PAin SoluTions In the Emergency Setting (PASTIES); a protocol for two open-label randomised trials of patient controlled analgesia (PCA) versus routine care in the Emergency Department.

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PAin SoluTions In the Emergency Setting (PASTIES); a protocol for two open-label randomised trials of patient controlled analgesia (PCA) versus routine care in the Emergency Department.

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Abstract

Introduction

Pain is the commonest reason that patients present to an Emergency Department (ED), but it is often not treated effectively. Patient controlled analgesia (PCA) is used in other hospital settings but there is little evidence to support its use in emergency patients.

We describe two randomised trials aiming to compare PCA to nurse titrated analgesia (routine care) in adult patients who present to the ED requiring intravenous (IV) opioid analgesia for the treatment of moderate to severe pain and are subsequently admitted to hospital.

Methods and analysis

Two prospective multi-centre open-label randomised trials of patient controlled analgesia versus routine care in emergency department patients who require IV opioid analgesia followed by admission to hospital; one trial involving patients with traumatic musculoskeletal injuries and the second involving patients with non-traumatic abdominal pain. In each trial, 200 participants will be randomised to receive either routine care or PCA, and followed for the first 12 hours of their hospital stay. The primary outcome measure is hourly pain score recorded by the participant using a visual analogue scale (VAS) over the 12 hour study period, with the primary statistical analyses based on the area under the curve of these pain scores. Secondary outcomes include total opioid use, side effects, time spent asleep, patient satisfaction, length of hospital stay, and incremental cost effectiveness ratio.

Ethics and dissemination

The study is approved by the South Central – Southampton A Research Ethics Committee (REC reference 11/SC/0151). Data collection will be completed by August 2013, with statistical analyses commencing after all final data queries are resolved. Dissemination plans include presentations at local, national and international scientific meetings held by relevant Colleges and societies. Publications should be ready for submission during 2014. A lay summary of the results will be available to study participants on request, and disseminated via a publically accessible website.

Registration details

The study is registered with the European Clinical Trials Database (EudraCT Number: 2011-000194-31) and is on the ISCRTN register (ISRCTN25343280).

Introduction

Pain is defined as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage" [1]. Pain is the commonest reason that patients present to the Emergency Department (ED), but it is often not treated effectively [2]. In a national survey of ED patients, 66% reported they were in pain [3]. The UK College of Emergency Medicine recommends that patients in severe pain should receive analgesia within 20 minutes of arrival in the ED, with regular reassessment and further action as required [4]. However, effective analgesia is often not achieved and almost half of patients recently surveyed thought more could be done to treat their pain in the ED [3].

Routine care for patients in moderate or severe pain often involves the administration of intravenous (IV) morphine, which is the standard opioid used in most hospitals and has been shown to be as effective as other opioids [5]. In EDs across the United Kingdom, analgesia for patients in severe pain is currently provided by nurse-delivered IV morphine administered over several minutes to achieve pain relief. This technique is safe and effective in the short term but places significant demands on nursing time, particularly when repeated doses are needed [6].

Once a patient is admitted to a hospital ward, severe pain may be managed using strong oral opioid analgesia or advanced pain management techniques. Best practice includes multimodal analgesia using regular paracetamol and non-steroidal anti-inflammatory drugs (NSAIDs) in addition to opioids. The decision to admit a patient to the ward has been shown to delay the delivery of effective analgesia in the ED – suggesting that this group of patients are at particular risk of poor pain management [7].
One solution may be to allow patients to deliver opioid analgesia themselves via a patient controlled analgesia (PCA) device. This device consists of a volumetric pump, which delivers a set IV dose of drug when a control button is pressed. The PCA system includes antisyphon and antireflux valves to minimize the risk of inadvertent drug delivery. The pump has a safety "lock out" period when it will not deliver a further dose of opioid. A protocol commonly used throughout many UK hospitals, in settings other than the ED, uses a 1mg bolus (1mg morphine) and lockout period of 5 minutes, and is derived from a broad evidence base [8-11]. PCA has been shown to be more effective in providing pain relief when compared to standard methods of analgesia delivery in areas such as post-operative care, burns, and in terminal care [12-15]. PCA is most effective in maintaining analgesia once baseline pain relief has been established [16].

