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Non operative treatment of children with appendicitis vs appendectomy – A feasibility study

Submission date 30/01/2017	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 08/02/2017	**Overall study status** Completed	
Last Edited 08/06/2023	**Condition category** Digestive System	

Plain English summary of protocol

Background and study aims
Acute appendicitis is a sudden, painful swelling of the appendix, and is the most common surgical emergency in children. People have around a 7-8% chance of developing appendicitis at some point in their lives and the most common age for appendicitis is in the early teens. An appendicectomy is considered the gold standard treatment for acute appendicitis by most surgeons and involves an operation to remove the appendix. Although appendicectomy is usually a simple procedure, it requires use of a general anaesthetic (medication to put patients to sleep during surgery) and there are other risks associated with surgery. Many parents find the idea that their child needs emergency surgery frightening and one they are keen to avoid if an alternative is available. An alternative approach to the treatment of children with acute appendicitis would be treatment with antibiotics. Whilst there is growing interest in the use of non-operative treatment with antibiotics, it is not yet known whether this approach is safe and effective. The aim of this study is to look at the feasibility of recruiting participants to take part in a study looking at the effectiveness and cost-effectiveness of non-operative treatment of acute appendicitis with antibiotics, to see if conducting a full scale study would be possible.

Who can participate?
Children aged 4-15 who have acute appendicitis.

What does the study involve?
Participants are randomly allocated to one of two groups. Those in the first group are treated with the current standard treatment which involves an operation to remove the appendix. Those in the second group are treated with antibiotics both through a drip and by mouth. Children in both groups are monitored closely during their time in hospital to make sure they are getting better. Once the doctors are happy with the patient's recovery and they are able to take fluid, food and painkillers by mouth, as well as move around, they are discharged home with any necessary information about appendicitis and their recovery. All patients attend three follow up appointments to ensure that they are healthy and not experiencing any issues. These appointments will take place six weeks, three months and six months after they are discharged from hosptial. At these visits and during the stay in hospital, parents are asked to fill in two short

questionnaires about their child's health status. Parents are also given the same questionnaires at discharge to fill in and return two weeks after they have gone home.

What are the possible benefits and risks of participating?
Participants who undergo surgery benefit from an improvement to their condition, as surgical removal of the appendix is the best known treatment for acute appendicitis. Having an operation will require general anaesthesia and involves a small number of risks related to surgery including bleeding, wound infection, a collection of pus in the abdomen, and in rare cases bowel obstruction requiring further surgery. There is also a 10% chance that the operation may show a healthy appendix, which means that the surgery was not necessary. In this case the appendix is removed anyway.
Participants treated with antibiotics benefit from avoiding surgery and the risks that it entails. If a child is treated with antibiotics, there is a small risk that the antibiotic treatment may not work. However, data collected on children with acute uncomplicated appendicitis who have been treated with antibiotics, suggest that it works in the majority of cases (97%). Children will be monitored closely whilst they are in hospital and if there is no improvement with antibiotic treatment, they will have an operation to remove the appendix. The other risk of antibiotic treatment is that the child will still have their appendix and may get appendicitis again. If this were to happen then they would have their appendix removed.

Where is the study run from?
1. Southampton Children's Hospital (UK)
2. St George's Hospital (UK)
3. Alder Hey Children's Hospital (UK)

When is the study starting and how long is it expected to run for?
July 2016 to October 2018

Who is funding the study?
National Institute for Health Research (UK)

Who is the main contact?
1. Miss Natalie Hutchings (public)
contract@soton.ac.uk
2. Mr Nigel Hall (scientific)
n.j.hall@soton.ac.uk

Study website
http://www.nets.nihr.ac.uk/projects/hta/1419290

Contact information

Type(s)
Public

Contact name
Miss Natalie Hutchings

Contact details
Southampton Clinical Trials Unit
Southampton General Hospital

Tremona Road
Southampton
United Kingdom
SO16 6YD
+44 23 8120 4128
contract@soton.ac.uk

