



FULL/LONG TITLE OF THE STUDY

ENDOPOL: dye chromoENDOscopy versus virtual chromoendoscopy for assessment of the ileo-anal pouch in patients with familial adenomatous POLyposis: a randomized controlled trial

SHORT STUDY TITLE / ACRONYM

Evaluation of the ileo-anal pouch in FAP (ENDOPOL)

PROTOCOL VERSION NUMBER AND DATE

Version 1 22.10. 2025

RESEARCH REFERENCE NUMBERS

IRAS Number:	365649
SPONSORS Number:	NA
FUNDERS Number:	NA

SIGNATURE PAGE

The undersigned confirm that the following protocol has been agreed and accepted and that the Chief Investigator agrees to conduct the study in compliance with the approved protocol and will adhere to the principles outlined in the Declaration of Helsinki, the Sponsor's SOPs, and other regulatory requirement.

I agree to ensure that the confidential information contained in this document will not be used for any other purpose other than the evaluation or conduct of the investigation without the prior written consent of the Sponsor

I also confirm that I will make the findings of the study publically available through publication or other dissemination tools without any unnecessary delay and that an honest accurate and transparent account of the study will be given; and that any discrepancies from the study as planned in this protocol will be explained.

For and on behalf of the Study Sponsor:

Signature: Date:

..../...../.....

Name (please print):

.....

Position:

.....

Chief Investigator:

Signature: Date:

Name: (please print):

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KEY STUDY CONTACTS

Insert full details of the key study contacts including the following

Chief Investigator	Dr Andrew Latchford Polyposis Registry St Mark's Hospital London North West University Healthcare NHS Trust Central Middlesex, Acton Lane London North West University Healthcare NHS Trust NW10 7NS andrew.latchford@nhs.net
Study Co-ordinator	Dr Benjamin Zare Polyposis Registry St Mark's Hospital London North West University Healthcare NHS Trust Central Middlesex, Acton Lane London North West University Healthcare NHS Trust NW10 7NS b.zare@nhs.net
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Joint-sponsor(s)/co-sponsor(s)	N/A
Funder(s)	No funding required
Key Protocol Contributors	Dr Andrew Latchford, Dr Benjamin Zare
Committees	N/A

STUDY SUMMARY

It may be useful to include a brief synopsis of the study for quick reference. Complete information and, if required, add additional rows.

Study Title	ENDOPOL: dye chromoENDOscopy versus virtual chromoendoscopy for assessment of the ileo-anal pouch in patients with familial adenomatous POLyposis: a randomized controlled trial
Internal ref. no. (or short title)	Evaluation of the ileo-anal pouch in FAP (ENDOPOL)
Study Design	international multi-centre randomised controlled trial
Study Participants	Adult patients with familial adenomatous polyposis and an ileal pouch-anal anastomosis (IPAA)
Planned Size of Sample (if applicable)	NA
Follow up duration (if applicable)	NA
Planned Study Period	5 years
Research Question/Aim(s)	1. To compare dye-based chromoendoscopy to virtual chromoendoscopy (narrow-band imaging(NBI) / blue laser imaging (BLI)) for the detection of clinical relevant adenomas greater than 5 mm in the ileo-anal pouch of patients with familial adenomatous polyposis (FAP) in an international multi-centre randomised controlled trial. 2. The secondary objectives are comparing: -Detection of advanced neoplasia in the ileal pouch, defined by advanced adenoma (≥10mm and/or adenoma with high-grade dysplasia) or cancer -Detection of adenomas 2-4mm, 5-9mm and ≥10mm in the pouch body and rectal cuff -Number of performed polypectomies -Interval for next surveillance endoscopy based on the personalised endoscopic surveillance protocol that is implemented in all centres of the European FAP Consortium -The InSiGHT polyposis staging system (IPSS) score (10) -Duration of endoscopy -Incidence of endoscopy-related complications -Number of adenomas in the rectal remnant and anal mucosa

FUNDING AND SUPPORT IN KIND

FUNDER(S) (Names and contact details of ALL organisations providing funding and/or support in kind for this study)	**FINANCIAL AND NON FINANCIALSUPPORT GIVEN**
No funding specifically for this study. A Dutch Grant was obtained by Professor Dekker, to facilitate the initial set up of the consortium.	

ROLE OF STUDY SPONSOR AND FUNDER

The protocol was drawn up purely by the consortium of European experts in familial adenomatous polyposis (FAP). There was no external input.