Despite the high prevalence of pain in ED patients there is very limited evidence relating to the use of PCA in this setting. Prior to commencing the PASTIES trial, only one small randomised trial of 86 adult patients with pain due to trauma presenting to the ED had been published [17], which concluded that PCA was as effective as standard nurse titrated analgesia. However, the trial data were collected during the patients' emergency department stay only, and did not continue to follow them after admission to a hospital ward. Having contacted the corresponding author of this paper, it would appear that the main issue with this

study was that the duration of active participation did not extend beyond 3 hours [18].

Three further relevant studies have been reported since the current study commenced, although all three studies were limited to a 2 hour period in the ED. The largest [19], a study done in North America, randomised 211 emergency patients with abdominal pain to one of three groups; standard care, PCA standard dose (1mg) bolus or PCA higher dose (1.5mg) bolus. It found that there was a significant reduction in pain in both PCA groups compared to standard care. A smaller study from Malaysia included patients presenting with pain of traumatic origin [20]; 96 patients in 2 centres were randomised to either standard care or PCA (1mg boluses), with a significant reduction reported in pain scores in the PCA group compared to the standard care group. The same 2 authors reported another smaller study of 47 patients with traumatic injury [21]. Patients were again randomized to receive either standard care or PCA (1mg boluses). This study found similar reductions in pain scores in the PCA group compared to standard care. These three recent studies provide further limited evidence of the short-term utility of PCA in emergency patients, but do not address the management of pain over the subsequent hours following hospital admission.

Cost analyses of the use of PCA versus standard analgesia have been carried out in a post-operative setting and suggest that PCA costs may be higher [22]. However, in the ED the heavy demands on nursing time of providing intravenous analgesia may offset the initial high setup costs of PCA analgesia; this current study will therefore determine the UK cost implications of PCA use in the emergency setting over the first 12 hours of hospital care. No previous or current studies have been identified that combine ED care with ongoing ward care to assess quality of pain relief beyond four hours, and no detailed analysis of the cost-effectiveness of PCA in this setting has previously been reported.

The aim of our study is therefore to compare PCA morphine to routine care (nurse titrated IV morphine in the ED and oral or parenteral morphine on the wards) in adult emergency patients who present in moderate or severe pain due to traumatic injuries or non-traumatic abdominal pain, and are then admitted to an inpatient ward.

Methods and analysis

Study design

The study comprises two contemporaneous multi-centre open-label randomised trials of PCA versus routine care in the Emergency Department. Patients presenting to the ED requiring IV analgesia and admission to hospital, with either traumatic musculoskeletal injury or non-traumatic abdominal pain, are potentially eligible for inclusion. Key outcome measures will be collected at baseline and then hourly for 12 hours. Whilst two separate trials are running (one of patients presenting with traumatic musculoskeletal injuries, the other of patients with non-traumatic abdominal pain), both are based on the same protocol, which is outlined below. Nevertheless, they are considered as two separate trials since they are powered separately.

Participants
Eligible patients are adults presenting to the ED with either traumatic injury or non-traumatic abdominal pain requiring IV opioid analgesia and hospital admission for at least 12 hours from the time of enrolment. Exclusion criteria are listed in Table 1. Study participants are patients who meet the screening criteria and are willing and able to give informed consent.

Study recruitment
Patients are screened by a research nurse on arrival at the ED. Following initial assessment and pain management, patients are approached by a research nurse and given a patient information sheet detailing the study. If they are happy to discuss the study further, any questions are answered at this stage. Patients are then fully assessed against the inclusion and exclusion criteria before written informed consent is obtained from patients willing and able to participate. Patients who decline to take part are not obliged to give a reason for declining but reasons are recorded by the research nurse if given.

Study procedures (see Figure 1)
After informed consent is obtained, the first VAS pain score is recorded, and the patient randomised (using a secure web-based randomisation system) to receive either PCA or routine care.

Participants in both groups then receive instructions on how to complete the VAS scores, which are entered into a mini flipchart. The participant turns the page of the flipchart after an entry is made, and the previous score is therefore not visible for comparison the next time a VAS score is recorded. Participants in the trauma group are instructed to record their pain scores on movement, while those in the abdominal group are asked to record their pain scores on deep breathing. Electronic timers (Casio F-91W digital watches) issue a bleep every hour as a reminder to the participant to complete the hourly score, but this bleep is not usually loud enough to wake the participant from sleep. Participants are also instructed how to record periods asleep on the booklet, using a tick box on each page.

