mediated interaction and the pure indirect effect) to show how much of the effect from ACEs on CP is attributable to mediation (ERDs and NCDs), or an interaction between variables, or both. Overall, ERDs considered in combination with NCDs accounted for a modest mediated proportion of the association between ACEs and CP ($p$<0.001). The mediated proportion due to ERDs jointly with NCDs ("natural indirect effect") was 11.0% for girls (95% CI 5.7%-16.2%)

and 9.2% for boys (4.5%-14.0%). The direct and interaction effects were not significant but accounted for more than 80% of the excess effect of ACEs on CP (table 2).

**Table 2.** Four-way decomposition* of the causal effects of ACEs on the risk of CP in the presence of ERDs and covariates

| | Girls | | Boys | |
|---|---|---|---|---|
| **Effect decomposition** | **Estimate (95% CI)** | **P-value** | **Estimate (95% CI)** | **P-value** |
| Total direct effect | 0.35 (0.27, 0.428) | <0.001 | 0.38 (0.29, 0.47) | <0.001 |
| Controlled direct effect (CDE; due neither to mediation nor interaction) | 0.10 (-0.31, 0.65) | 0.492 | 0.39 (-0.005, 0.79) | 0.053 |
| Reference interaction ($INT_{ref}$; due to interaction only) | 0.15 (-0.31, 0.61) | 0.528 | -0.05 (-0.41, 0.32) | 0.791 |
| Mediated interaction ($INT_{med}$; due to mediation and interaction) | -0.01 (-0.02, 0.01) | 0.528 | 0.003 (-0.02, 0.02) | 0.791 |
| Pure indirect effect or mediated main effect (PIE; due to mediation only) | 0.04 (0.02, 0.05) | <0.001 | 0.035 (0.02, 0.05) | <0.001 |
| Total effect risk ratio | 1.35 (1.27, 1.43) | <0.001 | 1.38 (1.29, 1.47) | <0.001 |
| | **Proportion, % (95% CI)** | **P-value** | **Proportion % (95% CI)** | **P-value** |
| Total direct effect | | | | |
| Proportion CDE (due neither to mediation nor interaction) | 0.48 (-0.85, 1.82) | 0.477 | 1.03 (0.09, 1.97) | 0.031 |
| Proportion $INT_{ref}$ (due to interaction only) | 0.42 (-0.92, 1.77) | 0.538 | -0.13 (-1.08, 0.82) | 0.789 |
| Proportion $INT_{med}$ (due to mediation and interaction) | -0.02 (-0.07, 0.04) | 0.539 | 0.01 (-0.04, 0.06) | 0.789 |
| Proportion PIE (due to mediation only) | 0.11 (0.06, 0.16) | <0.001 | 0.09 (0.04, 0.14) | <0.001 |
| Overall proportion mediated | 0.09 (0.06, 0.13) | <0.001 | 0.10 (0.06, 0.13) | <0.001 |
| Overall proportion attributable to interaction | 0.41 (-0.89, 1.70) | 0.538 | -0.12 (-1.03, 0.78) | 0.789 |
| Overall proportion eliminated | 0.52 (-0.82, 1.85) | 0.449 | -0.03 (-0.97, 0.91) | 0.949 |

*The four-way decomposition provides four estimates (i.e. CDE, $INT_{ref}$, $INT_{med}$, PIE) to show how much of the effect is attributable to mediation, or interaction, or both.

*The four-way decomposition can be interpreted as follows:

Controlled direct effect (CDE): Indicates how much of the effect of ACEs on CP would be if we intervened on ERDs (i.e. setting the ERDs on the same average level for all individuals), and what the proportion of the effect from ACEs on CP are explained through pathways independent of ERDs.

Reference interaction ($INT_{ref}$): Indicates how much of the effect on CP does not depend on the presence of ERDs (mediator); the effect is therefore *"unmediated"* when the exposure does not depend on changing the mediator.

Mediated interaction ($INT_{med}$): Indicates how much of effect on CP is dependent on an interaction between ACEs and ERD (i.e. the exposure and mediator operate only via interaction or operate at different levels depending on interactional effects).

Pure indirect effect (PIE): Indicates how much of the effect on CP is due to ERDs (i.e. mediator) in the absence of ACEs. The estimate will be zero only if the mediator affects the outcome when the exposure is present.

Proportion-eliminated: indicates the proportion of effect from ACEs on CP we would "*block*" if we intervened on ERDs.

## Sensitivity analyses

When comparing estimates from study phase one with estimates re-analysed in the complete birth cohort before exclusions (appendix C12), we found slightly higher adjusted weighted hazard ratios for the association between ACEs, ERDs and CP. However, as children had shorter length of follow-up (<2 years) in the complete birth cohort, the CP outcome may have occurred before the exposures of ACEs and ERDs, limiting estimates

comparability with the main analysis. For the mediation analysis, when excluding neurodevelopmental conditions or NCDs from the ERDs yielded comparable results in direction and magnitude of the effect on CP (difference in mediated proportions <1%; appendix C13).

## Discussion

In this two-phased study, we estimated the prevalence of and associations between ACEs, NCDs, ERDs and CP in children using a large representative birth cohort of mothers and children presenting to primary or secondary care. In phase one, we found that a substantial proportion of children had recorded ACEs in the early developmental period (41.9%). A smaller but significant proportion also presented with ERDs between 4 and 7 years of age (5.4%) or with CP between 7 and 16 years old (4.4%). Consistent with our primary hypothesis in phase one, we found that children with ACEs had a significantly higher risk of developing CP than children with no ACEs. We found that the risk of CP increased in a dose-response manner for children with more ACEs or more chronic health comorbidities relative to children with no ACEs or chronic health conditions. In phase two, we tested the hypothesis that ERDs would partially mediate the association between ACEs and CP. Consistent with our second hypothesis, we found that ERDs co-jointly with NCDs mediated about 10% of the total association between ACEs and CP. Combined, these findings highlight that children with early ACEs or ERDs who present to primary care during child development have an increased risk of developing CP.

Our findings align with the accumulating evidence that early adversity during the developmental period predisposes children to vulnerability to emotional and chronic health conditions. Our study extends previous studies on CP in children in multiple ways. Systematic reviews of cross-sectional and birth cohort studies highlight that ACEs are associated with CP and emotional difficulties,[45,109-112] but this evidence has mainly been limited to smaller cross-sectional samples and retrospective self-report measures. Similarly, whilst previous studies found a significant co-occurrence of CP and ERDs in children,[28,113] studies have not been large enough to ensure that ACEs and ERDs temporally preceded the

outcome of CP in children. We use prospectively recorded and clinically relevant data from both mothers and children, overcoming earlier limitations of recall bias and reverse causality of ACEs, ERDs and CP. Until now, CP and ERDs have mainly been considered co-occurring health outcomes later in life.

Consistent with Asmundson *et al.'s* shared vulnerability model of CP,[28] we found that ERDs mediated some of the effect of ACEs on CP, highlighting that ERDs may act as an important potential psychological mediator of CP.[28,39-44] Asmundson *et al.'s* model predicts that ERDs are transdiagnostic psychological precursors that increase the risk of pain and co-occurring mental health problems becoming chronic.[25,26,36,114-119] Whilst ERDs co-jointly with NCDs mediated a fairly small proportion of the effect from ACEs (~10%), this proportion translates to a relatively large mediation given that CP is considered a heterogeneous complex biopsychosocial presentation. It is likely that ERDs cumulatively contribute to the development of CP via interactions between ACEs and other risk factors of CP over time. We also found that ERDs on their own conferred a similar risk for CP as did exposure to four or more ACEs. Collectively, these findings add to a broader view that ERDs act as important and potentially modifiable early risk factors in children, common across multiple long-term health problems, including CP.[25,26,36,114-119]

**Limitations**

This study has several limitations. First, less than 50% of linkable children across data sources had more than 7-years of follow-up of GP records, resulting in potential selection bias. However, the primary source of loss to follow-up was that the GP practice itself stopped using the clinical EHR system connected to CPRD GOLD data source. GPs can opt to change clinical EHR systems depending on local offers or systems used by neighbouring NHS services. It is, however, very likely families will continue to be registered with a GP, as 99.9% of the English population are registered with a GP.

Second, the low prevalence estimates of CP, CM and mIPV in this study suggest under-recording relative to self-report measures in children, limiting the generalisability of the findings. For instance, CM or CP may only be recorded for the most severe cases and in

children with higher health morbidity. However, the current prevalence estimates may also reflect a general under-recognition of CP by health care professionals. CP is a complex condition to diagnose and manage,[120] requiring multidisciplinary and specialist clinic input, a rare resource in England.

Third, EHRs lack a deeper resolution of psychological constructs to study cognitive mechanisms. Nonetheless, most validated psychological measures in young children (<8 years old) focus almost exclusively on behavioural presentations validated against professional opinion (e.g. teacher, GPs, psychologist).[121] We used clinically relevant and prospectively captured ERDs by GPs or hospitals, including symptoms and diagnostic levels.

Finally, because we used an observational study design with a joint-mediator approach, we cannot rule out unmeasured confounding or isolate the mediated effect of ERDs, limiting causal interpretations.[122] However, CP is based on a biopsychosocial model where factors interact bidirectionally (i.e. no single causal direction), with considerable overlap across different dynamic biopsychosocial mechanisms, making causal analyses of single mediators of CP challenging.

**Implications**

In 2020, the Lancet Child and Adolescent Health commission published four transformative goals to improve care and research for children with CP and their families.[11] The primary goal is to increase awareness of the unmet need of children with CP who present to services for care but whose symptoms may remain unheard ("*make pain matter*").[11] Many health care professionals do not realise the bidirectional nature of CP,[123] - that is, pain often comes with significant psychosocial distress and can lead to life-long disability. We show that children with ACEs and ERDs are more likely to develop CP, supporting the notion that adversity and emotional difficulties can predispose children to CP. The findings highlight the importance of targeting early *"transdiagnostic"* psychological and developmental factors in childhood that could promote resilience. Primary care and hospitals represent a critical entry point for offering family support to prevent future harm from ongoing ACEs. Systemic implications include increased psychoeducation in primary

care, parent education about pain and children's need for emotional validation, and increased provision of integrated multidisciplinary approaches to managing children's pain and emotional needs.[11,29]

**Future research recommendations**

To our knowledge, this is the first study to examine the longitudinal relationship between clinically relevant ACEs, ERDs and CP. The aims were intentionally kept broad. Future longitudinal studies should continue refining the transdiagnostic process of ERDs to determine specific cognitive and behavioural treatment targets for CP in children. For instance, there is a need to explore which specific pain-related cognitive appraisals are most common to help develop new or adapt current CBT treatments for CP in older children. One potential avenue for development involves pain reprocessing therapy (PRT). PRT is a trauma-focused CBT (TF-CBT) informed approach that views pain-related cognitions as false alarms of a past injury,[124] analogous to TF-CBT for re-experiencing symptoms in PTSD (*"it's burning sensation, but we know that it's safe. It's a signal coming from your body…*"). Further research should also examine attachment and positive behavioural support-based mechanisms to inform developments of parent-based interventions for younger children who first present with ACEs or ERDs, and co-occuring pain complaints. Preliminary studies suggest, for instance, that CBT for parental anxiety alone might be as effective as individual child treatment for CP.[125]

**Contributors**

SS and LJ conceived the study. SS, RG and LJ designed the study. SS completed the statistical analyses. RG and LJ provided study supervision. SS and RG had full data access. All authors contributed to the interpretation of the data, manuscript revisions and had final responsibility for the decision to submit for publication.

**Data sharing**

This study uses data from the CPRD, a research service that provides primary care and linked data for public health research. CPRD data governance does not allow distribution or access to data to other parties outside of the approved study protocol. Researchers can apply for data access with a study protocol at https://www.cprd.com/ and would need approval by the Research Data Governance Secretariat. We provide all relevant code lists and coding scripts via https://acesinehrs.com/. All code is shared without investigator support.

**Declarations of interest**
All authors have completed the ICMJE uniform disclosure form (www.icmje.org/coi_disclosure.pdf) and declare no competing interests.

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This study was carried out as part of the CALIBER© resource. CALIBER, led by the UCL Institute of Health Informatics, is a research resource providing validated electronic health record phenotyping algorithms and tools for national structured data sources.[126]

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## Connecting narrative

Long before I started my career in psychology, I was interested in the enduring effects of childhood trauma and the factors that help children develop resilience. Adversity and trauma are, therefore, the underlying theme of all my research projects. The other connecting narrative is that all my projects use variations of electronic health records (EHRs) or routinely collected data to answer relatively broad research questions. As a research associate pre-clinical training, I had the opportunity to work in psychiatric epidemiology at UCL Great Ormond Street Institute of Child Health. I quickly fell in love with the scientific rigour of the epidemiological field and its ambitions to provide insights into questions at a national, service and policy level. This ambition often requires large samples, where EHRs offer a pragmatic and efficient solution. I developed skills in managing and manipulating *"big data".* Having started my clinical training, I was therefore keen to integrate my passion for EHRs and epidemiology into my clinical psychology research.

**CRL**

During my first clinical placement, I was placed in IAPT and had the privilege of learning TF-CBT to treat PTSD. Whilst the approach was relatively consistent in treating PTSD from single incident traumas, I found that there was larger variation in how people approached TF-CBT for PTSD from multiple different traumas. Everyone I asked seemed to have a different answer in how to treat multiple incident PTSD symptoms. Indeed, there were no TF-CBT protocols for multiple-incident PTSD available to clinicians in the service.

After completing my scoping search for previous systematic reviews, I discovered a large ongoing debate over whether TF-CBT were effective for PTSD from multiple-incident traumas. I found no previous reviews on the topic. Whilst, in theory, this question was simple and broad, it was a big challenge and required a tremendous and exhausting amount of work. The main challenge in completing the review involved developing a theoretically informed framework that could help meaningfully distinguish PTSD relating to single-incident trauma from multiple-incident traumas.

Also, once I started the review, almost two years had elapsed since I initially hatched the idea. My interest in the topic had faded against many other exciting research ideas. I was privileged to work alongside another trainee to complete the review. I am glad I persisted with the study. I learned to appreciate the vast amount of theoretical and clinical variations of TF-CBT that I now have in my tool kit that I can apply in practice.

**SIP**

The SIP was inspired by my supervisor (Prof Paul Salkovskis). Paul had heard concerns about the Trust experiencing challenges with “stranded” patients or delayed discharges (patients end up staying longer in hospital than expected). Whilst I had no expertise in the topic, I was excited that the SIP idea came directly from the Trust, ensuring the project was relevant to the service and could potentially lead to meaningful service improvements. It also suited my prior skills in using hospital admission data. At the time, I was on clinical placement at the Highfield inpatient unit for young people and had started gaining some insight into the importance of this topic.

The initial challenge with this project was the lack of standardised metrics and definitions over what constituted a *"delayed discharge" or “stranded patients”.* Without defined measures, how do we know there was a problem? This ambivalence could often leave me confused and questioning whether this SIP was needed. My supervisor helpfully guided me to refine the project aims. Discussions with the patient flow and transformation team and the head of service also helped refine the project directions.

I experienced significant delays in the data extraction process as the Trust was undergoing data system changes. This was anxiety-provoking, as I had planned to submit my SIP by my first university deadline and I felt already behind. As a potential backup up project and to help enrich the quantitative analysis, I conducted a qualitative phase. It proved difficult to recruit busy clinicians and required persistence and flexibility to manage competing demands of placements (e.g. sometimes visiting wards, etc.). I received support with recruitment from the Trust's clinical director and from my supervisor. I eventually

managed to interview multiple Consultant Psychiatrists covering different adult wards. The process was daunting but incredibly rewarding, and I am glad I've completed it. The project has helped me appreciate the complexity of different *"systems"* and the importance of integrated working across services.

**TDRP**

I was keen to develop a main research project that merged my interests in adversity and EHRs with clinically relevant psychological theories to help advance treatments for children. The project was developed with the help of my internal supervisor (Dr Louise Johns), who was interested in the link between trauma and chronic pain. I was lucky enough to find a seminal paper by Prof Asmundson who proposed several hypothetical studies suited for EHRs to further a biopsychosocial model on chronic pain. I was also very fortunate that my previous research supervisor (Prof Gilbert) agreed to be my external supervisor given their vast expertise on ACEs and EHRs.

Following a scoping search of previous studies, I found no studies on that had attempted Asmundson's recommendations. I quickly discovered, however, the sheer complexity of trying to answer research questions using predictions from a biopsychosocial model, potentially highlighting why no one had previously conducted a study to answer Asmundson's suggestions. The study design underwent several significant and iterative changes as the project progressed. The main challenge was to find an appropriate study design and analysis that could answer such a complex question. I changed the design several times based on discussions with my supervisors and collaborators, which required a significant amount of work. I learnt that testing hypotheses using causal analyses are complex tasks that requires an integration of sound formulation skills and statistical expertise to account for different biopsychososcial interactions. Overall, the project's biopsychosocial focus has reinforced the importance of working with researchers across disciplinary fields to ensure the theoretical and practical implications reflect multidisciplinary settings.

**Acknowledgements**

*Please note that project specific acknowledgements are listed at the end of each specific manuscript above. In this section, I provide acknowledgements applicable to the overall thesis. Names are listed in alphabetical order.*

First, I am incredibly grateful to the generosity of the patients and their families, along with the NHS staff and participating general practices, for their contribution to the research presented in this thesis.

Second, I would like to express my sincere gratitude to my supervisors Dr Louise Johns, Prof Ruth Gilbert, and Prof Paul Salkovskis, for their wisdom, tireless reviews of manuscripts and words of encouragement over the last three years. Their belief in me, expertise, perspective and scientific rigour have been invaluable in shaping me as a researcher and clinical psychologist. I look forward to many more years of collaboration.

Third, I am very appreciative to all the collaborators and co-authors who supported each project and took valuable time to meet, discuss ideas and review manuscripts. Thank you Angela Bird, Catherine Sage, Dr Matthew Jay, Dr Richard Howard and Dr Rob Bale.

Fourth, I would like to thank my course tutor Dr Reena Vohora and all my placement supervisors and teams for sharing their wisdom, providing inspiration and for supporting me.

Finally, I would like to thank my partner Rachel Ashwick for her never-failing patience, love and support throughout all the aspects of my training and life.

## Appendices

### Appendix A – Critical review of the literature

**A1:** Target journal: Instructions for authors

## About

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This confirms that any participant has consented to the inclusion of material pertaining to themselves, that they acknowledge that they cannot be identified via the manuscript; and that the participant has been fully anonymized by the author.
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    - The data that support the findings of this study are available on request from the corresponding author, [initials]. The data are not publicly available due to [restrictions e.g. their containing information that could compromise the privacy of research participants].
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  2. Search strings used for various platforms such as MEDLINE, Scopus etc.
  3. PICOS table (if relevant)
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**A2:** eTable. Search strategy OVID: AMED, Embase, Ovid MEDLINE(R), APA PsycInfo, Social Policy and Practice 1990-2022

| | | |
|---|---|---|
| 1 | ((trauma* adj3 stress) or (stress adj3 disorder*) or PTSD).ti,ab. | 158586 |
| 2 | limit 1 to english language [Limit not valid in Social Policy and Practice; records were retained] | 149596 |
| 3 | limit 2 to human [Limit not valid in AMED,Social Policy and Practice; records were retained] | 135942 |
| 4 | limit 3 to yr="1990 -Current" | 133251 |
| 5 | (randomi$ed or randomi$ation).ti,ab. | 20 |
| 6 | limit 5 to english language [Limit not valid in Social Policy and Practice; records were retained] | 20 |
| 7 | limit 6 to humans [Limit not valid in AMED,APA PsycInfo,Social Policy and Practice; records were retained] | 17 |
| 8 | limit 7 to yr="1990 -Current" | 17 |
| 9 | (RCT or (random* adj3 (administ* or allocat* or assign* or class* or cluster* or control* or determine* or divide* or distribut* or expose* or fashion or number* or place* or recruit* or subsitut* or treat*))).ti,ab. | 1450949 |
| 10 | limit 9 to english language [Limit not valid in Social Policy and Practice; records were retained] | 1348757 |
| 11 | limit 10 to humans [Limit not valid in AMED,APA PsycInfo,Social Policy and Practice; records were retained] | 1165731 |
| 12 | limit 11 to yr="1990 -Current" | 1130329 |
| 13 | (waitlist* or waitlist* or waitinglist* or wait* list* or ((waiting adj (condition or control)) or WLC)).m_titl. | 6392 |
| 14 | limit 13 to english language [Limit not valid in Social Policy and Practice; records were retained] | 5876 |
| 15 | limit 14 to humans [Limit not valid in AMED,APA PsycInfo,Social Policy and Practice; records were retained] | 5413 |
| 16 | limit 15 to yr="1990 -Current" | 5217 |
| 17 | ((psychother* or therap*) and (behavio* or cogniti* or process* or exposure*)).mp. or (CBT or "CT-PTSD" or "TF-CBT" or "narrative exposure therapy" or EMDR* or "eye movement desensi*").ti,ab. | 2564989 |
| 18 | limit 17 to english language [Limit not valid in Social Policy and Practice; records were retained] | 2361994 |
| 19 | limit 18 to humans [Limit not valid in AMED,APA PsycInfo,Social Policy and Practice; records were retained] | 1985580 |
| 20 | limit 19 to yr="1990 -Current" | 1857774 |
| 21 | 8 or 12 or 16 | 1134799 |
| 22 | 4 and 20 and 21 | 3823 |
| 23 | remove duplicates from 22 | 2050 |

