

Development and first-in-child feasibility clinical trial of a new MRI mini-capsule device to measure whole gut transit time in paediatric constipation

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A magnifying glass in the world of the medical device development – EPTRI webinar 25/11/2021

Rationale

- 10% of children suffer from constipation at some point in their life.
- 27,500/year in England are referred to secondary and tertiary care.
- Managing illness in these children can be challenging and the diagnosis often based on symptom reports.

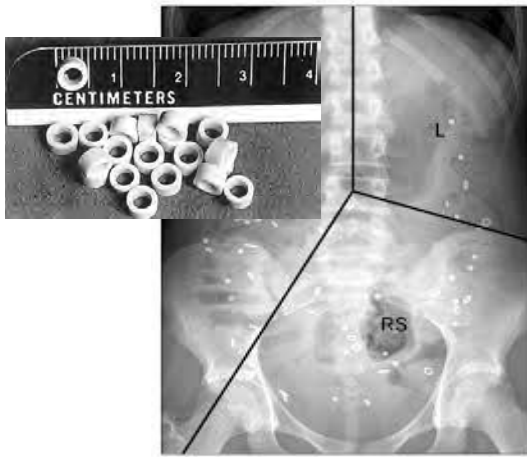
Koppen IGN *et al.* J Pediatr 2018, 198, 121-130
NICE Costing report. Clinical guideline 99. 2010.

Rationale

- An objective measure of the whole gut transit time (WGTT) available early in the clinical pathway can help with selection of therapy.
- Transit tests can distinguish between normal transit, anorectal retention or slow transit constipation.
- Useful when medical history and/or physical examination is unreliable.

Rationale

- Current X-ray radiopaque marker (ROM) method uses ionizing radiation, associated with risk of subsequent malignancy in children.
- Has poor anatomical definition of colon loops hence difficult to determine where the ROMs are.



X-ray test



Theory



Practice

Rationale

- Current X-ray radiopaque marker (ROM) method uses ionizing radiation, associated with risk of subsequent malignancy in children.
- Has poor anatomical definition of colon loops hence difficult to determine where the ROMs are.

Aim: to take this on with MRI – no ionizing radiation and higher quality cross-sectional imaging



X-ray test



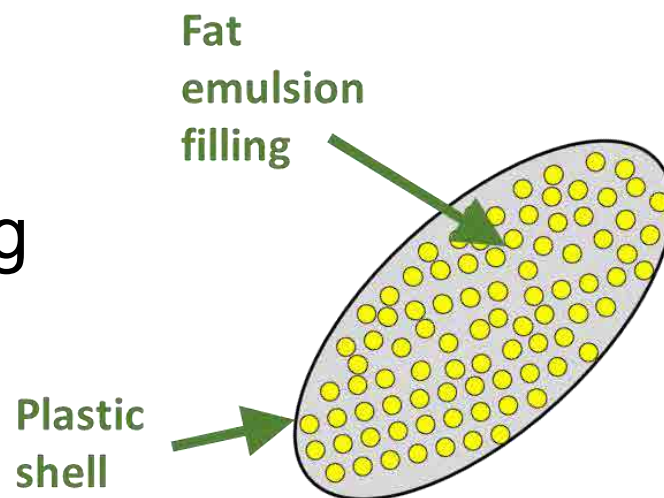
Theory



Practice

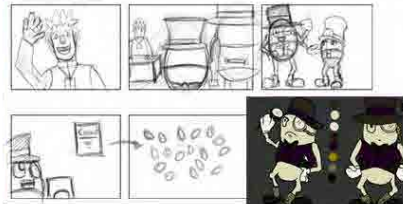
The new paediatric device

- EU Class IIa ingestible device.
- Small (8mm×4mm), inert, plastic mini-capsules, filled with a MRI-visible oil-in-water emulsion.
- Co-designed with our Young Persons Advisory Panel (YPAG) and manufactured by JEB Technologies