Interventions
Participants allocated to receive routine care are prescribed intravenous morphine while in the ED and oral morphine (or subcutaneous/intramuscular for those nil by mouth) when transferred to the hospital ward. Participants randomised to the PCA group receive instruction from the research nurse in how to operate the PCA device, which is set up by the ED nurses, and initiated with a 1mg morphine bolus and a 5 minute lock out. PCA is continued for a minimum period of 12 hours; in practice ongoing requirement for PCA is reviewed the following morning by the clinical team. Participants in both groups are prescribed multi-modal analgesia in addition, including paracetamol and a non-steroidal anti-inflammatory drug unless contra-indicated, and are also prescribed anti-emetics as required. Most outcome data are collected for 12 hours from the point at which the first pain score is completed. Length of hospital stay and final diagnosis at discharge are collected retrospectively.

Where possible, at the end of the 12 hour study period (or the following morning as appropriate), participants in both groups are visited by a research nurse to facilitate study data collection. The final page of the data collection booklet includes a five-point patient pain management satisfaction score ranging from 'perfectly satisfied' to 'not satisfied at all'. There is also a final pain VAS score, collected the following morning, which may be used to guide analysis of missing final data points.

Primary outcome measure

The primary outcome measure is the total pain experienced over the 12 hour study period, as captured by hourly completion of a visual analogue pain rating scale (VAS). The VAS is presented as a 100mm horizontal line with verbal anchors at each end of "no pain" and "worst pain possible". The study participant selects the point along the line (and marks this point with a pen) that reflects their current pain perception. Participants record VAS scores at 60-minute intervals over a 12 hour period. Periods of sleep are also recorded retrospectively by the participant.

Secondary outcome measures

Secondary outcome measures include total opioid dose, opioid side-effects, patient satisfaction with pain management, proportion of study period with VAS >44mm, proportion of study period spent sleeping, length of hospital stay, and incremental cost effectiveness ratio.

Total opioid dose is recorded from the prescribed medication administered as recorded on the patient's drug chart during the study period. Study observation charts are utilized for all study participants and are based on standard hospital charts: these are completed as part of routine care by ED nurses in the ED, and then by ward nurses after inpatient ward admission. Observations follow the standard of care in each centre. Typically, this involves observations 1 hourly for 4 hours, 2 hourly for 8 hours and 4 hourly thereafter. In practice, this will mean hourly vital signs in the ED and 2 hourly vital signs for the rest of the study period. Observations include heart rate (HR), blood pressure (BP), respiratory rate (RR), oxygen saturations (SpO_2), oxygen (O_2) flow rate, sedation score (AVPU) and nausea score (0-2). A research nurse reviews the observation charts after the 12 hour study period and transcribes out-of-range results into the study case report form (CRF). Following the participant's discharge, the length of stay in hospital and final diagnosis at discharge are obtained from the Patient Administration System (PAS) (or equivalent) by the research nurse and recorded in the CRF.

Randomisation and blinding

Randomisation to either PCA or standard care is undertaken via a secure web-based randomisation system. Research team members accessing the randomisation website do not know the allocation for an individual patient until the relevant details are entered and recruitment confirmed.

As pain experience over subsequent hours may be affected by the time of day of recruitment (those included later in the day will be scoring their pain during

night hours when they may spend a greater proportion of time asleep), randomisation is stratified by morning/afternoon admission, as well as by recruitment centre. Blinding is not possible for this study due to the nature of the intervention.

Sample size

The main objective of this study is to assess the magnitude of any difference in total pain scores between the PCA and standard care groups, for each population. Primary outcome data are being collected in terms of self-reported pain scores over time, with VAS measurements completed hourly over the 12-hour study period. Data will be conceptualised as a graph of VAS pain against time and used to produce an area under the curve (AUC) for each patient. This is a measure of overall pain experienced during the study period [23].

