BMJ Open

Pharmacological Emergency management of Agitation in Children and Young people: protocol for a randomised controlled trial of intraMuscular medication (PEAChY-M)

Elyssia M Bourke ,[1,2,3,4] Meredith L Borland ,[5] Amit Kochar,[6] Shane George ,[7,8] Deborah Shellshear,[9] Shefali Jani,[10,11] Kent Perkins,[12] Doris Tham,[13] Michael Solomon Gordon,[14,15] Kate Klein,[1,16] Chidambaram Prakash,[17] Katherine Lee,[2,18,19] Andrew Davidson,[19,20] Jonathan C Knott,[3,21] Simon Craig ,[22,23] Franz E Babl ,[1,2,3,24] On behalf of the Paediatric research in Emergency Departments International Collaborative (PREDICT)

To cite: Bourke EM, Borland ML, Kochar A, *et al*. Pharmacological Emergency management of Agitation in Children and Young people: protocol for a randomised controlled trial of intraMuscular medication (PEAChY-M). *BMJ Open* 2023;**13**:e067436. doi:10.1136/bmjopen-2022-067436

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2022-067436).

Received 23 August 2022
Accepted 20 February 2023

For numbered affiliations see end of article.

Correspondence to
Dr Elyssia M Bourke;
elyssia.bourke@mcri.edu.au

ABSTRACT

Introduction Acute severe behavioural disturbance (ASBD) is a condition seen with increasing frequency in emergency departments (EDs) in adults and young people. Despite the increasing number of presentations and significant associated risks to patients, families and caregivers, there is limited evidence to guide the most effective pharmacological management in children and adolescents. The aim of this study is to determine whether a single dose of intramuscular olanzapine is more effective than intramuscular droperidol at successfully sedating young people with ASBD requiring intramuscular sedation.

Methods and analysis This study is a multicentre, open-label, superiority randomised controlled trial. Young people aged between 9 and 17 years and 364 days presenting to an ED with ASBD who are deemed to require medication for behavioural containment will be recruited to the study. Participants will be randomised in a 1:1 allocation between a single weight-based dose of intramuscular olanzapine and intramuscular droperidol. The primary outcome is the proportion of participants who achieve successful sedation at 1-hour post randomisation without the need for additional sedation. Secondary outcomes will include assessing for adverse events, additional medications provided in the ED, further episodes of ASBD, length of stay in the ED and hospital and satisfaction with management.

Effectiveness will be determined using an intention-to-treat analysis, with medication efficacy determined as part of the secondary outcomes using a per-protocol analysis. The primary outcome of successful sedation at 1 hour will be presented as a percentage within each treatment group, with comparisons presented as a risk difference with its 95% CIs.

Ethics and dissemination Ethics approval was received from the Royal Children's Hospital Human Research Ethics Committee (HREC/69948/RCHM-2021). This incorporated a waiver of informed consent for the study. The findings will be disseminated in a peer-reviewed journal and at academic conferences.

Trial registration number ACTRN12621001238864.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This is the first interventional trial to compare intramuscular medication for the management of paediatric acute severe behavioural disturbance (ASBD) in the emergency department.
⇒ This study uses a randomised, controlled design to investigate the effectiveness of intramuscular olanzapine and intramuscular droperidol in young people with ASBD.
⇒ This study is being conducted across 10 EDs in Australia.
⇒ This is an open-label study with both treating clinicians and patients aware of the medication that they are being provided. Investigators and statisticians undertaking the data analysis will be blinded to the trial allocations until after the conclusion of the analysis.

INTRODUCTION

Acute severe behavioural disturbance (ASBD) is a common clinical condition in children and adolescents.[1 2] It poses significant physical and psychological risks to the patient and those caring for them.[3] These young people often present to the emergency department (ED) for management.

ASBD can be related to a range of underlying causes. In children and young people, common causes include mental health conditions, psychosocial problems and neurodevelopmental

disorders.[1 4] Less commonly, recreational substance use, self-poisoning or other organic causes are contributing factors. It is often difficult to elucidate the aetiology of the presentation prior to behavioural containment being achieved. As a result, these young people require urgent and effective management, thus allowing the treating clinician to assess the reason for their presentation and provide appropriate ongoing care.

ASBD is managed using a stepwise plan.[5] Non-pharmacological strategies are attempted first, followed by medication if required. Oral administration is the preferred option when medication is being used. The study team are undertaking a separate study of oral medications for the management of paediatric ASBD using a similar study design in patients in whom oral medication is deemed the most appropriate course of action, the protocol for which has also been published .[6] If the young person's behaviour cannot be contained with non-pharmacological strategies and they are either unwilling or unable to accept oral medication, and they pose a risk to themselves or others, they are provided with parenteral medication to achieve rapid behavioural control.[7] In most cases in the paediatric population, this parenteral medication would be provided by the intramuscular route.