L Marciani et al, patents: US11013427B2;
EP3166488B1; AU2015287435

Young people involvement



Young people involvement



Abrehart *et al.* *Research Involvement and Engagement* (2021) 7:2
<https://doi.org/10.1186/s40900-020-00243-0>

Research Involvement
and Engagement

COMMENTARY

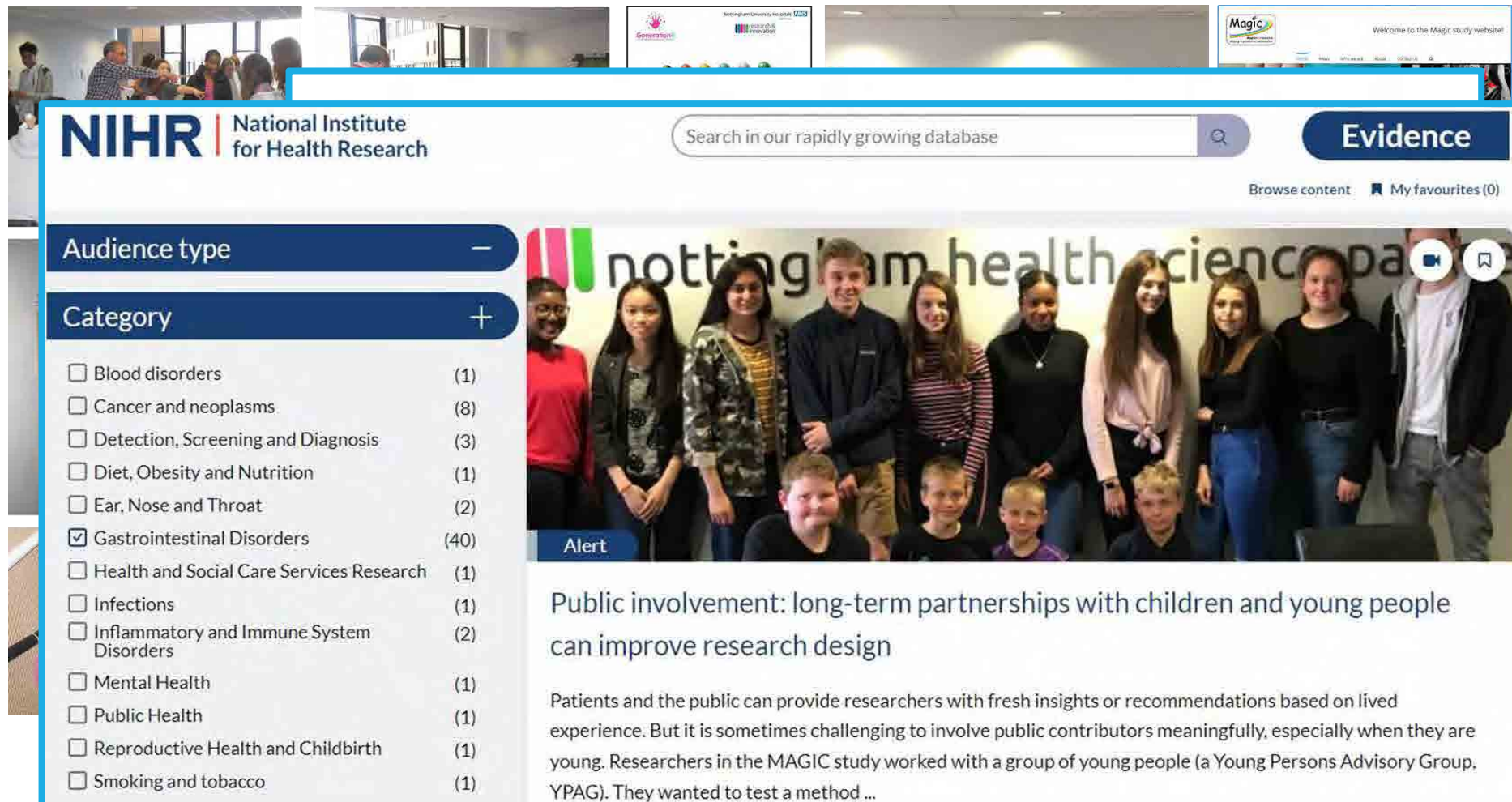
Open Access

“A little (PPI) MAGIC can take you a long way” : involving children and young people in research from inception of a novel medical device to multi-centre clinical trial
Roald Dahl, James and the Giant Peach (1961)



Nichola Abrehart^{1*†}, Kate Frost^{2†}, the Young Persons Advisory Group², Roy Harris¹, Andrew Wragg², Derek Stewart², Hayfa Sharif¹, Rachel Matthews³ and Luca Marciani¹

Young people involvement



The screenshot shows the NIHR Evidence website interface. At the top, there are several small images and logos, including 'Generations', 'NIHR Evidence', and 'Magic'. The main header features the NIHR logo and the text 'National Institute for Health Research'. A search bar is present with the text 'Search in our rapidly growing database'. To the right of the search bar is a button labeled 'Evidence'. Below the search bar, there are links for 'Browse content' and 'My favourites (0)'. On the left side, there is a sidebar with two main sections: 'Audience type' and 'Category'. The 'Category' section is expanded, showing a list of