Very few studies have addressed the question of what reduction in AUC might be a clinically significant analgesic effect. One study by Camu *et al.* demonstrated that a 20% reduction in the AUC for pain on movement was associated with a 26% absolute increase in the proportion of patients reporting their global rating of pain relief as very good or excellent (p=0.01) [24]. Conservatively, therefore, a difference in AUC of 15% between PCA and standard care groups was chosen to be of clinical significance. On a standardised AUC (scoring between 0 and 100) the standard care group is expected to have an average score of about 40 units, so 15% equates to a 6 point reduction. A standard deviation (SD) can be estimated from the research conducted by Camu *et al.* as about 15 units. Based on these assumptions, and using a two-tailed two sample t-test, with a type 1 error rate of 0.05, a sample size of 100 patients per group provides sufficient power (80%) to detect a between-group difference of 15%.

Statistical analyses

The primary analyses are all pre-specified and a detailed statistical analysis plan will be completed and signed-off by the data monitoring committee prior to the analyses commencing. Data will be reported and presented according to the CONSORT statement [25]. In the primary analyses data will be pooled across all participating recruitment centres, with adjustment for centre in all comparative analyses, and with adjustment for time of recruitment. 95% confidence intervals will be calculated and presented where possible.

The primary statistical analysis will follow an intention-to-treat approach, with the intent-to-treat population defined as all participants in the trial who completed the baseline and at least one other pain VAS. The primary outcome measure of total pain experienced will be captured using the area under the curve approach and will be compared between PCA and standard care groups using analysis of covariance, which will include the two stratification variables as covariates, both being considered as fixed effects, with a suitable transformation of the AUC considered if necessary. The estimate of the difference in mean AUC will be presented, together with a 95% confidence interval for the difference.

Continuous secondary outcomes will be compared between the two groups using analysis of covariance, with adjustment for stratification variables and a suitable

transformation of each variable considered if necessary. For each of the side effects, binary logistic regression will be used to estimate the odds ratio and 95% confidence interval for the group effect.

For the analysis of the participant's satisfaction with pain management, it is likely that the 5 point scale (ranging from 'perfectly satisfied' to 'not at all satisfied') will need to be recoded into fewer categories. Depending on how many recoded categories there are, either binary or ordinal logistic regression will be used to determine the odds ratio and 95% confidence interval for the group effect.

Missing data

It was anticipated prior to commencing the study that there would be some missing VAS scores and the original protocol specified how both missing data and periods when a participant indicated s/he was asleep should be handled within the analysis. However, inspection of the incoming combined primary outcome data suggests that there may be a relatively high proportion of participants with one or more missing pain VAS scores - in particular, indications of being asleep. As part of the development of the statistical analysis plan, more detailed rules for handling the missing pain VAS scores have been developed for each missing data scenario (sleep, spoilt, score missing but participant remained in trial, score missing because participant withdrawn from trial). In brief, this involves linear interpolation where the absent pain score(s) falls between two valid VAS scores, and last observation carried forward (LOCF) where the absent score(s) extends to the final 12-hour time point. The one exception to the latter is when it makes more sense to impute zero for the remaining scores, in particular if the patient is discharged because the pain has resolved; any other such potentially ambiguous situations will be judged on an individual basis, blinded to group allocation. Furthermore, a number of sensitivity analyses are also planned, such as treating all sleep periods as zero. The strategies have been discussed and agreed with the data monitoring committee and will be incorporated into the statistical analysis plan.

Economic evaluation

The trial will include a cost-effectiveness study from an NHS perspective. For the economic evaluation, the relative effectiveness of the intervention will be measured in terms of hours in moderate or severe pain averted. Details of the volume of resources used for pain management using the PCA or in usual management will be collected, ignoring resource use that is common to both study arms. Resource use will be costed using standard NHS costs. The main drivers of marginal cost in this study are likely to be medical and nursing time, but the evaluation will include the costs of medication, equipment and disposables and costs associated with length of stay. As part of the economic evaluation, an opportunistic sample of up to 20 patients in each arm of the trial will be observed by a research nurse and the time required for pain management by healthcare staff will be recorded. The results of the economic evaluation will be reported as incremental cost effectiveness ratios (ICERs) defined as the additional cost per hour in moderate or severe pain averted. Uncertainty around

the estimates of the ICER will be explored using probabilistic and deterministic sensitivity analysis.