A number of randomised controlled trials (RCTs) investigating parenteral medication management have been undertaken in the adult population.[8–12] There is no high-quality, prospective literature comparing the effectiveness or assessing the side effect profiles of these medications in the paediatric population.[7] Due to the increasing prevalence of paediatric ASBD presentations and key differences in the aetiological causes of ASBD in young people when compared with adults,[2] the research team conceived this study to determine the most effective intramuscular medication for the management of paediatric ASBD.

The choice of medications to include in the study was based on the available adult literature,[8–12] the agents currently recommended at the study hospitals[5 13–15] and a national Australian survey of the management practices and trial medication preferences of adult and paediatric emergency physicians for paediatric ASBD.[16] The regional guidelines suggested the use of droperidol, olanzapine or midazolam as possible primary agents.[5 13–15] In the national survey there was considerable variation in practice but droperidol, midazolam and olanzapine were the preferred agents to be included in a comparative trial. Using this evidence and following input from child and adolescent psychiatry teams at a number of study sites, the research team decided to compare droperidol and olanzapine. In this study, we aim to assess whether a single dose of intramuscular olanzapine is superior to a single dose of intramuscular droperidol in successfully sedating young people presenting with ASBD who require parenteral medication.

METHODS

Design

This is a multicentre, open-label, superiority RCT. The allocation ratio between comparison groups is 1:1. This trial protocol has been prepared using the Standard Protocol Items: Recommendations for Interventional Trials checklist.[17]

Patient and public involvement

The research team engaged a group of parent consumers with lived experience caring for children with mental health-related conditions including ASBD. These individuals were approached as they had supported their child through an episode of acute mental illness in the ED. The group were presented with an overview of the research and details of the protocol were explored during a number of meetings. They assisted in refining the study protocol and ensuring that the views of consumers were represented within the research.

These parent consumers will have ongoing involvement throughout the life of the study. Regular updates will be provided in a written format while data collection is being undertaken. Once the study results are available, they will be provided to parent consumers, allowing them a chance to comment on the findings, and their feedback will be incorporated into any publications or presentations. They will also be involved in the knowledge translation of the results of the study.

Setting and participants

Participants will be recruited at 10 EDs across Australia: Children's Hospital at Westmead Sydney, Gold Coast University Hospital, Grampian's Health Ballarat, Monash Children's Hospital Melbourne, Perth Children's Hospital, Queensland Children's Hospital Brisbane, Royal Children's Hospital Melbourne, Sunshine Coast University Hospital, Western Health Sunshine Hospital Melbourne and Women's and Children's Hospital Adelaide. We aim to recruit 35 participants per site between October 2021 and December 2024, to achieve our sample size of 348 participants. We believe this is feasible within the specified time frame based on our review of non-published audit data.

The Sedation Assessment Tool

There is no validated assessment tool for behavioural disturbance in children and adolescents presenting to the ED. Ideally such a tool would include a grading of both agitation and the possible resulting sedation or oversedation. In adult ASBD studies a range of tools including the Richmond Agitation Sedation Scale,[18] the altered mental status score[19] and observer assessment of alertness/sedation[20] have previously been used.

The only tool validated for use in the ASBD population in the ED which assesses both agitation and sedation on the same scale is the Sedation Assessment Tool (SAT),[21] which has been used in a number of adult studies.[22–24] It has not been validated in children and adolescents. This tool is a 7-point scale that assesses the patient's responsiveness and speech (figure 1). Using these descriptors, a score of +3 (highly agitated) to −3 (highly sedated) is determined. The score takes approximately 10 seconds to complete and has good inter-rater reliability.[21] We will use

SCORE	RESPONSIVENESS	SPEECH
+3	Combative, violent, out of control	Continual loud outbursts
+2	Very anxious and agitated	Loud outbursts
+1	Anxious and restless	Normal / Talkative
0	Responds easily to name, speaks in normal tone	Speaks normally
-1	Responds only if name is called loudly	Slurring or prominent slowing
-2	Physical stimulation	Few recognisable words
-3	No response to stimulation	Nil

Figure 1 Sedation Assessment Tool score.

the SAT to assess both eligibility of the young person and the primary outcome.

Inclusion and exclusion criteria

Full details of the inclusion and exclusion criteria are shown in box 1.

Young people aged between 9 and less than 18 years will be included if they have ASBD and the treating team is planning to administer intramuscular medication to manage their condition. Including an SAT of ≥+1 in the inclusion criteria ensures only participants with ASBD are enrolled.