**A3:** eTable. Selected study characteristics of the 144 included studies by trauma type

| Source & trauma group | Country | Intervention | Control arm (TAU) | Total n | Female | Age | Measure |
|---|---|---|---|---|---|---|---|
| **Accidents** | | | | | | | |
| ehlers2003 | England | CT-PTSD | Self-help booklet | 85 | - | 39.4 | CAPS |
| aldahadha2012 | Oman | EMDR | WL | 51 | 52.9 | 26.4 | TSI |
| blanchard2003 | USA | TF-CBT | PTSD psychotherapy | 78 | 73.1 | 40.6 | CAPS |
| Efendi2020 | Indonesia | TF-CBT | WL | 90 | 74.4 | 71.3 | CAPS |
| basoglu2005 | Turkey | TF-CBT (brief) | WL | 59 | 84.7 | 36.3 | CAPS |
| basoglu2007 | Turkey | TF-CBT (brief) | WL | 31 | 87 | 34 | CAPS |
| fauerbach2020 | USA | TF-CBT (brief) | Supportive counselling | 50 | 45 | 39 | DTS |
| fecteau1999 | Canada | TF-CBT (brief) | WL | 21 | 70 | 41.3 | CAPS |
| wu2014 | Hong Kong | TF-CBT (brief) | Self-Help Program | 60 | 32.07 | 39.4 | IES-R |
| dunne2012 | Australia | TF-CBT(Bryant, 1998) | WL | 26 | 50 | 32.54 | IES |
| beck2009 | USA | TF-CBT (group) | Minimal attention | 44 | 82 | 43.3 | CAPS |
| popiel2015 | Poland | PE | Paroxetine | 228 | 76.3 | 36.9 | PDS |
| **Assaults (sexual/physical)** | | | | | | | |
| nixon2016 | Australia | CPT | TAU | 47 | 97.8 | 31.2 | CAPS |
| covers2021 | Netherlands | EMDR | TAU | 57 | 100 | 25.8 | CAPS |
| rothbaum1997 | USA | EMDR | WL | 21 | 100 | 34.6 | PSS-I |
| echiverri-cohen2016 | USA | PE | Medication only | 49 | 74.5 | 37.7 | PSS-I |
| feeny2002 | USA | PE | WL | 72 | 100 | 34.9 | PSS-I |
| foa1991 | USA | PE | SIT | 55 | 100 | 31.8 | PSS-I |
| foa1999 | USA | PE | SIT | 96 | 100 | 34.9 | PSS-I |
| simon2008 | USA | PE | Placebo | 68 | 56.5 | 45.6 | SPRINT |
| schnurr2007 | USA | PE | PCT | 284 | 100 | 44.6 | CAPS |
| resick2002 | USA | PE | Minimal attention | 171 | 100 | 32 | CAPS |
| zoellner2019 | USA | PE | Sertraline | 200 | 24.5 | 37.4 | PSS-I |
| rothbaum2005 | USA | PE | WL | 74 | 100 | 33.8 | CAPS |
| ruglass2017 | USA | PE-Integrated (COPE) | Active monitoring | 110 | 36.3 | 44.8 | CAPS |
| mills2012 | Australia | PE-Integrated (COPE) | TAU | 103 | 62.1 | 33.7 | CAPS |
| echeburua1996 | Spain | TF-CBT | Progressive muscle relaxation | 20 | 100 | 22 | SS-PTSD |
| sijbrandij2007 | Netherlands | TF-CBT (brief) | WL | 143 | 60.1 | 37.6 | SI-PTSD |
| krakow2000 | USA | TF-CBT (group) | WL | 169 | 100 | 36.8 | PSS |
| **Mixed traumas (various)** | | | | | | | |
| maxwell2016 | USA | CPT | Memory specificity training | 18 | 81 | | MPSS |
| resick2015 | USA | CPT | PCT | 108 | 92.6 | 32.1 | PCL |
| falsetti2008 | USA | CPT (M-CET) | Minimal attention | 60 | 100 | 35 | MPSS |
| galovski2012 | USA | CPT (modified) | Symptom monitoring | 100 | 69 | 39.8 | CAPS |
| ehlers2005 | England | CT-PTSD | WL | 28 | 50 | 36.6 | PDS |
| ehlers2014 | England | CT-PTSD | WL | 121 | 58.67 | 39.9 | CAPS |
| hogberg2007 | Sweden | EMDR | WL | 24 | 20.83 | 43 | IES |
| karatzias2019 | Scotland/Northern Ireland | EMDR | TAU | 29 | 62 | 42.1 | PCL-5 |
| lee2002 | Australia | EMDR | SIT | 24 | 45.8 | 35.3 | IES |
| marcus1997 | USA | EMDR | TAU | 67 | 79 | 40.0 | IES |
| marcus2004 | USA | EMDR | SC | 67 | 79.1 | 42.4 | IES |
| steinert2016 | Cambodia | EMDR | WL | 86 | 60.7 | 27.6 | HTQ |
| carletto2016 | Italy | EMDR | Relaxation | 50 | 81 | 40.1 | SCID |
| vanderkolk2007 | USA | EMDR | Fluoxetine | 88 | 83 | 36.1 | CAPS |
| arntz2007 | Netherlands | PE | WL | 67 | 65.67 | 35 | PSS-SR |
| asukai2010 | Japan | PE | Medication only | 24 | 87.5 | 29.3 | CAPS |
| foa2013 | USA | PE | SC | 165 | 34.54 | 42.72 | PSS-I |
| fonzo2017 | USA | PE | WL | 66 | 65.1 | 36.72 | CAPS |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| frommberger2004 | Germany | PE | Paroxetine | 21 | 57.1 | 42.6 | CAPS |
| lovell2001 | England | PE | Relaxation | 77 | 35.6 | 47.5 | CAPS |
| marks1998 | England | PE | Relaxation | 87 | 36 | 38 | CAPS |
| øktedalen2015 | Norway | PE | IR | 67 | 57 | 45.2 | PSSSR |
| rothbaum2006 | USA | PE | Sertraline | 65 | 64.6 | 39.7 | SI-PTSD |
| vera2011 | Puerto Rico | PE | TAU | 14 | 0 | 45.8 | CAPS |
| markowitz2015a | USA | PE | Relaxation | 110 | 70 | 40.1 | CAPS |
| ghafoori2017 | USA | PE | PCT | 71 | 83.1 | 35.2 | PCL |
| coffey2016 | USA | PE | Health education | 126 | 46 | 34 | IES-R |
| brom1989 | USA | PE ("trauma desensitization") | WL | 112 | 79 | 42 | IES |
| akbarian2015 | Iran | TF-CBT | TAU | 40 | 78.6 | 31.6 | IES |
| hollifield2007 | USA | TF-CBT | WL | 84 | 65.6 | 42.2 | PSS-SR |
| cottraux2008 | France | TF-CBT | SC | 60 | 70 | 39 | PCL |
| bryant2006 | Australia | TF-CBT(Bryant, 1998) | SC | 87 | 61 | 33.7 | CAPS |
| hinton2011 | USA (Caribbean-Latino only clinic) | TF-CBT (CBT-CA) | Relaxation | 24 | 100 | 49.5 | PCL |
| monson2012a | USA/Canada | TF-CBT (Couple-focused) | WL | 80 | 75 | 37.1 | CAPS |
| davis2011 | USA | TF-CBT (ERRT) | WL | 47 | 75 | 47 | CAPS |
| sannibale2013 | Australia | TF-CBT (integrated; COMBINE) | Alcohol-support | 62 | 53 | 41.2 | CAPS |
| ivarsson2014 | Sweden | TF-CBT (online therapist guided) | Internet control | 62 | 82.3 | 46 | IES |
| ford2011 | USA | TF-CBT (TARGET) | PCT | 146 | 100 | 30.7 | CAPS |
| sloan2004 | USA | TF-CBT (WET) | Control writing | 51 | 100 | 18.9 | PDS |
| sloan2011 | USA | TF-CBT (WET) | Control writing | 42 | | 18.9 | PSS-I |
| vandam2013 | Netherlands | TF-CBT (Integrated; SWT) | TAU for SUD | 34 | 32.4 | 42.3 | PDS |
| saunders2015 | USA | TF-CBT (integrated; ICBT) | TAU | 126 | 61.9 | 32.17 | CAPS |
| Child maltreatment | | | | | | | |
| chard2005 | USA | CPT | Minimal attention | 71 | 100 | 32.77 | CAPS |
| rosner2019 | Germany | CPT | WL + treatment signposting | 88 | 85 | 18.1 | CAPS |
| bohus2013 | Germany | DBT-PTSD | TAU | 82 | 100 | 35.7 | CAPS |
| scheck1998 | USA | EMDR | Active listening | 67 | 100 | 20.9 | IES |
| perezdandieu2014 | France | EMDR-Integrated | TAU | 12 | 100 | 29.5 | PCL |
| cloitre2002 | USA | PE | Minimal attention | 58 | 100 | 34 | CAPS |
| feske2008 | USA | PE | TAU (mixed incl CBT) | 27 | 100 | 43.1 | PDS |
| debont2016/Vandenberg2015 | Netherlands | PE | WL | 155 | 54.2 | 41.2 | CAPS |
| mcdonagh2005 | USA | PE (modified) | PCT | 74 | 100 | 39.6 | CAPS |
| hien2017 | USA | PE-Integrated (COPE) | Active monitoring | 110 | 36.36 | 45 | MPSS-SR |
| mueser2008 | USA | TF-CBT | TAU | 108 | 78.7 | 44.2 | CAPS |
| mueser2015 | USA | TF-CBT | Psychoeducation | 201 | 70.05 | 44.7 | CAPS |
| jung2013 | Germany | TF-CBT (brief/online therapist guided) | WL | 34 | 100 | 37.2 | CAPS |
| **Emergency service personnel** | | | | | | | |
| alghamdi2015 | Saudi Arabia | NET | WL | 34 | 0 | 30.4 | SPTSS |
| difede2007 | USA | TF-CBT(Bryant, 1998) | TAU | 31 | 3 | 45.8 | PCL |
| **Intimate partner violence** | | | | | | | |
| orang2018 | Iran | NET | SC | 45 | 100 | 37.7 | PSS-I |
| kubany2003 | USA | TF-CBT | WL | 107 | 100 | 36.8 | CAPS |
| kubany2004 | USA | TF-CBT | WL | 107 | 100 | 42.2 | CAPS |
| **Military combat-related** | | | | | | | |
| forbes2012 | Australia | CPT | Therapy as usual (incl. CBT) | 59 | 3.4 | 53.4 | CAPS |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| kearney2021 | USA | CPT | Meditation-based intervention | 184 | 16.8 | 57.1 | CAPS |
| monson2006 | USA | CPT | WL | 60 | 10 | 54 | CAPS |
| suris2013 | USA | CPT | PCT | 129 | 85 | 46.1 | CAPS |
| carlson1998 | USA | EMDR | TAU | 35 | 0 | 48.3 | IES |
| jensen1994 | USA | EMDR | WL | 25 | 0 | 43.1 | M-PTSD |
| butler2018 | Germany | EMDR (+ group) | WL | 20 | 0 | 28.5 | PDS |
| foa2018 | USA | PE | PCT | 370 | 12 | 32.7 | PSS-I |
| nacasch2011 | USA | PE | TAU | 30 | 90 | 34.3 | PSS-I |
| nidich2018 | USA | PE | PTSD education | 202 | 17.8 | 47.0 | CAPS |
| rauch2018 | USA | PE | Sertraline hydrochloride | 223 | 13 | 34.5 | CAPS |
| thorp2019 | USA | PE | Relaxation | 87 | 0 | 65.5 | CAPS |
| keane1989 | USA | PE (Implosive) | WL | 24 | 0 | 34.6 | MMPI |
| back2019 | USA | PE-Integrated (COPE) | Relapse Prevention | 81 | 9.9 | 40.4 | CAPS |
| korte2017 | USA | PE-Integrated (COPE) | RP | 81 | 9.9 | 40.4 | PCL |
| norman2019 | USA | PE-Integrated (COPE) | PCT-Integrated coping skills | 119 | 10.1 | 41.6 | CAPS |
| mclay2011 | USA | VRET | TAU | 20 | 5 | 28.4 | CAPS |
| miyahira2012 | USA | VRET | Minimal attention | 42 | 100 | 35.5 | CAPS |
| ready2010 | USA | VRET | PCT | 11 | 0 | 57.5 | CAPS |
| stecker2014 | USA | TF-CBT (brief phone) | WL | 300 | 22.3 | 29.2 | PCL-M |
| ochsnermargolies2013 | USA | TF-CBT (CBT-I & nightmare rescripting) | WL | 40 | 10 | 37.7 | PSS-SR |
| church2013 | USA | TF-CBT (EFT) | TAU | 59 | 31.2 | 59.5 | PCL |
| geronilla2016 | USA | TF-CBT (EFT) | WL | 58 | 12 | 50 | PCL |
| castillo2016 | USA | TF-CBT (group) | SC | 86 | 100 | 35.9 | CAPS |
| schnurr2003 | USA | TF-CBT (group) | PCT | 360 | 0 | 50.7 | CAPS |
| cook2010 | USA | TF-CBT (Group; IRT) | Psychoeducation | 124 | 0 | 59.4 | CAPS |
| capone2018 | USA | TF-CBT (integrated; cognitive only) | TAU | 44 | 4.5 | 34.3 | CAPS |
| maguen2017 | USA | TF-CBT (IOK) | TAU | 33 | 0 | 61.2 | PCL |
| ulmer2011 | USA | TF-CBT (IRT) | WL | 22 | 38.1 | 46.0 | PCL-M |
| krupnick2017 | USA | TF-CBT (online therapist guided) | TAU | 34 | 8.82 | 40.1 | PCL |
| gray2019 | USA | TF-CBT (RTM) | WL | 74 | 0 | 48.6 | PCL |
| kent2011 | USA | TF-CBT (RTM) | WL | 39 | 33 | 54 | PDS |
| tylee2017 | USA | TF-CBT (RTM) | WL | 30 | 0 | 45.8 | PCL |
| **War trauma/organised violence** | | | | | | | |
| duffy2007 | Northern Ireland | CT-PTSD | WL | 58 | 39.66 | 43.9 | PDS |
| bolton2014 | Kurdistan/Iraq | CPT | WL | 281 | 58 | 40.23 | HTQ |
| weiss2015 | Iraq | CPT | WL | 342 | 30.9 | 43.4 | HTQ |
| acarturk2016 | Turkey | EMDR | WL | 98 | 74 | 33.7 | HTQ |
| shapiro2015 | Israel | EMDR | WL | 17 | 94.1 | 40 | IES |
| terheide2011 | Netherlands | EMDR | Stabilisation | 20 | 40 | 41.5 | HTQ |
| bichescu2007 | Romania | NET | Psychoeducation | 18 | 5.5 | 69.3 | CIDI |
| henseldittmann2011 | Germany | NET | SIT | 28 | | | CAPS |
| jacob2014 | Netherlands | NET | WL | 76 | | 37.6 | CAPS |
| neuner2010 | Germany | NET | TAU | 32 | 15.63 | 31.4 | PDS |
| neuner2004 | Uganda/Sudan | NET | SC | 43 | 60.4 | 33.2 | PDS |
| hijazi2014 | USA | NET | WL | 63 | 55.6 | 48.2 | HTQ |
| ertl2011 | Uganda | NET | WL | 85 | 55.3 | 18.3 | CAPS |
| robjant2019 | Eastern DR Congo | NET | TAU | 92 | 100 | 18 | PSSI |
| morath2014 | Germany | NET | WL | 34 | 41.18 | 28 | CAPS |
| stenmark2013 | Norway | NET | TAU | 81 | 30.86 | 35 | CAPS |
| adenauer2011 | Germany | NET | WL | 34 | 44.1 | 33.3 | CAPS |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| hermenau2013 | Germany | NET (FORTNET) | WL | 38 | 0 | 19 | PSS-I |
| carlsson2018 | Denmark | TF-CBT | SIT | 140 | 43.6 | 43.3 | HTQ |
| bryant2011 | Thailand | TF-CBT(Bryant, 1998) | SC | 28 | 96.4 | 43.1 | PSS-I |
| buhmann2018 | Denmark | TF-CBT | WL | 217 | 41 | 44.9 | HTQ |
| knaevelsrud2015 | Germany/Iraq | TF-CBT (online therapist guided) | WL | 159 | 71.7 | 28.1 | PDS |

Abbreviations: CAPS, Clinician Administered PTSD Scale; CBT, cognitive behavioural therapy; EMDR, eye movement desensitization and reprocessing; ET, exposure therapy; HTQ, Harvard Trauma Questionnaire; IES-R, Impact of Event Scale-Revised; PCL, PTSD Checklist; PDS, Posttraumatic Diagnostic Scale; PE, prolonged exposure therapy; PTSD, posttraumatic stress disorder; PSS, Posttraumatic Stress Scale; PSSI, PTSD Symptom Scale Interview; SIP, Structured Interview for PTSD; RCT, randomized clinical trial; SPRINT, short PTSD rating interview; WL, Waiting list; TAU, treatment as usual; SIT, stress inoculation training; PCT, Present-Centered Therapy for PTSD; SUD, Substance use disorder; CT-PTSD, Cognitive therapy for PTSD; CPT, Cognitive processing therapy; NET, Narrative Exposure Therapy; VRET, Virtual Reality Exposure therapy; RTM, Reconsolidation of Traumatic Memories; IOK, Impact of killing in war; COPE, Concurrent Treatment of PTSD and Substance Use Disorders Using Prolonged Exposure; EFT, Emotional Freedom Techniques; SC, Supportive Counselling.

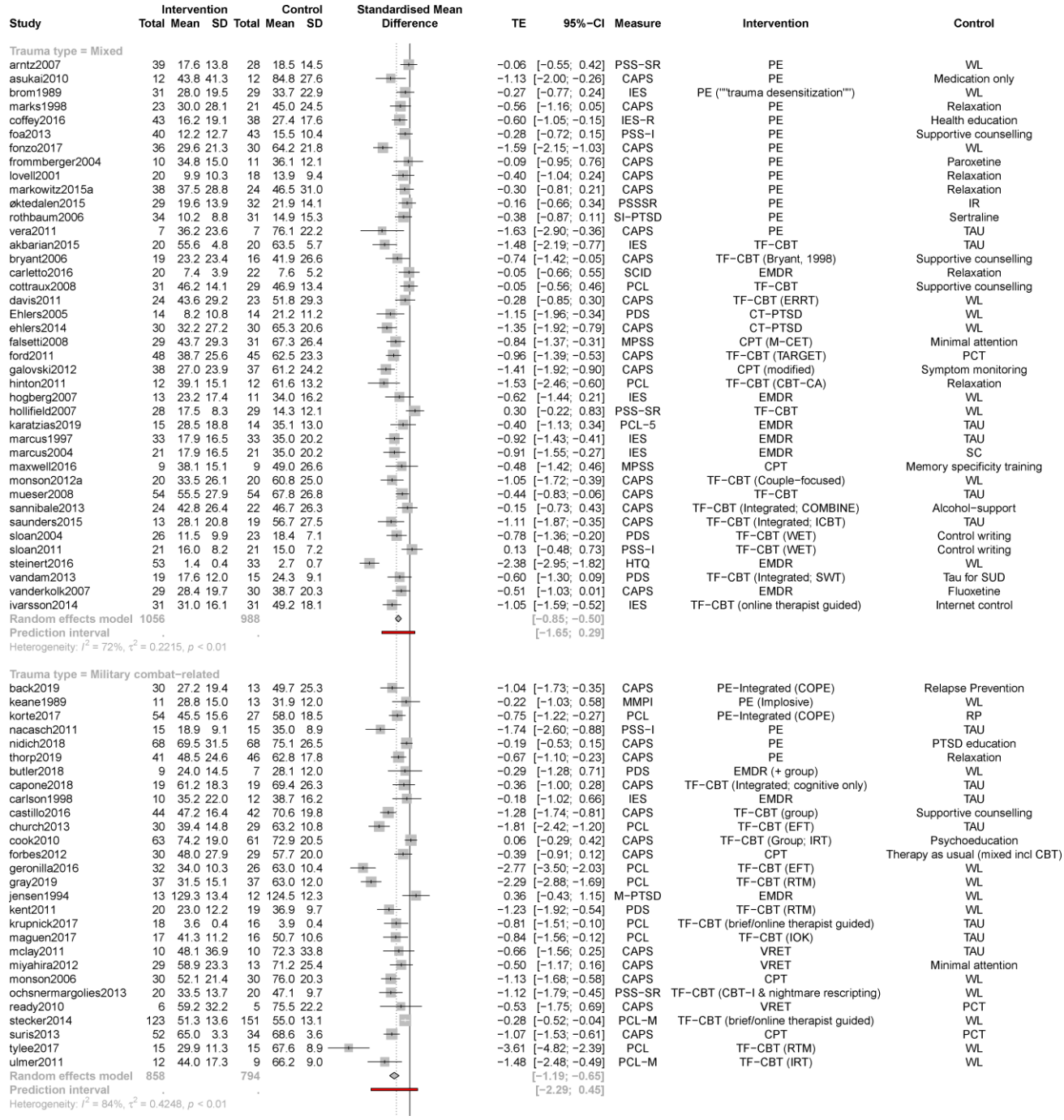
## **A4:** eTable**.** Individual risk of bias scores for the included 144 RCTS

| Source | Randomisation | Allocation Concealment | Outcome Assessors Masked | Outcome Measures Equal Valid and Reliable | Attrition Analysis | Treatment adherence measured by independent raters | Attrition greater than 20% | Risk of Bias |
|---|---|---|---|---|---|---|---|---|
| acarturk2016 | Yes | Yes | Yes | Yes | Yes | No | 0.286 | Low |
| adenauer2011 | Yes | Unclear | Unclear | Yes | Yes | No | 0.441 | Some |
| akbarian2015 | Yes | Yes | Yes | Yes | Yes | No | 0.3 | Low |
| aldahadha2012 | Unclear | Unclear | Unclear | Yes | No | No | - | High |
| alghamdi2015 | Yes | Unclear | Unclear | Yes | No | No | - | High |
| arntz2007 | Unclear | Unclear | Unclear | Yes | Yes | No | 0.4 | High |
| asukai2010 | Yes | Unclear | Yes | Yes | Yes | No | - | Some |
| back2019 | Yes | Yes | No | Yes | Yes | Yes | 0.48 | Low |
| basoglu2005 | Yes | Yes | Yes | Yes | Yes | Yes | - | Low |
| basoglu2007 | Yes | Yes | No | Yes | No | No | - | Some |
| bolton2014 | Yes | No | No | Yes | Yes | No | - | Some |
| beck2009 | Unclear | Unclear | Unclear | Yes | No | Yes | 0.25 | High |
| bichescu2007 | Unclear | Unclear | No | Yes | No | No | - | High |
| blanchard2003 | Unclear | Unclear | Yes | Yes | Yes | Yes | 0.204 | Some |
| bohus2013 | Unclear | Unclear | Yes | Yes | Yes | No | 0.27 | Some |
| brom1989 | Unclear | Unclear | Unclear | No | No | No | - | High |
| bryant2006 | Yes | Yes | Yes | Yes | Yes | Yes | 0.543 | Low |
| bryant2011 | Yes | Yes | Yes | Yes | Yes | No | - | Low |
| buhmann2018 | Yes | Yes | Unclear | Yes | Yes | No | - | Some |
| butler2018 | Unclear | Unclear | Unclear | Yes | No | No | - | High |
| capone2018 | Unclear | Unclear | Unclear | Yes | Yes | Yes | - | Some |
| carletto2016 | Yes | Unclear | Yes | Yes | No | No | - | Some |
| carlson1998 | Unclear | Unclear | No | Yes | No | No | - | High |
| carlsson2018 | Yes | Yes | Yes | Yes | No | No | 0.25 | Some |
| castillo2016 | Unclear | Unclear | Yes | Yes | Unclear | Yes | 0.233 | Some |
| chard2005 | Unclear | Unclear | Yes | Yes | Yes | Yes | - | Some |
| church2013 | Unclear | Yes | No | Yes | No | No | - | High |
| cloitre2002 | Unclear | Unclear | Yes | Yes | Yes | Yes | 0.21 | Some |
| coffey2016 | Yes | Unclear | Yes | Yes | Yes | Yes | 0.222 | Low |
| cook2010 | Yes | Unclear | Yes | Yes | Yes | Yes | 0.27 | Low |
| cottraux2008 | Yes | Yes | Yes | Yes | Yes | No | 0.3 | Low |
| covers2021 | No | No | Yes | Yes | Yes | Yes | - | Some |
| davis2011 | Unclear | Yes | Yes | Yes | Yes | No | 0.45 | Some |
| difede2007 | Unclear | Yes | Yes | Yes | Yes | No | - | Some |
| duffy2007 | Unclear | Unclear | Yes | Yes | Yes | No | - | Some |
| dunne2012 | Unclear | Unclear | No | Yes | Yes | No | - | High |
| echeburua1996 | Unclear | Unclear | Unclear | Yes | Yes | No | - | High |
| efendi2020 | No | No | No | Yes | No | No | - | High |
| ehlers2003 | Yes | Yes | Yes | Yes | Yes | No | - | Low |

