FORCE - Forearm Fracture Recovery in Children Evaluation

Protocol version 3.0
13th November 2019

Ethical approval

Obtained on the 16 November 2018 with reference number 18/WM/0324

Funding

This study is funded by the National Institute for Health Research, Health Technology Assessment (17/23/02)

Sponsorship

The University of Oxford is the sponsor of this study.

Registration

The study has been registered with the current controlled trials database under reference number ISRCTN13955395

Dates

Study start date: 16/11/2018

Study end date: 30/01/2021

Contents

Abbreviations

AE – Adverse Event

BNF – British National Formulary

CAT – Computer Adaptive Test

CI – Chief Investigator

CRF – Clinical Reporting Form

DSMC – Data and Safety Monitoring Committee

FORCE – Forearm Fracture Recovery in Children Evaluation

EQ-5D-Y – EuroQol - youth

GCP – Good Clinical Practice

HE – Health Economy/Economist

HRA – Health Research Authority

HTA- Health Technology Assessment

MRC – Medical Research Council

NICE -National Institute for Health and Care Excellence

OCTRU – Oxford Clinical Trials Research Unit

PAG - Parent Advisory Group

PI – Principal Investigator

PSSRU - Personal Social Services Research Unit

PROMIS - Patient Report Outcomes Measurement System

QA – Quality Assurance

QALY – Quality Adjusted Life Year

RCT- Randomised Controlled Trial

REC – Research Ethics Committee

RF – Research Fellow

SAE – Serious Adverse Event

SOP – Standard Operating Procedure

SWAT – Study Within A Trial

TMG – Trial Management Group

TRECA – TRials Engagement in Children and Adolescents

TSC – Trial Steering Committee

YPAG - Young Persons Advisory Group

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2. Synopsis

Study Title	The Forearm Fracture Recovery in Children Evaluation: *A multi-centre prospective randomised equivalence trial of a soft bandage and immediate discharge versus current treatment with rigid immobilisation for torus fractures of the distal radius in children*	
Acronym	FORCE	
Study Design	Multi-centre, multi-surgeon, parallel, two-arm, randomised controlled trial Trial is also acting as a 'host' to an engagement study, and sites will be cluster randomised to different forms of information provision. See Appendix 01	
Study Participants	Children 4 to 15 years old inclusive who have sustained a torus/buckle fracture of the distal radius with/without an injury to the ulna.	
Planned Sample Size	696	
Planned Study Period	01/10/18 – 30/01/21	
	Objectives	Outcome Measures
Primary	To quantify and draw inferences on observed differences in the Wong-Baker FACES Pain Rating Scale between soft bandage and immediate discharge versus rigid immobilisation and standard follow-up, at three days post randomisation.	Wong-Baker FACES
Secondary	1. To assess differences in the Wong-Baker FACES Pain Rating Scale between trial treatment groups at 1 day, 1, 3 and 6 weeks post randomisation 2. To determine differences in the use of regular analgesia between trial treatment groups at 1, 3 and 7 days post randomisation. 3. To quantify and draw inferences on functional recovery using the Patient Report Outcomes Measurement System (PROMIS) Upper Extremity Limb Score for Children Computer Adaptive Test between the trial treatment groups at 3 days, 1, 3 and 6 weeks post randomisation	Wong-Baker FACES Analgesia use PROMIS

	4. To quantify and draw inferences on observed differences in the EQ-5DY between trial treatment groups at 3 days, 7 days, 3 and 6 weeks post randomisation. 5. To determine differences in the number of days of school absence between trial treatment groups up to 6 weeks post randomisation. 6. To determine differences in the complication rate between trial treatment groups, including the need for further hospital attendance up to 6 weeks post-randomisation. 7. To investigate, using appropriate statistical and economic analysis methods, the resource use, and comparative cost effectiveness between trial treatment groups at 3 and 6 weeks post randomisation.	EQ-5DY School absence Complications Healthcare Resource use

3. Introduction

3.1 Background

Torus (buckle) fractures of the distal radius are the most common fractures in children. They result from trauma to growing bones and account for 500,000 UK emergency attendances annually[1].

Children's bones are very flexible compared with adult bones. In adults, a fracture leads to a complete disruption of the cortex of the bone, such that the broken bone is unstable and needs support from a cast or even surgical fixation. However, in children, the bones can 'buckle', such that there is deformation but no break in the cortex. Torus fractures are very low risk injuries for complications or deformity in the skeletally immature, and these fractures universally heal well[2].

There is considerable variation in the management of torus fractures. Treatment varies from the use of a removable rigid splint, to plaster cast immobilisation, to more flexible splints. The variation in practice has arisen from a longstanding taught doctrine of rigid immobilisation for fractures[3], tempered with newer evidence to suggest that simpler treatment methods are frequently as effective or perhaps even more effective[4-8]. The proponents of rigid forms of immobilisation (i.e. cast/ splint) argue that this maximises pain relief, and minimises the occurrence of complications, i.e. refracture. However, there is growing evidence to support the absence of complications with growing acceptance that rigid immobilisation may not improve pain control but will unduly restrict function, and that patients may safely be discharged at diagnosis[5,9]. Two systematic reviews support the abandonment of non-removable rigid casts in favour of splints removable at home[10,11].

The recent NICE non-complex fracture guidelines made recommendations on the management of these injuries[1]. The interventions considered as part of this review were non-removable rigid casts (i.e. fibreglass/ plaster of paris), soft casts, removable splints (removable half casts or manufactured wrist splints) and bandaging. The review focused on the outcomes of pain, return to normal activities, convenience and adverse outcomes. Overall the NICE review group concluded that bandaging was probably the optimal treatment approach, due the convenience, adequate pain control and the ability to promote early function. The NICE review concluded that torus fractures of the distal radius should not be immobilised in a non-removable rigid cast, and advocated discharge from the emergency department without a subsequent need for outpatient follow-up. NICE recommended that bandaging or soft casts should be the mainstay of treatment for torus fractures, but questioned whether any intervention was necessary at all. The guidelines were promoted widely through the 'Choosing Wisely Campaign' from the Academy of Medical Royal Colleges, which highlighted that non-removable rigid plaster casts bring little or no patient benefit, with thousands of unnecessary follow-up appointments[12]. NICE subsequently recommended a trial to determine the optimal intervention for torus fractures as one of the five research priorities within the non-complex fracture review, particularly addressing whether no immobilisation was as efficacious as splinting.

The best evidence for minimal immobilisation for the treatment torus fractures of the distal radius comes from the use of soft bandaging, in two small low-quality randomised trials comparing soft bandaging to rigid plaster casts[13,14]. These trials identified improved pain, improved function, less school absence and better convenience with bandaging, although there was a degree of parental anxiety about not using a splint/cast to treat a broken bone. There have been no trials comparing removable rigid splints to bandage treatment. The use of bandages has been trialled in a robust study amongst children with more severe wrist fractures (greenstick fractures)[15]. This trial compared soft bandaging to rigid casts, demonstrating that return to normal activities was faster amongst children for whom a soft bandage was used, with pain scores worse; yet of marginal clinical significance.