medical categories with checkboxes and counts. The main content area displays a search result for 'Public involvement: long-term partnerships with children and young people can improve research design'. The result includes a thumbnail image of a group of young people, an 'Alert' button, and a brief description of the study.

NIHR | National Institute for Health Research

Search in our rapidly growing database

Evidence

Browse content | My favourites (0)

Audience type —

Category +

- ☐ Blood disorders (1)
- ☐ Cancer and neoplasms (8)
- ☐ Detection, Screening and Diagnosis (3)
- ☐ Diet, Obesity and Nutrition (1)
- ☐ Ear, Nose and Throat (2)
- ☒ Gastrointestinal Disorders (40)
- ☐ Health and Social Care Services Research (1)
- ☐ Infections (1)
- ☐ Inflammatory and Immune System Disorders (2)
- ☐ Mental Health (1)
- ☐ Public Health (1)
- ☐ Reproductive Health and Childbirth (1)
- ☐ Smoking and tobacco (1)

Alert

Public involvement: long-term partnerships with children and young people can improve research design

Patients and the public can provide researchers with fresh insights or recommendations based on lived experience. But it is sometimes challenging to involve public contributors meaningfully, especially when they are young. Researchers in the MAGIC study worked with a group of young people (a Young Persons Advisory Group, YPAG). They wanted to test a method ...