Type(s)
Scientific

Contact name
Mr Nigel Hall

ORCID ID
http://orcid.org/0000-0001-8570-9374

Contact details
University Surgery Unit, MP 816
Southampton General Hospital
Southampton
United Kingdom
SO16 6YD
+44 23 8077 7222
n.j.hall@soton.ac.uk

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
32463

Study information

Scientific Title
The title given on the patient information sheet is: CONservative TReatment of Appendicitis in Children a randomised controlled Trial CONTRACT (Feasibility)

Acronym
CONTRACT

Study objectives
The aim of this study is to assess the feasibility of recruiting participants in order to inform the feasibility of a large randomised controlled trial looking at whether non-operative treatment of acute uncomplicated appendicitis in children is effective, and cost effective.

Ethics approval required
Old ethics approval format

Ethics approval(s)
South Central – Hampshire A Research Ethics Committee, 22/11/2016, ref: 16/SC/0596

Study design
Randomised; Interventional; Design type: Treatment, Drug, Management of Care, Surgery, Active Monitoring

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Specialty: Children, Primary sub-specialty: Gastroenterology, Hepatology and Nutrition; UKCRC code/ Disease: Oral and Gastrointestinal/ Diseases of appendix

Interventions
Participants are randomised using an online randomisation system in a 1:1 ratio between the 2 treatment arms. Minimisation will be used for age, gender, duration of symptoms before randomisation and centre.

Treatment Arm A: Non Operative Treatment
Patients will be treated in hospital with a minimum of 24 hours intravenous antibiotics followed by oral antibiotics until the doctors feel they meet criteria for discharge. They will be monitored during their stay in hospital to ensure recovery and if at any stage they are deteriorating, or have not improved by 48 hours post randomisation, they will be referred for an appendicectomy. Time in hospital may vary for each patient but it is expected that the patient will be in hospital for a minimum of 48 hours. The follow up will be for 6 months from the date of first discharge from hospital.

Treatment Arm B: Appendicectomy
Patients will be treated with intravenous antibiotics until it is time for their operation. The operation will require a general anaesthetic to remove the appendix, either by laparoscopic or open surgery. Time in hospital may vary for each patient depending on their recovery rate. Standard care estimates the patient will be in hospital for a few days. Again, the follow up will be for 6 months from the date of first discharge from hospital.

The follow up period involves 3 appointments at 6 weeks, 3 months and 6 months. All patients, or a member of their family, will be asked to complete 2 questionnaires at randomisation, discharge, 2 weeks, 6 weeks, 3 months and 6 months. Patients will also be asked to complete a diary card for the 2 weeks immediately after discharge and an extra questionnaire at the 6 weeks and 6 months follow up appointments.

Intervention Type
Other

Primary outcome measure
Proportion of eligible patients recruited to the study over 12 months is measured by the number of patients who consent and are randomised into the study by 12 months divided by the total number of patients who were eligible and screened for the study by 12 months.

Secondary outcome measures
1. Willingness of parents and children to be enrolled in, and surgeons to recruit to, a randomised study comparing operative versus non-operative treatment and identify anticipated recruitment rate - measured in parallel qualitative workstream through patient/parent interviews, surgeon surveys and focus groups
2. Identify strategies to optimise surgeon-family communication to inform the future RCT – measured in parallel qualitative workstream during interviews with families and surgeons up to 6 months following recruitment consultation
3. Enhance the design of a future RCT from the perspectives of stakeholders at participating sites (children, parents, surgeons and nurses) - measured in parallel qualitative workstream during interviews with families, surgeons and nurses up to 6 months following recruitment consultation, in surgeon survey, and focus groups with surgeons
4. Assess the equipoise and willingness of UK paediatric surgeons to participate in a future RCT – measured in parallel qualitative workstream with surgeon survey and focus groups
5. Clinical outcomes of trial treatment pathways including:
5.1. Overall success of initial non-operative treatment (measured as the number of patients randomised to Treatment Arm A, discharged from hospital without appendicectomy)
5.2. Complications of disease and treatment (measured during hospital stay and 6 month follow-up period)
5.3. Rate of recurrent appendicitis during 6 month follow-up period