To summarise, there are several options for the treatment of torus fractures of the distal radius, with key differences relating to the degree of immobilisation provided, and the follow-up required. Non-removable rigid casts are no longer recommended for the treatment of these injuries. Removable splints immobilise the wrist and may provide the best pain relief. Soft bandaging restricts movement the least and may promote early function, but concern remains about pain and the potential for complications, despite evidence to the contrary. We therefore propose a trial of soft bandage versus immobilisation with a splint as per current practice.

Current Practice

As part of the feasibility work for the proposed trial, a telephone survey of Accident and Emergency departments treating children was conducted to ascertain current practice. A clinician (emergency nurse practitioner, registrar or consultant) provided information in 100 UK Emergency Departments regarding their current protocol concerning torus fractures. Amongst these units, a manufactured removable splint was used in 54 centres, a removable half-cast in 41 centres and a soft-cast in 5 centres. Follow-up and/or repeated X-ray imaging in an orthopaedic department was used in 60 of the 100 centres. No centres used a bandage as treatment for this injury.

Why is this important?

Given the very large number of these injuries, identifying the optimal treatment strategy could have profound effects on childhood pain, school absences and cost to the NHS. Even apparently minor modifications in the care pathway of a very common fracture, such as discontinuing the use of manufactured wrist-splints (approx. £3-9 per splint) could have very large financial implications across the NHS (e.g. £1.5 - £4.5m annual saving for discontinuing the use of wrist splints alone). A multicentre trial is likely to have wider financial benefits by promoting best practice across the NHS, such as reducing the reliance on follow-up outpatient visits and follow-up radiographs.Given the high annual incidence of these fractures, coupled with the recommendation from NICE of a trial and uncertainty around the optimal method of treatment we propose:

A multi-centre prospective randomised equivalence trial of a soft bandage and immediate discharge, versus current treatment with rigid splint immobilisation for torus fractures of the distal radius in children

4. Trial design

4.1 Trial summary

The proposed project is a two-phased study. Phase 1 (Internal Pilot) will confirm the expected rate of recruitment in a large-scale multi-centre randomised controlled trial. Phase 2 (Main phase) will be the proposed randomised controlled trial in a minimum of 10 centres treating children's fractures across the UK.

Internal Pilot

The internal pilot will take place at 6 centres over a period of 6 months. The aim of this initial phase will be to determine the number of eligible and recruited patients in the centres over the course of 6 months as well as optimise the electronic data collection procedures. Screening logs will be kept at each site to record children presenting with an undisplaced wrist fracture, to determine the number of patients assessed for eligibility and reasons for any exclusion. In addition, the number of eligible and recruited patients, and the number of patients who decline consent/withdraw, will be recorded.

The Data Safety and Monitoring Committee (DSMC) will make a recommendation to the Trial Steering Committee (TSC) regarding trial continuation in the event that the recruitment target for the internal pilot is not met. If the trial is stopped, then all trial patients will be followed up per protocol. If the trial continues into the main phase, patients from the internal pilot will be included in the final analysis.

Main RCT

The main trial will be recruiting from a minimum of 10 centres treating children's fractures across the UK.

Trial Structure

All children presenting at trial centres with an acute torus fracture of the distal radius are potentially eligible to take part in the trial. After consent has been gained, a local research associate will collect baseline demographic data, pain-intensity using the Wong-Baker FACES Pain Scale, Patient Report Outcomes Measurement System (PROMIS) Upper Extremity Score for Children and health-related quality of life using the EQ-5DY.

A randomisation sequence, stratified by centre and age group (4-7 years and ≥8 years) will be produced by the trial statistician and administered online. Each patient will be randomly allocated (1:1) to either a regimen of a soft bandage and immediate discharge, or rigid immobilisation (as per current practice at the treating centre) and follow-up as per current practice at the treating centre.

4.2 Objectives

The aim of this pragmatic randomised controlled trial is to evaluate the clinical and cost-effectiveness of soft bandage immobilisation and immediate discharge, compared to rigid splint immobilisation and follow-up as per the protocol of the treating centre, for the treatment of torus fractures of the distal radius in children.

The primary objective is:

To quantify and draw inferences on observed differences in the Wong-Baker FACES Pain Rating Scale between soft bandage and immediate discharge versus rigid immobilisation and standard follow-up, at three days post randomisation.

The secondary objectives are:

1. To assess differences in the Wong-Baker FACES Pain Rating Scale between trial treatment groups at 1 day, 7 days, 3 weeks and 6 weeks post randomisation

2. To determine differences in the use of regular analgesia between trial treatment groups at 1 day, 3 days and 7 days post randomisation.

1. To quantify and draw inferences on functional recovery using the Patient Report Outcomes Measurement System (PROMIS) Upper Extremity Limb Score for Children Computer Adaptive Test (a validated measure of childhood upper limb function) between the trial treatment groups at 3 days, 7 days, 3 weeks and 6 weeks post randomisation

3. To quantify and draw inferences on observed differences in the EQ-5DY (a validated assessment of Health-related Quality of Life) between trial treatment groups at 3 days, 7 days, 3 weeks and 6 weeks post randomisation.

4. To determine differences in the number of days of school absence between trial treatment groups up to 6 weeks post randomisation.

5. To determine differences in the complication rate between trial treatment groups, including the need for further hospital attendance up to 6 weeks post-randomisation.

6. To investigate, using appropriate statistical and economic analysis methods, the resource use, and comparative cost effectiveness between trial treatment groups at 3 and 6 weeks post randomisation.

4.3 Outcome measures

The primary outcome measure for this study is the ***Wong-Baker FACES Pain Rating Scale***[16]***.*** This is a validated self-reported tool. It is an ordinal assessment of pain using a series of six facial-expressions to illustrate the degree of pain intensity. A numerical rating is assigned to each face (from 0, "no hurt" to 10, "hurts worst"). It has been validated for use amongst children over 3 years old, including in the paediatric emergency department[17]; with its use being most established from 5 years-old[4,18]. It has been identified to be an excellent measure of pain when estimating the effect of treatment interventions in the emergency department, and it highly correlated to the visual analogue scale ($r=0.90$ $p<0.001$)[17]. Test-retest reliability is excellent, $r=0.90$, $p<0.001$[19]. Wong-Baker scale is widely used in clinical practice, forming part of the Royal College of Emergency Medicine 'Composite tool for the assessment of pain in children' produced in 2013 as part of a best practice guideline[20], and was recently specifically highlighted for use by the NICE major trauma guidelines[21].