ROLES AND RESPONSIBILITIES OF STUDY MANAGEMENT COMMITEES/GROUPS & INDIVIDUALS

A European Consortium was set up, to look at outcomes of endoscopy in patients with FAP, having highlighted it as an area of need. To our knowledge, there are no studies comparing dye chromoendoscopy to virtual chromoendoscopy in the setting of a pouch in FAP.

The consortium comprises:

Hospital Clinic de Barcelona	Maria Pellise, Francesc Balaguer
Hospital General Universitario de Alicante	Rodrigo Jover
Hospital Edouard Herriot Lyon	Jean-Christophe Saurin
The Maria Sklodowska-Curie Memorial Cancer Center	Michal Kaminski
Sant'Orsola Malpighi University Hospital Bologna	Luigi Ricciardiello
University Medical Center Mainz	Helmut Neumann
St. Mark’s Hospital London	Andrew Latchford, Benjamin Zare
Netherlands Cancer Institute/LUMC	Monique van Leerdam
Amsterdam UMC, location AMC	Evelien Dekker, Roel Hompes, Barbara Bastiaansen, Patrick Bossuyt

It is this group of European experts who developed the concepts and protocols for this study.

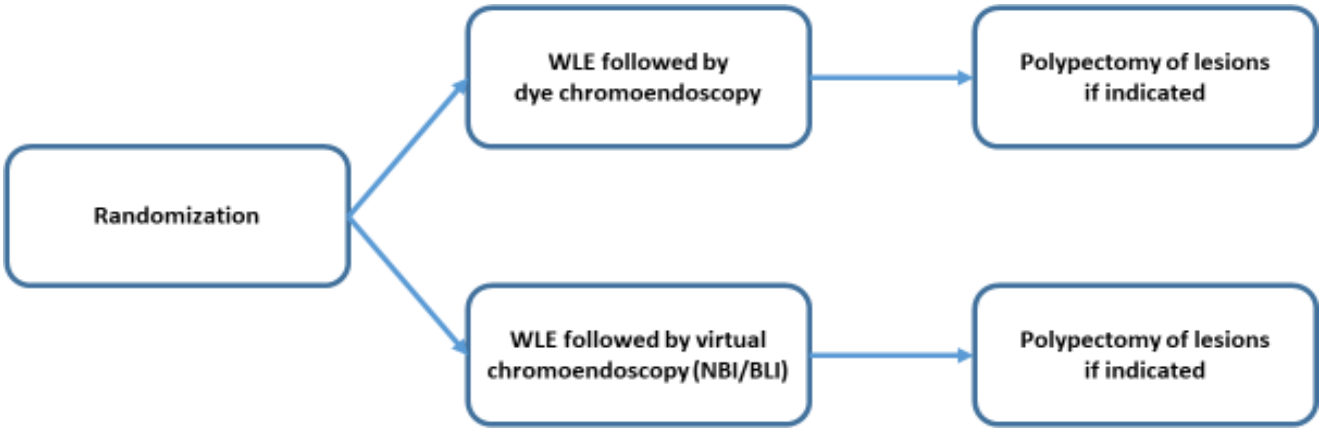
Patient and Public involvement has not been sought. Patients with FAP already undergo endoscopic procedures for their surveillance. The current study is to formalise the optimal polyp detection method during follow up, which fits within current national and European guidelines and removes the inter-endoscopist variability.

PROTOCOL CONTRIBUTORS

The protocol was developed purely by the clinical members of the consortium with no external input from funders or sponsors.

KEY WORDS: FAP
Endoscopy
Surveillance

STUDY FLOW CHART



STUDY PROTOCOL

ENDOPOL: dye chromoENDOscopy versus virtual chromoendoscopy for assessment of the ileo-anal pouch in patients with familial adenomatous POLyposis: a randomized controlled trial

1 BACKGROUND

Familial adenomatous polyposis (FAP) is an autosomal dominant inherited condition, characterized by formation of hundreds to thousands of polyps throughout the entire colon and rectum. When left untreated, nearly 100% of all FAP patients develop colorectal cancer (CRC) at a median age of 35-45 years (1). To prevent patients from developing CRC, patients undergo prophylactic colectomy. The preferred surgical procedures for FAP are a proctocolectomy with ileal pouch-anal anastomosis (IPAA) or a subtotal colectomy with ileorectal anastomosis (IRA) or ileal distal sigmoidal anastomosis (IDSA)(2).

