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Non-operative treatment of children with appendicitis vs appendectomy

Submission date
27/07/2021

Recruitment status
Recruiting

Registration date
28/07/2021

Overall study status
Ongoing

Last Edited
18/08/2024

Condition category
Digestive System

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

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 the 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 effectiveness and cost-effectiveness of non-operative treatment of acute appendicitis with antibiotics.

Who can participate?
Children aged 4-15 years 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 6 weeks and 4, 8 and 12 months after they are discharged from hosptial. At these visits and during the stay in hospital, parents are asked to fill in a questionnaire about their child’s health status.

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?
Southampton Clinical Trials Unit (UK)

When is the study starting and how long is it expected to run for?
January 2021 to September 2027

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

Who is the main contact?
1. Miss Jessica Kelly (public)
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2. Mr Nigel Hall (scientific)
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Study website
https://www.southampton.ac.uk/ctu/trialportfolio/listoftrials/contract2.page#trial_overview

Contact information

Type(s)
Public

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Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
302249

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
IRAS 302249, NIHR131346

Study information

Scientific Title
CONservative TReatment of Appendicitis in Children – a randomised controlled Trial (CONTRACT 2)

Acronym
CONTRACT 2

Study objectives
The aim of this study is to assess whether non-operative treatment of acute uncomplicated appendicitis in children is effective and cost-effective.

Ethics approval required
Ethics approval required

Ethics approval(s)

Approved 01/12/2021, South Central - Hampshire A Research Ethics Committee (Temple Quay House, 2 The Square, Temple Quay, Bristol, BS1 6PN, United Kingdom; +44 (0)207 104 8196; hampshirea.rec@hra.nhs.uk), ref: 21/SC/0317

Study design
Randomized controlled trial with internal pilot

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 to request a participant information sheet

Health condition(s) or problem(s) studied
Appendicitis

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 12 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 12 months from the date of first discharge from hospital.

The follow-up period involves four appointments at 6 weeks, 4, 8 and 12 months. All patients, or a member of their family, will be asked to complete questionnaires at randomisation, 1 week, 2 weeks, 3 weeks, 4 weeks, 6 weeks, 4 months, 8 months and 12 months. Patients will also be asked to complete a diary smartphone app for the 3 weeks immediately after discharge

Intervention Type
Mixed

Primary outcome measure
Treatment success, defined as recovery from acute appendicitis and having none of the following: negative appendicectomy, complication requiring intervention under general anaesthesia, failure of non-operative treatment during initial hospital admission (treated with appendicectomy), recurrent appendicitis. Measured at 1 year following randomisation.

Secondary outcome measures
1. Negative appendicectomy recorded by research nurse at hospital discharge, 6 weeks
2. Intra-abdominal abscess recorded by research nurse at hospital discharge, 6 weeks
3. Reoperation recorded by research nurse at hospital discharge, 6 weeks, 4, 8, 12 months
4. Bowel obstruction recorded by research nurse at hospital discharge, 6 weeks, 4, 8, 12 months
5. Wound infection recorded by research nurse at hospital discharge, 6-week review
6. Other wound complication recorded by research nurse at hospital discharge, 6-week review
7. Antibiotic failure recorded by research nurse at hospital discharge, 6-week review
8. Length of hospital stay recorded by research nurse at hospital discharge, 6 weeks, 4, 8, 12 months
9. Histology of appendix recorded by research nurse at hospital discharge, 6 weeks, 4, 8, 12 months
10. Adverse events recorded by research nurse at hospital discharge, 6 weeks, 4, 8, 12 months
11. Recurrent appendicitis recorded by research nurse at 6 weeks and 4, 8, 12 months
12. Readmission to hospital recorded by research nurse at 6 weeks and 4, 8, 12 months
13. Patient's quality of life measured using Child Health Utility (CHU9D) by smartphone app and research nurse at hospital discharge, 1, 2, 3, 4, 6 weeks and 4, 8, 12 months
14. Healthcare resource use recorded using shortened Client Service Receipt Inventory (CSRI) by research nurse at 6 weeks and 4, 8, 12 months
15. Death recorded by research nurse at hospital discharge, 6 weeks, 4, 8, 12 months
16. Was pain relief taken? (Y/N) recorded by smartphone app daily for 3 weeks following discharge
17. Able to do normal daily activities (Y/N) recorded by smartphone app daily for 3 weeks following discharge
18. Attended school (Y/N) recorded by smartphone app daily for 3 weeks following discharge
19. Able to do full activities (Y/N) recorded by smartphone app daily for 3 weeks following discharge
20. Parents missed work (Y/N) recorded by research nurse and smartphone app at hospital discharge and daily for 3 weeks following discharge