Ethics and dissemination

Ethical considerations

The protocol is designed to conform to the principles of the Declaration of Helsinki and has been approved by the South Central – Southampton A Research Ethics Committee (REC reference 11/SC/0151). A Clinical Trial Authorisation has been obtained from the Medicines and Healthcare products Regulatory Agency (MHRA) and the study runs in compliance with the Medicines for Human Use (Clinical Trials) Regulations 2004 and subsequent amendments, the principles of GCP, the Research Governance Framework for Health and Social Care (Second edition, 2005) and the Data Protection Act 1998. The study has been adopted by the NIHR Clinical Research Network (CRN).

The study is sponsored by Plymouth Hospitals NHS Trust and approved by the participating trust's Research and Development (R&D) departments at investigator sites. The study is managed by the UKCRC-registered Peninsula Clinical Trials Unit at Plymouth University (Registration No: 31).

A Trial Management Team meets regularly to discuss the progress of the trial, and address any issues that arise. A Trial Steering Committee (TSC), with an independent chair, meets approximately every six months to oversee the conduct and safety of the trial. A Data Monitoring Committee (DMC), comprising two independent clinicians and one independent statistician, meets approximately every six months to oversee the data management and any issues relating to patient safety. The DMC provides recommendations to the TSC following each meeting.

The main ethical consideration is that emergency patients in pain are being asked to participate in a research study. However, all patients are initially treated according to their needs, and only once the patient has received appropriate initial analgesia and made more comfortable are they approached regarding the study.

Timelines and dissemination plans

Approval from a NHS Research Ethics Committee was obtained in May 2011. Recruitment and training of staff involved in the project occurred in June 2011, and recruitment of participants started in July 2011. Additional trial centres were added, to improve recruitment, during 2012.

Patient recruitment will complete in July 2013. Statistical analyses will commence once final data collection and monitoring has concluded, and it is anticipated that the first publications will be ready for submission by early 2014.

As well as the submission of research articles to appropriate peer-reviewed journals, research findings will be submitted for presentation at local, national and international scientific meetings held by, for example, the College of

Emergency Medicine, Faculty of Pain Medicine and Royal College of Anaesthetists. In particular, effective dissemination of research findings throughout the Emergency Medicine community within the UK and overseas is anticipated with one of the study authors (JB) currently chairing the UK Clinical Effectiveness Committee of the College of Emergency Medicine. A lay summary of the results will be available to study participants on request, and disseminated via a publically accessible website.

Conclusions

The lack of evidence regarding the effectiveness of PCA to manage pain in patients presenting to Emergency Departments indicates the need for well-designed clinical trials to investigate this subject. This study, comprising two trials in different populations of patients in pain presenting to the ED, has been designed to investigate whether PCA is more effective than standard care in managing pain in the ED and during the following hours of hospital admission. This is the first study to follow-up participants from emergency admission to the hospital ward, and will therefore give a pragmatic answer to the question of whether PCA should be used in these patients.

Author's contributions

JS, MR and RS conceived the idea of the study and JS, MR, RS, PE, AB, and CP were responsible for the initial study design. CH, SC and JB further contributed to the final study design. SC and PE designed the plan for data analysis with input from all other authors. All authors contributed to the planning of the study, have critically revised successive drafts of the manuscript, and have approved the final version.

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Table 1: exclusion criteria

Criteria	Rationale
Patients over 75 years	Altered plasma levels of opioid in this age group for a given standard dose of PCA
Patients with a reduced conscious level (Glasgow Coma Score (GCS)<15)	Will not be able to give informed consent
Inability to operate a PCA device	Will not be able to complete the intervention
Patients who cannot understand the study information	e.g. due to pre-existing dementia, learning difficulties, or intoxication. Will not be able to give informed consent
Patients with chronic pain	Altered pain processing or opioid tolerance
Patients who are opioid tolerant or have active opioid addiction	Abnormal response to opioids or potential opioid misuse
Patients with a history of renal failure	Accumulation of active opioid metabolites
Allergy or other contraindication to morphine	
Hypotension (systolic blood pressure <90mmHg)	Morphine may exacerbate hypotension
Patients in police custody, or prisoners	
Inability to gain IV access	Will not be able to receive IV morphine
Patients who are likely to be definitively treated in the ED and discharged, or who are likely to require transfer for surgery direct from the ED	Will not be able to complete 12 hours of VAS scoring
Patients who are pregnant or breast-feeding	Altered drug metabolism and foetal/infant opioid effects
Patients on other predetermined analgesia pathway	e.g. regional anaesthesia
Previous participation in this study	
Current participation in another Clinical Trial of an Investigational Medicinal Product (CTIMP)	