The remaining inclusion criteria will ensure that the participant's ASBD is being managed in the least restrictive means feasible while preserving patient and staff safety.

Exclusion criteria include a range of safety and pragmatic factors. Children and adolescents with known long QT syndrome will be excluded due to the risk (although small) of iatrogenic long QT with olanzapine.[25] Young people who are known to be pregnant will be excluded due to sparse safety data for the study medications in pregnancy.[26] Those potential participants who had a previous non-response to either study medication or whose parent/guardian refuses one of the two study medications will be excluded to ensure that no young person is enrolled to receive a medication that had previously been ineffective. Patient and parent/guardian reports, established behavioural management plans and medical records will be used to determine prior medication ineffectiveness.

Participants whom the clinician deems as being more suitable to receive medication via an alternative route of administration or an alternative therapy will also be excluded from the study.

The remaining exclusion criteria—that participants can only be enrolled in PEAChY-M once and cannot be enrolled in its sister trial PEAChY-O (a study comparing oral olanzapine to oral diazepam for ASBD in young people who are able to accept oral sedation) during the same admission—are to avoid complications with non-independence of observations, and the difficulty of following two protocols simultaneously.

Outcome

The primary outcome and most of the secondary outcomes of the trial are being assessed relative to the time of randomisation. This approach was chosen to ensure that all processes which would occur day-to-day in the ED—including the time taken to locate, dispense, prepare and administer the medication—were accounted for. In addition to these outcomes assessing the effectiveness of the trial intervention; the efficacy of the medications being used will also be determined.

Box 1 Inclusion and exclusion criteria

Inclusion criteria

⇒ Aged between 9 years and 17 years and 364 days.
⇒ Sedation Assessment Tool score of ≥+1 as determined by an emergency department (ED) clinician (medical practitioner) (ie, patient deemed to be in a state of acute severe behavioural disturbance (ASBD)).
⇒ Concerted attempts at non-pharmacological management of the participant's ASBD have failed.
⇒ ED clinician determines that medication is required to assist with management of the participant's ASBD and the young person is either unable or unwilling to accept oral medication.

Exclusion criteria

⇒ Known, documented or reported allergy or previous serious side effect to either olanzapine or droperidol.
⇒ Known, documented or reported non-response to either olanzapine or droperidol.
⇒ Accompanying parent/guardian requests or refuses either olanzapine or droperidol.
⇒ Obvious reversible aetiology for agitation that has been identified and not yet treated (eg, hypotension, hypoxia, hypoglycaemia).
⇒ Known pregnancy.
⇒ Known long QT syndrome.
⇒ Clinician decision that alternative route of drug administration or therapy is more appropriate.
⇒ Participants who have been enrolled in PEAChY-O[a] during the present ED admission.
⇒ Participants who have been enrolled in PEAChY-M during a prior ED admission.

[a]*PEAChY-O – Pharmacological Emergency management of Agitation in Children and Young People – a randomised controlled trial of Oral medication is a second trial being run concurrently by the research team.*

Box 2 Secondary outcomes

⇒ Medication-related adverse events (AEs) reported from randomisation until measurement of the primary outcome.
⇒ Medication-related AEs reported from after the measurement of the primary outcome until the participant is discharged from hospital.
Note: extrapyramidal side effects are being monitored for 48 hours post hospital discharge. This is performed through medical record review. No in person or phone follow-up is being conducted.
⇒ Further episodes of acute severe behavioural disturbance in the emergency department (ED) from randomisation until discharge from the ED.
⇒ Injuries to staff from randomisation until the participant's discharge from the ED.
For example: soft tissue injuries sustained from being punched or kicked.
⇒ Injuries to participants and/or their parents or guardian from randomisation until the participant's discharge from the ED.
For example: injuries related to physical or mechanical restraints inclusive of skin erythema or bruising.
⇒ Length of stay (LOS) in the ED and in hospital (from time of randomisation).
⇒ Disposition on discharge from the ED.
For example: discharged home or admitted to a mental health unit.
⇒ Staff, participant and carer satisfaction with the management provided, assessed 1-hour post randomisation.
⇒ Healthcare resource use and costs incurred from time of randomisation until ED discharge.
⇒ Healthcare resource use and costs incurred from time of randomisation until hospital discharge.
⇒ Clinician assessment of whether successful sedation was achieved at 1-hour post randomisation.
⇒ Whether a participant is administered their randomised medication or not.
⇒ Whether a participant is administered the prescribed weight-based dose or not.