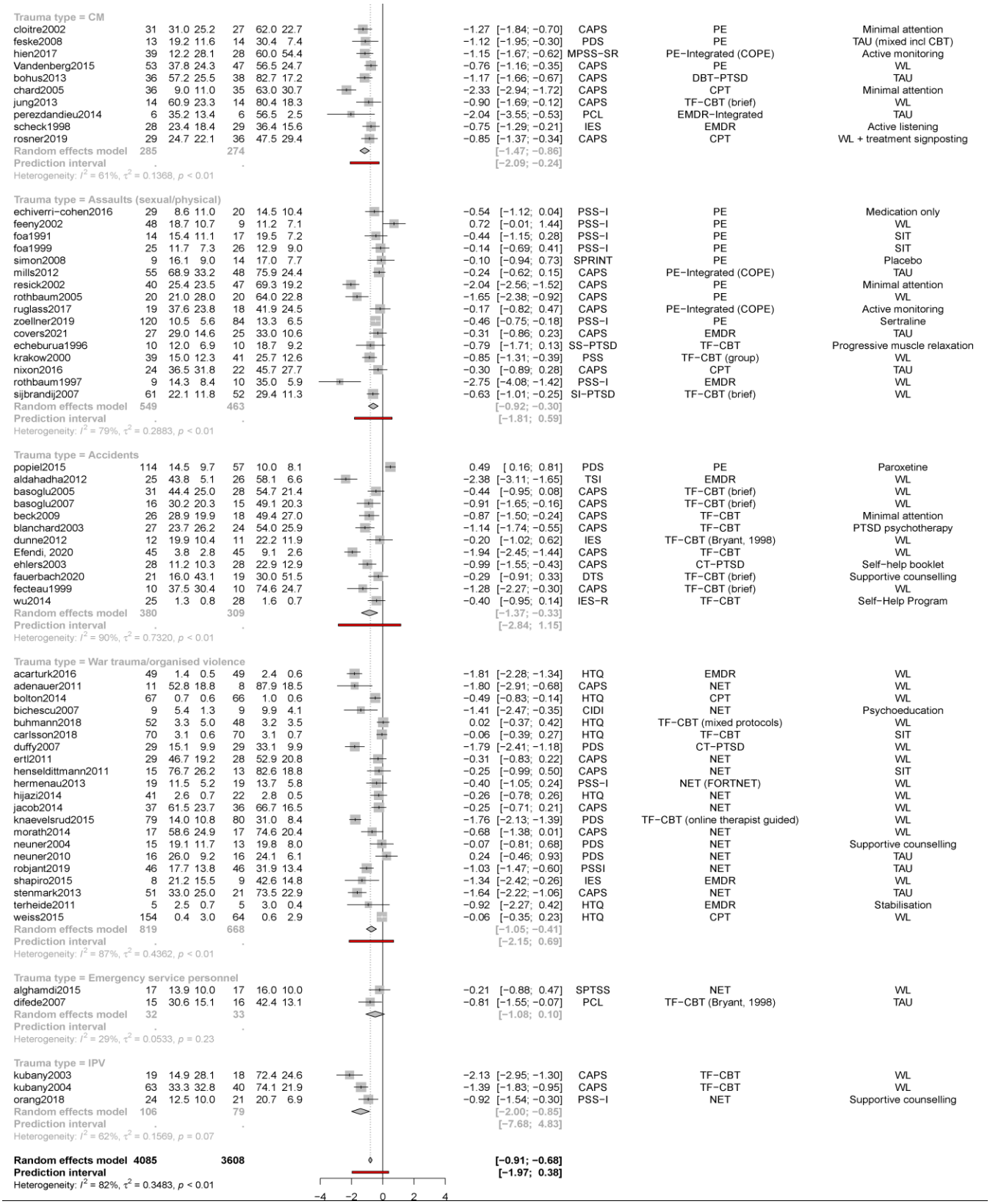
| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| ehlers2005 | No | No | No | Yes | No | Yes | - | High |
| ehlers2014 | Unclear | Yes | Yes | Yes | Yes | Yes | - | Low |
| ertl2011 | No | No | Yes | Yes | Yes | Yes | - | Some |
| falsetti2008 | Unclear | Unclear | Yes | Yes | No | Yes | 0.383 | Some |
| fauerbach2020 | No | Yes | No | Yes | Yes | No | - | Some |
| fecteau1999 | Unclear | Unclear | No | Yes | No | Yes | - | High |
| feeny2002 | No | Yes | Yes | Yes | No | No | - | Some |
| feske2008 | Unclear | Unclear | Unclear | Yes | No | No | 0.22 | High |
| foa1991 | Unclear | Unclear | Yes | Yes | No | No | - | High |
| foa1999 | Unclear | Unclear | Yes | Yes | Yes | Yes | - | Some |
| foa2013 | Unclear | Unclear | Yes | Yes | Yes | Yes | 0.43 | Some |
| foa2018 | No | Yes | Yes | Yes | Yes | Yes | - | Low |
| fonzo2017 | Yes | Unclear | Unclear | Yes | Yes | Yes | 0.23 | Some |
| forbes2012 | Yes | Yes | Yes | Yes | Yes | Yes | 0.22 | Low |
| ford2011 | Yes | No | Yes | Yes | Yes | No | - | Some |
| frommberger2004 | Unclear | Unclear | Unclear | Yes | No | No | 0.24 | High |
| galovski2012 | Yes | Yes | Yes | Yes | Yes | Yes | 0.3 | Low |
| geronilla2016 | Unclear | Unclear | Unclear | Yes | No | No | 0.224 | High |
| ghafoori2017 | Yes | Unclear | No | Yes | Yes | Yes | 0.7 | Some |
| gray2019 | Yes | Yes | Yes | Yes | Yes | Yes | - | Low |
| henseldittmann2011 | Yes | Yes | No | Yes | Yes | No | 0.25 | Some |
| hermenau2013 | Yes | No | Yes | Yes | Yes | No | - | Some |
| hien2017 | Yes | Yes | Yes | Yes | Yes | Yes | 0.374 | Low |
| hijazi2014 | Yes | Yes | Unclear | Yes | Yes | No | - | Some |
| hinton2011 | Unclear | Unclear | Unclear | Yes | No | No | - | High |
| hogberg2007 | Yes | Yes | Yes | Yes | No | Yes | - | Low |
| hollifield2007 | Yes | Yes | Yes | Yes | Yes | No | 0.27 | Low |
| ivarsson2014 | Yes | Yes | Yes | Yes | Yes | Unclear | 0.226 | Low |
| jacob2014 | Yes | Unclear | Yes | Yes | Yes | Yes | - | Low |
| jensen1994 | Unclear | Unclear | No | Yes | No | No | - | High |
| jung2013 | Unclear | Unclear | Yes | Yes | Yes | No | - | Some |
| karatzias2019 | Unclear | Unclear | Yes | Yes | Yes | No | - | Some |
| keane1989 | Unclear | Unclear | No | No | No | No | - | High |
| kearney2021 | Yes | Yes | Yes | Yes | Yes | Yes | - | Low |
| kent2011 | Unclear | Unclear | Unclear | Yes | Yes | No | - | High |
| knaevelsrud2015 | Yes | Yes | No | Yes | Yes | No | 0.411 | Some |
| korte2017 | No | No | No | Yes | No | No | - | High |
| krakow2000 | Unclear | Unclear | Unclear | Yes | No | No | 0.45 | High |
| krupnick2017 | Unclear | Unclear | Unclear | Yes | Yes | No | 0.471 | High |
| kubany2003 | Unclear | Unclear | Yes | Yes | Yes | No | 0.35 | Some |
| kubany2004 | Unclear | Unclear | Yes | Yes | Yes | No | 0.35 | Some |
| lee2002 | No | No | No | Yes | No | Yes | - | High |
| lovell2001 | Yes | Unclear | Yes | Yes | Yes | Yes | - | Low |
| maguen2017 | Unclear | Unclear | Unclear | Yes | No | No | - | High |
| marcus1997 | Yes | Unclear | No | Yes | No | No | - | High |
| marcus2004 | Yes | Unclear | No | Yes | No | No | - | High |
| markowitz2015a | Yes | Unclear | Yes | Yes | Yes | Yes | 0.25 | Low |
| maxwell2016 | Yes | Unclear | Yes | Yes | Yes | Yes | 0 | Low |
| mcdonagh2005 | Unclear | Unclear | Yes | Yes | Yes | Yes | 0.33 | Some |
| mclay2011 | Unclear | Unclear | Unclear | Yes | No | No | - | High |
| mills2012 | Yes | Yes | Yes | Yes | Yes | Yes | 0.238 | Low |
| miyahira2012 | Unclear | Unclear | Unclear | Yes | No | No | 0.476 | High |
| monson2006 | Unclear | Unclear | Yes | Yes | Yes | Yes | - | Some |
| monson2012a | Yes | Yes | Yes | Yes | Yes | Yes | 0.225 | Low |
| morath2014 | Unclear | Unclear | Yes | Yes | Yes | No | - | Some |
| mueser2008 | Yes | Yes | Yes | Yes | Yes | Unclear | - | Low |
| mueser2015 | Yes | Yes | Yes | Yes | Unclear | No | 0.25 | Some |
| nacasch2011 | Unclear | Yes | Yes | Yes | Yes | No | - | Some |
| neuner2004 | Yes | No | No | Yes | No | No | - | High |
| neuner2010 | Unclear | Unclear | Yes | Yes | Yes | No | - | Some |
| nidich2018 | Yes | Yes | Yes | Yes | Yes | Yes | - | Low |
| nixon2016 | Yes | Yes | No | Yes | Yes | No | - | Some |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| ochsnermargolies2013 | Unclear | Unclear | No | Yes | Yes | Unclear | 0.25 | High |
| øktedalen2015 | Yes | Yes | Yes | Yes | Yes | Yes | - | Low |
| orang2018 | Unclear | Unclear | Yes | Yes | No | Unclear | 0.244 | High |
| perezdandieu2014 | Unclear | Unclear | Unclear | Yes | Yes | No | - | High |
| popiel2015 | Unclear | Yes | Yes | Yes | Yes | Mixed | 0.39 | Low |
| ready2010 | Unclear | Unclear | Yes | Yes | No | No | - | High |
| resick2002 | Unclear | Unclear | Yes | Yes | Yes | Yes | 0.33 | Some |
| resick2015 | Unclear | Unclear | Yes | Yes | Yes | Yes | 0.519 | Some |
| robjant2019 | Yes | Unclear | Yes | Yes | Yes | No | - | Some |
| rothbaum1997 | Unclear | Unclear | Yes | Yes | No | Yes | - | Some |
| rothbaum2005 | Unclear | Unclear | Yes | Yes | No | Yes | - | Some |
| rothbaum2006 | Unclear | Unclear | Yes | Yes | Yes | No | - | Some |
| ruglass2017 | Yes | Yes | Yes | Yes | Yes | Yes | - | Low |
| sannibale2013 | Unclear | Yes | Yes | Yes | Yes | No | 0.25 | Some |
| saunders2015 | Unclear | Unclear | No | Yes | Yes | No | - | High |
| scheck1998 | Yes | No | No | Yes | No | No | - | High |
| schnurr2003 | Yes | Yes | Yes | Yes | Yes | Yes | - | Low |
| schnurr2007 | Yes | Yes | Yes | Yes | Yes | Yes | 0.29 | Low |
| shapiro2015 | Unclear | Unclear | Yes | Yes | No | No | 0.24 | High |
| sijbrandij2007 | Yes | Yes | No | Yes | Yes | Yes | - | Low |
| sloan2004 | Unclear | Unclear | No | Yes | Yes | Unclear | - | High |
| sloan2011 | Unclear | Unclear | Yes | Yes | No | Unclear | - | High |
| stecker2014 | Yes | Unclear | Unclear | Yes | No | No | 0.217 | High |
| steinert2016 | Unclear | Unclear | Yes | Yes | Yes | No | - | Some |
| stenmark2013 | No | Unclear | No | Yes | Yes | No | 0.33 | High |
| suris2013 | Yes | Unclear | Yes | Yes | Yes | No | 0.519 | Some |
| terheide2011 | Yes | Yes | Yes | Yes | Yes | No | - | Low |
| thorp2019 | Unclear | Unclear | Yes | Yes | Yes | Yes | 0.241 | Some |
| tylee2017 | Unclear | Unclear | No | No | No | No | - | High |
| ulmer2011 | Unclear | Unclear | No | Yes | Yes | No | - | High |
| vandam2013 | Yes | Yes | No | Yes | Yes | No | - | Some |
| vandenberg2015 | Yes | Yes | Yes | Yes | Yes | Yes | - | Low |
| vanderkolk2007 | Unclear | Unclear | Yes | Yes | Yes | Yes | - | Some |
| vera2011 | Unclear | Unclear | Unclear | Yes | No | No | - | High |
| weiss2015 | Yes | No | Yes | Yes | Yes | No | - | Some |
| wu2014 | No | Yes | No | Yes | Yes | No | - | Some |
| zoellner2019 | Yes | Unclear | Yes | Yes | Yes | Yes | 0.26 | Low |
| echiverri-cohen2016 | No | No | Yes | Yes | No | Yes | - | Some |
| simon2008 | Yes | Unclear | Yes | Yes | No | Unclear | - | Some |
| marks1998 | Yes | Yes | Yes | Yes | No | Yes | - | Low |
| rosner2019 | Yes | Yes | Yes | Yes | Yes | Yes | - | Low |
| rauch2018 | Yes | Yes | Yes | Yes | Yes | Yes | - | Low |
| norman2019 | Yes | Yes | Yes | Yes | Yes | Yes | - | Low |

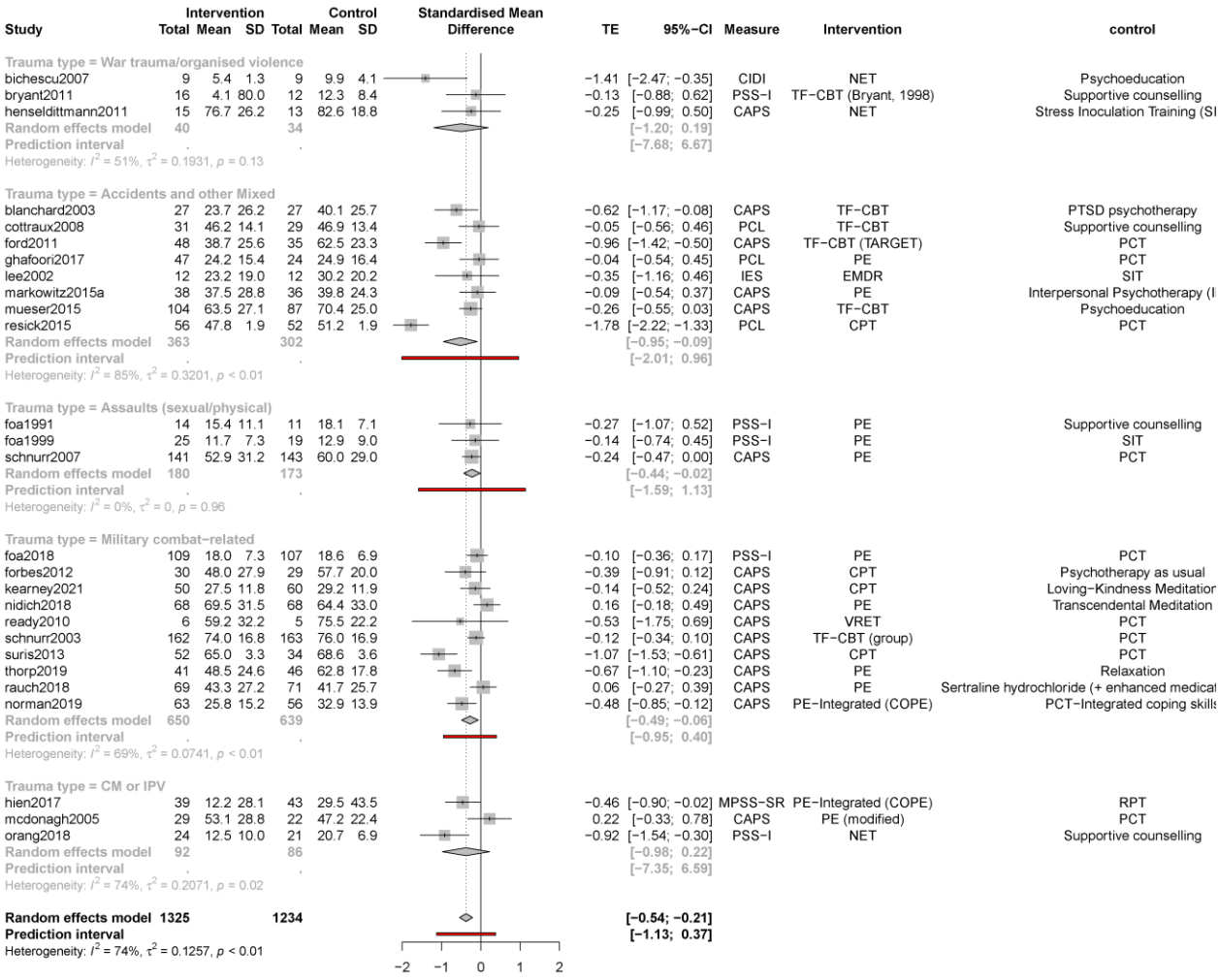
**A5:** eFigure. Forest plot of individual study estimates of TF-CBT intervention vs TAU by trauma type, intervention and outcome measures



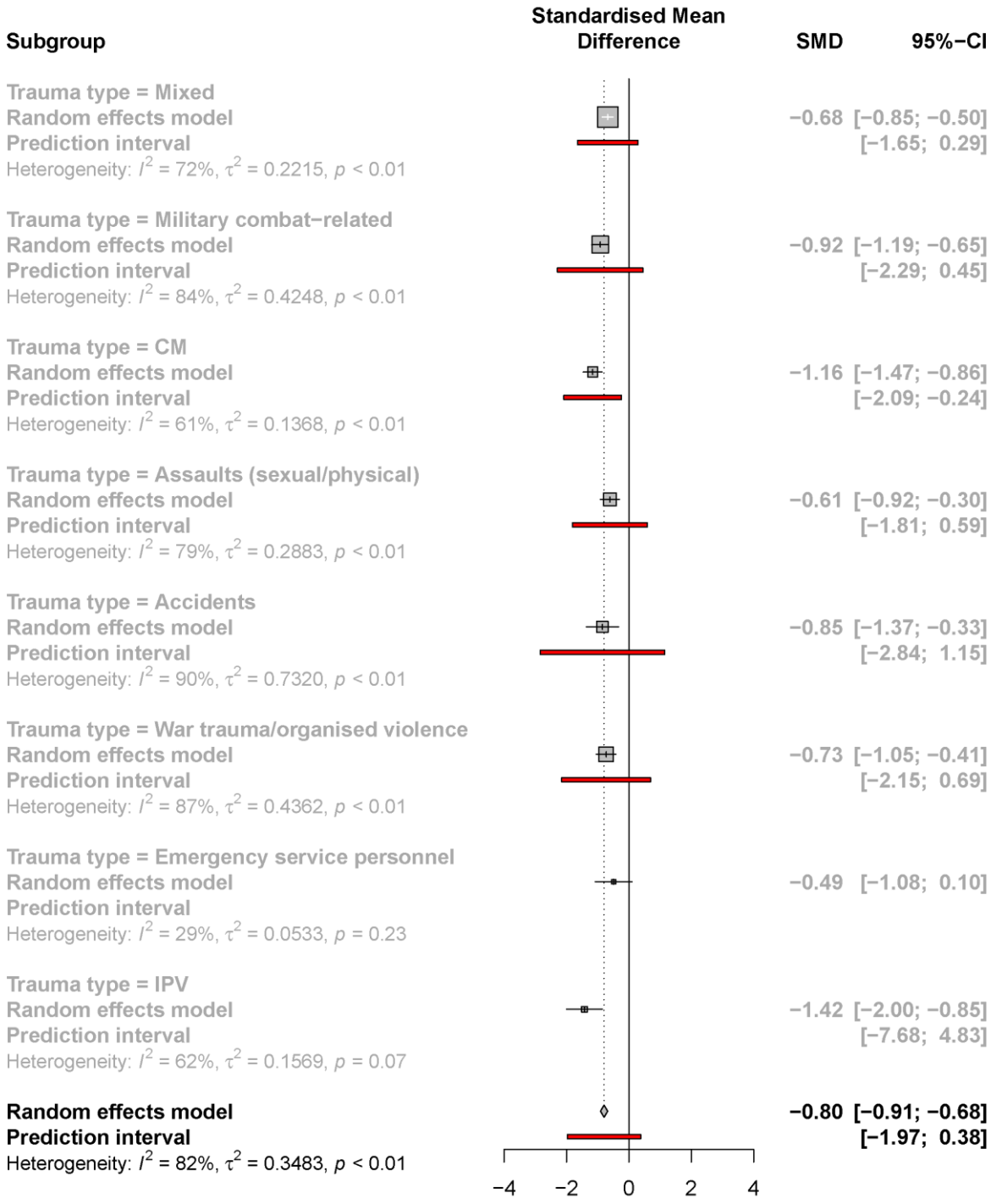
**A5:** eFigure. Forest plot of individual study estimates of TF-CBT intervention vs TAU by trauma type, intervention and outcome measures (continued)



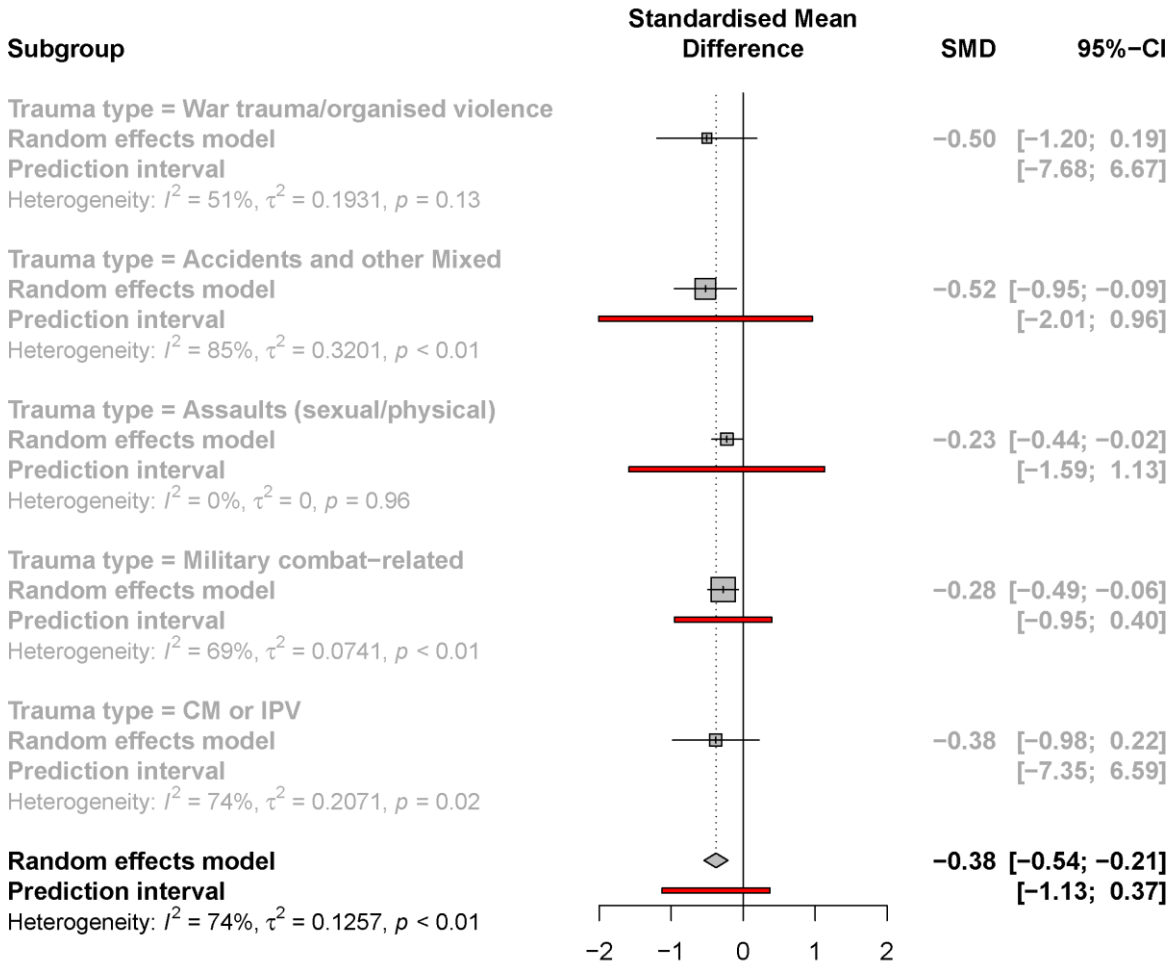
**A6:** eFigure. Forest plot of individual study estimates of TF-CBT vs active comparator groups by trauma type, intervention and outcomes