The secondary outcome measures in this trial are:

Functional Recovery - Patient Report Outcomes Measurement System (PROMIS Bank v2.0) Upper Extremity Score for Children Computer Adaptive Test (CAT) – PROMIS is a collection of patient-reported health status tools available for children and adults that were developed to be disease nonspecific in collaboration with the US National Institute for Health[22,23]. These tools can be administered to healthy children as well as to children with a variety of chronic health conditions. They are, self-reported from 8-years old, and proxy-reported below 8-years. The PROMIS Pediatric item banks were developed using a strategic item generation methodology adopted by the PROMIS Network utilising item response theory. Field-testing occurred among 4129 children aged 8 to 17 years old[24]. All raw scores generated from PROMIS instruments are translated into standardized T scores with a population mean of 50 and an SD of 10. The population mean refers to the mean of the calibration sample, which, for paediatric and parent proxy instruments, is composed of a higher percentage of patients with chronic illness. Lower T scores indicate a worse outcome in the remaining domains: mobility, peer relationships, and upper-extremity function. PROMIS is available in full (30 questions), short-form (8 questions) or as a computer adaptive test "CAT" (average 8-questions). A CAT enables the answer from one question to inform the choice of the next so each child completing a CAT could answer a distinct set of questions to arrive at their score.

The PROMIS Upper Extremity Score for Children is a tool that measures the functional recovery of upper limb function. It has been demonstrated to have convergent validity with other tests used in the assessment of arm function in children with congenital limb abnormalities[25]. Disabilities of the Arm Shoulder and Hand Score (DASH $r=0.80$ $p<0.001$) and Pediatric Outcomes Data Collection Instrument ($r=0.70$ $p<0.001$) (DASH is an adult measure of upper limb function with items of limited relevance to children, and PODCI is a general measure of disability). PROMIS Upper Extremity Score for Children also correlates better than other measures to physiological tests of upper limb function (Grip Strength and Pinch Strength $r>0.6$ $p<0.05$). In the congenital limb population the PROMIS test was also the only tool without ceiling effects (when using the computer adaptive test but not a short form). The PROMIS Upper Extremity Score for Children appears to be the best tool to assess functional recovery in this group of patients. There is now agreement from an international group planning multicentre paediatric orthopaedic trials (IMPACCT), that the PROMIS Upper Extremity Tool is the preferred outcome to assess upper limb function in children.

Analgesia Use - It is established that the analgesia used in the management of torus fractures are simple over-the-counter medications; paracetamol and ibuprofen. Patients are typically asked to purchase these over-the-counter, or out of daytime hours may be given a short supply. Information concerning the use of analgesia will be sought at a binary level to their use in the last 24 hours.

Quality of life - **EQ-5D-Y**; This is the youth version of the EQ-5D-3L, which is a validated, generalised, health related quality of life questionnaire consisting of 5 domains related to daily activities with a 3-level answer possibility. EQ-5D-Y has been especially adapted in terms of language for children from 8–18 years[26,27]. A proxy version is available for younger children. Its age appropriateness in terms of feasibility, reliability and validity in children and adolescents has been established[27]. There is currently ongoing work, to produce EQ-5D-Y value sets for use in children and adolescents. Our

interim solution is to apply adult EQ-5D value sets to the EQ-5D-Y classification, but to use the EQ-5D-Y valuation system if ready before the FORCE trial is complete.

Days of Absence from school/childcare – School absence, due to injury, will be recorded.

Complications - All complications will be recorded. Particular note will be made of hospital re-attendance for any reason including inadequate analgesia, refracture or worsening of the fracture.

Healthcare Utilisation – This will be monitored for the economic analysis. Unit cost data will be obtained from national databases such as the BNF and PSSRU Costs of Health and Social Care. Where these are not available the unit cost will be estimated in consultation with the Oxford University Hospitals finance department. NHS costs and patients' parents out-of-pocket expenses will be recorded via a short questionnaire which will be administered at three and six weeks post injury.

Throughout the internal pilot phase, completion rates of outcome measures will be carefully monitored. A review of these rates will be discussed by the trial management group on a monthly basis, with potential interventions, such as paper CRF's or reminder phone calls, discussed and implemented prior to the start of the main RCT recruitment phase.

Data Collection.

The parent/guardian and/or child (for children over the age of 12 with parents' agreement) will be prompted to complete the questionnaires with, or on behalf of, the child at day 1, day 3, day 7, 3 weeks and 6 weeks. A direct link to the on-line questionnaire will be sent via a text message or email. If the parent/guardian and/or child have not responded to the initial and reminder messages within a specified timeframe (the time allowed will vary for each of the time points), we will attempt to call the parent/guardian to obtain the outcome data for the time point over the telephone. Exact timelines and frequency of phone calls will be specified in the data management plan for this trial.

Once the final questionnaire is completed, a £10 gift voucher will be offered as compensation for any costs (i.e. mobile phone data) incurred whilst completing the outcome measure assessments.

TIME POINT	**Data COLLECTION**
Baseline	Wong-Baker scale, PROMIS Upper Extremity for Children CAT and EQ-5DY.
1 day [CRF via text message/email/telephone]	Wong-Baker scale and Use of Analgesia (Y/N)
3 days [CRF via text message/email/telephone]	Wong-Baker scale ***(primary outcome)***, PROMIS CAT, Use of immobilisation (Y/N), Use of Analgesia (Y/N), EQ-5DY.

7 days [CRF via text message/email/telephone]	Wong-Baker scale, Use of immobilisation (Y/N), Use of Analgesia (Y/N), PROMIS CAT and EQ-5DY.
21 days [CRF via text message/email/telephone]	Wong-Baker scale, Use of immobilisation (Y/N), Days of school absence, PROMIS CAT, EQ5DY and Economics questionnaire.
6 weeks [CRF via text message/email/telephone]	Wong-Baker scale, PROMIS CAT, EQ5DY, Days of school absence, and Economics questionnaire

Table 1 Data collection time points

4.4 Sample size

The primary outcome is the 6-point Wong-Baker FACES Pain Rating Scale (Wong-Baker scale) at 3 days, a validated scale for self-reporting pain in children that is preferred by children[18]. The Wong-Baker scale has a minimally clinical important difference (MCID) of 1 face, which was determined in the setting of the paediatric emergency department[17]. The Wong-Baker scale demonstrates a very high correlation with the VAS, with each face corresponded to approximately 17mm on the VAS and a clinically important difference in pain[17]. Each face equates to 2 points on the 6-category Wong-Baker scale. This trial will demonstrate equivalence of a soft-bandage to rigid immobilisation assessing the difference in means on the Wong-Baker scale at 3-days post randomisation. Assuming an equivalence margin of 1 point (half the MCID), 90% power, 1-sided 2.5% significance and assuming that the standard deviation is 2.3 (based on results from a feasibility study) 278 patients would be required to show equivalence. Allowing 20% loss to follow-up inflates this to 348 (174 per arm).

Consideration must also be made of the fact that Wong-Baker scale is a categorical outcome that may behave non-linearly in some instances (i.e. the magnitude of pain within the intervals is not uniform), with non-linearity most likely in younger age-groups, tending to linearity in those over 8-years old[28]. We therefore have powered the trial for equivalence separately in the two subpopulations (<8 and ≥8years), which is also important for secondary outcomes.

We plan on recruiting a minimum of 696 patients, a minimum of 348 in the 4-7 year age group and a minimum of 348 in the 8-15 age group. (PASS 13 Power Analysis and Sample Size Software (2014). NCSS, LLC. Kaysville, Utah, USA, ncss.com/software/pass).