After (procto-)colectomy, patients remain at risk of developing adenomas or cancer in the retained rectum but interestingly most patients with IPAA will also develop adenomas in the pouch over time. The 5, 10 and 15-year risks of developing adenomas in the pouch after IPAA are 7–16%, 35–42% and 75%, respectively (3). The incidence of cancer after IPAA is

1-2% (4, 5). Whether this risk of polyposis and cancer is reflected in the considerable risk of pouch excision in the long-term is still unknown. However, nowadays more and more patients suffer from extensive polyposis sometimes requiring pouch excision. Therefore, high quality pouchoscopy including polypectomy is needed.

The current ESGE guideline on polyposis syndromes recommends 1 to 2-yearly endoscopic surveillance of the pouch with polypectomy for adenomas >5mm (6). No recommendation is provided on which imaging technique should be used to optimise polyp detection.

White-light endoscopy (WLE), narrow-band imaging (NBI) and blue laser imaging (BLI) have been widely used as the standard of care to assess the retained rectum or ileo-anal pouch after prophylactic (procto-)colectomy. In some dedicated FAP centres, however, endoscopists prefer the use of dye-based chromoendoscopy for polyp-detection in the ileo-anal pouch. Ileal adenomas in the pouch may be more flat or sessile with a different shape compared to colorectal adenomas and may be easily overlooked. Moreover, pouch carcinomas might develop / be diagnosed shortly after endoscopic surveillance (4). This raises the question as to whether pouch adenomas may be more easily missed compared to colorectal adenomas and extra measures should be taken.

For adenoma detection in the rectum, pouch and duodenum in patients with FAP, some studies showed that the use of dye-chromoendoscopy results in higher detection rates (of mainly small polyps) (4, 7, 8). The use of dye-based chromoendoscopy in the pouch has only been described in a small subgroup of 33 patients within a larger study, demonstrating higher adenoma detection rates compared to WLE (4). However, chromoendoscopy is time-consuming and detecting more small adenomas (<5mm) might not be relevant in a condition such as FAP. That having been said, another recent study found that dye chromoendoscopy led to a higher detection of large (>10mm) duodenal adenomas when compared to WLE (9).

To our knowledge, no studies have compared dye chromoendoscopy to virtual chromoendoscopy. Whether the use of chromoendoscopy leads to better detection of clinically relevant adenomas, such as adenomas >5mm or advanced adenomas, compared to virtual chromoendoscopy, is unclear. Regardless, optimising endoscopic surveillance techniques in FAP patients is of great importance, not only to prevent patients from developing cancer but also to avert the need for a second surgery in the form of a pouch excision.

2 RATIONALE

To our knowledge, no studies have compared dye chromoendoscopy to virtual chromoendoscopy in this setting, and whether the use of either leads to better detection of clinically relevant adenomas remains uncertain at present.

Within St Mark's Hospital, virtual chromoendoscopy is mainly used, but in some cases, dye chromoendoscopy is also utilised. And, in other European centres, dye chromoendoscopy is primarily employed. With this research, we aim to compare these techniques.

Guidelines recommend surveillance intervals in patients with FAP and a pouch. Whilst these do allow for the use of dye-spray, given the current lack of evidence upon which a recommendation could be made, they do no currently specifically dictate either form of chromoendoscopy over the other.

At present, this study falls within the national and European guidelines but seeks to standardise practice and provide a clear dataset from which we may optimise the outcomes of surveillance.

3 THEORETICAL FRAMEWORK

Randomising patients at the time of procedure will ensure objective assessment of the performance of dye versus virtual chromoendoscopy. Prospectively collecting data on surveillance outcome performed using either respective chromoendoscopy technique, in a standardised way, will allow better interpretation of outcomes of surveillance and provide data upon which follow-up guidelines may be made more standardised.

4 RESEARCH QUESTION/AIM(S)

1. To compare dye-based chromoendoscopy to virtual chromoendoscopy (NBI/BLI) for the detection of clinical relevant adenomas greater than 5 mm in the ileo-anal pouch of patients with FAP

2. To measure/assess a number of cofactors for changeability / association with either chromoendoscopy technique (see 'Objectives').

4.1 Objectives

Primary Objective:
The primary objective of this study is to compare dye-based chromoendoscopy to virtual chromoendoscopy (NBI/BLI) for the detection of clinical relevant adenomas greater than 5mm in the ileo-anal pouch of patients with FAP in an international multi-centre randomised controlled trial.