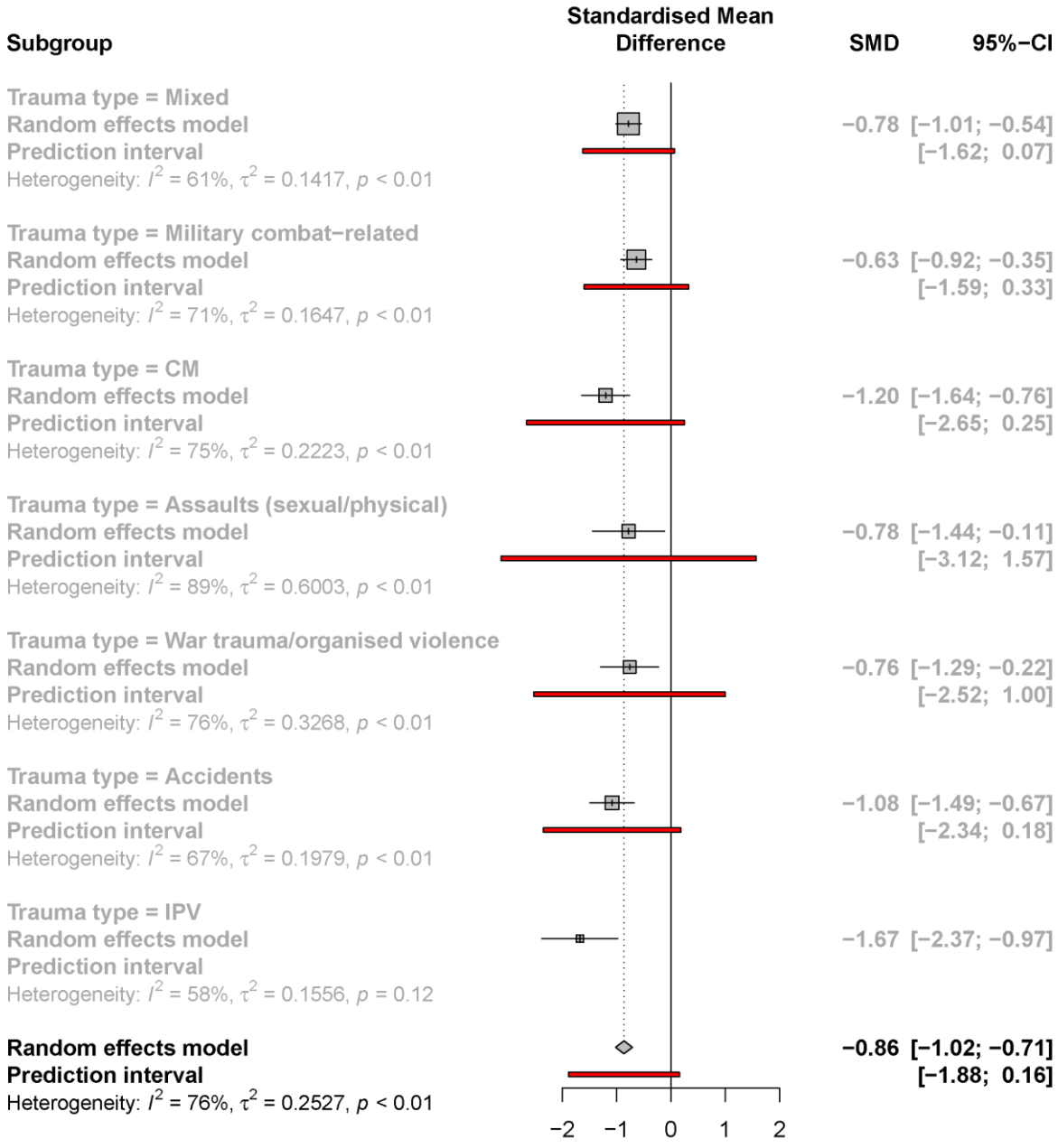
**A7:** eFigure. Forest plot of subgroup analyses for TF-CBT vs TAU by trauma type any PTSD outcome measure



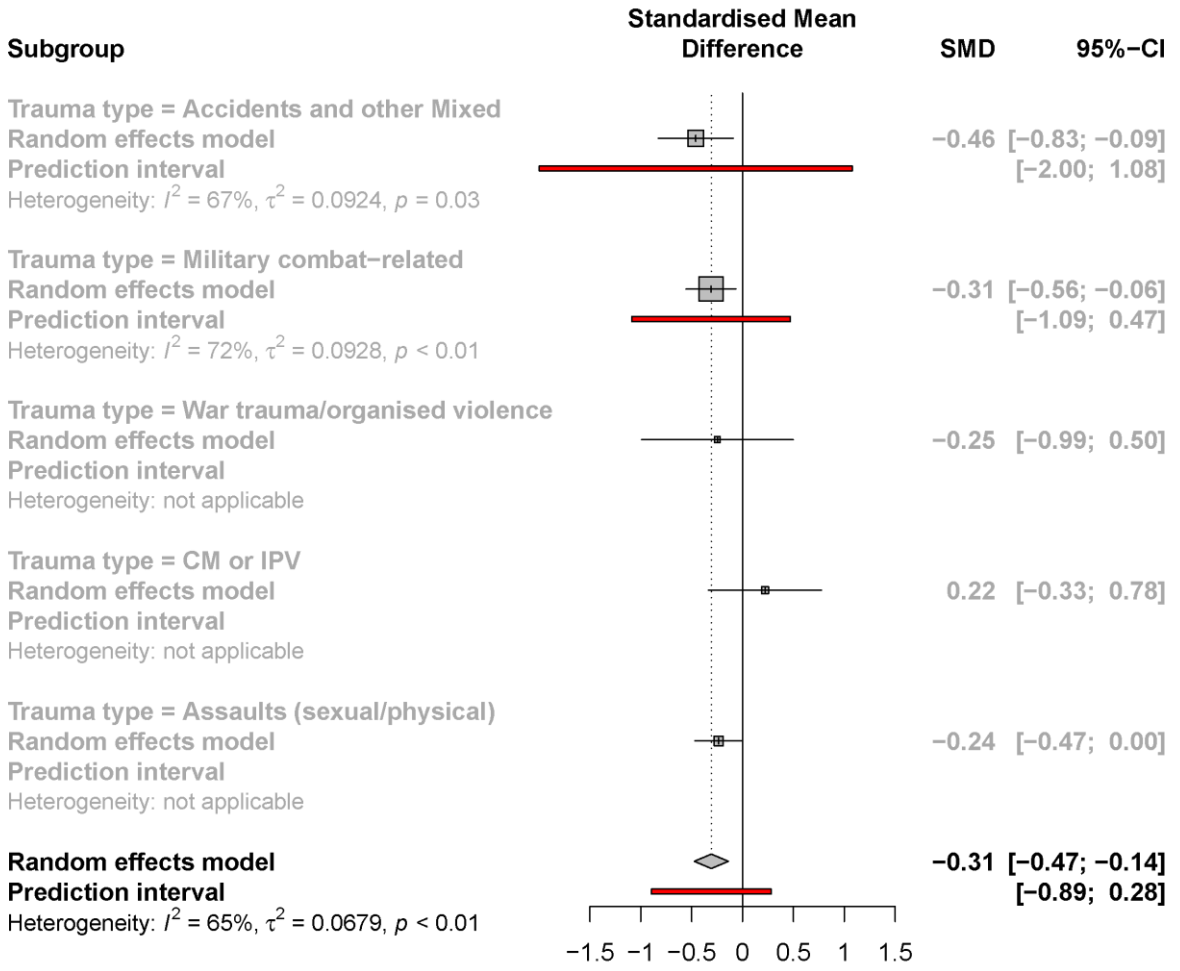
**A8:** eFigure. Forest plot of subgroup analyses for TF-CBT vs active comparator groups by trauma type any PTSD outcome measure



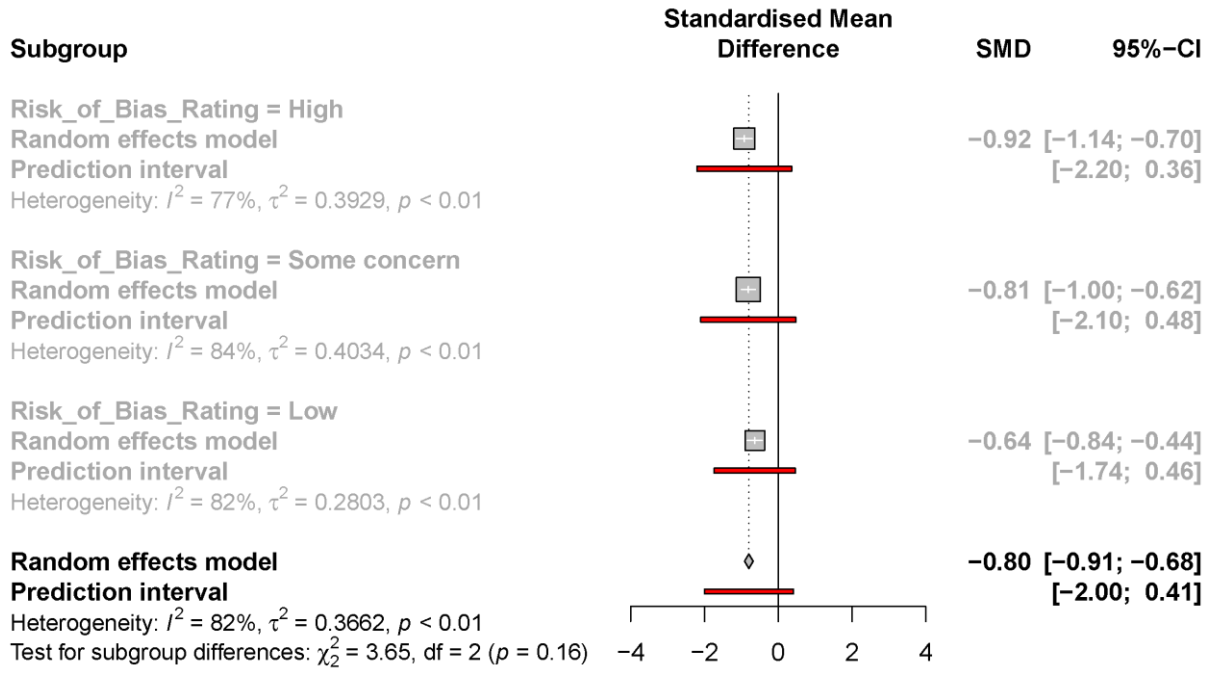
**A9:** eFigure**.** Forest plot of subgroup analyses for TF-CBT vs TAU groups by trauma type CAPS only



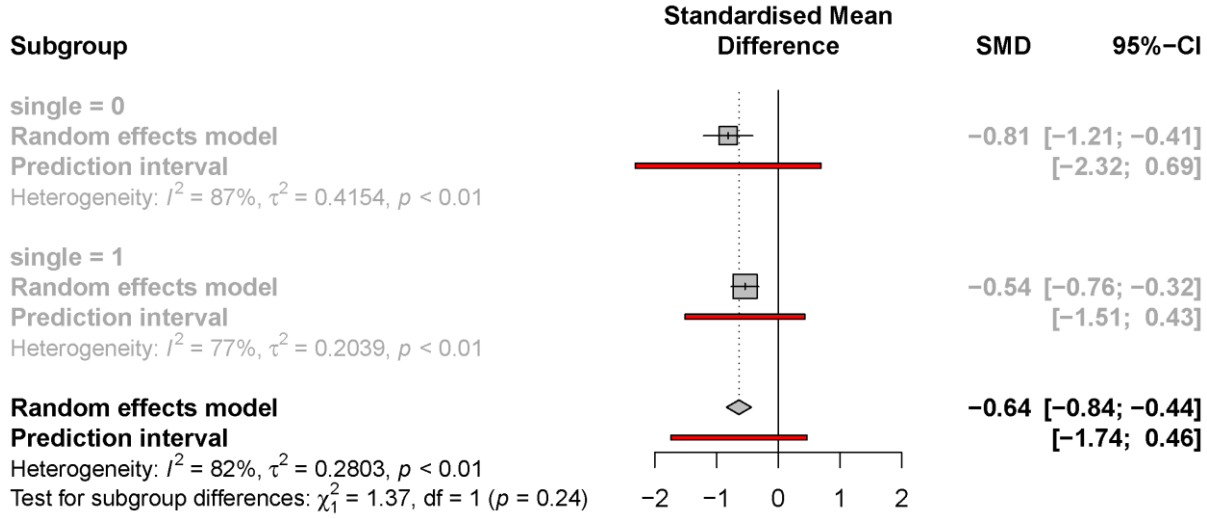
**A10:** eFigure. Forest plot of subgroup analyses for TF-CBT vs active comparator groups by trauma type CAPS only



**A11:** eFigure. Forest plot of subgroup analyses for TF-CBT vs TAU by overall risk of bias (any PTSD measure)




**A12:** eFigure. Forest plot of subgroup analyses for single vs multiple-incident trauma (TF-CBT vs TAU) high quality studies only



**A13:** eTable**.** Serial exclusion of individual studies from the main random-effects meta-analysis of 132 RCTs on TF-CBT vs. TAU (influential analysis investigation)

| Excluded study | Overall estimate | LCI | UCI | $t^2$ | $I^2$ |
|---|---|---|---|---|---|
| arntz2007 | -0.785 | -0.9002 | -0.6699 | 0.3475 | 81.90% |
| asukai2010 | -0.7768 | -0.8919 | -0.6617 | 0.348 | 82.00% |
| back2019 | -0.7772 | -0.8924 | -0.6620 | 0.3486 | 82.00% |
| marks1998 | -0.7839 | -0.8990 | -0.6687 | 0.3481 | 82.00% |
| cloitre2002 | -0.7751 | -0.8902 | -0.6600 | 0.3475 | 81.90% |
| coffey2016 | -0.7808 | -0.8965 | -0.6651 | 0.3516 | 82.00% |
| debont2016 | -0.7791 | -0.8948 | -0.6634 | 0.3515 | 82.00% |
| echiverri-cohen2016 | -0.7811 | -0.8965 | -0.6657 | 0.3499 | 82.00% |
| feeny2002 | -0.7892 | -0.9034 | -0.6750 | 0.341 | 81.70% |
| feske2008 | -0.7768 | -0.8919 | -0.6617 | 0.3481 | 82.00% |
| foa1991 | -0.7815 | -0.8968 | -0.6663 | 0.349 | 82.00% |
| foa1999 | -0.7842 | -0.8994 | -0.6690 | 0.3482 | 81.90% |
| foa2013 | -0.7835 | -0.8990 | -0.6680 | 0.3501 | 81.90% |
| fonzo2017 | -0.7722 | -0.8869 | -0.6576 | 0.3439 | 81.80% |
| frommberger2004 | -0.7834 | -0.8984 | -0.6684 | 0.3477 | 82.00% |
| hien2017 | -0.776 | -0.8913 | -0.6608 | 0.3485 | 81.90% |
| keane1989 | -0.7827 | -0.8979 | -0.6676 | 0.3482 | 82.00% |
| korte2017 | -0.7795 | -0.8951 | -0.6639 | 0.3511 | 82.00% |
| lebeau2008 | -0.7834 | -0.8984 | -0.6683 | 0.3478 | 82.00% |
| lovell2001 | -0.7839 | -0.8990 | -0.6687 | 0.3481 | 82.00% |
| markowitz2015a | -0.7831 | -0.8985 | -0.6677 | 0.3495 | 82.00% |
| mills2012 | -0.784 | -0.8995 | -0.6685 | 0.3501 | 81.90% |
| nacasch2011 | -0.7727 | -0.8874 | -0.6580 | 0.3452 | 81.90% |
| nidich2018 | -0.7845 | -0.9000 | -0.6690 | 0.3501 | 81.80% |
| øktedalen2015 | -0.7842 | -0.8995 | -0.6690 | 0.3485 | 81.90% |
| popiel2015 | -0.7893 | -0.9016 | -0.6770 | 0.3256 | 80.70% |
| resick2002 | -0.7677 | -0.8812 | -0.6543 | 0.3347 | 81.30% |
| rothbaum2005 | -0.7726 | -0.8874 | -0.6579 | 0.345 | 81.80% |
| rothbaum2006 | -0.7825 | -0.8980 | -0.6671 | 0.3502 | 82.00% |
| ruglass2017 | -0.7836 | -0.8988 | -0.6684 | 0.3483 | 82.00% |
| thorp2019 | -0.7802 | -0.8960 | -0.6645 | 0.3519 | 82.00% |
| Vandenberg2015 | -0.7795 | -0.8953 | -0.6637 | 0.3523 | 82.00% |
| vera2011 | -0.7751 | -0.8899 | -0.6603 | 0.3468 | 82.00% |
| zoellner2019 | -0.7825 | -0.8988 | -0.6662 | 0.3564 | 82.00% |
| acarturk2016 | -0.7696 | -0.8834 | -0.6557 | 0.3377 | 81.40% |
| adenauer2011 | -0.7737 | -0.8884 | -0.6589 | 0.346 | 81.90% |
| akbarian2015 | -0.7738 | -0.8887 | -0.6590 | 0.3462 | 81.90% |
| aldahadha2012 | -0.767 | -0.8806 | -0.6533 | 0.3366 | 81.50% |
| alghamdi2015 | -0.7833 | -0.8985 | -0.6681 | 0.3484 | 82.00% |
| basoglu2005 | -0.782 | -0.8975 | -0.6665 | 0.3502 | 82.00% |
| basoglu2007 | -0.7782 | -0.8934 | -0.6630 | 0.3488 | 82.00% |
| bass2014 | -0.782 | -0.8980 | -0.6661 | 0.3537 | 82.00% |
| beck2009 | -0.7784 | -0.8937 | -0.6631 | 0.3494 | 82.00% |
| bichescu2007 | -0.7756 | -0.8905 | -0.6607 | 0.3472 | 82.00% |
| blanchard2003 | -0.7762 | -0.8914 | -0.6610 | 0.3484 | 82.00% |
| bohus2013 | -0.7758 | -0.8911 | -0.6606 | 0.3485 | 81.90% |
| brom1989 | -0.7834 | -0.8987 | -0.6680 | 0.3493 | 82.00% |
| bryant2006 | -0.7855 | -0.9005 | -0.6705 | 0.3466 | 81.90% |
| buhmann2018 | -0.786 | -0.9010 | -0.6711 | 0.3458 | 81.70% |
| butler2018 | -0.7818 | -0.8969 | -0.6668 | 0.3481 | 82.00% |
| capone2018 | -0.7823 | -0.8976 | -0.6670 | 0.3491 | 82.00% |
| carletto2016 | -0.7847 | -0.8998 | -0.6696 | 0.3475 | 81.90% |
| carlson1998 | -0.7829 | -0.8980 | -0.6678 | 0.348 | 82.00% |
| carlsson2018 | -0.7855 | -0.9007 | -0.6704 | 0.3472 | 81.70% |
| castillo2016 | -0.7747 | -0.8898 | -0.6596 | 0.3473 | 81.80% |
| chard2005 | -0.766 | -0.8792 | -0.6528 | 0.3329 | 81.30% |
| church2013 | -0.7706 | -0.8850 | -0.6563 | 0.3418 | 81.70% |

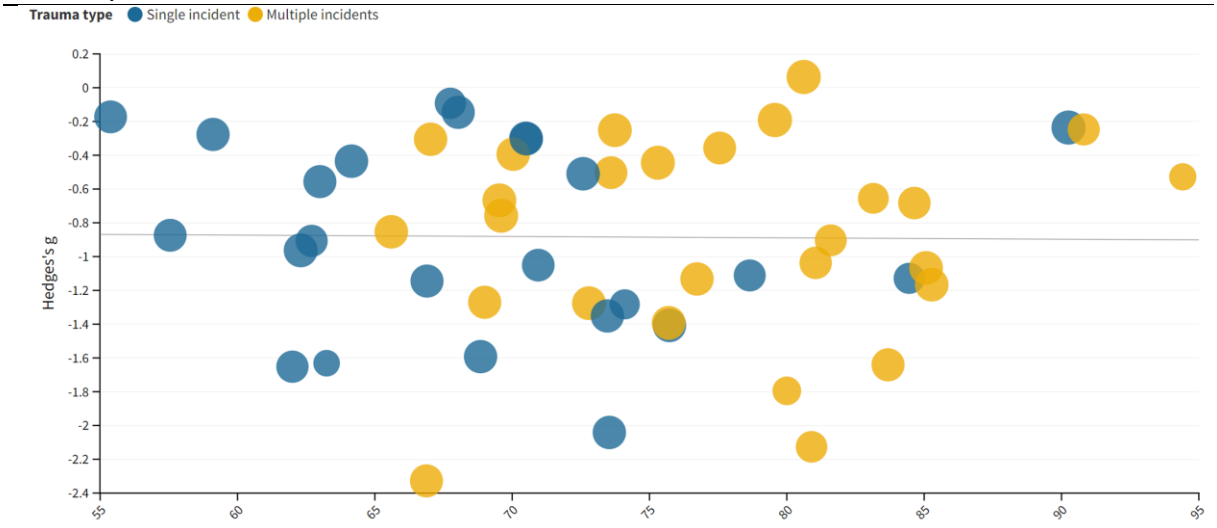
| | | | | | |
|---|---|---|---|---|---|
| cook2010 | -0.7864 | -0.9012 | -0.6717 | 0.3442 | 81.60% |
| cottraux2008 | -0.7851 | -0.9002 | -0.6699 | 0.3474 | 81.90% |
| covers2021 | -0.7829 | -0.8982 | -0.6675 | 0.3494 | 82.00% |
| davis2011 | -0.7831 | -0.8984 | -0.6678 | 0.349 | 82.00% |
| difede2007 | -0.7789 | -0.8941 | -0.6636 | 0.349 | 82.00% |
| duffy2007 | -0.7708 | -0.8852 | -0.6564 | 0.3421 | 81.70% |
| dunne2012 | -0.7829 | -0.8980 | -0.6678 | 0.3481 | 82.00% |
| echeburua1996 | -0.779 | -0.8941 | -0.6639 | 0.3486 | 82.00% |
| Efendi2020 | -0.7685 | -0.8821 | -0.6549 | 0.336 | 81.40% |
| ehlers2003 | -0.7774 | -0.8928 | -0.6621 | 0.3494 | 82.00% |
| Ehlers2005 | -0.7766 | -0.8917 | -0.6615 | 0.348 | 82.00% |
| ehlers2014 | -0.7744 | -0.8894 | -0.6594 | 0.3467 | 81.90% |
| ertl2011 | -0.783 | -0.8984 | -0.6677 | 0.3495 | 82.00% |
| falsetti2008 | -0.7787 | -0.8942 | -0.6632 | 0.3502 | 82.00% |
| fauerbach2020 | -0.7828 | -0.8981 | -0.6676 | 0.3489 | 82.00% |
| fecteau1999 | -0.7761 | -0.8911 | -0.6611 | 0.3476 | 82.00% |
| forbes2012 | -0.7823 | -0.8978 | -0.6669 | 0.35 | 82.00% |
| ford2011 | -0.7776 | -0.8932 | -0.6620 | 0.3508 | 82.00% |
| galovski2012 | -0.7737 | -0.8886 | -0.6588 | 0.3458 | 81.80% |
| geronilla2016 | -0.7639 | -0.8767 | -0.6510 | 0.3306 | 81.20% |
| gray2019 | -0.7662 | -0.8794 | -0.6530 | 0.3329 | 81.30% |
| henseldittmann2011 | -0.7828 | -0.8979 | -0.6676 | 0.3484 | 82.00% |
| hermenau2013 | -0.782 | -0.8973 | -0.6667 | 0.3492 | 82.00% |
| hijazi2014 | -0.7834 | -0.8987 | -0.6680 | 0.3492 | 82.00% |
| hinton2011 | -0.7744 | -0.8893 | -0.6595 | 0.3466 | 81.90% |
| hogberg2007 | -0.7801 | -0.8953 | -0.6649 | 0.3488 | 82.00% |
| hollifield2007 | -0.7876 | -0.9021 | -0.6731 | 0.3428 | 81.70% |
| jacob2014 | -0.7836 | -0.8990 | -0.6682 | 0.3496 | 81.90% |
| jensen1994 | -0.7865 | -0.9013 | -0.6718 | 0.3452 | 81.90% |
| jung2013 | -0.7782 | -0.8934 | -0.6630 | 0.3487 | 82.00% |
| karatzias2019 | -0.7818 | -0.8970 | -0.6666 | 0.3488 | 82.00% |
| kent2011 | -0.7757 | -0.8908 | -0.6606 | 0.3478 | 82.00% |
| knaevelsrud2015 | -0.7691 | -0.8823 | -0.6558 | 0.3327 | 81.10% |
| krakow2000 | -0.7786 | -0.8942 | -0.6630 | 0.351 | 82.00% |
| krupnick2017 | -0.7789 | -0.8942 | -0.6636 | 0.3492 | 82.00% |
| kubany2003 | -0.7698 | -0.8840 | -0.6555 | 0.3417 | 81.70% |
| kubany2004 | -0.7735 | -0.8884 | -0.6587 | 0.3454 | 81.80% |
| maguen2017 | -0.7787 | -0.8939 | -0.6634 | 0.3491 | 82.00% |
| marcus1997 | -0.778 | -0.8935 | -0.6626 | 0.3501 | 82.00% |
| marcus2004 | -0.7781 | -0.8934 | -0.6628 | 0.3492 | 82.00% |
| maxwell2016 | -0.7808 | -0.8960 | -0.6657 | 0.3485 | 82.00% |
| mclay2011 | -0.7798 | -0.8950 | -0.6647 | 0.3486 | 82.00% |
| miyahira2012 | -0.7812 | -0.8965 | -0.6659 | 0.3493 | 82.00% |
| monson2006 | -0.7762 | -0.8914 | -0.6609 | 0.3486 | 81.90% |
| monson2012a | -0.777 | -0.8923 | -0.6618 | 0.3487 | 82.00% |
| morath2014 | -0.7798 | -0.8951 | -0.6645 | 0.3493 | 82.00% |
| mueser2008 | -0.7823 | -0.8981 | -0.6665 | 0.3523 | 82.00% |
| mueser2015 | -0.7842 | -0.9001 | -0.6683 | 0.3529 | 81.80% |
| neuner2004 | -0.784 | -0.8991 | -0.6689 | 0.3476 | 82.00% |
| neuner2010 | -0.7863 | -0.9011 | -0.6715 | 0.3455 | 81.90% |
| nixon2016 | -0.7829 | -0.8982 | -0.6676 | 0.3491 | 82.00% |
| ochsnermargolies2013 | -0.7765 | -0.8917 | -0.6613 | 0.3483 | 82.00% |
| orang2018 | -0.778 | -0.8933 | -0.6627 | 0.3493 | 82.00% |
| perezdandieu2014 | -0.7743 | -0.8890 | -0.6596 | 0.3461 | 81.90% |
| ready2010 | -0.7802 | -0.8952 | -0.6652 | 0.3482 | 82.00% |
| robjant2019 | -0.7769 | -0.8924 | -0.6615 | 0.3501 | 81.90% |
| rothbaum1997 | -0.7703 | -0.8846 | -0.6561 | 0.3426 | 81.80% |
| sannibale2013 | -0.7841 | -0.8993 | -0.6689 | 0.3482 | 81.90% |
| saunders2015 | -0.7767 | -0.8919 | -0.6616 | 0.3482 | 82.00% |
| scheck1998 | -0.7794 | -0.8949 | -0.6639 | 0.3503 | 82.00% |
| shapiro2015 | -0.776 | -0.8910 | -0.6611 | 0.3475 | 82.00% |
| sijbrandij2007 | -0.7807 | -0.8966 | -0.6648 | 0.3531 | 82.00% |