Efficacy outcomes

⇒ The proportion who achieve successful sedation, as determined by a Sedation Assessment Tool score of ≤0, without the requirement of additional medication at 1-hour post randomisation.
⇒ Time from randomisation to medication administration.

Descriptive outcomes

⇒ LOS in the ED (from time of triage).
⇒ LOS in the hospital (from time of triage).

The primary outcome is the proportion of participants who achieve *successful sedation* without the requirement for additional sedation 1-hour post randomisation. *Successful sedation* will be assessed by the treating clinician and is defined as reaching an SAT of ≤0 (figure 1).

Secondary outcomes (box 2) include the number of adverse events (AEs); length of stay (LOS); injuries to staff, participants or parents/guardians; disposition; satisfaction with care; associated costs and whether a participant is administered the medication. The time frames at which each outcome is determined are detailed in box 2.

Efficacy outcomes include assessing the primary outcome in those participants who are administered the medication within 30 min of randomisation and assessing the secondary outcomes in this population. The time taken for the young person to be administered the medication from randomisation will also be assessed.

Descriptive outcomes include the LOS in ED and LOS in hospital from the time of ED triage.

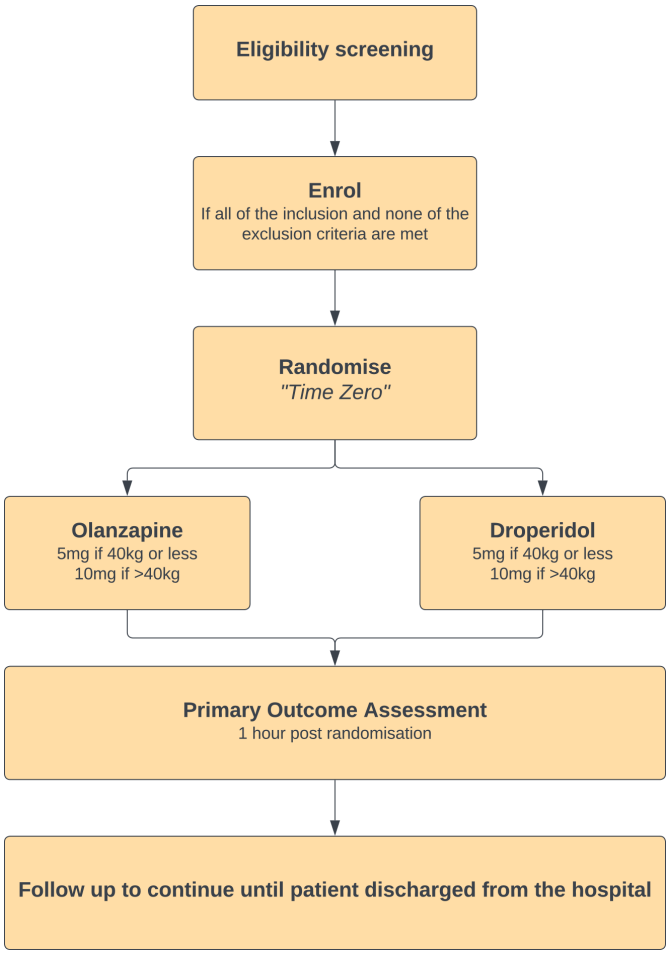

Figure 2 PEAChY-M trial enrolment process.

Patient recruitment, study procedure and data collection

ED healthcare staff will identify patients who are potentially eligible. Enrolment can occur at any time during an ED admission. If a potential participant meets all inclusion and no exclusion criteria they will then be enrolled by the ED clinician (figure 2). A waiver of informed consent has been approved for this study, so informed consent is not a requirement of enrolment.

The research team provided extensive education on the inclusion and exclusion criteria, data collection and other trial processes to ED clinicians, nursing staff and mental health clinicians as the key staff involved in the care of these young people in the ED prior to commencement of the trial. Ongoing education will be provided while the trial is being conducted.

Randomisation will be conducted using sealed opaque envelopes produced according to a computer-generated randomisation schedule. Once the participant has been enrolled, the ED clinician will open the next randomisation envelope, which will reveal the trial drug allocation. This is an open label study so the clinician and participant

will be aware of the medication to which the participant has been randomised. The rationale for making this an open label study is to ensure that clinicians will be able to rapidly identify class-specific AEs that may occur and treat these appropriately. Additionally, to blind the trial medication, a 'double dummy' approach would need to be used as intramuscular olanzapine is a yellow liquid and intramuscular droperidol is clear. Providing an extra intramuscular injection to each participant would expose these participants to an unnecessary burden.

Medication dosing will be weight based, with participants weighing <40 kg receiving 5 mg of either drug and those weighing 40 kg or greater receiving 10 mg. If the child's weight is not known, it will be estimated using the clinician's best guess. Only one dose of medication will be provided as part of the trial, with no dose modification allowances.