The new paediatric device



JEB Technologies
Limited



Feasibility clinical study

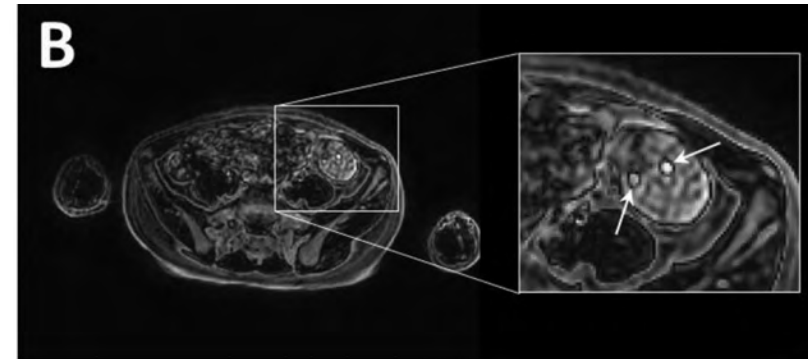
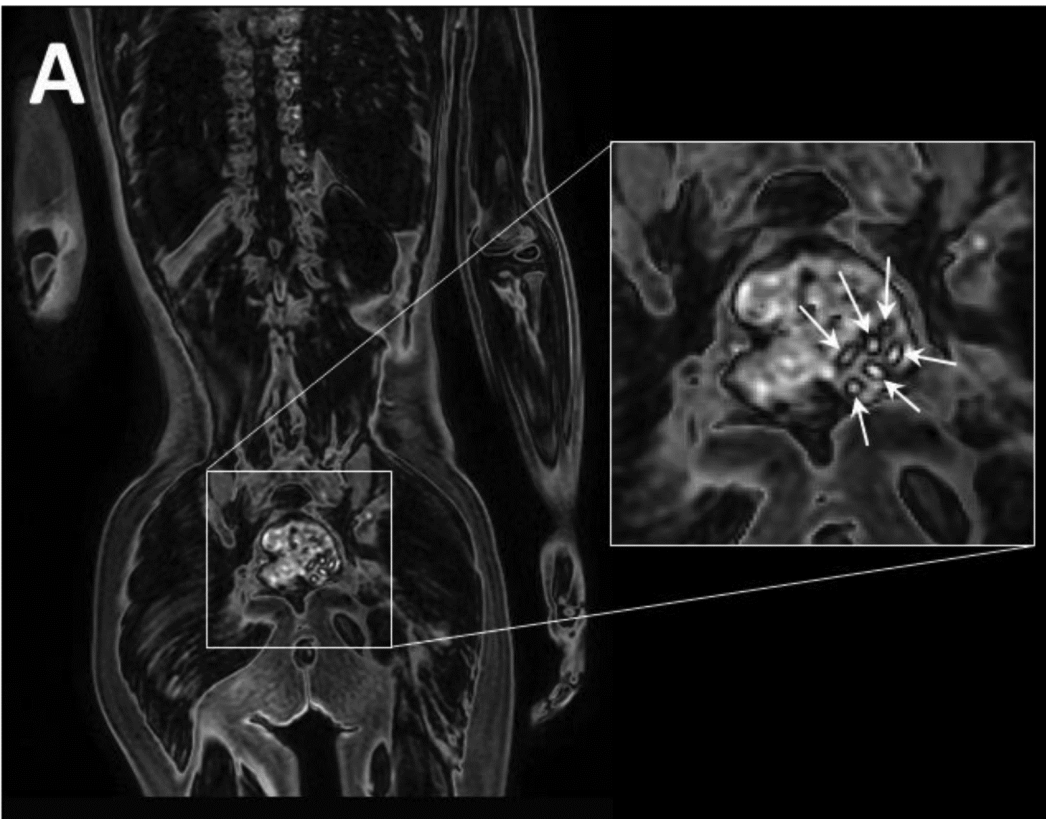
- First-in-child study of new device: safety and acceptability.
- 16 patients + 19 healthy participants age 7-18 years old.
- 24 mini-capsules each day for 3 days (a common X-ray ROMs protocol). MRI at Day 4 and if needed Day 7 (also Day 28 for this first study only).
- Whole gut transit time calculated from the count of the mini-capsules in the gut (as ROMs).

Feasibility clinical study

- The MRI test was well accepted and safe.
- The mini-capsules were imaged in the colon successfully by MRI, providing bright signal against colonic chyme on the derived in-phase minus out-of-phase images.