Secondary Objectives:
The secondary objectives are comparing:
- Detection of advanced neoplasia in the ileal pouch.
- Detection of adenomas at three different size thresholds in the pouch body and rectal cuff, specifically
- Detection of adenomas in the rectal remnant and anal mucosa
- The InSiGHT polyposis staging system (IPSS) score (10)
- Assessment of frequency of polypectomy
- Evaluation of the duration of endoscopy
- Complications and safety signals related to procedures
-Examination of the interval between surveillance endoscopies based on the personalised endoscopic surveillance protocol that is implemented in all centres of the European FAP Consortium

4.2 Outcome

Primary Study Endpoint:
Incidence of clinically relevant adenomas greater than 5mm in the ileo-anal pouch, comparing dye-based chromoendoscopy to virtual chromoendoscopy (NBI/BLI).

Secondary Study Endpoints:
- Incidence of advanced neoplasia – defined by advanced adenoma (≥10mm and/or adenoma with high-grade dysplasia) or cancer – in the pouch globally
- Incidence of adenomas 2-4mm, 5-9mm and ≥10mm in the pouch body and rectal cuff, respectively
- Number of adenomas in the rectal remnant and anal mucosa
- Scoring on the InSiGHT polyposis staging system (IPSS) score (10)
- Number of polypectomies performed per procedure
- Length of individual procedures
- Incidence of endoscopy-related complications
- Interval between surveillance endoscopies (based on the ‘Personalized endoscopic surveillance’ protocol already being implemented across centres in the European FAP Consortium)

The outcomes are important clinical endpoints assessing the safety and effectiveness of endoscopic surveillance with each respective form of chromoendoscopy in patients with FAP. These data are useful to inform clinical practice and modify existing guidelines.

5 STUDY DESIGN/METHODS, DATA COLLECTION AND DATA ANALYIS

This study is designed as an international multi-centre randomised controlled trial with an estimated duration of 2 years. Patients will undergo their scheduled regular surveillance pouchoscopy, performed by endoscopists with extensive experience with FAP. Prior to the endoscopy, patients will be randomly assigned to undergo pouchoscopy with dye-based chromoendoscopy or with NBI/BLI. After diagnostic assessment, adenomas with an indication for endoscopic intervention will be removed.

STUDY DESIGN/METHODS

5.6 Randomisation, blinding and treatment allocation

Randomisation is performed by an independent computer-generated random numbers program (Castor EDC). All participating centres have access to this tool. Prior to pouchoscopy, randomisation will be performed prior to the procedure in a 1:1 ratio. Block size in a 2-4-6 randomisation will be used to ensure same distributions (dye-based chromoendoscopy versus NBI) for each centre. Stratification by centre will be performed to account for potential variations in patient characteristics and procedural protocols among different centres. Blinding is not feasible due to the distinct visual aspects involved in virtual and dye chromoendoscopy, which is also the case for patients undergoing pouchoscopy under mild sedation.

DATA COLLECTION

5.7 Study procedures

Sedation

Procedures will be performed without sedation, under conscious sedation using intravenous midazolam and fentanyl, or deep sedation with propofol, at the discretion of the endoscopist and patient.

Bowel preparation

Participants will be prepared with bowel preparation (oral or enema), according to usual local policy. The quality of bowel preparation is assessed and irrigation with fecal debris is performed when needed. Quality of bowel preparation is assessed using the Boston Bowel Preparation Score (BBPS) (for one segment) (11). When the BBPS is <2, the endoscopy will be discontinued, and the patient will be rescheduled.

Sequence of the endoscopy and obtaining measurements

The pouchoscopy begins with a first examination with WLE, in which the polyp burden will be described according to the table below. In all patients the pouch length, height of rectal cuff and the length of rectal remnant will be described. To ensure uniformity the lengths will be measured after the pouch has been completely deflated. The length of the pouch body will be determined with the endoscope measuring from the transition of anal mucosa to the pouch until the transition of the pouch

to the pre-pouch ileum. The length of the rectal remnant will be determined from the dentate line until the transition to the pouch body/ileoanal anastomosis.

Reporting of polyp size and reliability checking

For assessing size and polyp burden the variability may be high between endoscopists, especially in assessing polyps smaller than 5mm.

The visualisation of biopsy forceps with a known size will be advised to be employed in determining polyp size. In addition, however, during this study endoscopists will assess endoscopy images for polyp burden and corresponding size – the assessments will be analysed after which the interrater reliability will be determined. A week later the assessments will also be repeated, in order to determine the intrarater reliability. If the reliability tends to be good for smaller polyps (<5 mm), they will be included in the study and reported.