The time at which the randomisation envelope is opened will be time zero for the study.

Participants will be observed for 1 hour from randomisation, at which time the primary outcome will be assessed by the treating clinician or ED nurse responsible for care of the patient. The treating clinician will document the primary and other secondary outcomes measured at this time on a paper-based case report form (CRF) (online supplemental file 1). They will also record details of when the medication was administered. Data on AEs during the ED admission will also be collected on the paper CRF, as will the clinician's assessment of the likely cause of the ASBD. They will be asked to determine if, in their opinion, the participant was successfully sedated. The clinician will also provide details on what non-pharmacological de-escalation techniques were used while the young person was in the ED. They will complete a satisfaction survey at this 1-hour post randomisation time point and provide one to the young person and/or guardian to complete if feasible. A participant information form will also be offered to the young person and/or their guardian at this time point to those who are willing and able to accept this handout.

The data for the remaining secondary outcomes collected more than 1 hour following randomisation will be obtained retrospectively from the participant's medical record.

Data management

Data collected on the paper CRF and from the medical records will be entered into a password-protected database enabled through the REDCap (Research Electronic Data Capture)[27] web-based application hosted by the Murdoch Children's Research Institute (MCRI). This database will only be accessible to trained research staff. All data entered into this database will be de-identified. The identifiable paper-based CRFs and satisfaction surveys will be kept in a locked office, accessible only to the researchers at the local site.

All sites will maintain a separate password-protected logbook on a secure online database containing re-identifying information for data queries.

All investigators and statisticians involved in the analysis of the data will be blinded to the trial intervention until after the data analysis is complete.

Oversight of data collection and auditing of data entry compliance will be undertaken both remotely and through conducting regular site visits in line with the Clinical Monitoring Plan for the study. If there is a need to re-identify data for clarification, this will be done by the principal investigator (PI) at a site level.

All data will be retained in line with the ethics and governance requirements of the local site.

This study has a Trial Steering Committee (TSC) consisting of the chief principal investigator, trial coordinator, site PIs, trial statistician and a number of other study team members. The TSC will meet regularly to discuss the progress of the trial, review recruitment and AEs. This will ensure there is a forum for contemporaneously identifying and addressing issues.

An independent Data Safety Monitoring Board (DSMB) has been established for this study. It includes two independent clinicians experienced in the care of young people with ASBD and the conduct and monitoring of RCTs, and a biostatistician who is experienced in the monitoring of RCTs. The role of the PEAChY-M DSMB is to review data related to recruitment, safety and trial conduct. No interim analyses of the effectiveness or efficacy data will be performed. Data will be reviewed by the DSMB members in both an aggregated format in the open report and in the closed report in treatment groups labelled 'A' and 'B'. The DSMB will review all data within 6 months of commencement of recruitment and then yearly. Following each meeting, the DSMB can recommend to continue the trial unchanged, continue with modifications or terminate the trial.

Statistical methods

Sample size and power calculation

Assuming conservatively that 60% of participants reach successful sedation without the requirement for additional medication at 1-hour post randomisation (primary outcome) in the intramuscular droperidol group, which could be hypothesised from previous literature,[7–12] 165 participants would be required in each group in order to have 80% power to detect a 15% increase in the percentage reaching successful sedation without additional medication in the intramuscular olanzapine group (to 75%), based on a two-sided test with alpha=0.05. In order to allow for a 5% loss of follow-up (a conservative estimate given the short time frame of the primary outcome), we aim to recruit a total of 348 participants (approximately 174 per group).

Randomisation

Participants will be randomised in a 1:1 ratio between olanzapine and droperidol. The randomisation schedule will be computer generated by an independent statistician in the Clinical Epidemiology and Biostatistics Unit at the MCRI using block randomisation with variable block