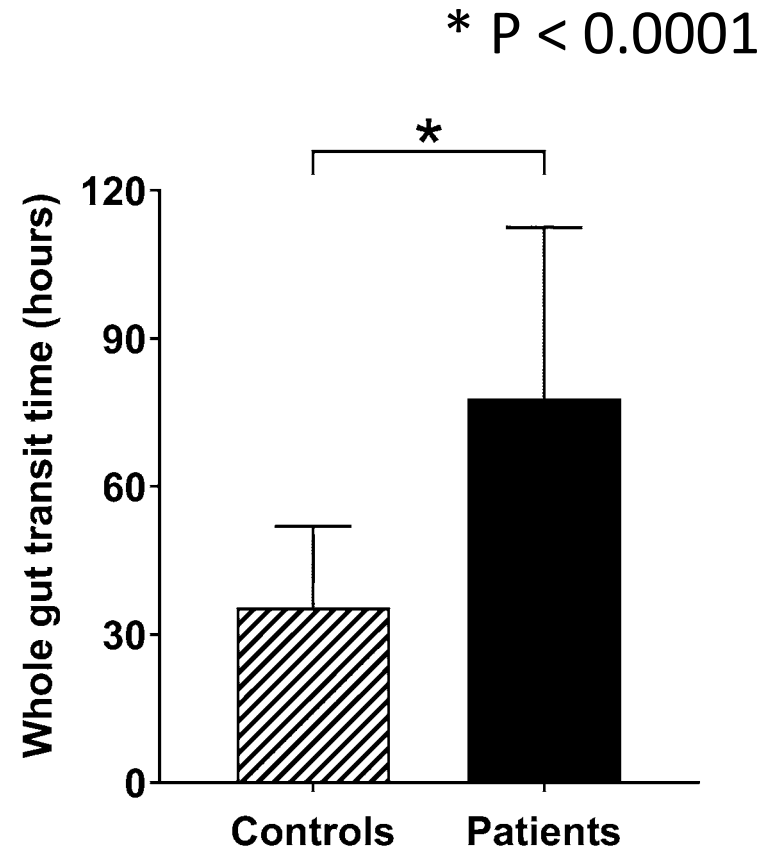
Feasibility clinical study



MRI images from a
7 year old patient
participant

Feasibility clinical study

- The transit time was longer in the patient group.
- The last MRI scan confirmed exit of the device in all participants.



Feasibility clinical study

- The transit time was longer in the constipated group.
- The last MRI confirmed the diagnosis of constipation and the device in all patients.

ORIGINAL ARTICLE: GASTROENTEROLOGY

OPEN

Feasibility Study of a New Magnetic Resonance Imaging Mini-capsule Device to Measure Whole Gut Transit Time in Paediatric Constipation

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ABSTRACT

Objective: In England, 27,500 children are referred annually to hospital with constipation. An objective measure of whole gut transit time (WGTT) could aid management. The current standard WGTT assessment, the x-ray radiopaque marker (ROM) test, gives poor definition of colonic anatomy and the radiation dose required is undesirable in children. Our objective was to develop an alternative magnetic resonance imaging (MRI) WGTT measure to the x-ray ROM test and to demonstrate its initial feasibility in paediatric constipation. **Methods:** With the Nottingham Young Person's Advisory Group we developed a small (8 × 4 mm), inert polypropylene capsule shell filled with MRI-visible fat emulsion. The capsule can be imaged using MRI fat and water in-phase and out-of-phase imaging. Sixteen patients with constipation and 19 healthy participants aged 7 to 18 years old were recruited. Following a common ROM protocol, the participants swallowed 24 mini-capsules each day for 3 days and were imaged on days 4 and 7 using MRI. The number of successful studies (feasibility) and WGTT were assessed. Participants' EuroQol Visual Analogue Scale were also collected and compared between the day before the taking the first set of mini-capsules to the day after the last MRI study day.

Results: The mini-capsules were imaged successfully in the colon of all participants. The WGTT was 78 ± 35 hours (mean ± standard deviation) for patients, and 36 ± 16 hours, $P < 0.0001$ for healthy controls. Carrying out the procedures did not change the EuroQol Visual Analogue Scale scores before and after the procedures.

Conclusions: Magnetic Resonance Imaging in Paediatric Constipation was a first-in-child feasibility study of a new medical device to measure WGTT in paediatric constipation using MRI. The study showed that the new method is feasible and is well tolerated.