| | | | | | |
|---|---|---|---|---|---|
| sloan2004 | -0.7791 | -0.8945 | -0.6637 | 0.3499 | 82.00% |
| sloan2011 | -0.7859 | -0.9008 | -0.6711 | 0.346 | 81.90% |
| stecker2014 | -0.7843 | -0.9004 | -0.6681 | 0.3552 | 81.80% |
| steinert2016 | -0.7649 | -0.8776 | -0.6522 | 0.3292 | 81.10% |
| stenmark2013 | -0.7719 | -0.8865 | -0.6573 | 0.3435 | 81.70% |
| suris2013 | -0.7767 | -0.8921 | -0.6613 | 0.3496 | 81.90% |
| terheide2011 | -0.7784 | -0.8934 | -0.6635 | 0.348 | 82.00% |
| tylee2017 | -0.765 | -0.8783 | -0.6517 | 0.335 | 81.40% |
| ulmer2011 | -0.775 | -0.8899 | -0.6601 | 0.3469 | 82.00% |
| vandam2013 | -0.7804 | -0.8957 | -0.6651 | 0.3493 | 82.00% |
| vanderkolk2007 | -0.7814 | -0.8969 | -0.6659 | 0.3504 | 82.00% |
| weiss2015 | -0.7857 | -0.9008 | -0.6706 | 0.3469 | 81.60% |
| wu2014 | -0.7822 | -0.8976 | -0.6668 | 0.3498 | 82.00% |
| ivarsson2014 | -0.7769 | -0.8922 | -0.6615 | 0.3492 | 82.00% |
| **Overall estimate** | -0.779 | -0.8936 | -0.6644 | 0.3471 | 81.90% |

**A14:** eTable. Meta-regressions of the association between overall effect size and study characteristics

| **TF-CBT vs. TAU** | | | | | **Test of Moderators** | |
|---|---|---|---|---|---|---|
| **Predictor** | **Studies** | **Estimate** | **LCI** | **UCI** | ***Q*** | ***P*** |
| Mean age | 131 | -0.0035 | -0.0158 | 0.0088 | 0.3129 | 0.5759 |
| Proportion of women | 129 | -0.0028 | -0.0063 | 0.0006 | 2.6305 | 0.1048 |
| Baseline CAPS score | 51 | -0.001 | -0.0203 | 0.0179 | 0.0145 | 0.9042 |

**A15:** eFigure. Bubble plot of meta-regressions examining association of CAPS baseline severity and overall estimate of TF-CBT vs. TAU

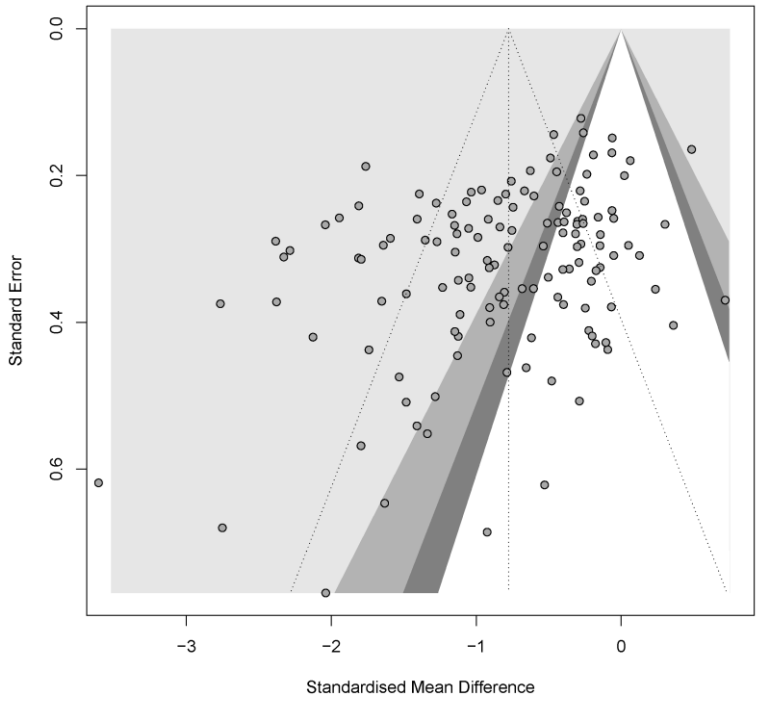



The plots shows the mean CAPS baseline score of the intervention arm from each RCT in relation to the effect size of TF-CBT against TAU, with relatively even amount of study of both sides of the regression line (indicating no association).

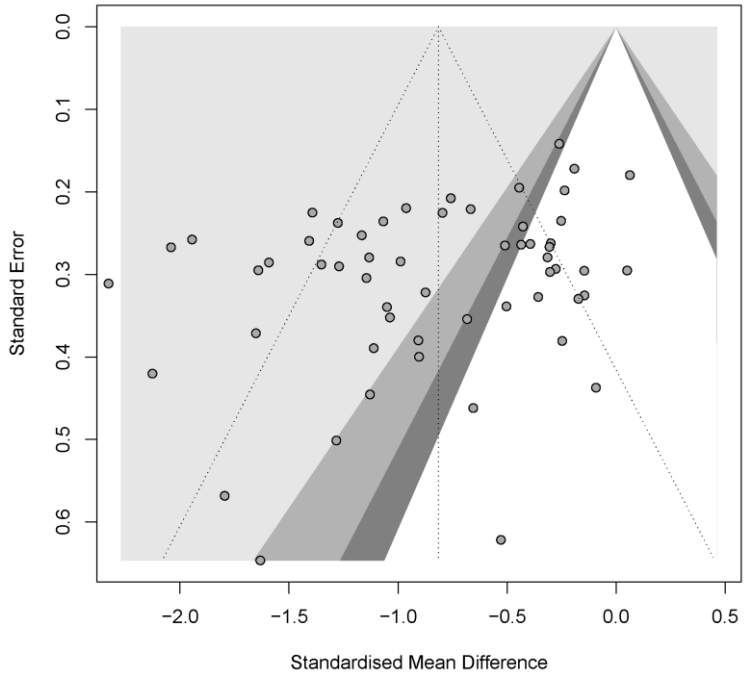
The pooled mean CAPS score of all 51 RCTs with available data were:
Baseline: 73.52 (8.8) [range: 55.4-94.4]
End of treatment: 42.22 (15.7) [range: 9.0-76.7]

**A16:** eFigure**.** Funnel plot assessment for the overall estimate of studies reporting on TF-CBT against TAU

**A. All 133 RCTs**



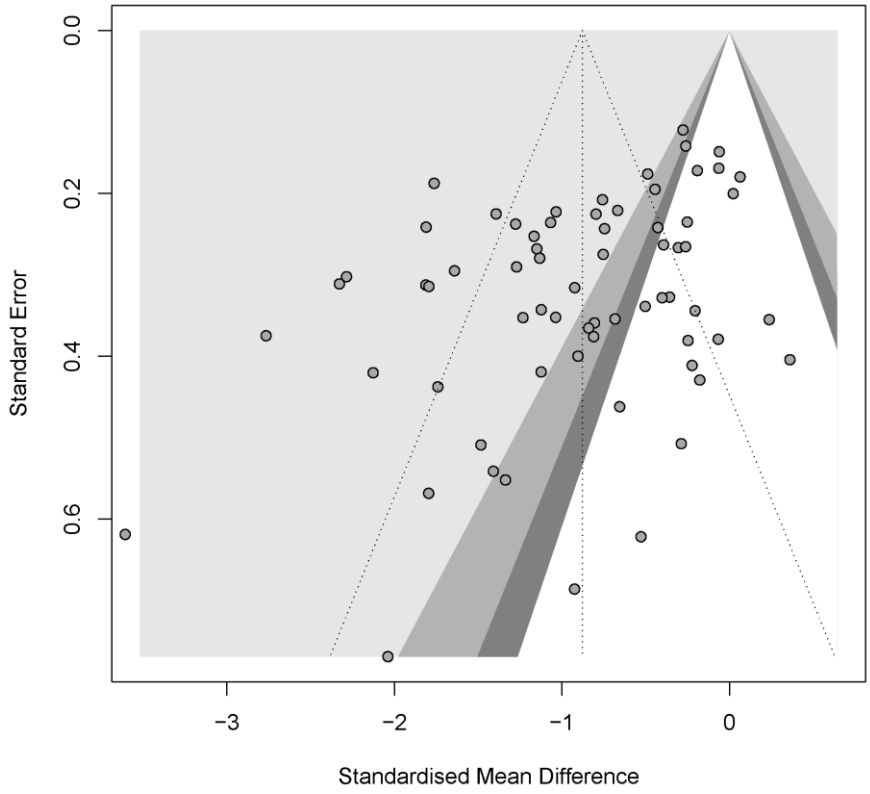

**B. 51 RCTs with CAPS outcome measure only**



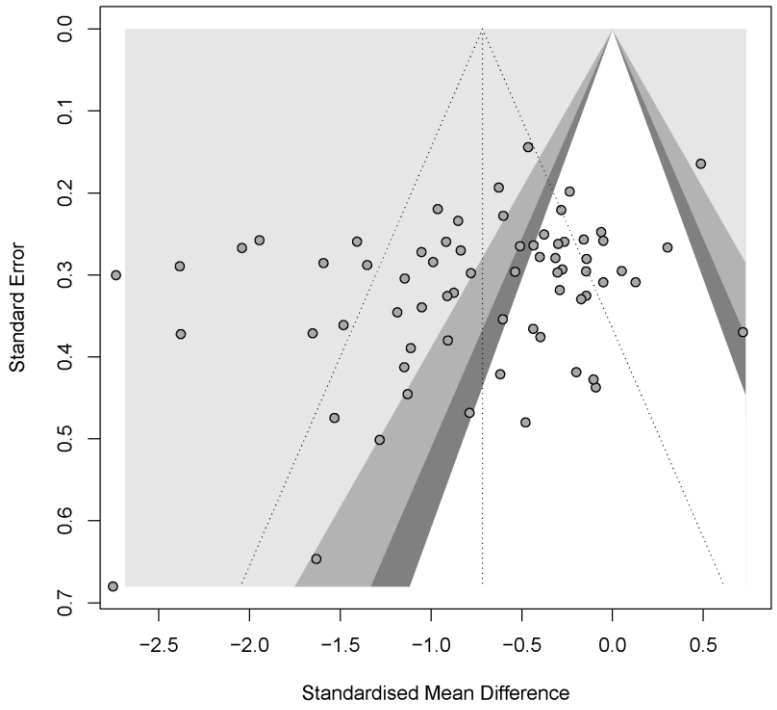

The dashed black vertical line depicts the observed overall summary effect , with attached lines representing 95% confidence intervals for individual effect estimates, assuming no bias. The grey shaded funnel plot funnel represents the 95% confidence intervals, and the dark blue funnel represents the 99% confidence intervals represent effect estimates imputed by trim-and-fill.
Overall: Egger's test: bias -2.45, *p*-value <0.0001; Rank test: -1556.0, *p*=0.0022
Overall CAPS only: Egger's test: bias -2.24, *p*-value =0.0303; Rank test: -228.0, *p*=0.1071

**A17:** eFigure. Funnel plot assessment of estimate of studies reporting on TF-CBT by trauma group

**A.** multiple-incident trauma studies only




**B**. Single-incident trauma studies




Multiple-incident trauma estimates: Egger's test: bias -3.32, *p*-value =0.0015; Rank test: -328.0, *p*=0.0574
Single-incident trauma estimates: Egger's test: bias -2.43, *p*-value =0.013; Rank test: -409.0, *p*=0.0269

## **A18:** References of included studies


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## Appendix B – Service improvement project

**B1:** Instructions for authors target journal

*BMJ Quality & Safety* (formerly *Quality & Safety in Health Care*) is a leading international peer review journal in this growing area of quality and safety improvement. It provides essential information for those wanting to reduce harm and improve patient safety and the quality of care. The journal reports and reflects research, improvement initiatives and viewpoints and other discursive papers relevant to these crucial aims with contributions from researchers, clinical professionals and managers and experts in organisational development and behaviour.

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- **What is already known on this topic** – *summarise the state of scientific knowledge on this subject before you did your study and why this study needed to be done*
- **What this study adds** – *summarise what we now know as a result of this study that we did not know before*
- **How this study might affect research, practice or policy** – *summarise the implications of this study*

This will be published as a summary box after the abstract in the final published article.

**B2:** eMethods. Interview schedule (qualitative phase 1) delayed discharges and transfers of care

**Introductions**

- Thank you, [NAME] for making the time in your busy schedule to meet with me today.

➔ Complete If: audio recording previously agreed to in emails: [Is it ok if I audio record? – Ill tell you a bit more about this soon.]

- Interviewer introduces him/herself (name, position, affiliations, professionals' roles and responsibilities, and interests.)
- I do clinical mental health placements across oxford health and as part of our training we do research. I've been asked to do a project on delayed transfers of care, and I am doing interviews to learn about staff views on discharge decisions related to delayed transfers of care in adult mental health hospitals.

- Participant introduces him/herself (name, where from).

- Thank you. I audio record our conversation to make sure I understood correctly and for transcription purposes. We may use very short quotations to illustrate key points. If we use such quotes, we will ensure that any identifiable information will be removed. We won't be making copies of the interview available to anyone else other than my supervisor (Insert name).

➔ Complete if: no written confirmation for terms exists (e.g. email confirmation). [This interview will take approximately 20-30 minutes. I hope you allow me to record our conversation today to make sure I understood correctly and for transcription purposes. Your participation is voluntary, and you can remove yourself from the study at any time until the interviews are anonymised. I will give you time to read the consent form. I am happy to answer any questions you have once you read the form. If you're happy to proceed, please sign the form and we can begin. *(Participant reviews and signs consent form) ]*

- Before we begin, do you have any questions?

**Clinical experiences with patient discharge**

1. **Can you tell me what you understand of the term delayed transfer of care from your hospital?**

Ok, thank you for that. That makes sense. For the purpose of this project, by a DTOC we mean: "that a patient is deemed ready to be discharged or transferred but are they're still occupying a bed due to non-clinical reasons."

Prompts:

Why is it important? Do you think it's a problem?

2. **Can you describe a recent experience where a patient was approaching discharge with potential of being delayed from your hospital? Can you tell me more about this?**

Prompts:

a. What was the process in making the decision to discharge or not?
   i. Who were the key decision makers?

ii. Who was ultimately responsible for the decisions
iii. Was this a typical way delays was managed from the unit?
iv. How were you involved in the decision that the patient was ready (or not) for transfer/discharge?
v. In your opinion, was this patient ready to be transferred from unit to the community?

**Barriers and facilitators**

**3. From your experience, what are the barriers to earlier discharge or transfers from the ward?**

**4. From your experience, what works to minimise delayed transfer patients from the unit?**

Prompts (q3-q4):

b. In your experience, what does not work with the current process?
c. From your experience, what are important treatment factors that influence delayed transfer of care from the unit?
d. From your experience, what are important patient factors that influence delayed transfer of care from the unit?
e. How do you think your perceptions of 'clinical responsibility' influence your decision-making in practice?

**Guidelines, tools, local initiatives**

**5. Does your [MENTAL HEALTH UNIT/WARD] use guidelines, protocols or checklists to assist with determining which patients are ready for discharge?**

Prompts:

a. Please describe these tools and how they are used?
b. Are these tools based on any specific guidelines or recommendations?
c. In your view, are these tools effective?
d. Why? Why not?

**Additions/summary**

**6. Of all of the things we talked about today please identify what you would consider the three most important things that could speed up delayed discharges from hospital ward.**

*Time saving alternative:* **Is there anything you thought I would ask but did not, or anything else that you think is important for us to consider?**

**Questions/Conclusions**

- These are all the questions I have for you. Do you have any questions for me about the research project or interview?
- Thank you for your input, I really appreciate that you took the time to talk to me.

**B3:** eTable. Relevant NHS trust metrics for psychiatric length of stays and delayed discharges by different monitoring organisations

| Monitoring organisation | Metric name | Definitions and measures required by organisation from NHS |
|---|---|---|
| NHS England,[80] and The Care Act (2014): Care and Support (Discharge of Hospital Patients) Regulations (2014) | Delayed transfer of care (DTOC) | DTOCs refers to a patient who is occupying a bed after being deemed medically fit for discharge. Most DTOCs are attributed to reasons beyond hospitals direct control, such as waiting for social care or community assessments. The metric was developed to help identify improvement areas and support a support consistent notification for alerting community and social services on likely assessment needs and services post-discharge. When DTOCs are attributed to Social care or council, the NHS trust can claim reimbursement sum up to £155 per day (schedule 3 of the Care Act 2014) for each delayed day. Many NHS trusts do not claim this reimbursement.<br><br>All delayed transfers of care (DTOCs) in mental health in-patient settings must be reported at a patient-level in the Mental Health Services Data Set (MHSDS). They must also be reported in the monthly SitRep (MSitDT) return.[10]<br><br>However, mandatory DTOC reporting stopped beginning of COVID-19, and reliable data collection of individual level DTOCs has not yet been achieved. More than half of submissions were deemed unreliable in July 2019 (MHSDS).[81] |
| | DTOC beds:<br>DTOC rate: | Total delayed days in a month divided by the number of days in that month<br>Total number of days a bed was occupied by a delayed patient as a percentage of the total number of occupied beds. |
| CQC | RPIR ID - CHS7. Bed Occ & LOS: "Bed Occupancy and Length of Stay" in the last 12-months | Provide by ward and by month for one year:<br>• The bed occupancy (in-patient days/available bed days):<br>• Length of stay (leave must be including Home Leave, Mental Health Leave of Absence or Mental Health Absence Without Leave)*<br>*Patients admitted and discharged on the same day have a LOS of zero days |
| | CQC rating scheme: "Responsive/Effective" (R3.6, E4): | Potential criteria for ratings of "Effective/ Responsive":<br>Good: appointments, care and treatment only cancelled or delayed when absolutely necessary<br>Requires improvement: there may be delays or poor coordination when people are referred or discharged or when they transition to other services.<br>Inadequate: There are significant delays to discharge, transition or referral |
| Getting it Right the First Time (GRIFT) NHS improvement network | 5. Adult acute in-patient<br>5.13 Acute in-patient length of stay profile | Proportion of Occupied bed days (excluding leave), Adult acute bed occupancy including and excluding leave, exceeding different length of stay as follows:<br>• 0-3 days<br>• 4-13 days<br>• 14-59 days<br>• 60-89 days OR >60 days overall<br>• 90 days or longer<br>Adult acute admissions – patients no fixed abode<br>DTOC rate<br>DTOC days lost by provider |
| The Mental Health Act 1983 of | *Section 2 – Admission for Assessment* | Legally approves compulsory admission of a patient for assessment up to 28 days in hospital. Section 2 of the mental health act defines hospital stays less than 28 days as "a short stay" (an arbitrary cut-off). |

| | | |
|---|---|---|
| England and Wales | | |
| **Financial measures** | | |
| NHS payment tariffs[82] | Number of days in hospital for specific conditions that are exceeding "expected number of days" | NHS's payment by result system pay hospitals on a fixed price tariff based on patients expected LOS, which varies depending on patient needs. Hospitals are paid less for days that exceed a patient's expected LOS. Higher rates of longer LOS can therefore cause significant financial stress on NHS trusts. Hospitals receives on average less money for any "excess day" in hospital whilst losing income on waiting admissions |

**B4:** eTable. Comparison estimates of means length of stay for adult acute psychiatric admissions in England

The lack of standard definitions over what constitutes an "excessive LOS" in psychiatry may partly explain why so little is known about the factors influencing longer LOS, delayed discharges and effective prevention.

In 2019, the NHS Long Term Plan set targets for all NHS trusts to reduce the average LOS of acute in-patient admissions to 32 days. However there is currently no referenced data source that confirm how the 32 day cut-off is derived.[13]

**NHS England Hospital Episode Statistics Adult Mental Health**[41]

Notably, as seen in table below the mean LOS for adult psychiatric admissions range between 47-51 days in national data sources (2016-2021), with similar estimates reported in published studies (e.g. 51 days).[83]

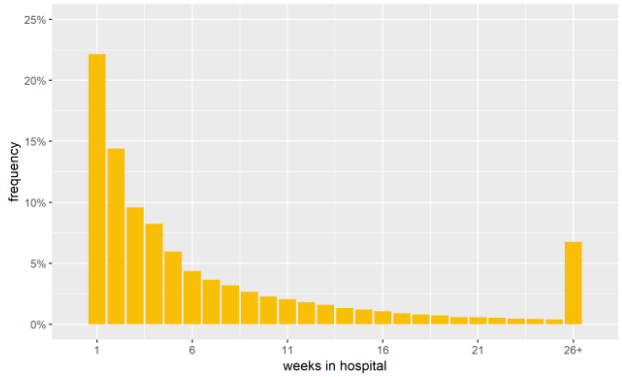
**NHS England Hospital Admitted Patient Care Activity for Adult Mental Health in England by complete financial year**

| Year period | Finished consultant episodes | Admissions | Gender and age | | | | LOS | | Admission type | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | Male | Female | Unknown | Mean age | Mean | Median | Emergency | Planned |
| 2020 | 67,204 | 44,435 | 35,484 | 31,650 | 70 | 41 | 47 | 19 | 33,171 | 6,382 |
| 2019 | 77,048 | 54,695 | 41,620 | 35,366 | 62 | 40 | 48 | 20 | 40,397 | 7,956 |
| 2018 | 95,197 | 69,007 | 51,708 | 43,416 | 73 | 40 | 48 | 19 | 49,631 | 10,878 |
| 2017 | 102,052 | 75,384 | 56,013 | 45,997 | 42 | 40 | 49 | 19 | 54,240 | 11,585 |
| 2016 | 101,152 | 76,512 | 54,681 | 46,428 | 43 | 41 | 51 | 19 | 53,590 | 12,491 |

**The Strategy unit. Royal college of psychiatrist commissioned report (2019)**[8]

Extracted content linked to figure below: "*The average (mean) length of stay in a mental health bed in 2016/17 was approximately seven weeks (median four weeks). The length of stay distribution is broad and right-skewed. More than one third of patients are discharged within two weeks, but seven per cent are still in hospital after six months. Most very short duration stays in mental health units (e.g. <= 3 days) occur when patients discharge themselves contrary to clinical advice or consent."* (pp.1 88 Wyatt et al., 2019)

Figure 2v: Distribution of length of stay (weeks) in mental health beds, England 2016/17




*Source: Hospital Episode Statistics – Admitted Patient Care*

| **B5:** eTable. Individual risk items from local risk assessment extracted from CRIS (Yes/No/Not assessed) | |
|---|---|
| 1 | Self-Harm |
| 2 | Suicide |
| 3 | Self-Neglect |
| 4 | Physical Health / Falls |
| 5 | Misuse of Medication |
| 6 | Alcohol and Substance Misuse |
| 7 | Accidental Harm (Outside the Home) |
| 8 | Disengagement / Non-Compliance with Care |
| 9 | Risk From Others |
| 10 | Violence and Aggression |
| 11 | Fire-Setting |
| 12 | Sexual Offending |
| 13 | Specific Risks to Others |
| 14 | Risk to Children OR Child at Risk from Adult / Others |
| 15 | Multi-Agency Public Protection Arrangements (MAPPA) |
| 16 | Damage to Property |
| 17 | Unlawful Restrictions / DoLS |
| 18 | Absconding / Escaping / Wandering |

**B6:** eMethods. More information on statistical methods and procedures

Give the lack of standardised and clinically meaningful outcomes of hospital stays and delays, we provided estimates for three different outcomes as frequently reported in meta-analyses.[16,30,35,43-47] Each outcome applied a different statistical approach.