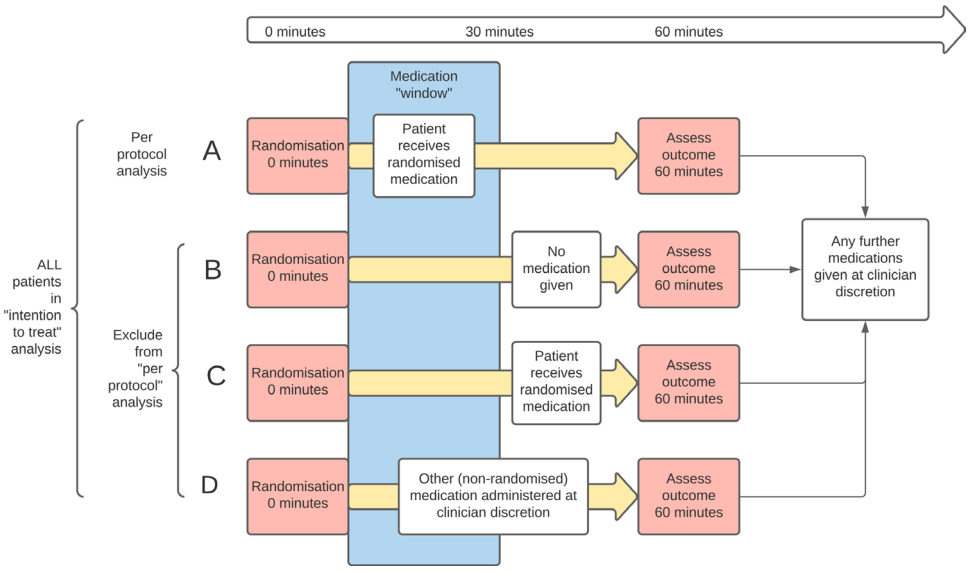

Figure 3 Summary of inclusions and exclusions from the intention-to-treat versus the per-protocol analysis.

size (with blocks of size 2, 4 and 6), stratified by site (10 strata). Treatment allocation will be via opaque, sealed envelopes.

Population to be analysed

The main objectives of the trial—those relating to effectiveness—will be analysed following the intention-to-treat principle. All participants, regardless of whether or not they are administered the medication to which they are randomised, will be included in this analysis according to their randomised group.

The secondary efficacy objectives will be assessed using a per-protocol analysis including only participants who are administered the medication to which they have been randomised within 30 min of randomisation (figure 3 provides details of who will be excluded from the per-protocol analysis).

Methods of analysis

Baseline and demographic characteristics will be summarised by randomised group in both the intention-to-treat and per-protocol populations as means and SD for continuous variables (or medians and IQR for non-parametric variables) and number and percentage for categorical variables.

Effectiveness objectives

The primary outcome, successful sedation without the need for additional medication at 1-hour post randomisation, will be summarised as the number and percentage in each treatment group. The estimand of interest is the risk difference (RD) which will be estimated using binomial regression with an identity link function adjusted for site, as used in the randomisation. The estimated RD will be reported along with its 95% CI and p value.

AEs will be presented as the number and percentage of participants with one or more events from randomisation to 1 hour and until ED or hospital discharge—or 48 hours post discharge in the case of extra-pyramidal side effects (EPSEs)—and the number and type of events, by group.

Further episodes of ASBD and injuries to staff and the participants themselves in the ED will be summarised as the number and percentage of participants with one or more of each type of event post randomisation as well as the number of events, by group. The proportion of participants with one or more of each of these events will be compared between groups using an RD estimated from binomial regression adjusted for site, reported with its 95% CI and p value.

LOS in the ED and LOS in hospital from the time of randomisation, will be summarised as a mean and SD on the log scale by group. These outcomes will be compared between groups using a mean difference on the log scale estimated using linear regression applied to the logged values adjusted for site. The results will be reported as a mean difference on the log scale along with its 95% CI and the corresponding p value.

Disposition on discharge from the ED will be presented as the number and percentage of participants with each disposition destination, by randomised group.

Participant, carer and staff satisfaction regarding the medication provided will be summarised as a mean and SD by group. These outcomes will be compared using a mean difference between groups estimated via linear regression adjusted for site. The results will be reported with its 95% CI and the corresponding p value.

Costs will be totalled in each category of staff time, medication, equipment and total ED and total hospital costs from the time of randomisation. Total costs will be compared between groups using the mean difference in cost per patient estimated using a generalised linear model, with the link function and distribution informed by the appropriate goodness of fit tests (Pregibon link test and modified Park test).[28] The results will be reported as the point estimate of the marginal effect

of the trial group on mean costs and its 95% CI and p value.

The proportion of participants who are administered each intervention according to their random allocation will be summarised as the number and percentage per randomised group. The proportion of participants not administered the medication in each group will be compared using an RD estimated from binomial regression adjusted for site, reported with its 95% CI and p value.

The proportion of participants receiving their weight-based dose in each group will be compared using an RD estimated from binomial regression with results reported with its 95% CI and p value.

Efficacy objectives

The proportion who are successfully sedated in each group will be summarised as the number and percentage in each treatment group in the per-protocol population. The estimand of interest is the RD which will be estimated using binomial regression with an identity link function. The estimated RD will be reported along with its 95% CI and p value.