4.5 Methodology

4.5.1 Eligibility

Patients will be eligible for this study if:

- There is radiographic evidence of a torus fracture of the distal radius whereby there is a cortical deformation within the distal third of the radius but no break in the cortex. These may be associated with an ipsilateral fracture to the ulna (the ulna fracture may be buckle, greenstick or otherwise).
- They are aged 4 to 15 years old inclusive.

- Randomisation must occur at the site able to definitively treat the injury (i.e. a centre able to take the decision regarding the definitive treatment approach, which will typically be the emergency department).

Patients will be excluded from participation in this study if:

- The injury is more than 36 hours old.
- The treating clinician judges that there is a cortical disruption of the radius on radiographs (i.e. a greenstick fracture).
- They have sustained an additional fracture at the time of the index fracture (with the exception of ipsilateral ulna fractures)
- There is evidence that the patient and/or parent/guardian would be unable to adhere to trial procedures or complete follow-up, such as insufficient English language comprehension, developmental delay or a developmental abnormality or no access by parents to a mobile telephone with internet access.

4.5.2 Recruitment and consenting

We recognise that, unlike amongst adults, there is a very large seasonal variation in fractures in children. Approximately three times more fractures are seen in mid-summer compared to mid-winter, with weather significantly influencing the incidence of fractures – correlating with time spent playing outside[29]. The expected recruitment rate will be adapted to accommodate this large seasonal variation. We anticipate achieving a conservative rate of 10 patients per month per centre over a one-year period. Hospitals identified to be recruiting sites for this study have between 200 and 400 eligible cases per year. Recruitment rates in similar studies have shown to be as high as 85%. We have opted for a more conservative rate of 50%.

During the 6 months internal pilot phase between Nov '18 and April '19, we expect recruitment rates to vary between 3 and 8 patients/centre/month (Winter months with fewer fractures). We expect that between 120 and 140 patients will be recruited from the 6 pilot centres. If less than target recruitment rates are achieved in this internal pilot phase the DSMC will provide the TSC with a recommendation with regards the continuation of the study.

Following the internal pilot phase, the recruitment rate will increase to between 12 and 15 patients/centre/month (Summer months with increased number of fractures). A further 4-6 sites will be enrolled with recruitment being completed within a further 12-14 months.

Informed consent will be obtained by the local research associate. A member of the clinical team will approach the patient and their parent/guardian initially about the study. If the patient/parent/guardian is interested they will be introduced to the research associate assigned to the study. The research associate will present the patient with the age-appropriate Participant Information Sheet or online study information (as per cluster randomisation of the site, set out in Appendix 01) and verbal explanation of the trial procedures. The patient/parent/guardian will then be given the opportunity to discuss any issues related to the trial with the research associate and members of their family and friends. The parent/guardian will then be asked to sign an electronic informed consent form, and children from 8 years will be

invited to sign an electronic assent form. Assent should be taken where appropriate, however the absence of assent does not exclude the patient from the study if consent has been obtained from the parent/ legal representative. If a child indicates dissent or indicates they do not what to take part, the child will not be included in the study.

Any new information that arises during the trial that may affect participants' willingness to take part will be reviewed by the Trial Steering Committee; if necessary this will be communicated to all participants by the Trial Coordinator. A revised consent form will be completed if necessary.

4.5.3 Trial ID

When a patient is randomised, sufficient non-identifiable details will be logged prior to treatment, by the clinical team using a secure, encrypted, web-based system, provided by the Oxford Clinical Trials Research Unit (OCTRU). Basic information including the patient initials, age and eligibility checks will be entered. The patient will then receive a trial ID that will be used on all relevant and non-public facing trial documentation.

4.5.4 Randomisation

The patient will be randomised after consent. All hospital treatment areas have access to the internet so will access the randomisation service in real time i.e. there will be no delay in patient treatment.

Consented participants will be randomised to one of two intervention groups (1:1) using a computer randomisation service provided by OCTRU. Randomisation allocation will be implemented using stratification by centre and age (4-7 years, ≥8 years) with randomisation schedules prepared by the trial statistician and embedded in the online system.

Stratification by centre will help to ensure that any clustering effect related to the centre will be equally distributed in the trial arms. The catchment area (the local population served by the hospital) will be similar for all of the hospitals; each hospital being a children's injury unit dealing with these fractures on a daily basis. All of the recruiting hospitals, and indeed all hospitals throughout the NHS, use these techniques as part of their normal practice i.e. staff will already be equally familiar with both forms of treatment. This cannot eliminate the *clinician-specific effect* of an individual at any one centre[30]. However, since the procedures are commonplace across the NHS, many clinicians will be involved in the management of this group of patients; likely between 20 and 50 clinicians at each centre, including consultants, trainees and specialist nurses. Therefore, we anticipate that each individual clinician will only treat a handful of those enrolled in the trial, reducing the risk of a clinician-specific effect upon the outcome in any one centre.

Stratification by age will ensure that the treatments are balanced across the age groups. This will take into account differences in the properties of the primary outcome by age, with the score tending to linearity in those around 8-years onwards, but behaving non-linear for those under 8-years[28]. Furthermore there is a discontinuity within the secondary outcome instruments, i.e. self-reports ≥8 years old, and proxy-reports <8 years old for secondary outcomes. The trial therefore considers children <8 years, separately to those ≥8 years to ensure the maximum validity of the result generated, and to maximise the generalisability of the trial results.

4.5.5 Pre and Post randomisation withdrawals/exclusions

Participants (or their parents/guardians) may decline to continue to take part in the trial at any time without prejudice. A decision to decline consent or withdraw will not affect the standard of care the patient receives. Participants (or their parents/guardians) can withdraw by contacting the research team by telephone or e-mail. Upon withdrawal of the patient, any data collected up until the time of withdrawal will be retained by the research team and included in the final analysis. Contact details for these patients will be destroyed. Withdrawn patients or patients deemed ineligible after consent will not be replaced.

4.5.6 Blinding

Patients and their parents/guardians cannot be blinded to their treatment. The treating clinician will of course, not be blinded to the treatment they are providing. However, the treating clinical team will take no part in the follow-up assessment of the patients. The outcome data will be collected directly from the patient and/or their parents/guardians. Outcome assessors will be blinded to the participant's treatment allocation.

4.6 Technologies assessed

All of the hospitals involved in this trial are familiar with both treatment techniques. All of the patients will receive analgesia at the discretion of the treating clinician as per local guidelines. In the absence of local guidelines, clinicians should adhere to the Royal College of Emergency Medicine best practice guidelines for the management of acute pain in children[20].

This trial will compare two approaches to treat torus fractures of the distal radius in children.

4.6.1 Soft bandage immobilisation and immediate discharge

A simple bandage, such as a gauze bandage or similar, will be offered to participants. The use/discontinuation of the bandage will be at the discretion of the child and their parents. The bandage technique involves application to the wrist from the middle of the forearm to the level of the metacarpophalangeal joints. Patients will be discharged from the emergency department, after randomisation, without the need for outpatient follow-up (as per NICE guidance). It will be advised that the child may return to activities as pain allows, a point of contact for any ongoing concern will be provided and no specific restrictions are in place. It will be advised that the bandage should not be worn for more than 3 weeks.