What Is Known

- Current methods for assessing whole gut transit time include the traditional abdominal x-ray and radiopaque markers.
- X-ray radiopaque marker methods expose children and young people ionizing radiation in the range 0.03 to 0.11 mSv.
- >X-ray radiopaque markers produce 2-dimensional radiographs in which the bowel and location of the radiopaque markers may be difficult to distinguish.

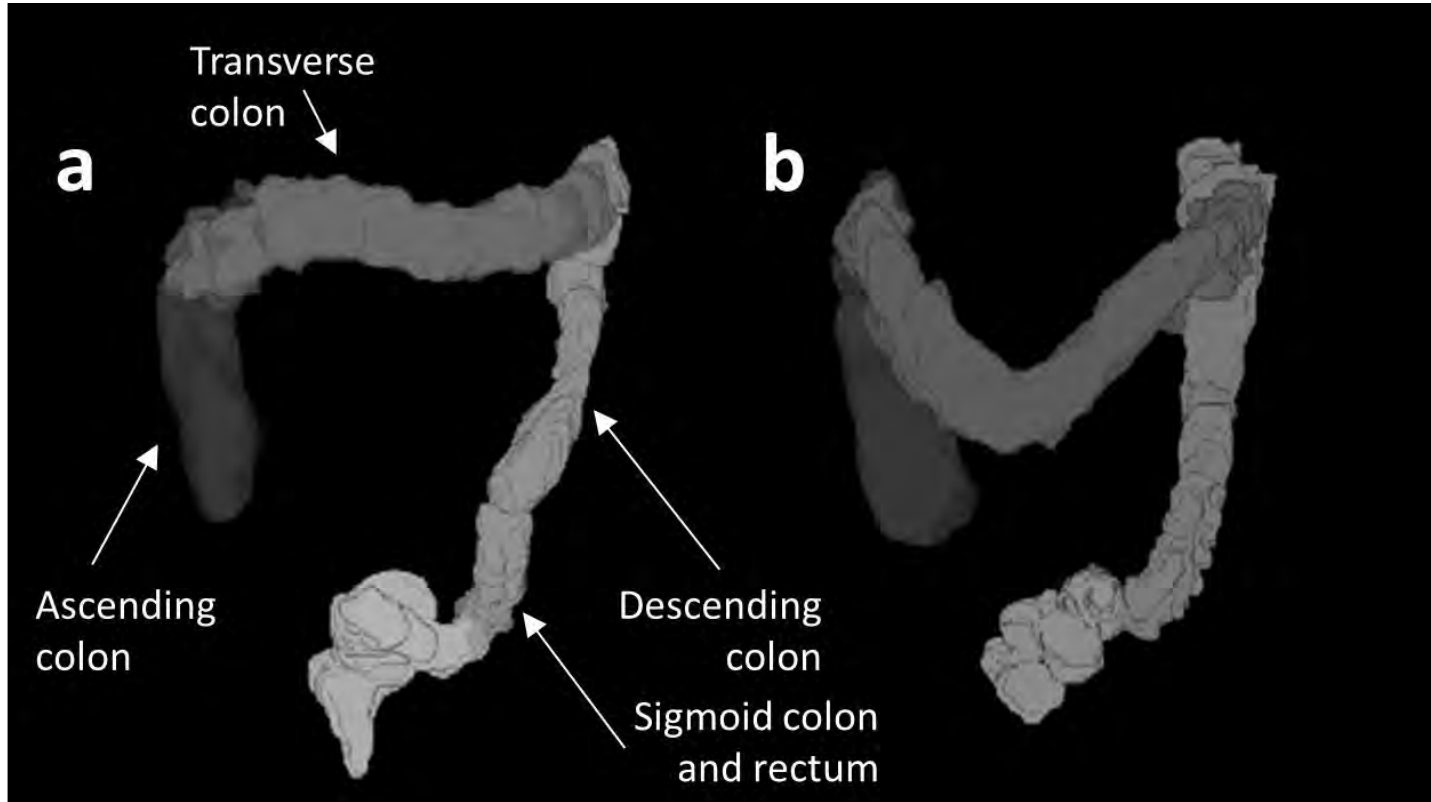
What Is New

- We developed a new, magnetic resonance imaging visible mini-capsule, specifically aimed at children and young adults.
- This first-in-child feasibility study showed that whole gut transit time can be measured in paediatric constipation using the new mini-capsule device in conjunction with magnetic resonance imaging.