Time from randomisation to medication administration will be presented as a mean and SD on the log scale by group in the per-protocol population. This outcome will be compared between groups using a mean difference on the log scale estimated using linear regression applied to the logged values. The results will be reported with its 95% CI and the corresponding p value.

Because the analysis of the efficacy objectives will be conducted in the per-protocol population, the analysis will not represent a randomised comparison and, hence, confounding may be present. Given this, results for all of the efficacy objectives will be presented adjusted for the following potential confounders:

- Site (as used in randomisation).
- Baseline SAT score.
- Age of participant.
- Time from randomisation.

We will also explore whether there are other baseline factors where there is a clinically relevant difference and will adjust for these factors in a secondary, post-hoc analysis.

Descriptive objectives

The LOS in ED and in hospital from the time of the participant's triage will be summarised as a mean and SD for all randomised participants.

Interim analyses

A DSMB has been convened as described earlier. This committee will be given summary data on the AEs that occur during the trial, along with data on recruitment and compliance with the protocol in the intention-to-treat population. There are no interim analyses planned of effectiveness or efficacy data.

Ethical issues and dissemination

Ethical approval to undertake the study was provided by the Royal Children's Hospital Human Research Ethics Committee (HREC/69948/RCHM-2020). This approval incorporated a waiver of informed consent under the National Statement on Ethical Conduct in Human Research.[29] All participating sites have obtained governance approvals from their local Human Research Ethics Committees.

As previously described, prior to the commencement of the study the research team engaged a consumer advisory group to seek advice regarding the structure of the protocol and the acceptability of the waiver of informed consent. A waiver of informed consent was endorsed by the consumer advisory group, as they felt that an ED encounter with a child presenting with ASBD would not be an appropriate setting to enter into a detailed discussion about risks and benefits of treatment, and that providing treatment in a timely manner was very important.

This trial was registered with the Australian and New Zealand Clinical Trial Registry on 13 September 2021 prior to recruitment commencing. The Universal Trial Number for this study is U1111-1268-9279.

The MCRI serves as the primary sponsor for this trial. The overall decision regarding all aspects of the trial falls to the PEAChY-M TSC with input from MCRI as the trial sponsor. The study funders do not have direct decision-making or input into the day-to-day running of the trial, data interpretation or study publications.

This protocol paper is based on V.2.0 dated 12 September 2022 of the PEAChY-M protocol.

Once the study has concluded we will present the results at relevant conferences and will publish the results in an international peer-reviewed journal. There are no limitations or restrictions on publication of this data.

Risk management, AEs and patient safety

There are no foreseeable risks additional to standard clinical care to patients by participating in this study. Both medications being used in this study are currently used as standard of care for paediatric ASBD in Australia and are listed in the doses being trialled on multiple clinical practice guidelines.[5 13–15] AEs will be closely monitored while the participant is in the ED and treated using standard clinical care algorithms. All AEs will be reported to the study's independent DSMB. All serious AEs, suspected unexpected serious adverse reactions and urgent safety measures will be reported to the trial sponsor, lead HREC and local governance bodies in line with the expectations set out in the National Health and Medical Research Council safety monitoring and reporting in clinical trials involving therapeutic goods guideline.[30]

Time plan

Recruitment has commenced at of the 10 sites. We plan to complete recruitment by the end of 2024.

DISCUSSION

Our study is the first interventional study comparing any intramuscular medications for the management of paediatric ASBD in the ED. It will provide useful effectiveness and efficacy data for these two medications that can be used to improve clinical care in this area. It will provide valuable information regarding the potential adverse effects of each medication in this patient population.

Our study design has a number of limitations. The trial is open-label. This was necessary to ensure that any AEs that occurred could be recognised and rapidly acted on. This also means that clinical staff who are determining the SAT score will be aware of the study drug allocation. All investigators and the statisticians analysing the trial data will, however, be blinded to treatment allocation until the end of the study. Second, for feasibility and logistical reasons it is not possible to collect 'time to effective sedation' as the primary outcome.

This study will have an impact on clinical practice in the emergency department but also more broadly. Paediatric patients with ASBD are a rapidly increasing patient population in whom limited research has been undertaken to determine the most effective medications for behavioural containment. We therefore anticipate our study to have significant clinical utility once the results are available.