Overall study start date
01/07/2016

Completion date
31/10/2018

Eligibility

Key inclusion criteria
1. Child age 4 – 15 years (<16 years and >3 years)
2. Clinical diagnosis, either with or without radiological assessment, of acute appendicitis which prior to study commencement would be treated with appendicectomy
3. Written informed parental consent, with child assent if appropriate

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
Planned Sample Size: 65; UK Sample Size: 65

Total final enrolment
57

Key exclusion criteria
1. Clinical signs or radiological findings to suggest perforated appendicitis
2. Presentation with appendix mass
3. Previous episode of appendicitis or appendix mass treated non-operatively
4. Major anaesthetic risk precluding allocation to the appendicectomy arm
5. Known antibiotic allergy preventing allocation to non-operative treatment arm
6. Antibiotic treatment started at referring institution (defined as 2 or more doses administered)
7. Cystic fibrosis
8. Positive pregnancy test
9. Current treatment for malignancy

Date of first enrolment
13/02/2017

Date of final enrolment
28/02/2018

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Southampton Children's Hospital
University Hospital Southampton NHS Foundation Trust
Tremona Road
Southampton
United Kingdom
SO16 6YD

Study participating centre

St George’s Hospital
St George’s University Hospitals NHS Foundation Trust
Blackshaw Road
Tooting
London
United Kingdom
SW17 0QT

Study participating centre
Alder Hey Children’s Hospital
Alder Hey Children’s NHS Foundation Trust
East Prescot Road
Liverpool
United Kingdom
L14 5AB

Sponsor information

Organisation
University Hospital Southampton NHS Foundation Trust

Sponsor details
Research & Development Department
SGH, Level E, Laboratory & Pathology Block, SCBR, MP 138
Tremona Road
Southampton
England
United Kingdom
SO16 6YD

Sponsor type
Hospital/treatment centre

ROR
https://ror.org/0485axj58

Funder(s)

Funder type
Government

Funder Name

National Institute for Health Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Findings will be disseminated locally, nationally and internationally through local meetings, presentation to international meetings (e.g. British Association of Paediatric Surgeons Annual Congress) and submission to high quality peer reviewed journals for publication. Study participants will receive a summary of the findings written by our Study Specific Advisory Group (SSAG, see PPI section) including information on how to seek further advice should they so wish. The SSAG will prepare a report for dissemination amongst regional CRN Young Persons Advisory Groups (YPAGs). Members of the SSAG will be encouraged to contribute to reports of the PPI activity within this study and these will be submitted to the INVOLVE conference.

Whilst the academic output from this trial will be a number of high quality publications, the findings of the feasibility work related to recruitment will be made available as early as possible (subject to compliance with necessary copyright and IP agreements) with the intention that other researchers will benefit from the work done in the CONTRACT study and use this to optimise recruitment to other ongoing and planned RCTs. This will be done with support from the CRN and the MRC Trials Methodology Hubs. The COS protocol will be registered with the COMET initiative and the COS added to the COMET database once complete.

Intention to publish date
31/10/2019

Individual participant data (IPD) sharing plan
The current data sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Other publications	qualitative study	30/03/2020	27/11/2020	Yes	No

Protocol article	protocol	02/03/2018	27/11/2020	Yes	No
Results article	results	13/01/2021	18/01/2021	Yes	No
Protocol article	protocol	01/02/2021	26/02/2021	Yes	No
Results article		01/02/2023	07/02/2023	Yes	No
Other publications		07/06/2023	08/06/2023	Yes	No
HRA research summary			28/06/2023	No	No