Overall study start date
01/01/2021

Completion date
01/09/2027

Eligibility

Key inclusion criteria
1. Children aged 4–15 years
2. Clinical diagnosis, 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
Child

Lower age limit
4 Years

Upper age limit
15 Years

Sex
Both

Target number of participants
376

Key exclusion criteria
1. Complicated appendicitis score of 4 or greater
2. Clinical or radiological findings to suggest perforated appendicitis
3. Presentation with appendix mass
4. Previous episode of appendicitis or appendix mass treated non-operatively
5. Major anaesthetic risk precluding allocation to the appendicectomy arm
6. Known antibiotic allergy preventing allocation to non-operative treatment arm
7. Positive pregnancy test

Date of first enrolment
31/01/2022

Date of final enrolment
31/12/2025

Locations

Countries of recruitment
England

Northern Ireland

Scotland

United Kingdom

Wales

Study participating centre
University Hospital Southampton
Southampton
United Kingdom
SO16 6YD

Study participating centre
Alder Hey Hospital
Liverpool
United Kingdom
L12 2AP

Study participating centre
St George's Hopsital
London
United Kingdom
SW17 0QT

Study participating centre
Manchester Childrens Hospital
Manchester
United Kingdom
M13 9WL

Study participating centre
United Leeds Teaching Hospitals NHS Trust
Trust Offices
Leeds General Infirmary
Great George Street
Leeds
United Kingdom
LS1 3EX

Study participating centre
Bristol Childrens Hospital
Bristol
United Kingdom
BS1 3NU

Study participating centre
Great North Children’s Hospital
Newcastle
United Kingdom
NE7 7DN

Study participating centre
Chelsea & Westminster Hospital
London
United Kingdom
SW10 9NH

Study participating centre
Leicester Royal Infirmary
Leicester
United Kingdom
LE1 5WW

Study participating centre
Cardiff Hospital
Cardiff
United Kingdom
CF14 4HH

Study participating centre
Evelina Children’s Hospital
London
United Kingdom
SE1 7EH

Study participating centre
King's College Hospital
London
United Kingdom
SE5 9RS

Study participating centre
The Royal Belfast Hospital for Sick Children
274 Grosvenor Road

Belfast
United Kingdom
BT12 6BA

Study participating centre
Birmingham Childrens Hospital
Steelhouse Lane
Birmingham
United Kingdom
B4 6NH

Study participating centre
Royal Hospital for Sick Children (Glasgow)
1345 Govan Road
Glasgow
United Kingdom
G51 4TF

Study participating centre
Royal Alexandra Children's Hospital
Eastern Road
Brighton
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BN2 5BE

Study participating centre
Oxford Radcliffe Hospital NHS Trust
The John Radcliffe
Headley Way
Headington
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United Kingdom
OX3 9DU

Study participating centre
James Paget University Hospital
Lowestoft Road
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Great Yarmouth
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NR31 6LA

Sponsor information

Organisation
University Hospital Southampton NHS Foundation Trust

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R&D Dept, E Level, L123
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SO16 6YD
+44 (0)23 8120 5146
sponsor@uhs.nhs.uk

Sponsor type
Hospital/treatment centre

Website
http://www.uhs.nhs.uk/home.aspx

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
Current publication and dissemination plan as of 29/12/2021:
Planned publication in a high-impact peer-reviewed journal. The protocol will be made available online.

We will send participants a summary of the study results, unless they have told us they prefer not to receive this. The summary will also be available on the Southampton Clinical Trial Unit CONTRACT 2 website to members of the public. The findings will also be published in updates to participants and through contacts with patient groups.

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Previous publication and dissemination plan:
Planned publication in a high-impact peer-reviewed journal. The protocol will be made available online, link to follow when finalised.

Intention to publish date
01/09/2028

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request following the process outlined at https://www.southampton.ac.uk/ctu/about/index.page, with requests made via ctu@soton.ac.uk. The type of data required will have to be requested and stipulated in the request (but all are available for request from 3 months after the publication. The researchers will ask participants for their permission to access their child's hospital data from a data warehouse such as NHS digital or an equivalent devolved organisation. This optional part of the trial will allow the trial to report on long-term follow-up. The people who analyse the information will not be able to identify the child and will not be able to find out the child's name, NHS number or contact details. Data is anonymous.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No