4.6.2 Rigid splint immobilisation

A rigid splint will be applied that is either manufactured to conform to the wrist (e.g. futura splints), or is moulded onto the wrist (i.e. backslab). The study is pragmatic and the exact type of splint will not be prescribed to treating clinicians. A record will be made of the type of splint used. Treatment advice and follow-up will be as per the usual practice of the treating centre.

4.6.3 Rehabilitation

Physiotherapy does not typically form a part in the management of these injuries, and no specific guidelines will be offered to clinicians or patients.

4.7 Complications and Serious Adverse Event management

Serious adverse events are defined as any *untoward and unexpected medical occurrence that: 'Results in death'*, '*Is life-threatening'*, '*Requires hospitalisation or prolongation of existing inpatients´ hospitalisation'*, '*Results in persistent or significant disability or incapacity'*, '*Is a congenital anomaly or birth defect' or 'any other important medical condition which, although not included in the above, may require medical or surgical intervention to prevent one of the outcomes listed'*.

All serious adverse events (SAE) will be directly entered onto the electronic Serious Adverse Event reporting form and the central research team will be notified by email within 24 hours of the investigator becoming aware of the event. Once notified, causality and expectedness will be confirmed by the Chief Investigator or trial nominated clinician. SAEs that are deemed to be unexpected and related to the trial will be notified to the Research Ethics Committee (REC) within 15 days. All such events will be reported to the TSC and DSMC at their next meetings. All participants experiencing SAEs will be followed-up as per protocol until the end of the trial.

Complications that are foreseeable in the treatment of torus fractures do not need to be reported immediately, provided they are recorded in the 'Complications' section of the Case Report Forms and/or Patient Questionnaires. For this trial, such an event is recall to hospital outpatient/emergency department with a diagnosis of an alternative fracture pattern, or a worsening fracture deformity (+/- the need for differing inpatient or outpatient treatment).

4.8 End of trial

The end of the trial will be defined as the collection/receipt of the last follow-up questionnaire from the last participant.

5. Data Management

The Case Report Forms will be designed by the trial coordinator in conjunction with the trial management team. Patients will be asked to provide their contact details as well as the contact details of up to two alternative friends or family members. Experience from numerous orthopaedic trauma trials has highlighted that collection of this additional data reduces loss to follow-up substantially.

Data will be collected in electronic format from participants with direct entry onto the trial database, including the collection of documentary evidence of consent and assent. Electronic data collection has the major advantage of building "data logic" into forms, minimising missing data, data input errors and ensuring the completeness of consent and assent forms. All data entered will be encrypted in transit between the client and server. All electronic patient-identifiable information will be held on a server located in an access controlled server room at the University of Oxford. The data will be entered into a GCP compliant data collection system and stored in a database on the secure server, accessible only to the research team based on their role within the study. The database and server are backed up to a secure location on a regular basis.

Details of the data collected, where it is stored and who has access to it along with a fair processing statement will be available for the public to see on the study website.

Paper forms with patient-identifiable information will be held in secure, locked filing cabinets within a restricted area. The patient-identifiable data will be kept separately from the outcome data obtained from/about the patients (both paper and electronic). Patients will be identified by a trial ID only. Direct access to source data/documents will be required for trial-related monitoring and/or audit by the Sponsor, NHS Trust or regulatory authorities as required. All paper and electronic data will be retained for at least one year after completion of the trial and Consent/Assent forms will be kept until the youngest participant reaches 21 years of age.

The trial will be reported in line with the CONSORT statement.

5.1 Statistical Analysis

A separate statistical analysis plan (SAP) with full details of all statistical analyses planned for the data of this study will be drafted early in the trial and finalised prior to any primary outcome analysis. The SAP will be reviewed and will receive input from the TSC and DSMC.

Any changes or deviations from the original SAP will be described and justified in the protocol, final report and/or publications, as appropriate. It is anticipated that all statistical analysis will be undertaken using Stata (StataCorp LP, www.stata.com) or other well-validated statistical packages.

In equivalence trials a maximum clinical difference (ΔT) is pre-specified at a level within which the two treatments can be considered not to differ in any clinically meaningful way. Therefore the null hypothesis is that the difference is greater than ΔT exists in either direction, H0: $\Delta \leq -\Delta T$ or $\Delta \geq \Delta T$ and the trial is targeted to disprove this in favour of the alternative that no clinical difference exists, HA: $-\Delta T < \Delta < \Delta T$.

All analyses will be carried out on the intention-to-treat population (that is all patients will be analysed in the group they were randomised to regardless of actual treatment received). Analyses will be repeated for the per protocol population (patients excluded from the per-protocol population will be pre-specified in the SAP) and only if both results from the intent-to-treat and per protocol analysis show equivalence will equivalence be claimed[31,32].

The results of the analysis of the primary outcome should be one of the following:

- The confidence interval for the difference of the two treatment lies entirely within the equivalence range, -ΔT to ΔT, so that equivalence may be concluded with only a small probability of error.
- The confidence interval covers at least some points that lie outside the equivalence range, so that differences of potential clinical importance remain a real possibility and equivalence cannot be safely concluded.
- The confidence interval lies wholly outside the equivalence range (though this is unlikely in this context)

As well as assessing both intent to treat and per protocol analyses, if equivalence is demonstrated this will also form part of an additional sensitivity analysis to assess the range of potential biases that could have results from loss to follow-up, protocol deviations and withdrawal.

Standard descriptive statistics will be used to describe the demographics between the treatment groups reporting means and standard deviations or medians and interquartile ranges as appropriate for continuous variables and numbers and percentages for binary and categorical variables. All comparative outcomes will be presented as summary statistics and reported together with 95% confidence intervals and all tests will be carried out at a 5% two-sided significance level.

The Wong-Baker Scale at 3-days post-randomisation is the primary outcome of the study and will be compared between treatment groups as the dependent variable in a multivariable linear regression model, including all patients, adjusting for the stratification factors. An unadjusted t-test will also be undertaken. Separate analyses of patients in the two subpopulations will be undertaken (<8 and ≥8years) using the same methodology. Additional analyses utilizing all the time-points using multi-level modeling will also be undertaken for completeness. EQ-5D-Y is an important secondary outcome, though the development of 'value sets' for use in children and adolescents is ongoing. Our interim solution is to apply adult EQ-5D value sets to the EQ-5D-Y classification, but to use the EQ-5D-Y valuation system if ready before the FORCE trial is complete.

5.2 Economic evaluation

An economic evaluation will be conducted as part of the trial design to estimate the cost-effectiveness. The average staff time and time to deliver the rigid immobilisation and soft bandage treatment will recorded at each centre, as well as other materials, and consumables involved. Data will be collected on the health service resources used in the treatment of each trial participant during the period between randomisation and 6 weeks post-randomisation. At 3 and 6 weeks post-randomisation, parents/guardians will be asked to complete economic questionnaires profiling their child's hospital (inpatient and outpatient) and community health resource use and as well as their own out-of-pocket expenditures and costs associated with their lost productivity. Unit cost data will be obtained from national databases such as the BNF and PSSRU Costs of Health and Social Care[33] .