Functional constipation in childhood is common, with estimated prevalence of 14% (1–5). The diagnosis is based on symptom and is defined according to the Rome IV diagnostic criteria (6–8).

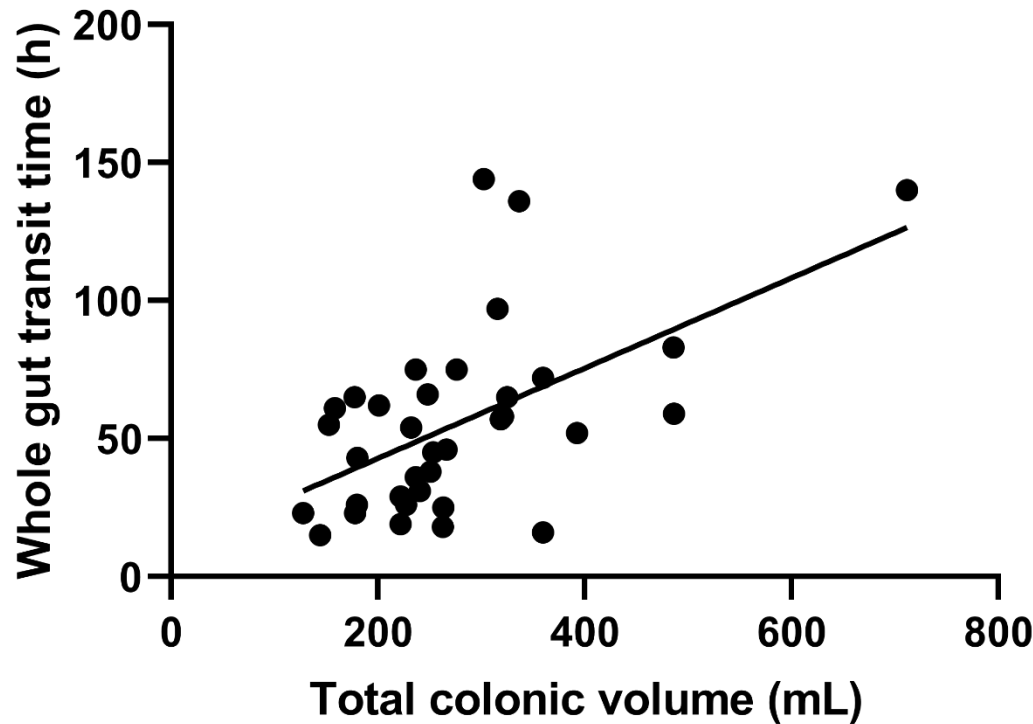
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Feasibility clinical study



(a) Patient, 9 years old, weight 48 Kg, height 130 cm, BMI 21.4 kg/m². TCV= 237 mL / **WGTT = 75 Hours**. **(b)** Healthy control, 10 years old, weight 42 Kg, height 145 cm, BMI = 19.9 kg/m². TCV = 227 mL/ **WGTT = 26 Hours**.

Additional insights: transit and volumes



Coefficient of correlation $R=0.56$, $p=0.0005$.