**Multiple imputations of missing data**

We examined whether significant differences existed across all outcomes using complete case analyses compared with patients with missing values. We found no significant differences, and we assumed values were missing at random. We imputed missing values for all variables listed in the main manuscript table 1 with missing data.

We used R's MICE package to create 20 imputed datasets (20 iterations for each imputation). For each missing value, the package retains the average (or mode) of imputed values from imputed datasets, rounded to the nearest integer within each imputation. Categorical variables were imputed using logistic regression models. Continuous variables were log-transformed where necessary and imputed using Bayesian linear regressions. We pooled values using Rubin's rule fitted to each statistical model (e.g. logistic or cox-regression models). We incorporated hospital ID's into the model to account for potential differences in practices between hospitals.

**Locally defined delayed discharge (LOS > 56 days): adjusted logistic regression models**

We fitted adjusted multivariable logistic regression models to examine the association between each predictor and the primary outcome (yes/no). Where possible, we adjusted all models for age, sex, admission year and ward of discharge. We also accounted for clustering effects from specific hospitals by including the hospital ID as a cluster variable in the calculation of robust standard errors (SE) based on the sandwich estimator. We adjusted all estimates for sex, admission year, and age groups to account for uneven distributions (e.g. single sex in-patient units).

**Differences in mean length of stay: Generalised linear regression models with estimated marginal means**

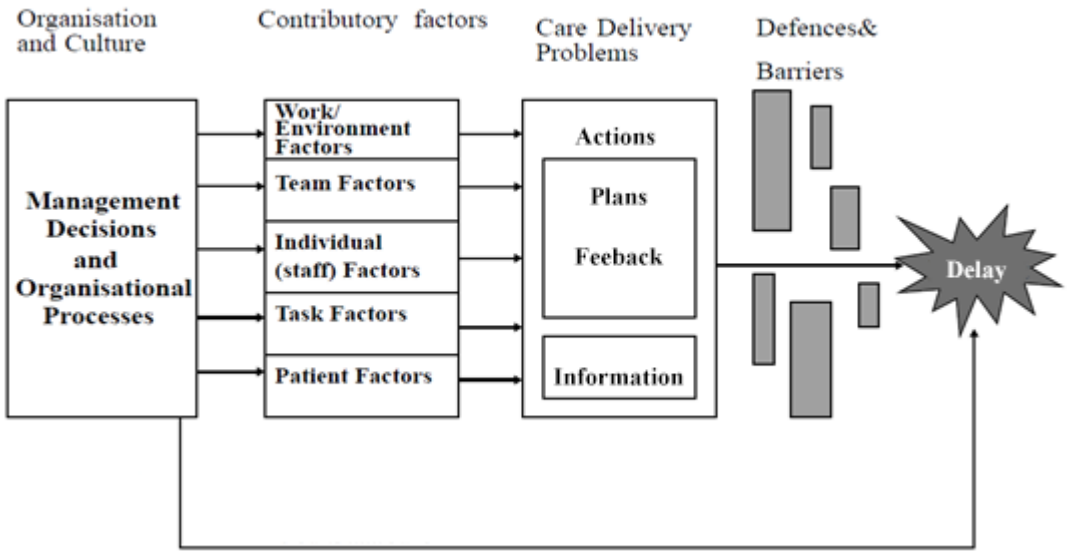
We used adjusted mixed-effects linear regression models to examine predictors impact on patients' length of stay (LOS) in days. We converted estimates to adjusted mean LOS using the Least-Squares means (lsmean) package in R. The lsmean package provides Estimated Marginal Means (EMM) based on averages of predictors over a reference grid. The reference grid is the set of all combinations of reference levels (overall predictor variables). As most LOS data is left-skewed (high distribution of shorter LOS), we applied general mixed effects models (GMM) to relax the normality assumption and analysed LOS under a "skewed-normal distribution" assumption.[84] We used GMM over transforming variables following the arguments described by Manning (2005).[85] We applied GGM in lme4 and ggeffects package in R.

**One-year readmissions: Cox-proportional hazards models**

To examine predictors association with re-admission within one year of discharge we used cox proportional hazard models, with time from discharge to readmission (number of days) used as the underlying time scale. Patients were censored at 1-year post-discharge

or the study end date, whichever came first. We examined the proportional hazards assumption using Schoenfeld residuals and log-log plots, which showed no evidence of violations for any model.

**B7:** eFigure. Adapted Framework from Vincent et al. on contributory factors to clinical outcomes




Adapted from Reason (1997),[86] and Vincent et al. (1998)[42]

**B8:** eTable. Longitudinal case example covering 16 years (2005-2021) of patient who became a delayed discharge in the Trust due to "hospital dumping" resulting in repeated admissions as obtained from case notes reviews

| Time | Dates | Patient journey |
|---|---|---|
| | | **History** |
| | 2005-2015 | Fortnightly home visits from CPN |
| | 06/2011 | [start of electronic record] Is on CPA, receives fortnightly home visits from CPN in CMHT (medication drop), not significant concerns/manages well but with some police contacts |
| | 05/2012 | Tenancy at risk (verbally abusive to neighbours) – medical impression: psychosis increased, not taking meds. |
| | 09/2012 | Police arrest – "burglary" Marked decrease in hygiene; MHA –"not detainable" |
| | 03/2013 | CPA review: tenancy at risk: Needs supportive housing; Lodger in flat vulnerable exploitation — drug use |
| 11y 6mo | 03/2013 | The only family is a single parent –" wants patient in hospital" – "cant cope on their own" – referral to supported accommodation options |
| | 05/2013 | Switch CPN |
| | 04/2014 | Risk of tenancy - Damage to property |
| | 08/2014 | Housing estate looking to evict – police agrees to support by visiting each week to keep tenancy |
| | 09/2014 | Switch CPN |
| | 02/2015 | AMHT Discharge from treatment function – "no evidence of mental illness at that time" |
| | 09/2015 | Criminal Justice Liaison & Diversion: "arrested for street robbery with force" |
| | 12/2015 | Rejection for alternative housing referral, attempt to prevent homelessness |
| | 11/2016 | Several GP contacts – GP re-refers to AMHT |
| | 11/2016 | **Evicted – homeless – drug use** |
| | 11/2016 | AMHT accepts GP referral (MDT meeting) – no clear signs of mental from referral, offer 3-month package for trial engagement |
| 1y 1mo | 11/2016 | Arrested and imprisoned |
| | 02/2017 | Prison release |
| | | Intermittent stay at hostel - Homeless |
| | 12/2017 | Police arrest for arson |

| | | |
|---|---|---|
| 1y 1mo | 12/2017 | **Placed in local mental health housing - Social worker arrangements** |
| | 01/2018 | Police custody for damages to cars and property |
| | 09/2018 | Local housing contacts AMHT duty – no medication adherence, drug misuse, psychosis - damage to property |
| | 10/2018 | Local housing discusses eviction with plans to evict |
| 1-3 days | 02/2019 | **Admission PICU: place of safety – Police escort** |
| | 02/2019 | Discharged from ward with monitoring (e.g. social worker home visits) + Call from community saying cannot meet needs |
| 5 wk | 02/2019 | **Admission adult acute in-patient** – psychosis, damage to property, poor medication adherence |
| | | Health complexities - Hepatitis C + picking scabs, infection control, refuse medication |
| | 02/2019 | Ward rounds "not fit for discharge" (no other barriers documented) |
| | | AMHT CCO needs identified – community non-available |
| | 02/2019 | Supported accommodation looking to evict and gained "Order for possession" |
| | | Temporary CCO AMHT assigned and get involved contacting supported accommodation |
| | 02/2019 | Ward in-patient social worker get involved and contact supported accommodation with dismay |
| | 03/2019 | Ward rounds – "Not fit" (housing identified as issues) |
| | 03/2019 | CCO AMHT attends ward round - no action plans/ Unable to discharge as no secure housing |
| 10mo, 2wks | 03/2019 | **Delayed discharge starts (Date deemed fit for discharge by medical review)** |
| | 03/2019 | No updates regarding housing from anyone. Consultant contacts in-patient social worker |
| | 04/2019 | In-patient social worker discusses supported housing option |
| | 05/2019 | In-patient social worker gathering info from Response to refer to "Housing first (wait time) |
| | 05/2019 | Inpatient social worker liaison with 3 placement options (housing first, supported accommodation) |
| | 05/2019 | Plan confirmed (supported accommodation referral sent) |
| | 05/2019 | Supported accommodation assessment<br>New CCCO AMHT allocated<br>Placement option added for planning discharge on homeless pathway<br>Patient refuses to attend local mental health housing assessment |
| | 06/2019 | supported accommodation assessment completed with patient and in-patient social worker<br>Inpatient social worker referrals - Response home support with care package |
| | 06/2019 | Supported accommodation response: rejection |
| | | Inpatient social worker appeals rejection and find alternative supported accommodation |
| | 07/2019 | In-patient social worker contact family to update (mum) |
| | 08/2019 | Meeting about rejection from supported accommodation |
| | 08/2019 | Patient visit holder house with CCO AMHT |
| | 08/2019 | Holder house funding rejected |
| | 09/2019 | Housing first assessment completed with patient and in-patient worker |
| | 10/2019 | Housing first referral accepted – no available houses not yet fully developed and not able to administer all medication etc. Patient no capacity to weigh up administer medication x2 day |
| | 11/2019 | In-patient social worker identified "pilot project" as placement interim option until housing first becomes available. Liaison, assessment, and referral procedures initiated. |
| | 01/2020 | Pilot project referral (only staffed until 19:30) – needs meds at 20:00 |
| | 01/2020 | Pilot project - Delays with care staff being able to administer certain medications etc |
| 34 wks | 02/2020 | **Discharged on s17 extended leave*** |
| | 02/2020 | Pilot project – Staff report patient linked to various destruction to property and refusal of medication, unable to provide medication |
| | 05 to 09/2020 | Pilot project requesting recall |
| | 10/2020 | Multiagency safeguarding meeting regarding<br>Trying to prevent hospital admission as "vehicle" to move housing |
| 4 wks | 10/2020 | **OOA Transferred** |
| 14 wks (+3d) | 11/2020 | **Admission back to local ward - Ambulance escort** |
| | 11/2020 | Pilot project - Placement pressure to not return patient (Our teams' opinion is the patient needs a longer-term rehab) |
| | 01/2021 | Ward rounds and MDT (care coordinator only met 15 min) |
| | | Returning to placement with CMHT support (family wants person back in hospital recalled) |
| 5wks (+4d) | 02/2021 | **Discharge back to pilot project on extended S17*** |
| | | Placement with home visits from care coordinator |
| | 03/2021 | Placement breakdown (challenging behaviours) |
| | 03/2021 | **Admission to local ward: Recalled S17 leave** |

*Some patients are temporarily discharged as a leave of absence from the hospital under Section 17 of the Mental Health Act (1983). A leave of absence relates to a trial period to confirm that a patient is either medically optimised or safe for permanent discharge. Any delay relating to this discharge is not a DTOC and hence is not reportable. However, where a patient has been deemed suitable for discharge and has to return to hospital care because there is a lack of post-discharge support, then this would count as a reportable DTOC, with each delayed day following the patient being ready for discharge being countable, including the period covered by the leave of absence.

**B9:** eTable. Result from the multivariable risk prediction model of potential delayed discharges (LOS>56 days) using a penalised logistic regression model with Least Absolute Shrinkage and Selection Operator (LASSO)

| Significant variable (predictors) | Coefficient estimate |
|---|---|
| 1. Section 117 | 1.474127 |
| 2. Dementia | 1.167019 |
| 3. Bipolar | 0.503338 |
| 4. Learning/Intellectual disability | 0.484249 |
| 5. Psychosis | 0.469971 |
| 6. Self-neglect risk item (imputed) | 0.426117 |
| 7. Disengagement in care risk item (imputed) | 0.341469 |
| 8. Covid-19 positive | 0.311631 |
| 9. Aggression and violence risk item (imputed) | 0.229217 |
| 10. Homeless/no fixed abode | 0.167608 |
| 11. Falls risk item (imputed) | 0.095594 |
| 12. Black ethnicity | 0.081915 |
| 13. RskTOtrid risk item (imputed) | 0.070053 |
| 14. RskFOtrid item (imputed) | 0.046955 |
| 15. Most deprived (1-2 IMD) imputed | 0.033361 |
| 16. age | 0.003858 |
| 17. Time to care coordinator assignment (None) | -1.24064 |
| 18. ward stay observation desc. Intermittent | -0.48155 |
| 19. ward stay observation desc. General | -0.44948 |
| 20. Personality disorder | -0.43404 |
| 21. Time to care coordinator assignment (1-2 weeks) | -0.43273 |
| 22. Time to care coordinator assignment (1 week) | -0.35254 |
| 23. ward stay observation desc. Within arms lengths | -0.2437 |
| 24. Trauma- and stressor-related disorders | -0.2154 |
| 25. Suicideid risk item (imputed) | -0.17464 |
| 26. ActHrmid risk item (imputed) | -0.14123 |
| 27. RskCdnid risk item (imputed) | -0.10839 |
| 28. Time to care coordinator assignment (2-3 weeks) | -0.06693 |
| 29. SubMisid risk item (imputed) | -0.06541 |
| 30. SlfHrmid risk item (imputed) | -0.06163 |
| 31. Least deprived (IMD 5) (imputed) | -0.04766 |
| 32. ward capacity in % | -0.00821 |
| 33. number of ward admissions in the month of admission | -0.00037 |
| **Non-significant predictors (any variable with a coefficient of zero were excluded)** | |
| 34. Time to care coordinator assignment (3-4 weeks) | |
| 35. ward AMHB Sapphire | |
| 36. ward AMHO Allen | |
| 37. ward AMHO Ashurst | |
| 38. ward AMHO Phoenix | |
| 39. ward AMHO Vaughan Thomas | |
| 40. ward AMHO Wintle | |
| 41. Anxiety disorders | |
| 42. Drug misuse | |
| 43. Eating disorders | |
| 44. Mental disorder | |
| 45. Neurodevelopmentaldisorder | |
| 46. imd 5 imp3 | |
| 47. imd 5 imp4 | |
| 48. adm n cat0 | |
| 49. adm n cat1 | |
| 50. adm n cat2 | |

51. Admission type Planned (imputed)
52. Sex/gender
53. ASD
54. Depression
55. AsbEscid risk item (imputed)
56. DmgPrpid risk item (imputed)
57. FireSetid risk item (imputed)
58. MAPPAid risk item (imputed)
59. MUsfMedid risk item (imputed)
60. SexOffid risk item (imputed)
61. ULawRstid risk item (imputed)
62. Total number of risk items endorsed (imputed)

**B10:** eTable. Adjusted odds ratios for delayed discharges and adjusted hazard ratios for specific mental health diagnosis

| | **Delayed discharge (LOS >56 days)** | | **One year readmission** | | |
|---|---|---|---|---|---|
| ICD code | aOR | p-value | aHZ | p-value | Diagnosis term |
| F20.0 | 3.32 (2.6-4.25) | 0 | 1.41 (1.08-1.83) | 0.012 | Paranoid schizophrenia |
| F20.9 | 2.78 (1.53-5.03) | 0.001 | 0.98 (0.59-1.63) | 0.931 | Schizophrenia, unspecified |
| F23.9 | 0.46 (0.27-0.77) | 0.003 | 0.64 (0.25-1.62) | 0.343 | Acute and transient psychotic disorder, unspecified |
| F25.0 | 3.86 (2.58-5.79) | 0 | 1.61 (1.22-2.13) | 0.001 | Schizoaffective disorder, manic type |
| F25.9 | 2.88 (2.02-4.1) | 0 | 1.36 (1.11-1.66) | 0.003 | Schizoaffective disorder, unspecified |
| F29 | 1.03 (0.79-1.34) | 0.842 | 0.42 (0.25-0.7) | 0.001 | Unspecified nonorganic psychosis |
| F31.1 | 0.9 (0.6-1.33) | 0.584 | 1.14 (0.84-1.54) | 0.409 | Bipolar affective disorder, current episode manic without psychotic symptoms |
| F31.2 | 0.98 (0.73-1.33) | 0.9 | 0.83 (0.57-1.21) | 0.333 | Bipolar affective disorder, current episode manic with psychotic symptoms |
| F31.9 | 1.23 (0.82-1.83) | 0.313 | 1.17 (0.59-2.32) | 0.656 | Bipolar affective disorder, unspecified |
| F32.2 | 0.34 (0.22-0.54) | 0 | 0.25 (0.1-0.68) | 0.006 | Severe depressive episode without psychotic symptoms |
| F32.3 | 1.43 (1.19-1.71) | 0 | 0.7 (0.53-0.93) | 0.012 | Severe depressive episode with psychotic symptoms |
| F43.2 | 0.2 (0.07-0.56) | 0.002 | 0.34 (0.1-1.12) | 0.076 | Adjustment disorders |
| F60.3 | 0.28 (0.22-0.36) | 0 | 2.12 (1.73-2.59) | 0 | Emotionally unstable personality disorder |

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## Appendix C – Theoretically driven research project

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|---|---|
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| | |
|---|---|
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| **Authors' names**<br>Separate with commas. No full stops after initials. If there is a very large number of authors we may suggest that they form a group whose name will appear in the article byline. List ORCiD iD alongside respective authors | Ingela Radestad (0000-0000-0000-0000), Gunnar Steineck, C Nordin, B Sjogren |
| **Address for each author**<br>Separate each part of address with a comma (don't use a separate line for each part) Please include postcodes<br>**Authors' names and positions** | Centre for Caring Sciences, Karolinska Institute, S-171 76 Stockholm, Sweden Ingela Radestad midwife Unit of Cancer Epidemiology, Radiumhemmet, Karolinska Institute Gunnar Steinbeck associate professor Department of Womens Health, Karolinska Institute B Sjogren associate professor Department |

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A competing interest - often called a conflict of interest - exists when professional judgment concerning a primary interest (such as patients' welfare or the validity of research) may be influenced by a secondary interest (such as financial gain, academic promotion, or personal rivalry). It may arise for the authors of an article in *The BMJ* when they have a financial interest that may influence, probably without their knowing, their interpretation of their results or those of others.
We believe that, to make the best decision on how to deal with an article, we should know about any competing interests that authors may have, and that if we publish the article readers should know about them too. We are not aiming to eradicate such interests across all article types in *The BMJ*. However, certain articles (see below) fall under a stricter policy announced in 2014. This means that authors whose financial conflicts of interest are judged to be relevant by the BMJ team are not permitted to write these articles. We also ask our staff and reviewers to declare any competing interests.
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**Research**

We have produced a checklist to help authors decide whether *The BMJ* is the right journal for their research. If the work does not seem to fit in *The BMJ*, it may be better sent straight to another journal with a more specialist or local readership or a higher acceptance rate.

To learn more about the kind of research articles we give priority to, and what services we offer to authors of research, please read the editorial "Publishing your research study in the *BMJ*?". Please note that we welcome studies - even with "negative" results - as long as their research questions are important, new, and relevant to general readers and their designs are appropriate and robust.

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Please ensure that the discussion section of your article comprises no more than a page and a half and follows this overall structure, although you do not need to signpost these elements with subheadings:

- *Statement of principal findings*
- *Strengths and weaknesses of the study*
- *Strengths and weaknesses in relation to other studies, discussing important differences in results*
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This video gives more detailed advice on writing each section of a research paper for *The BMJ*.

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Please ensure that the structured abstract is as complete, accurate, and clear as possible and has been approved by all authors. We may screen original research articles by reading only the abstract.

Abstracts should be 250- 300 words long: you may need up to 400 words, however, for a CONSORT or PRISMA style abstract. MEDLINE can now handle up to 600 words. Abstracts should include the following headings, but they may be modified for abstracts of clinical trials or systematic reviews and meta-analyses according to the requirements on the the CONSORT extension for abstracts and the PRISMA extension for abstracts, respectively.

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• **Interventions** - what, how, when and for how long. This heading can be deleted if there were no interventions but should normally be included for randomised controlled trials, crossover trials, and before and after studies.
• **Main outcome measures** - those planned in the protocol, those finally measured (if different, explain why).
• **Results** - main results with (for quantitative studies) 95% confidence intervals and, where appropriate, the exact level of statistical significance and the number need to treat/harm. Whenever possible, state absolute rather than relative risks.
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When writing your abstract, use the active voice but avoid "we did" or "we found". Numbers over 10 do not need spelling out at the start of sentences. p-values should always be accompanied by supporting data, and denominators should be given for percentages. Confidence intervals should be written in the format (15 to 27) within parentheses, using the word "to" rather than a hyphen. Abstracts do not need references.

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We want your piece to be easy to read but also as scientifically accurate as possible. We encourage authors to review the "Statistical Analyses and Methods in the Published Literature or The SAMPL Guidelines" while preparing their manuscript.
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For a clinical trial:

• Absolute event rates among experimental and control groups.
• RRR (relative risk reduction).
• NNT or NNH (number needed to treat or harm) and its 95% confidence interval (or, if the trial is of a public health intervention, number helped per 1000 or 100,000).

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For a case control study:

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• PPV and NPV (positive and negative predictive values)

The box stating 'what is known' and 'what this study adds' should also reflect accurately the above information. Under what this study adds, please give the one most useful summary statistic eg NNT.

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Reporting guidelines promote clear reporting of methods and results to allow critical appraisal of the manuscript. We ask that all manuscripts be written in accordance with the appropriate reporting guideline. Please submit as supplemental material the appropriate reporting guideline checklist showing on which page of your manuscript each checklist item appears. A complete list of guidelines can be found in the website of the Equator Network. Below is the list of most often used checklists but others may apply.
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A cover letter is your opportunity to introduce your study to the editor, highlighting the most important findings and novelty. Please also include in the letter the following information:

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As co production of research with patients and the public is relatively new we appreciate that not all authors will have involved them in their studies. We also appreciate that patient / public involvement may not be feasible or appropriate for all papers. We therefore continue to consider papers where they were not involved.

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The Patient and Public Involvement section should provide a brief response to the following questions, tailored as appropriate for the study design reported:

• At what stage in the research process were patients/public first involved in the research and how?
• How were the research question(s) and outcome measures developed and informed by their priorities, experience, and preferences?
• How were patients/public involved in the design of this study?
• How were they involved in the recruitment to and conduct of the study?
• Were they asked to assess the burden of the intervention and time required to participate in the research?
• How were (or will) patients and the public be involved in choosing the methods and agreeing plans for dissemination of the study results to participants and wider relevant communities? You may find this link helpful.
In addition to considering the points above we advise authors to look at guidance for best reporting of patient and public involvement as set out in the GRIPP2 reporting checklist.