Health related quality of life will be estimated using the EuroQol EQ-5D-Y[26,27]. Responses to the EQ-5D will be converted into health preference scores using established methods[34,35].

Missing data will be explored and managed using similar methods to the main statistical analysis. A within-trial evaluation will be conducted from a UK NHS and Personal Social Services perspective[36] using the FORCE trial data. An incremental cost-effectiveness analysis, expressed in terms of incremental cost per quality-adjusted life year (QALY) gained will be performed using bivariable regression. Results will be presented using incremental cost-effectiveness ratios (ICERs), net benefit and value of information. Further, sensitivity analyses will consider the broader issue of the generalisability of the study results, including a broader societal perspective to include out-off pocket expenses borne by participants' parents, informal care provided by family and friends and parents' income loss.

6. Trial Oversight

The trial will be conducted in accordance with the Medical Research Council's Good Clinical Practice (MRC GCP) principles and guidelines, the Declaration of Helsinki, Oxford Clinical Trials Research Unit SOPs, relevant UK legislation and this Protocol. GCP-trained personnel will conduct the trial.

The day-to-day management of the trial will be the responsibility of the Trial Manager, supported by the OCTRU administrative staff. This will be overseen by the Trial Management Group, who will meet monthly to assess progress. It will also be the responsibility of the Trial Manager to undertake training of the research staff at each of the trial centres. The trial statistician, health economist and the information specialist will be closely involved in setting up data capture systems, design of databases and clinical reporting forms. A TSC and a DSMC will be set up.

6.1 Trial Supervision

Day-to-day management of the trial will be overseen by a Trial Management Group which is made up of the Investigators listed in Section 1 and staff working on the project within OCTRU. A TSC -with an independent Chairperson - and DSMC will be set up.

The TSC, which includes independent members provides overall supervision of the trial on behalf of the funder. Its terms of reference will be agreed with the HTA and will be drawn up in a TSC charter which will outline its roles and responsibilities. Meetings of the TSC will take place at least once a year during the recruitment period.

An outline of the remit of the TSC is to:

- monitor and supervise the progress of the trial towards its interim and overall objectives
- review at regular intervals relevant information from other sources
- consider the recommendations of the DSMC
- inform the funding body on the progress of the trial.

The DSMC is a group of independent experts external to the trial who assess the progress, conduct, participant safety and, if required critical endpoints of a clinical trial.

The study DSMC will adopt a DAMOCLES charter which defines its terms of reference and operation in relation to oversight of the trial. They will not be asked to perform any formal interim analyses of effectiveness. They will, however, review accruing data, summaries of the data presented by treatment group, and will assess the screening algorithm against the eligibility criteria. They will also consider emerging evidence from other related trials or research and review related SAEs that have been reported. They may advise the chair of the Trial Steering Committee at any time if, in their view, the trial should be stopped for ethical reasons, including concerns about participant safety. DSMC meetings will be held at least annually during the recruitment phase of the study. Full details including names will be included in the DSMC charter.

6.2 Quality control

We will institute a rigorous programme of quality control. The research manager in conjunction with the trial coordinator will be responsible for ensuring adherence to the trial protocols at the

trial sites. Quality assurance checks will be undertaken by the CTU to ensure integrity of randomisation, study entry procedures and data collection. The CTU has a quality assurance manager who will monitor this trial by conducting regular (at least once in the lifetime of the study, more if deemed necessary) inspections of the Trial Master File. Furthermore the processes of consent taking, randomisation, registration, provision of information and provision of treatment will be monitored. Written reports will be produced for the TSC, informing them if any corrective action is required.

Additionally, the study may be monitored, or audited by sponsor or host sites in accordance with the current approved protocol, GCP, relevant regulations and standard operating procedures.

6.3 Funding

This study is funded by the National Institute for Health Research Health Technology Assessment (17/23/02).

6.4 Insurance and Indemnity Arrangements

The Sponsor has a specialist insurance policy in place - Newline Underwriting Management Ltd, at Lloyd's of London - which would operate in the event of any participant suffering harm as a result of their involvement in the research. Standard NHS cover for negligent harm is in place for NHS procedures. There will be no cover for non-negligent harm.

6.5 Ethical and Regulatory Consideration

6.5.1 Declaration of Helsinki

The Investigator will ensure that this study is conducted in accordance with the principles of the Declaration of Helsinki.

6.5.2 Guidelines for Good Clinical Practice

The Investigator will ensure that this study is conducted in accordance with relevant regulations and with Good Clinical Practice.

6.5.3 Approvals

The protocol, informed consent form assent form, participant information sheet and other study materials will be submitted to an appropriate Research Ethics Committee (REC), and HRA for written approval.

The Investigator will submit and, where necessary, obtain approval from the above parties for all substantial amendments to the original approved documents.

6.5.4 Reporting

The CI shall submit once a year throughout the study, or on request, an Annual Progress report to the REC Committee, HRA (where required) host organisation and Sponsor. In addition, an End of Study notification and final report will be submitted to the same parties.

6.5.5 Participant Confidentiality

The study staff will ensure that the participants' anonymity is maintained. The participants will be identified only by a participant ID number on all study documents and any electronic database, with the exception of the CRF, where participant initials may be added. All documents

will be stored securely and only accessible by study staff and authorised personnel. The study will comply with the General Data Protection Regulation (GDPR) and the Data Protection Act, which requires data to be de-identified as soon as it is practical to do so.

6.5.6 Expenses and Benefits

A £10 gift voucher will be offered for participation in the research project. These funds are offered to compensate for any cost and inconvenience participant families may have incurred by using their mobile phone or computer to complete the outcome measure assessments.

6.5.7 Ethical considerations

The two interventions used in this study are both standard clinical practice and currently offered to patients across the UK. As per recent NICE guidance, it is recommended that '*children with torus fractures are discharged after first assessment and advise parents and carers that further review is not usually needed*' [1]. The NICE guideline will be followed

amongst those allocated to a soft bandage, whilst participants allocated to rigid splints will be followed up according to the local policy of the treating hospital (be that following the NICE guideline or otherwise).

We are aware that being part of a study, particularly a study involving randomisation, may be a concern for some parents. We are working closely with the NIHR-funded TRECA (Trials Engagement in Children and Adolescents) team (University of York) who have a wealth of experience in the preparation of documentation presented to parents and children. In addition, the research associates at the recruiting sites have all got extensive experience in working with children and parents.

Recompense for data costs caused considerable debate amongst our PPI forum (through the NIHR Young Persons Advisory Group and Parents Advisory Group). It was recognised that cost may be a barrier to participation for some families (i.e. particularly those from more deprived groups, who frequently use pay-as-you-go data tariffs); whilst others believed that automatically offering recompense for participation would be a barrier to them – as they believed the NHS could ill-afford to make such payments. Agreement was therefore made to offer a payment of £10 to cover reasonable out of pocket expenses to rather than for this to be automatically provided. We have incorporated this approach in our trial.