Additional insights: transit and volumes

Whole gut transit time (h)

200

150

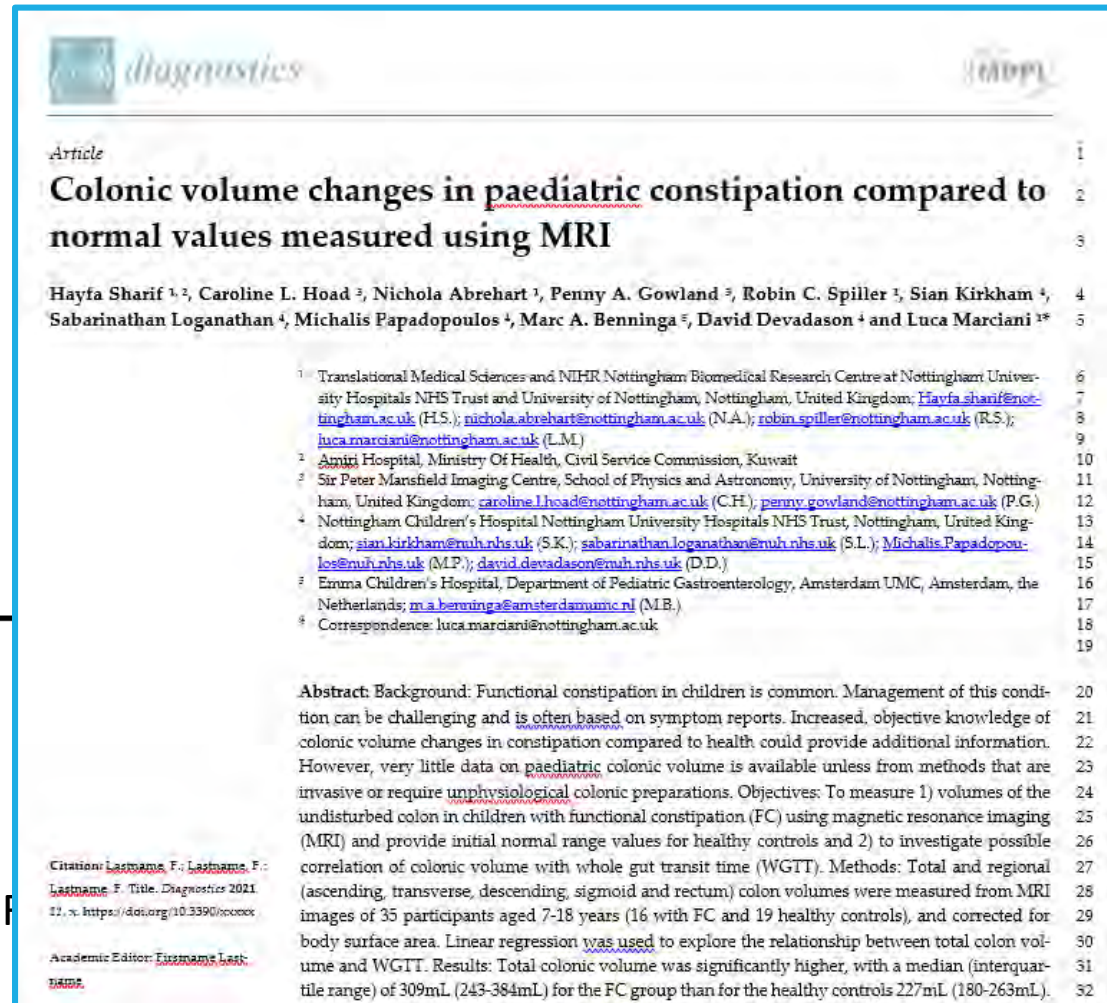
100

50

0

0

Coefficient of correlation r



Next steps: MAGIC2

- Current second grant funded by NIHR i4i.
- Partnership with JEB Technologies, young persons and parents.
- CE marking.
- Multi-centre clinical efficacy study.
- High volume production.
- Commercialisation.



FUNDED BY

NIHR | National Institute
for Health Research

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