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**If information detailing whether there was patient and public involvement, or not, is missing in the submitted manuscript we will request authors to provide it.**

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Where they have been involved we consider it good practice for authors to name and thank them in the contributorship statement after seeking their permission to do so;

and to clearly identify them as patient/public contributors. When they have contributed substantially and meet authorship criteria they should be invited to coauthor the manuscript.

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**Links to selected examples of Patient and Public Involvement statements in published BMJ research papers showing patient and carer involvement at various stages of the research process.**
Comparison of the two most commonly used treatments for pyoderma gangrenosum: results of the STOP GAP randomised controlled trial
Evidence based community mobilization for dengue prevention in Nicaragua and Mexico
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Real world effectiveness of warfarin among ischemic stroke patients with atrial fibrillation: observational analysis from Patient-Centered Research into Outcomes Stroke Patients Prefer and Effectiveness Research (PROSPER) study.
**Example PPI statements to adapt for use in a paper**
Examples to guide the wording for PPI statements

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• If appropriate, invite the original author[s] to participate in the re-analysis.
• If a month elapses without a response from the authors, please email the head of research for The BMJ (presently eloder@bmj.com) and cc papersadmin@bmj.com.
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In two or three single sentence bullet points, please summarise the state of scientific knowledge on this topicbefore you did your study, and why this study needed to be done. Be clear and specific, not vague.

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In one or two single sentence bullet points, give a simple answer to the question “What do we now know as a result of this study that we did not know before?” Be brief, succinct, specific, and accurate. For example: "Our study suggests that tea drinking has no overall benefit in depression." You might use the last sentence to summarise any implications for practice, research, policy, or public health. For example, your study might have asked and answered a new question (one whose relevance has only recently

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**Original raw data** if you think they will help our reviewers (and maybe readers), or if we specifically request them. Please note our policy on data sharing, explained above.
**Video and audio files** that will add educational value to your article, for example by explaining the intervention in a trial.
**A video abstract** that summarizes your findings and that will be posted on bmj.com with your paper. You can find additional information about video abstracts here and here.
**Public and patient involvement materials** used in your research.
**Copies of any non-standard questionnaires and assessment schedules** used in the research.
**Copies of patient information sheets** used to obtain informed consent for the study or to comprise or deliver the intervention in a clinical trial.
**Copies of closely related articles you have published** (this is particularly important when details of the study methods are published elsewhere).
**Copies of any previous reviewers' reports on this article**. We appreciate that authors may have tried other journals before sending their work to *The BMJ*, and find it helpful if you let us know how you have responded to previous reviewers' comments.

**C2:** eMethods. Development and refinement of codes for chronic pain and emotion regulation difficulties (ERDs)

We followed previously developed methods for identifying and validating clinically relevant indicators of CP and ERDs.[46] We first systematically searched assembled code lists of presentations meeting the criteria for potential ERDs and CP. The CP code list was reviewed by a clinical expert (RH; Consultant in Anaesthesia and Pain Medicine for children), and the ERD code list was reviewed by the first author (SS) and a clinical expert (LJ). The reviewers rated the importance of each code on a scale from 1 (not relevant) to 3 (very likely relevant).

Having compiled a relevant list of codes representing potential ERDs and CP indicators, we created reference standard indicators by identifying specific diagnostic codes that described ERDs or CP. For CP, this code list included GP referrals to specialist clinics or prescriptions of higher potency pain analgesics. All codes not included in either reference standard acted as potential candidate candidates of CP or ERDs. We then obtained frequency counts for all unique codes. Codes with similar descriptions that had less than 100 unique observations in the data were grouped into composite candidate indicators. Codes with 100 or more unique observations in the data were treated as standalone candidate indicators.

To determine the relevance of the developed candidate indicators of CP or ERDs, we used data driven variable selection model based on risk prediction. We used a random forest model (RF) with the Boruta selection filter.[100] RF-Bortua is a supervised machine learning (ML) algorithm that automatically determines the relevance of candidate indicators based on their consistent association with the reference standard indicators. The algorithm aims to provide a compact list of indicators that accurately identify the target conditions (i.e. reference standards of CP or ERDs). RF Boruta uses permuted variable importance scores (PIMP) to determine the relevance of individual candidate indicators. In brief, PIMP indicates how much the overall model prediction of the reference standard relies on a single candidate indicator. Each indicator receives a ranking based on the PIMP. RF-Boruta also adds “shadow indicators” (copies of original candidate indicators) into the mix of candidate indicators. Shadow indicators contain randomly mixed values with similar underlying distribution, but their PIMP score is removed. These shadow indicators act as reference points to determine inclusion. RF-Boruta then repeats the risk prediction model 100 times, ranks each indicator's PIMP score; and systematically examines indicators ranking against

the shadow indicators. Significant differences between indicators are determined against a "*binomial distribution*" using standard Z tests. The algorithm stops when all indicators have an established decision. eFigures 1 and 2 show boxplots summarising the distribution of RF-Boruta decisions to retain or exclude candidate indicators of ERDs and CP, respectively. The colours mark the final decision (green=retain, red=exclude, yellow=needs review). The boxplot shows the average PIMP for each code, and the whiskers of the boxplots show the worst and best shadow in each iteration (in blue).

RF-Boruta has shown optimal performance when compared against seven other variable selection models and expert review.[127-129] RF models have also shown to outperform clinical judgement in risk prediction and outperform traditional methods to validate measures,[130,131] as the model can use the patient's complete recorded history to make calculated decisions. RF models have previously been used for identifying highly accurate indicators of ACEs,[76] psychosis and predictions of suicide using data from EHRs.[132,133]

**C3:** eMethods. Expert review and ratings of CP indicators – example form

**Chronic pain in children - GP and hospital codes**
There is currently no validated indicators for identifying chronic pain (CP) in children using English electronic health records. By reviewing all available codes/measures/prescriptions in our data, we have identified potentially relevant codes for classifying CP in children between 5-18 years old in EHRs from CPRD (GP visits) and HES-APC (Hospital admissions).

As an expert, we would like you to please verify each code's relevance below on a scale "not relevant to relevant/likely CP" for its relevance and appropriateness to classify CP. We use the broad CP definition as provided by ICD-11 (below). However, mainly use your professional judgement to rate each code on their individual basis regardless of context (e.g. dynamic and protective factors), considering recorded presentations/conditions in children with CP you've seen clinically. Please note coded-EHRs generally show low sensitivity (under recording) and high specificity of diagnostic specialist conditions like CP.

Brackets "(e.g. n=)" shows number of recordings per 100,000 children.

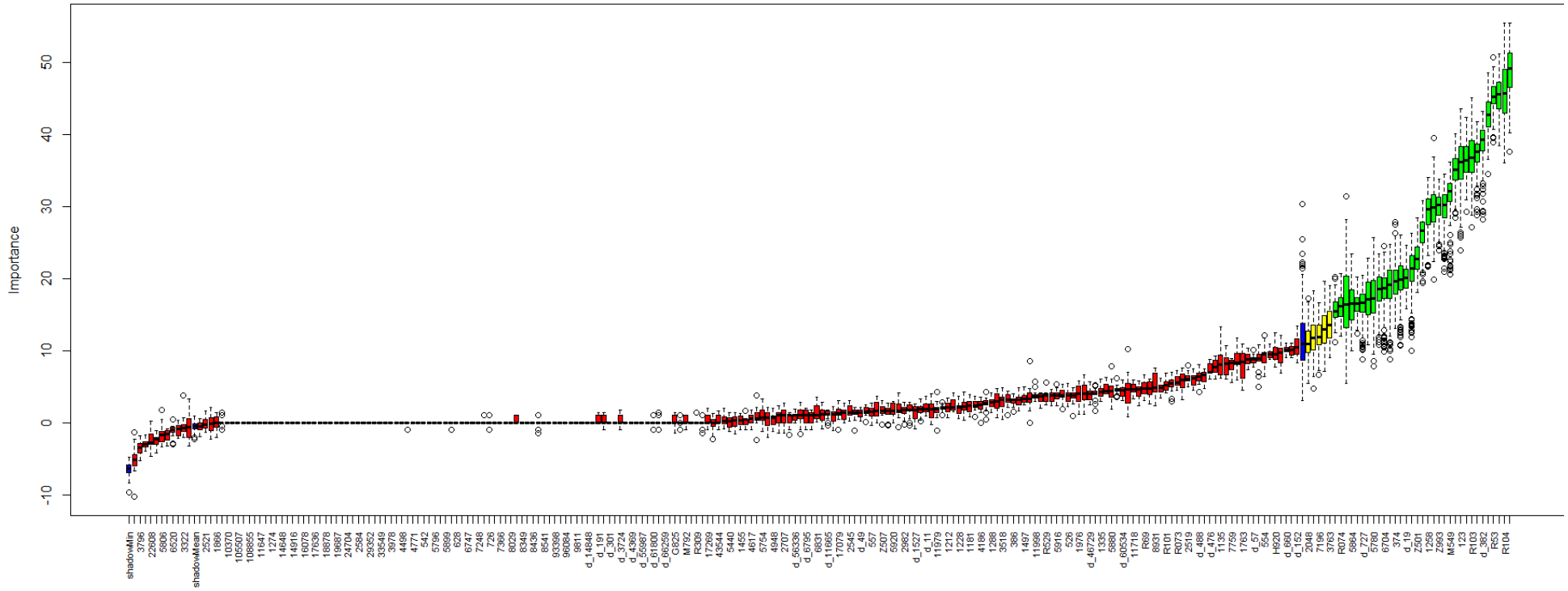
**ICD-11 definition**
Pain is an unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage. Chronic pain is pain that persists or recurs for longer than 3 months. Chronic pain is multifactorial: biological, psychological and social factors contribute to the pain syndrome.
https://icd.who.int/browse11/l-m/en#/http%3a%2f%2fid.who.int%2ficd%2fentity%2f1581976053

Required
1.Your name:

2.Hospital admissions - How relevant is this code for identifying CP in children?

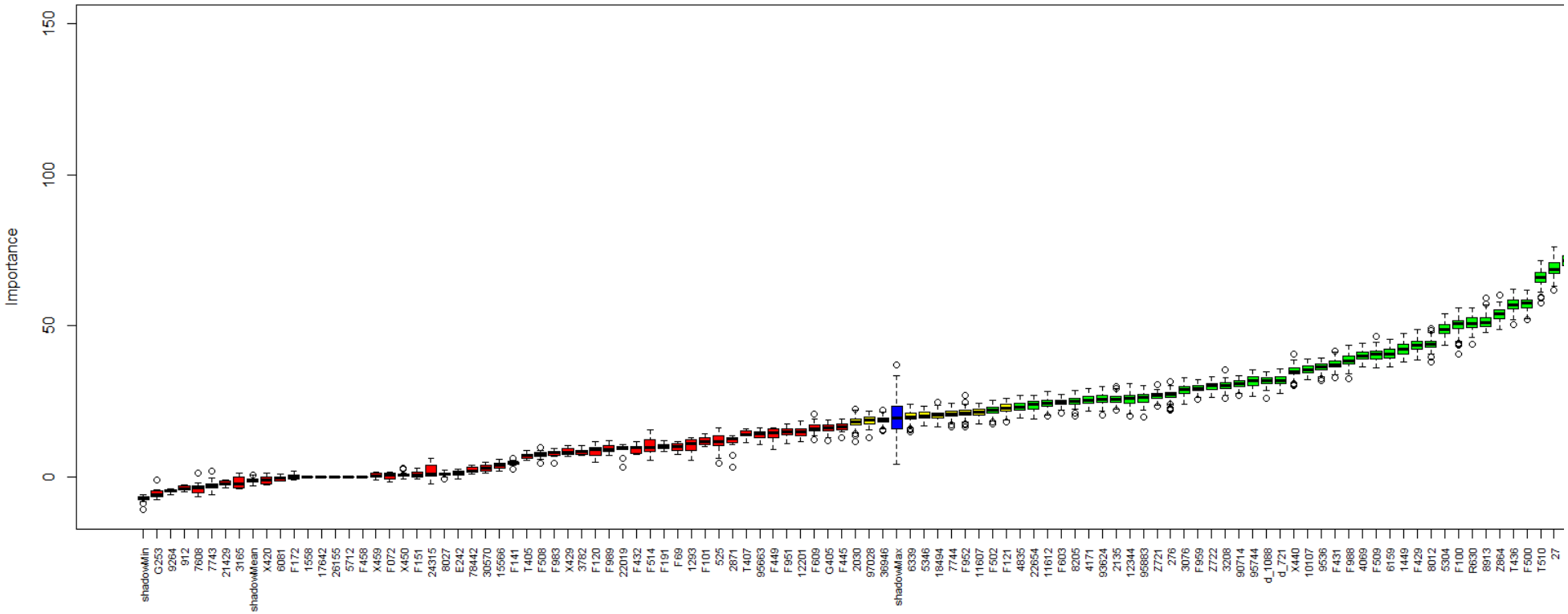
| EXAMPLE FORM | Not all relevant | Maybe | Very likely/relevant |
|---|---|---|---|
| M542 - Cervicalgia (186) | ○ | ○ | ○ |
| M791 - Myalgia (131) | ○ | ○ | ○ |
| R522 - Other chronic pain (49) | ○ | ○ | ○ |
| R521 - Chronic intractable pain (16) | ○ | ○ | ○ |

**C4:** eFigure. Selection of additional chronic pain (CP) codes via consistent risk association with the CP reference standard among children 5-18 years old using a random forest Boruta variable selection algorithm



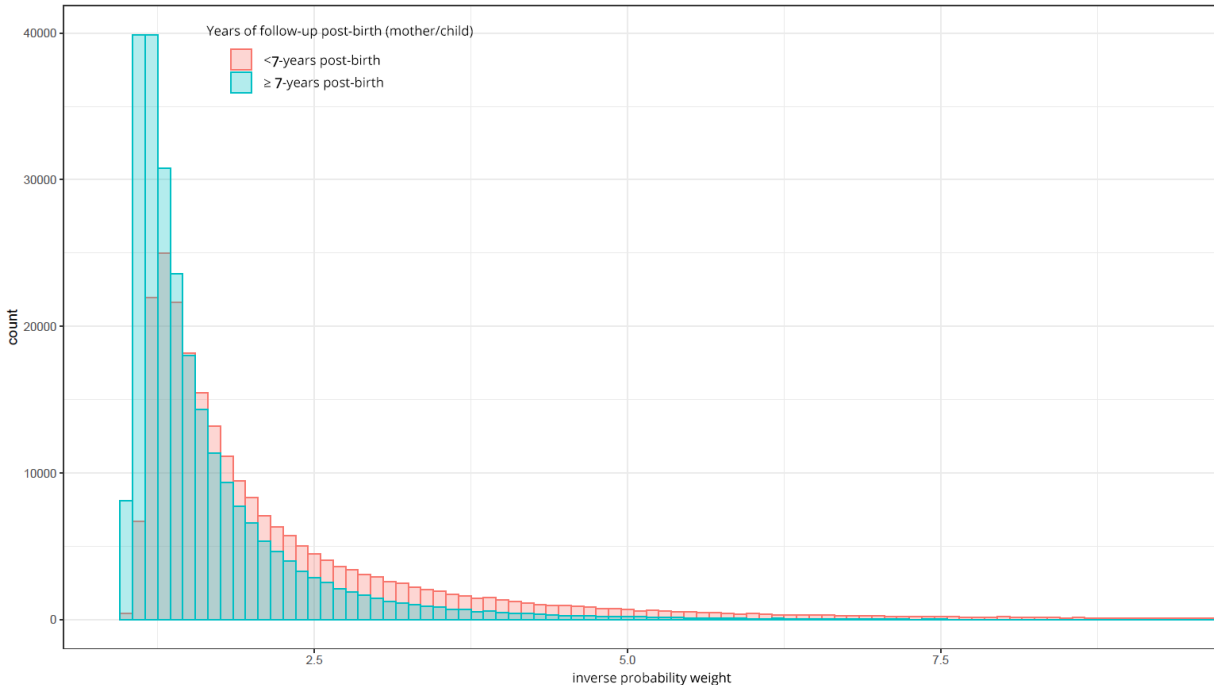

eFigure C3 shows a boxplot summarising the distribution of RF-Boruta decisions to retain or exclude codes of CP. The colours mark Boruta's final decision (green= retain, red=exclude, yellow=needs review). The boxplot shows the average PIMP for each code, and the whiskers of the boxplots show ranges. The worst and best shadow in each iteration is marked in blue.

**C5:** eFigure. Selection of additional emotion regulation difficulties (ERDs) codes (anxiety and emotion-related disorders) via their consistent risk association with the ERDs reference standard among children 5-18 years old using a random forest Boruta variable selection algorithm

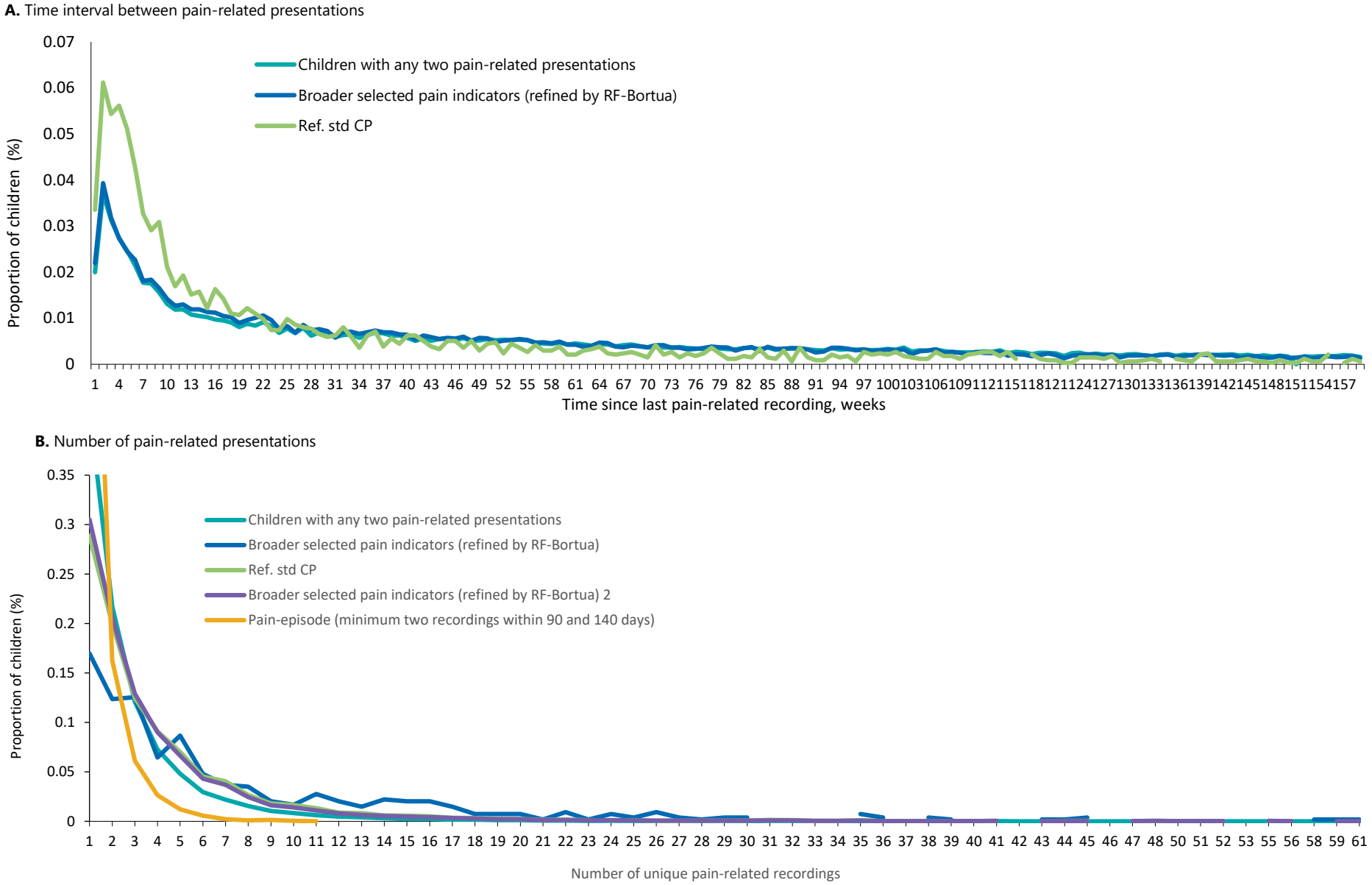



eFigure C4 shows a boxplot summarising the distribution of RF-Boruta decisions to retain or exclude codes of ERDs. The colours mark Boruta's final decision (green= retain, red=exclude, yellow=needs review). The boxplot shows the average PIMP for each code, and the whiskers of the boxplots show ranges. The worst and best shadow in each iteration is marked in blue.