Patient information leaflets have been written to include children aged 4-7 years old, above 8 years old and for parents/guardians. We discussed this in detail with the NIHR young persons advisory group (YPAG - who principally range in age between 11 and 17 years old), parents advisory group (PAG), health care professional and our PPI advisors (Phoebe Gibson and Jenny Preston (who leads PPI across NIHR CRN Child)). It was felt that a single leaflet would be appropriate for 'older' child to convey issues of assent and randomisation, as the study was relatively simple and language could be tailored to cover all children. We invited the YPAG children to dissect the adult PIS to identify sections that were relevant for them, and to review the final structure - they were clear that they wanted the PIS to include the core study details, but not the finer elements of data protection and GDPR. To ensure that older children have access to any further details that they may wish to read, we have added a statement to the older

child PIS to identify that "Further details of the study can be found in the adult version of the information leaflet given to your parent/guardian, and available online at www.forcestudy.org/info."

6.6 Dissemination

The study monograph will be prepared by the trial management team at the completion of the trial. No patient identifiable information will be contained in any form of dissemination of study results.

Dissemination will be via traditional and novel methods:

- Conference: Traditional conference dissemination will focus on presentations to include the key professional stakeholders (emergency medicine doctors, orthopaedic surgeons, emergency nurse practitioners and trainees in emergency medicine and orthopaedics).
- Publications: Key outputs will be published in high-impact journals with publicity sought in other professional journals (e.g. Pulse, HSJ, Nursing Times). We will ensure that plain English summaries are published alongside the full paper, along with links to other digital media on the trial website to explain the trial result in an accessible format – i.e. an explainer video and infographic. Given the frequency of the injury, this is also likely to be of interest to international press-outlets.
- Policy Makers: We will ensure the development of links with key organisations such as NICE, NHS Information Centre, NHS England and Quality Observatories to contribute to and capitalise on their networks. Most importantly the outputs will directly contribute to the NICE non-complex fracture guidelines, and will be directly relevant to the widely publicised Choosing Widely Campaign.
- Public Dissemination: To ensure a broad campaign we will target a range of social media outlets (e.g. twitter and blogs such as MumsNet) with the explainer video and infographic. We will seek to engage the NHS Dissemination centre, and seek to publish 'digital story' as part of the 'NIHR Signal'. Finally, will produce a Wikipedia page for this injury (currently absent) and update this with the trial result.

7. Project Timetable and Milestones

We propose a 2 year study starting in July 2018. The planned trial timetable is shown below, with key milestones indicated and responsible parties identified:

Month	By date	Activity	Milestone	Responsibility
-4-0		Ethic submission	REC approval	CI/RF
0-4	July 2018	Start Trial/ Appoint staff		CI
			1st TSC/DSMC meeting	CI/TM
		Finalise trial protocol	Protocol final version	TMG
	Oct 2018	Complete data capture systems	CRF final version	CI/TS/TM
5-8	Nov 2018	Open recruitment at internal pilot site 1+2	1st trial site online	TM/CI
	Dec 2018	Open recruitment at internal pilot site 3-6	4 pilot sites online	TM/CI
	April 2019	Finish internal pilot recruitment	14 centre months recruitment	TM/CI
			2nd TSC/DSMC meeting	
9-18	May 2019	Start staggered launch 2 centres/month		TM/CI
	July 2019	Complete site initiations	All 10 sites recruiting	TM/CI
	Jun 2020	End recruitment	696 patients enrolled	
19-20	Aug 2020	Complete 6 week follow-up all sites	Completed follow-up	
21-24	Oct 2020	Statistical analysis		TS
		Health economics analysis		HE
	Dec 2020	Data review all patients	DSMC report	DMEC via TSC to HTA
			Final TSC meeting	TSC
	Jan 2021	Final report HTA	HTA report	TMG

CI Chief Investigator, RF Research Fellow, TMG Trial Management Group, TM Trial Manager, TSC Trial Steering Committee, DSMC Data Safety and Monitoring Committee, TS Trial Statistician, HE Health Economist

8. Protocol Amendments:

Amendment No.	Protocol Version	Date issued	Author(s) of changes	Details of Changes made
2	2.0	09Jan2019	Daniel Perry, Louise Spoors, Juul Achten, Jackie Martin-Kerry	**4.3 Outcomes: School Absence –** added "School absence, due to injury, will be recorded." **4.5.1 Inclusion Criteria (and throughout) –** changed to "4- 15yrs." **4.5.1 Inclusion Criteria –**changed to "Mobile telephone with internet access." **4.5.2 Recruitment and Consenting -** A slight amendment and addition for clarification was required regarding child assent **4.5.5 Withdrawals –** amended as no longer patient facing **4.6.2 Rigid splint immobilisation –** the treatment advice has been clarified in line with the patient facing document **4.7 Adverse Events –** changed to "Complications and Serious Adverse Event Management". Adverse events were removed and these will be reported as complications in the case report forms. **5.2 Economic evaluation -** minor modification as required by the health economist **Protocol Amendment: Appendix 1 TRECA SWAT**

6	3.0	13Nov2019	Louise Spoors, Dan Perry, Juul Achten, Amrita Athwal	**1. Contact details –** update of trial management group members **4.5.2 Recruitment and consenting** – changed further recruitment period from 6-8 months to 12-14 months **7. Project Timetable and Milestones –** dates amended: End recruitment changed from Dec 2019 to Jun 2020, Complete follow-up changed from Feb 2020 to Aug 2020, Statistical and Health Economic Analysis changed from May 2020 to Oct 2020, Data review changed from Jun 2020 to Dec 2020 and Final HTA report changed from Jul 2020 to Jan 2021

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10. APPENDIX 01 – TRECA (TRials Engagement in Children and Adolescents) Study – SWAT ('Study Within A Trial') in FORCE study

Aims

The overarching aims of TRECA are to evaluate the impact of multimedia information resources (MMIs) on:

- trial recruitment and retention, and
- quality of decision-making about participation in healthcare trials involving children and adolescents.

Background and rationale

The effectiveness and safety of healthcare interventions is best determined through randomised controlled trials (RCTs) (1, 2). However, major barriers to the successful conduct and outcome of clinical trials are levels of recruitment and retention. In the UK, only a small proportion of trials actually recruit successfully to time and target (3). There is now international recognition of the importance of paediatric clinical trials to inform healthcare decisions for children and adolescents (4, 5). High quality trials involving children are essential to ensure that medication and treatments used in children are effective and safe (4, 6).

A potential barrier to recruitment and retention is the information provided to potential trial participants (1). How children and parents make decisions regarding participation in research and what information is important to them, both remain areas of uncertainty (7, 8). Conventionally, participant information about a trial is provided in printed form. These documents should be understandable to potential trial participants and assist their decision-making (9). However, the format of this information has received recurrent criticism, notably for being too long, difficult and technical (10-13). Furthermore, the content of trial sheets is mostly guided by regulatory agencies and can be inconsistent with what patients want to know (8, 10, 14). A number of studies report that trial participants do not understand information contained within participant information sheets (15) and that the information can be very wordy and overwhelming (10, 16). Potential participants who have lower levels of literacy are most likely to be affected by this (17). Furthermore, good graphic design is often lacking in participant information sheets, such as a structure that aids navigation of the information, and visual appeal to invite and engage the reader. For example, written information should inform a decision about participation, but may act more as a prospectus for the trial and as a contract between researchers and the participant (18). Re-writing, redesigning and user testing of trial information can produce an understandable and preferred resource (19).