Figure legend

Figure 1: trial schematic

References

1. Merskey H. Pain terms: a list with definitions and notes on usage. Recommended by the IASP Subcommittee on Taxonomy. *Pain* 1979;6(3):249.
2. Todd KH, Ducharme J, Choiniere M, et al. Pain in the emergency department: results of the pain and emergency medicine initiative (PEMI) multicenter study. *J Pain* 2007;8(6):460-6.
3. Commission TH. Emergency Department Survey 2008. *http://www.cqc.org.uk/_db/_documents/Full_national_results_with_historical_comparisons.pdf* 2008.
4. College of Emergency Medicine CEC. Clinical audit standards 2009. *Accessed at: http://www.collemergencymed.ac.uk* 2009.
5. Plummer JL, Owen H, Ilsley AH, et al. Morphine patient-controlled analgesia is superior to meperidine patient-controlled analgesia for postoperative pain. *Anesth Analg* 1997;84(4):794-9.
6. Lvovschi V, Aubrun F, Bonnet P, et al. Intravenous morphine titration to treat severe pain in the ED. *Am J Emerg Med* 2008;26(6):676-82.
7. Arendts G, Fry M. Factors associated with delay to opiate analgesia in emergency departments. *J Pain* 2006;7(9):682-6.
8. Owen H, Plummer JL, Armstrong I, et al. Variables of patient-controlled analgesia. 1. Bolus size. *Anaesthesia* 1989;44(1):7-10.
9. Owen H, Szekely SM, Plummer JL, et al. Variables of patient-controlled analgesia. 2. Concurrent infusion. *Anaesthesia* 1989;44(1):11-3.
10. Macintyre PE. Safety and efficacy of patient-controlled analgesia. *Br J Anaesth* 2001;87(1):36-46.
11. Walder B, Schafer M, Henzi I, et al. Efficacy and safety of patient-controlled opioid analgesia for acute postoperative pain. A quantitative systematic review. *Acta Anaesthesiol Scand* 2001;45(7):795-804.
12. Choiniere M, Grenier R, Paquette C. Patient-controlled analgesia: a double-blind study in burn patients. *Anaesthesia* 1992;47(6):467-72.
13. Hudcova J, McNicol E, Quah C, et al. Patient controlled opioid analgesia versus conventional opioid analgesia for postoperative pain. *Cochrane Database Syst Rev* 2006(4):CD003348.
14. White PF. Use of patient-controlled analgesia for management of acute pain. *JAMA* 1988;259(2):243-7.
15. Dolin SJ, Cashman JN, Bland JM. Effectiveness of acute postoperative pain management: I. Evidence from published data. *Br J Anaesth* 2002;89(3):409-23.
16. Rees DC, Olujohungbe AD, Parker NE, et al. Guidelines for the management of the acute painful crisis in sickle cell disease. *Br J Haematol* 2003;120(5):744-52.
17. Evans E, Turley N, Robinson N, Clancy M. Randomised controlled trial of patient controlled analgesia compared with nurse delivered analgesia in an emergency department. *Emerg Med J* 2005;22(1):25-9.
18. Clancy M. Personal communication. 2009.
19. Birnbaum A, Schechter C, Tufaro V, et al. Efficacy of patient-controlled analgesia for patients with acute abdominal pain in the emergency department: a randomized trial. *Acad Emerg Med* 2012;19(4):370-7.

20. Rahman NH, Desilva T. A Randomized Controlled Trial of Patient-controlled Analgesia Compared with Boluses of Analgesia for the Control of Acute Traumatic Pain in the Emergency Department. *J Emerg Med* 2012;43(6):951-7.
21. Rahman NH, DeSilva T. The effectiveness of patient control analgesia in the treatment of acute traumatic pain in the emergency department: a randomized controlled trial. *Eur J Emerg Med* 2012;19(4):241-5.
22. Choiniere M, Rittenhouse BE, Perreault S, et al. Efficacy and costs of patient-controlled analgesia versus regularly administered intramuscular opioid therapy. *Anesthesiology* 1998;89(6):1377-88.
23. Matthews JN, Altman DG, Campbell MJ, et al. Analysis of serial measurements in medical research. *BMJ* 1990;300(6719):230-5.
24. Camu F, Van Aken H, Bovill JG. Postoperative analgesic effects of three demand-dose sizes of fentanyl administered by patient-controlled analgesia. *Anesth Analg* 1998;87(4):890-5.
25. Moher D, Hopewell S, Schulz KF, et al. CONSORT 2010 explanation and elaboration: updated guidelines for reporting parallel group randomised trials. *BMJ* 2010;340:c869.