Author affiliations
[1]Emergency Research, Murdoch Children's Research Institute, Parkville, Victoria, Australia
[2]Department of Paediatrics, University of Melbourne, Parkville, Victoria, Australia
[3]Department of Critical Care, University of Melbourne, Parkville, Victoria, Australia
[4]Emergency Deparment, Grampians Health, Ballarat, Victoria, Australia
[5]Emergency Department, Perth Children's Hospital, Nedlands, Western Australia, Australia
[6]Emergency Department, Women and Children's Hospital Adelaide, Adelaide, South Australia, Australia
[7]Children's Critical Care Service, Gold Coast University Hospital, Southport, Queensland, Australia
[8]School of Medicine and Menzies Health Institute Queensland, Griffith University, Nathan, Queensland, Australia
[9]Emergency Department, Queensland Children's Hospital, South Brisbane, Queensland, Australia
[10]Emergency Department, Children's Hospital at Westmead, Westmead, New South Wales, Australia
[11]Children's Hospital at Westmead Clinical School, The University of Sydney, Sydney, New South Wales, Australia
[12]Emergency Department, Sunshine Coast University Hospital, Sunshine Coast, Queensland, Australia
[13]Paediatric Emergency Department, Western Health, Footscray, Victoria, Australia
[14]Psychological Medicine, Monash Health, Clayton, Victoria, Australia
[15]Monash University, Monash University, Clayton, Victoria, Australia
[16]Emergency Department, The Royal Children's Hospital Melbourne, Parkville, Victoria, Australia
[17]Department of Psychiatry, The Royal Children's Hospital Melbourne, Parkville, Victoria, Australia
[18]Clinical Epidemiology and Biostatistics (CEBU), Murdoch Children's Research Institute, Parkville, Victoria, Australia
[19]Melbourne Children's Trials Centre, Murdoch Children's Research Institute, Parkville, Victoria, Australia
[20]Department of Anaesthesia, Royal Children's Hospital Melbourne, Parkville, Victoria, Australia
[21]Emergency Department, The Royal Melbourne Hospital City Campus, Parkville, Victoria, Australia
[22]Department of Paediatrics, Monash University, Clayton, Victoria, Australia
[23]Emergency Department, Monash Medical Centre Clayton, Clayton, Victoria, Australia
[24]Emergency Department, Royal Childrens Hospital, Parkville, Victoria, Australia

Twitter Elyssia M Bourke @elyssiabourke, Meredith L Borland @MeredithBorland, Shane George @shanegeorge77 and Simon Craig @DrSimonCraig

Acknowledgements This study is being conducted on behalf of the Paediatric Research in Emergency Departments International Collaborative (PREDICT) research network and the Australasian College of Emergency Medicine Clinical Trials Network (ACEM CTN). The authors would like to thank our parent consumers Dr Kathleen Alleaume-Ross, Ms Jodie Miers, Mr MD Kabir and Ms Diana Mercuri for their involvement in the study design process. The authors would also like to acknowledge participating patients and emergency department staff.

Contributors EMB, FEB, SC, MLB, AD and JCK were integral in conceiving the study. EMB, MLB, AK, SG, DS, SJ, KK, KL, AD, JCK, SC and FEB were involved in the development of the trial protocol. KL provided statistical oversight of the study protocol. EMB wrote the first draft of the protocol paper and MLB, AK, SG, DS, SJ, KP, DT, MSG, KK, CP, KL, AD, JCK, SC and FEB provided feedback. EMB, MLB, AK, SG, DS, SJ, KP, DT, MSG, KK, CP, KL, AD, JCK, SC and FEB have read and approved the final version.

Funding This study is being funded by the Medical Research Futures Fund Million Minds Grant, Canberra, Australia (GNT1179137), the Western Australian Child Research Fund Grant (Round 8), Perth, Australia (N/A) and an Emergency Medicine Foundation (EMF) Grant (Round 38), Brisbane, Queensland (EMLE-234R38-2022). EMB is funded by an NHMRC postgraduate scholarship (GNT2005279). FEB is funded by a grant from the Royal Children's Hospital Foundation and a NHMRC Investigator Grant (GNT2017605). This study is supported by the Melbourne Children's Trials Centre at MCRI. The Royal Children's Hospital and the MCRI are supported by the Victorian Government's Operational Infrastructure Support, Australia (N/A).

Competing interests None declared.

Patient and public involvement Patients and/or the public were involved in the design, or conduct, or reporting, or dissemination plans of this research. Refer to the Methods section for further details.

Patient consent for publication Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request. The authors support data sharing. The PEAChY-M trial will collect identifiable individual patient data that are subject to restriction due to ethics, consent and privacy. Anonymised participant data and data dictionary will be available on request from the corresponding author where possible within these constraints for use.

ORCID iDs
Elyssia M Bourke http://orcid.org/0000-0001-5617-0955
Meredith L Borland http://orcid.org/0000-0002-5326-5008
Shane George http://orcid.org/0000-0002-8880-1245
Simon Craig http://orcid.org/0000-0003-2594-1643
Franz E Babl http://orcid.org/0000-0002-1107-2187

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