**C6:** eFigure. Inverse probability weights for loss to follow-up at 7-years post-birth



**C7:** eFigure. Distribution of pain-related presentations obtained from different tested CP indicators showing (A) distribution of time-interval between visits and distribution of (B) number of pain-related recordings in children between 7 and 16 years old



**C8:** eTable. Global Burden of Disease 2019 Cause Hierarchy of the five most common non-communicable diseases in children and adolescents included in this study (excluding mental and musculoskeletal disorders)

| Cause ID | Cause Name | Hierarchy Level | Cause Outline | GBD Estimate 2019 for 10-24 years old YLL rates per 100,000 population |
|---|---|---|---|---|
| **409** | **Non-communicable diseases** | **1** | **B** | **686.93 (656.33-718.10)** |
| **410** | **Neoplasms** | **2** | **B.1** | **281.8 (254.3-298.9)** |
| 444 | Lip and oral cavity cancer | 3 | B.1.1 | 1.7 (1.59-1.82) |
| 447 | Nasopharynx cancer | 3 | B.1.2 | 1.73 (1.56-1.93) |
| 450 | Other pharynx cancer | 3 | B.1.3 | 0.39 (0.34-0.46) |
| 411 | Esophageal cancer | 3 | B.1.4 | 0.5 (0.46-0.55) |
| 414 | Stomach cancer | 3 | B.1.5 | 2.28 (2.11-2.47) |
| 441 | Colon and rectum cancer | 3 | B.1.6 | 6.24 (5.77-6.72) |
| 417 | Liver cancer | 3 | B.1.7 | 4.9 (4.53-5.30) |
| 453 | Gallbladder and biliary tract cancer | 3 | B.1.8 | 0.27 (0.25-0.29) |
| 456 | Pancreatic cancer | 3 | B.1.9 | 1.62 (1.46-1.79) |
| 423 | Larynx cancer | 3 | B.1.10 | 0.28 (0.27-0.30) |
| 426 | Tracheal, bronchus, and lung cancer | 3 | B.1.11 | 5.57 (5.09-6.11) |
| 459 | Malignant skin melanoma | 3 | B.1.12 | 5.8 (3.70-6.72) |
| 462 | Non-melanoma skin cancer | 3 | B.1.13 | 0.43 (0.39-0.47) |
| 429 | Breast cancer | 3 | B.1.14 | 2.34 (2.15-2.54) |
| 432 | Cervical cancer | 3 | B.1.15 | 1.37 (1.15-1.57) |
| 435 | Uterine cancer | 3 | B.1.16 | 0.2 (0.18-0.22) |
| 465 | Ovarian cancer | 3 | B.1.17 | 4.86 (4.18-5.76) |
| 438 | Prostate cancer | 3 | B.1.18 | 0.35 (0.28-0.55) |
| 468 | Testicular cancer | 3 | B.1.19 | 6.68 (5.87-7.58) |
| 471 | Kidney cancer | 3 | B.1.20 | 3.78 (3.48-4.12) |
| 474 | Bladder cancer | 3 | B.1.21 | 0.57 (0.53-0.61) |
| 477 | Brain and nervous system cancer | 3 | B.1.22 | 57.22 (37.71-64.02) |
| 480 | Thyroid cancer | 3 | B.1.23 | 0.9 (0.85-0.99) |
| 483 | Mesothelioma | 3 | B.1.24 | 0.33 (0.28-0.38) |
| 484 | Hodgkin lymphoma | 3 | B.1.25 | 7.86 (6.89-10.24) |
| 485 | Non-Hodgkin lymphoma | 3 | B.1.26 | 22.78 (21.2-24.98) |
| 486 | Multiple myeloma | 3 | B.1.27 | 0.32 (0.26-0.37) |
| 487 | Leukaemia | 3 | B.1.28 | 64.64 (60.62-69.01) |
| 489 | Other malignant neoplasms | 3 | B.1.29 | 74.01 (62.15-80.22) |
| 490 | Other neoplasms | 3 | B.1.30 | 1.86 (1.34-2.27) |
| 491 | **Cardiovascular diseases** | 2 | B.2 | 77.7 (73.20-82.30) |
| 492 | Rheumatic heart disease | 3 | B.2.1 | 2.56 (2.28-2.84) |
| 493 | Ischemic heart disease | 3 | B.2.2 | 13.4 (12.25-14.9) |
| 494 | Stroke | 3 | B.2.3 | 21.97 (20.11-24.22) |
| 498 | Hypertensive heart disease | 3 | B.2.4 | 1.28 (0.94-1.53) |
| 504 | Non-rheumatic valvular heart disease | 3 | B.2.5 | 3.56 (3.23-3.95) |
| 499 | Cardiomyopathy and myocarditis | 3 | B.2.6 | 17.83 (15.54-21.24) |
| 500 | Atrial fibrillation and flutter | 3 | B.2.7 | - |
| 501 | Aortic aneurysm | 3 | B.2.8 | 2.81 (2.54-3.10) |
| 502 | Peripheral artery disease | 3 | B.2.9 | - |
| 503 | Endocarditis | 3 | B.2.10 | 3.36 (1.70-4.20) |
| 507 | Other cardiovascular and circulatory diseases | 3 | B.2.11 | 10.9 (9.71-13.94) |
| 508 | Chronic respiratory diseases | 2 | B.3 | 17.9 (16.60-20.50) |
| 509 | Chronic obstructive pulmonary disease | 3 | B.3.1 | 5.09 (4.58-6.07) |
| 510 | Pneumoconiosis | 3 | B.3.2 | 0.08 (0.07-0.11) |
| 515 | Asthma | 3 | B.3.3 | 7.2 (6.56-8.26) |
| 516 | Interstitial lung disease and pulmonary sarcoidosis | 3 | B.3.4 | 3.02 (1.96-3.61) |
| 520 | Other chronic respiratory diseases | 3 | B.3.5 | 2.54 (2.16-3.63) |
| 526 | Digestive diseases | 2 | B.4 | 27.00 (25.30-28.70) |
| 521 | Cirrhosis and other chronic liver diseases | 3 | B.4.1 | 10.44 (9.47-11.81) |
| 992 | Upper digestive system diseases | 3 | B.4.2 | 1.45 (1.30-1.63) |
| 529 | Appendicitis | 3 | B.4.3 | 1.06 (0.83-1.38) |
| 530 | Paralytic ileus and intestinal obstruction | 3 | B.4.4 | 3.85 (3.19-4.60) |
| 531 | Inguinal, femoral, and abdominal hernia | 3 | B.4.5 | 0.23 (0.21-0.26) |
| 532 | Inflammatory bowel disease | 3 | B.4.6 | 2.90 (2.42-3.32) |

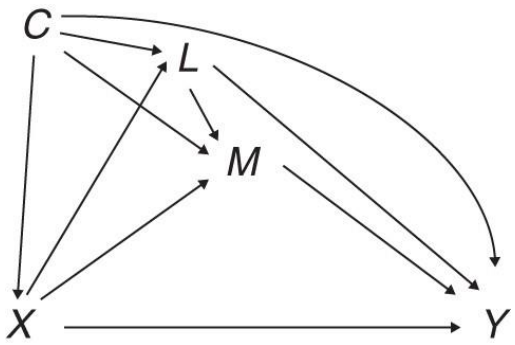
| | | | | |
|---|---|---|---|---|
| 533 | Vascular intestinal disorders | 3 | B.4.7 | 1.05 (0.95-1.19) |
| 534 | Gallbladder and biliary diseases | 3 | B.4.8 | 0.62 (0.42-0.70) |
| 535 | Pancreatitis | 3 | B.4.9 | 3.38 (2.97-3.79) |
| 541 | Other digestive diseases | 3 | B.4.10 | 1.99 (1.21-2.46) |
| 542 | **Neurological disorders** | 2 | B.5 | 72.00 (67.80-76.40) |
| 543 | Alzheimer's disease and other dementias | 3 | B.5.1 | - |
| 544 | Parkinson's disease | 3 | B.5.2 | 0.06 (0.05-0.07) |
| 545 | Idiopathic epilepsy | 3 | B.5.3 | 36.86 (33.68-39.59) |
| 546 | Multiple sclerosis | 3 | B.5.4 | 1.16 (0.75-1.53) |
| 554 | Motor neuron disease | 3 | B.5.5 | 3.91 (3.62-4.2) |
| 972 | Headache disorders | 3 | B.5.6 | - |
| 557 | Other neurological disorders | 3 | B.5.7 | 29.99 (27.94-32.10) |
| **974** | **Diabetes and kidney diseases** | **2** | **B.8** | **15.4 (14.40-16.40)** |
| 587 | Diabetes mellitus | 3 | B.8.1 | 6.82 (6.42-7.28) |
| 589 | Chronic kidney disease | 3 | B.8.2 | 8.5 (7.81-9.18) |
| 588 | Acute glomerulonephritis | 3 | B.8.3 | 0.10 (0.08-0.11) |
| 653 | Skin and subcutaneous diseases | 2 | B.9 | 1.30 (0.80-1.80) |
| 654 | Dermatitis | 3 | B.9.1 | - |
| 655 | Psoriasis | 3 | B.9.2 | - |
| 980 | Bacterial skin diseases | 3 | B.9.3 | 1.03 (0.63-1.47) |
| 658 | Scabies | 3 | B.9.4 | 0.07 (0.02-0.10) |
| 659 | Fungal skin diseases | 3 | B.9.5 | - |
| 660 | Viral skin diseases | 3 | B.9.6 | - |
| 661 | Acne vulgaris | 3 | B.9.7 | - |
| 662 | Alopecia areata | 3 | B.9.8 | - |
| 663 | Pruritus | 3 | B.9.9 | - |
| 664 | Urticaria | 3 | B.9.10 | - |
| 665 | Decubitus ulcer | 3 | B.9.11 | - |
| 668 | Other skin and subcutaneous diseases | 3 | B.9.12 | 0.20 (0.14-0.29) |
| **640** | **Other non-communicable diseases** | **2** | **B.12** | **112 (101.5-131.70)** |
| 641 | Congenital birth defects | 3 | B.12.1 | 62.24 (50.97-78.48) |
| 594 | Urinary diseases and male infertility | 3 | B.12.2 | 3.57 (3.27-4.15) |
| 603 | Gynaecological diseases | 3 | B.12.3 | 0.12 (0.10-0.22) |
| 613 | Hemoglobinopathies and haemolytic anaemias | 3 | B.12.4 | 5.83 (5.33-6.41) |
| 619 | Endocrine, metabolic, blood, and immune disorders | 3 | B.12.5 | 40.18 (34.69-54.8) |
| 680 | Oral disorders | 3 | B.12.6 | - |

**C9:** eMethods. Additional information on using a counterfactual framework for mediation analysis

In contrast to traditional mediation analyses based on Baron and Kenny's seminal work (1986), we employed a counterfactual framework for causal mediation analysis.[96,134] In this section, we summarise components from the counterfactual framework relevant to this study. More details of the framework can be found elsewhere.[96,134]

***The counterfactual framework.*** The counterfactual framework can incorporate semi-parametric models (e.g., Cox regression) and is the recommended method for *causal* mediation analysis.[96,135] Under the counterfactual framework, we aim to decompose the causal effect into four pathways: the controlled direct effect ("*neither due to mediation or interaction*"), reference interaction ("*due to interaction only*"), mediated interaction ("*due to mediated interaction*") and pure indirect effect ("*due to mediation only*"). This decomposition provides maximum insight into how much of the effect is explained by different causal approaches, including mediation and interaction. The four-way decomposition requires the study design and data analysis to meet five rigorous causal assumptions (A),[95,96]:

- A1=control must be made for exposure (X) outcome (Y) confounding;
- A2=control must be made for the mediator (M)-outcome (Y) confounding;
- A3= control must be made for exposure (X)-mediator (M) confounding;




- A4= there should be no mediator-outcome-confounders that are themselves affected by the exposure (L; herein termed "*intermediate confounder";*);
- A5=the exposure should temporally precede the outcome.

Violations in any of the above assumptions (A1-A5) can give rise to very misleading and biased results. It should also be noted that no causal inferences can be made when violating the assumption of temporality (A5; e.g., conducting mediation analysis on cross-sectional data only).[67,95,96] We used a birth cohort study (longitudinal design - temporality) with data to control for all hypothesised confounders, thus meeting causal assumptions A1-A3. However, as described by De Stavola et al.,[97] birth cohort studies often violate the fourth assumption (A4) regarding *"no intermediate confounding".* This violation happens because a myriad of factors (L) during child development interact with the exposure and the mediator,

and causally contribute to the outcome (Y).[97] Control can often not be made for all possible interactions. As shown in the simplified causal directed acyclic graph below (figure 3), this study violates the causal assumption of no "*intermediate confounders*" (A4). ACEs may be causally linked to multiple different health conditions (i.e. leading to intermediate confounding), which may affect both ERDs and CP (figure 3)

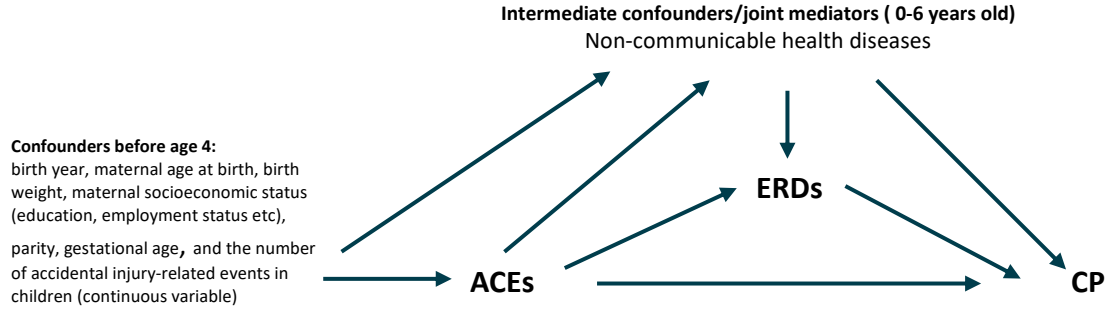



**Figure 3.** Simplified* causal directed acyclic diagram
**Does not show all interrelationships between confounding variables under each heading*

Additionally, calculating the indirect and direct effect in the presence of intermediate confounding (L) requires statistical methods beyond simple linear regressions. It is not sufficient to use a regression model and control for the intermediate confounder (e.g., as in the Baron and Kenny approach), as this approach would block the "X ->L -> Y" direct-effect relationship needed to calculate indirect effects (mediation). On the other hand, ignoring "L" in a regression model would result in confounded mediated estimates, as L is confounding the relationship between M and Y.

***A joint mediator approach.*** There are currently few statistical analyses that can handle intermediate confounders using time-to-event data.[136] VanderWeele et al.,[95] suggested four different methods to circumvent the *"no intermediate confounder"* causal assumption statistically. In this study, we adopted a "join mediator" approach (the first approach suggested by VanderWeele *et al*.[95]), treating ERDs and NCDs as joint mediators of ACEs whilst adjusting for baseline confounders. This approach also mirrors NICE practice guidelines that children should receive joint interventions (i.e. mediators) for co-occurring NCDs and ERDs.[98] Whilst this approach is unable to separate the specific effect from ERDs on CP, we statistically account for the intermediate confounder assumption (A4), leading to less confounded and biased results than single mediator approach (e.g. Baron and Kenny approach; which ignores the intermediate confounding assumption).

Still, a join-mediator approach can provide useful insights into the mechanisms behind ACEs, ERDs and CP. First, children with ERDs and NCDs are unlikely to receive treatment for

only one of the presentations, and findings are therefore likely to mirror effects seen in practice.[98] Second, alternative approaches suggested by VanderWeele et al.,[95] includes redefining the *"natural effect",*[136] path analysies and using weighting-based estimators. However, these approaches are statistically more complex, challenging to interpret and weight-based approaches can lead to biased standard errors that can be severely bias. These approaches also requires correctly specifying the conditions (e.g. temporal order, role etc) of exposure, mediators, and covariates.[136] However, correct specification in analytic models of CP is very challenging, as CP is based on a biopsychososcial model and depend on bidirectional relationships and interactions. Taken together, we choose the joint mediator approach as best suited for our study aims and underlying data structure.

**Additional information on data management and software**

We conducted all analyses on University College London's secure analytic server (the Data Safe Haven; certified to ISO27001 information security standards), using Stata 16 and R (version 4.2) with the survival, medflex, caret, boruta, hmisc, rms, mice and tidyverse packages.

We followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE),[137] and the Reporting of studies Conducted using Observational Routinely-collected health Data statement (RECORD) in reporting this study.[138] Details of the statistical analyses are provided in the appendix.

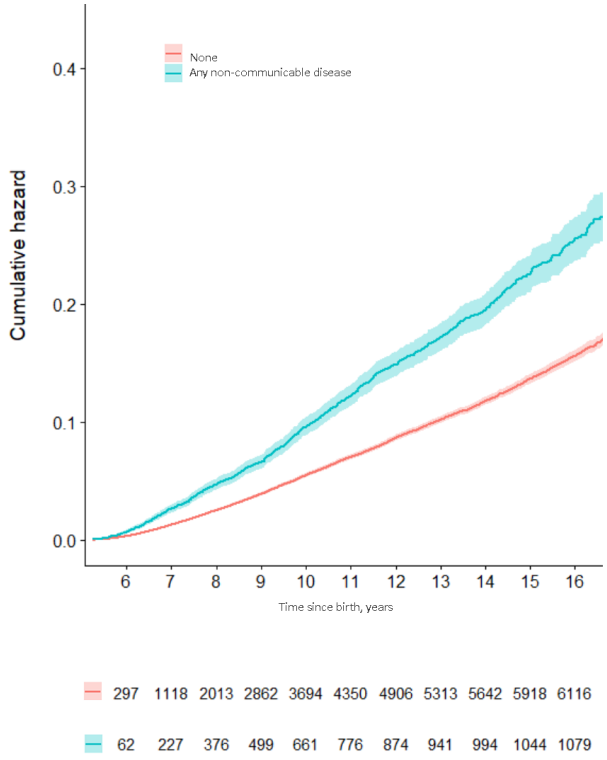
## Additional results

**C10:** eTable. Results from the logistic regression model used to predict censoring at 7-years post-birth

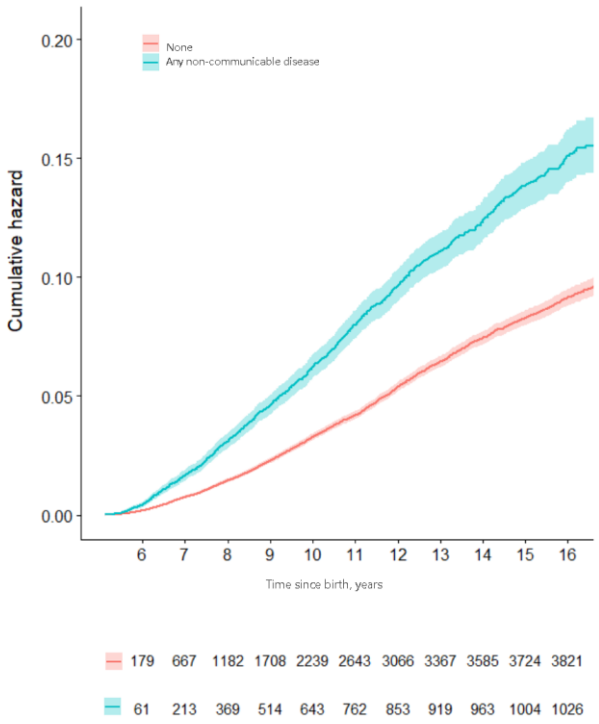
| | Odds Ratio (95 CI) | Robust Std. Err. | z | P-value |
|---|---|---|---|---|
| **Maternal socioeconomic status quintile*** | | | | |
| 1 (least deprived) | *REF* | | | |
| 2 | 1.21 (1.18-1.23) | 1.18 | 1.23 | 0 |
| 3 | 1.32 (1.29-1.35) | 1.29 | 1.35 | 0 |
| 4 | 1.34 (1.31-1.37) | 1.31 | 1.37 | 0 |
| 5 (most deprived) | 1.46 (1.43-1.50) | 1.43 | 1.5 | 0 |
| **Region of England, GP practice** | | | | |
| East midlands | *REF* | | | |
| East England | 0.53 (0.51-0.55) | 0.51 | 0.55 | 0 |
| Northeast | 0.43 (0.41-0.45) | 0.41 | 0.45 | 0 |
| Northwest | 0.36 (0.34-0.38) | 0.34 | 0.38 | 0 |
| London | 0.34 (0.32-0.35) | 0.32 | 0.35 | 0 |
| South Central | 0.39 (0.38-0.41) | 0.38 | 0.41 | 0 |
| Southeast Coast | 0.28 (0.27-0.29) | 0.27 | 0.29 | 0 |
| South Nest | 0.39 (0.38-0.41) | 0.38 | 0.41 | 0 |
| West Midlands | 0.37 (0.36-0.39) | 0.36 | 0.39 | 0 |
| Yorkshire & The Humber | 0.57 (0.54-0.59) | 0.54 | 0.59 | 0 |
| **Maternal age at birth, years*** | 0.97 (0.97-0.97) | 0.97 | 0.97 | 0 |
| **Type of ACEs (not exclusive)** | | | | |
| AFE | 0.87 (0.86-0.89) | 0.86 | 0.89 | 0 |
| Any CM or mIPV | 1.26 (1.21-1.31) | 1.21 | 1.31 | 0 |
| MSM | 1.36 (1.32-1.40) | 1.32 | 1.4 | 0 |
| mMHPs | 0.89 (0.88-0.91) | 0.88 | 0.91 | 0 |
| **Birth years*** | 1.22 (1.22-1.22) | 1.22 | 1.22 | 0 |
| **Number of children** | 0.51 (0.5-0.51) | 0.50 | 0.51 | 0 |
| **Number of days enrolled with pratice before birth** | 1 (1.00-1.00) | 1.00 | 1.00 | 0 |

## **C11:** eFigure. Cumulative incidence of chronic pain by any non-communicable disease and sex

**A.** Girls - Incidence of CP by any NCD




**B.** Boys - Incidence of CP by any NCD




Number at risk presented for each strata underneath each year since birth

## Results from sensitivity analyses

**C12:** eTable. Adjusted and weighted hazard ratios of chronic pain in children between 7 and 16-years old by ACEs and ERDs in the selected cohort (n=179207) and the complete linkable cohort (n=494191)

| | Weighted & adjusted HR (95%CI) | |
|---|---|---|
| **ACEs** | **Girls** | **Boys** |
| Any ACE | 1.39 (1.31-1.46) | 1.33 (1.24-1.42) |
| *Complete linkable cohort* | 1.42 (1.36-1.48) | 1.45 (1.38-153) |
| Any CM/mIPV | 1.30 (1.12-1.51) | 1.67 (1.44-1.93) |
| *Complete linkable cohort* | 1.98 (1.75-2.23) | 1.42 (1.26-1.60) |
| mMHPs | 1.44 (1.37-1.52) | 1.41 (1.32-1.50) |
| *Complete linkable cohort* | 1.42 (1.36-1.49) | 1.47 (1.39-1.55) |
| AFE | 1.28 (1.21-1.35) | 1.33 (1.24-1.42) |
| *Complete linkable cohort* | 1.37 (1.30-1.45) | 1.34 (1.27-1.40) |
| MSM | 1.22 (1.09-1.38) | 1.12 (0.97-1.30) |
| *Complete linkable cohort* | 1.25 (1.13-1.38) | 1.17 (1.03-1.32) |
| **ERDs** | 1.92 (1.72-2.14) | 1.77 (1.60-1.96) |
| *Complete linkable cohort* | 2.14 (1.96-2.33) | 2.08 (1.91-2.26) |
| **ERDs excl. Neurodevelopmental** | 1.97 (1.76-2.20) | 1.78 (1.59-2.00) |
| *Complete linkable cohort* | 2.19 (2.01-2.40) | 2.16 (1.97-2.37) |

Risks of CP in children between 7 and 16-years old. Circles represents adjusted and weighted hazard ratios (HR). Horizontal lines represents the 95% confidence interval. HRs are adjusted for children's birth year and region. Weights are based on the inverse probability for loss-to-follow-up at 7-years post-birth using maternal age, region, number of non-birth-related hospital admissions, IMD, number of days enrolled with practice before birth, ACEs and CP as predictors. We accounted for clustering effects of siblings in the calculation of the robust standard errors based on the sandwich estimator. Abbreviations: ACE=Adverse childhood experience, AFE=Adverse family environments, CM=Child maltreatment, CI=Confidence interval, ERDs=Emotions regulation difficulties (anxiety, emotion, depressive and self-harm presentations), HZ=Hazard ratio, mIPV=Maternal intimate partner violence, mMHPs=Maternal mental health problems, MSM=Maternal substance misuse.

**C13:** eTable. Four-way decomposition of the causal effects of ACEs on the risk of CP in the presence of ERDs (excluding neurodevelopmental conditions) and covariates

| | Girls | | Boys | |
|---|---|---|---|---|
| **Effect decomposition** | **Estimate (95% CI)** | **P-value** | **Estimate (95% CI)** | **P-value** |
| Total effect | 0.35 (0.27, 0.43) | <0.001 | 0.38 (0.29, 0.47) | <0.001 |
| Controlled direct effect (due neither to mediation nor interaction) | 0.12 (-0.39, 0.63) | 0.648 | 0.41 (-0.04, 0.86) | 0.076 |
| Reference interaction (due to interaction only) | 0.19 (-0.27, 0.69) | 0.438 | -0.07 (-0.49, 0.36) | 0.760 |
| Mediated interaction (due to mediation and interaction) | -0.01 (-0.03, 0.01) | 0.439 | 0.003 (-0.02, 0.02) | 0.760 |
| Pure indirect effect or mediated main effect (due to mediation only) | 0.04 (0.03, 0.06) | <0.001 | 0.03 (0.02, 0.05) | <0.001 |
| Total effect risk ratio | 1.35 (1.27, 1.43) | <0.001 | 1.38 (1.29, 1.47) | <0.001 |
| | **Proportion, % (95% CI)** | **P-value** | **Proportion % (95% CI)** | **P-value** |
| Proportion controlled direct effect (due neither to mediation nor interaction) | 0.34 (-1.1, 1.79) | 0.641 | 1.08 (-0.02, 2.18) | 0.054 |
| Proportion reference interaction (due to interaction only) | 0.56 (-0.90, 2.01) | 0.452 | -0.17 (-1.29, 0.94) | 0.757 |
| Proportion mediated interaction (due to mediation and interaction) | -0.02 (-0.08, 0.04) | 0.453 | 0.01 (-0.04, 0.06) | 0.757 |
| Proportion pure indirect effect or mediated main effect (due to mediation only) | 0.12 (0.06, 0.13) | <0.001 | 0.08 (0.04, 0.13) | <0.001 |
| Overall proportion mediated | 0.10 (0.06, 0.13) | <0.001 | 0.09 (0.06, 0.13) | <0.001 |
| Overall proportion attributable to interaction | 0.54 (-0.86, 1.93) | 0.453 | -0.18 (-1.23, 0.87) | 0.757 |
| Overall proportion eliminated | 0.66 (-0.79, 2.1) | 0.373 | -0.08 (-1.82, 1.02) | 0.882 |

Proportion-eliminated: indicates the proportion of effect from ACEs on CP we would "*block*" if we intervened on ERDs.