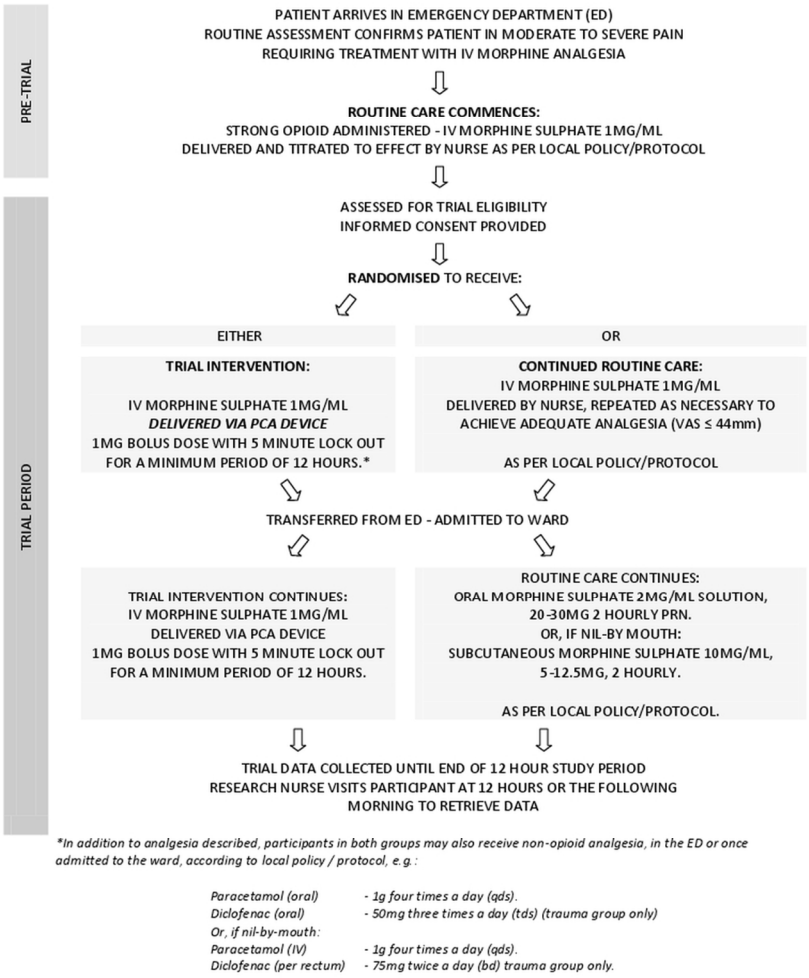

Figure 1: trial schematic
90x127mm (300 x 300 DPI)

CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	1
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	2
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	3-4
	2b	Specific objectives or hypotheses	4
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	4-8
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	
Participants	4a	Eligibility criteria for participants	5
	4b	Settings and locations where the data were collected	5
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	5-6
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	6
	6b	Any changes to trial outcomes after the trial commenced, with reasons	
Sample size	7a	How sample size was determined	7
	7b	When applicable, explanation of any interim analyses and stopping guidelines	
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	6
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	6
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	6
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	6
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those	N/A

		assessing outcomes) and how	
	11b	If relevant, description of the similarity of interventions	N/A
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	7-8
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	7-8
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	FIGURE 1 for flow diagram
	13b	For each group, losses and exclusions after randomisation, together with reasons	N/A
Recruitment	14a	Dates defining the periods of recruitment and follow-up	N/A
	14b	Why the trial ended or was stopped	N/A
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	N/A
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	N/A
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	N/A
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	N/A
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	N/A
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	N/A
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	8
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	N/A
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	N/A
Other information			
Registration	23	Registration number and name of trial registry	2
Protocol	24	Where the full trial protocol can be accessed, if available	N/A – protocol paper
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	11

*We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see www.consort-statement.org.