An alternative for providing information to potential trial participants is through the use of multimedia information (MMI) (17, 20, 21), such as a website that presents key information using a combination of video, animation, text and diagrams. However,

research is needed to identify and evaluate different ways of presenting multimedia to children and parents (10). Multimedia presentation can be understood through reading, listening and watching and allows people with different preferences to use the resource effectively (17). The FORCE study MMIs contain all information that would be found in the written participant information about the FORCE study, but will focus on information deemed important for children, adolescents and their parents when deciding whether to participate in a trial (8, 20). Information will be available through animation, video clips, pictures and written text.

Study design

Phase one of TRECA occurred in the preparatory stages, and informed the development of the materials used within the FORCE study SWAT (Study Within a Trial). Phase one involved participatory design with children and adolescents with long-term health conditions, their parents and clinicians involved in paediatric trials. Interviews were undertaken to identify the needs and preferences concerning information about trials and the way they would like this information presented. This has informed the development of the MMIs used within this SWAT. User testing was also undertaken to ensure that families could find information easily and understand the information.

Phase two of TRECA involves evaluating the MMIs in a series of embedded trials hosted within healthcare trials following the addition of host trial-specific content to the MMI. FORCE is one of six trials participating in the TRECA study. The MMIs will be tested for their impact on decisions about trial participation taken by children and adolescents and/or parents and behaviours (rates of recruitment to, and retention in, the host trials).

The FORCE study will use a cluster randomised design where recruiting sites will be randomised to use either conventional PIS or a MMI to provide information to potential participants of FORCE.

Patients

All patient approached for participation in FORCE will be eligible for inclusion in TRECA.

Consent

Within the overarching application for TRECA to the HRA, the sponsor (University of York) and research ethics committee (Yorkshire & The Humber – Bradford Leeds Research Ethics Committee ref: 17/YH/0082; IRAS ID 212761), agreed that informing and consenting patients/parents specifically about the collaboration with TRECA would be confusing and may overburden patients and parents with information. This could compromise the results of the study. The additional patient burden related to TRECA consists of one brief optional anonymous questionnaire. This was described as 'very minimal' input by the PPI members who reviewed this information. Anonymised FORCE data concerning recruitment and retention will be provided to the TRECA team to evaluate the efficacy of MMIs. Hence, patients/parents will not be specifically informed about their host trial's involvement in TRECA and will not be asked to provide specific consent for the TRECA aspects of the host trials.

Cluster randomisation and blinding

Sites were reviewed for variation in hospital type (teaching hospital status), expected recruitment rates and what the usual treatment was for minor fractures. Sites did not vary greatly in any of these aspects. Randomisation was undertaken using Microsoft Excel to determine which sites would be randomised to MMI and those randomised to PIS. Blinding of local site staff to the TRECA allocation is not possible due to the nature of the 'intervention'. Moreover, due to the way the regulatory system is set-up, with sites receiving information in relation to all study amendments, it is not possible to prevent site staff from becoming aware of the alternative mode of information delivery to the one they are allocated to. We recognise this to be a limiting factor. However, to mitigate this potentially confounding factor, we do not 'train' sites in the delivery of the alternative method, in fact we actively discourage them to review it in detail as it might affect the way they will deliver the trial information to patients.

The FORCE study is cluster randomised and patients will not be aware that an alternative method of information delivery will be used in other trial hospitals. Patients will therefore be blinded to the intervention.

MMI development

The MMI templates developed in Phase one of TRECA have been adapted to suit the FORCE study. The MMIs are based on information from the FORCE study participant information sheets (PIS). The MMIs also include generic animations that cover elements about trials, including:

- what is a trial?

- why do we do trials?
- who is in a research team
- assent and consent

In addition, the FORCE study MMIs have an explainer animation about the FORCE study on the front/home page of the MMIs. The idea is that this explainer covers the main features of the trial in approximately 60 seconds of animation.

MMI delivery

The FORCE MMIs will be presented by the research team member to individuals approached to participate in the FORCE study. This will be done using a dedicated tablet computer at each participating FORCE site using the MMIs. Recruiting researchers will provide the MMI in the same way that they use the PIS during discussions. Participants will also be able to access the MMIs at home (via smartphone, tablet or PC) and will be provided with the link to the relevant MMI to review after they have made a decision about whether to participate in the FORCE study.

MMIs will be version controlled as per any patient-facing document. All versions of the website (with version numbers) will be uploaded on the UK Web Archive curated by the British library in order to maintain copies of the website indefinitely.

Outcome measures

Objective measures are the rates of recruitment to, and retention in, each host trial. Quality of decision-making will also be assessed. The primary outcome for phase two of the TRECA study is the recruitment rate to each host trial.

For **recruitment,** this is defined as the proportion of patients who agreed to participate, from the total approached. For **retention,** this is derived from the number and timing of study drop outs, i.e. those who do not complete all follow up questionnaires.

The **quality of decision making** will be assessed through a questionnaire. Families will be asked to complete a brief decisional scale, adapted from one used within the REFORM trial (22) and drawing conceptually on the SURE (23) and DelibeRATE scales.

As far as possible, we aim to obtain decision quality scores both from individuals who decide to participate in the host trial and those who decline.

Data collection

Recruitment data

Data on recruitment to the host trial will be recorded automatically within the host trial dataset. In order to assess any potential moderating influences of other variables on the effectiveness of the MMIs, we will aim to obtain data within each host trial of children and adolescents' age, gender and Index of Multiple Deprivation (IMD) decile,

according to allocation in the TRECA interventions and to FORCE study participation decision.

Specifically the data requested by TRECA from the FORCE study will be anonymised data that includes for each patient:

- Screening ID and Participant ID (if patient consents)
- TRECA arm used at site
- Allocation within FORCE
- Age (years) and gender of child participant
- IMD decile (measure for socio-economic status)
- Retention in FORCE (whether completed final follow up questionnaire)

Decision-making questionnaires

All patients/parents who are approached for participation in the FORCE study will be given the decision-making questionnaire that is used across TRECA studies. Hard copy questionnaires will be provided to people approached to participate in FORCE, as soon as is practicable after their decision about whether to participate in FORCE has been made. Families will be asked to return the questionnaires by post in stamped self-addressed envelopes.

Analysis

The results from the FORCE study embedding the TRECA MMIs will be analysed. A joint FORCE and TRECA paper will be written based on these data and submitted to a peer-reviewed journal. It is anticipated that authors will comprise of key members of the FORCE management team and TRECA Study Advisory Group.

A meta-analysis of data from all six trials that embed TRECA will also be undertaken and submitted to a peer-reviewed journal to show overall impact of TRECA MMIs.

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