Polyp burden scoring tables will be employed to assess polyp burden according to specific location – pouch body or rectal remnant – and in summation.

Polyp burden scoring tables

Segment (Length)	Number of polyps with WLE
Pouch body ☐ cm	☐ 2-4mm ☐ 5-9mm ☐ ≥10mm
Rectal remnant ☐ cm	☐ 2-4mm ☐ 5-9mm ☐ ≥10mm
Total polyp burden	☐ **2-4mm** ☐ **5-9mm** ☐ **≥10mm**

Segment (length)	Number of polyps with chromoendoscopy
Pouch Body ☐ cm	☐ 2-4mm ☐ 5-9mm ☐ ≥10mm
Rectal remnant ☐ cm	☐ 2-4mm ☐ 5-9mm ☐ ≥10mm
Total polyp burden	☐ **2-4mm** ☐ **5-9mm** ☐ **≥10mm**

Legend: A: 0-10 B: 10-20 C: > 20

Subgroup-specific endoscopy sequence

[All in keeping with current standard practice/guidelines for endoscopic surveillance]

- Group A (Dye-based chromoendoscopy)

  The pre-pouch ileum, pouch body and rectal cuff are diffusely dyed using a spray catheter with indigo carmine. Then the endoscope is advanced to the pre-pouch ileum from where withdrawal and mucosal inspection is performed in spiral fashion. The size in millimetre (mm) and location of detected lesions (pouch body and rectal remnant) is documented using the polyp burden scoring table above. The size of adenomas will be measured using a closed or open biopsy forceps with a known size. Retroflexion is performed to assess the rectal cuff.

  After thorough inspection and documentation, adenomas with an indication for polypectomy will be resected using standard polypectomy techniques.

  Indications for polypectomy include:

  - polyps >5mm in the pouch body

  - polyps >2mm in the rectal cuff

  - polyps suspicious for HGD or early cancer

- Group B (Virtual chromoendoscopy)

  The pre-pouch ileum, pouch body and rectal cuff are diffusely dyed using a spray catheter with indigo carmine. Then the endoscope is advanced to the pre-pouch ileum from where withdrawal and mucosal inspection is performed in spiral fashion. The size in millimetre (mm) and location of detected lesions (pouch body and rectal remnant) is documented using the polyp burden scoring table above. The size of adenomas will be measured using a closed or open biopsy forceps with a known size. Retroflexion is performed to assess the rectal cuff.

  After thorough inspection and documentation, adenomas with an indication for polypectomy will be resected using standard polypectomy techniques.

  Indications for polypectomy include:

  - polyps >5mm in the pouch body

  - polyps >2mm in the rectal cuff

  - polyps suspicious for HGD or early cancer

General quality parameters

Quality parameters will be collected for each pouchoscopy:

- Adjusted BBPS in pouch

- Procedural time (including all of: introduction of endoscope, irrigation, dying when chromoendoscopy is used, withdrawal with inspection, retroflexion, removal and retrieval of polyps)

Post-procedure follow-up

As for regular care, patients will be asked to keep track of any adverse events occurring after the pouchoscopy and contact the hospital when needed. Next surveillance pouch endoscopy will be scheduled according to the centres usual policy.

DATA ANALYSIS

5.8 Statistical analysis

Normally distributed variables will be presented as means (±standard deviation), variables with skewed distributions as medians (interquartile range). Categorical variables will be presented as frequencies (%) and will be compared using the Chi-square test or Fisher's exact test. Number of adenomas between the both groups will be compared, with the method depending on the type of distribution, using an unpaired t-test or the Mann-Whitney U test. P- value less than 0.05 will be considered to indicate statistically significant differences. To minimize the potential bias due to missing data, only participants with data on the study parameters will be included in this analysis.

5.4 Data handling

Data will be held in the routine hospital medical systems accessible by the participants usual medical team and a study file. Data that leaves the Trust will be anonymised. Patients will be allocated a study number, and all data will reference this; no patient identifiable information will leave the Trust or be accessible to anyone other than those usually involved in the patients care. Anonymised data will be held centrally in an online database (EDC Castor).

6 STUDY SETTING

The data that are collected are done so by individual sites within the consortium. They anonymise the data collected, and these are then held centrally in an online database (EDC Castor).

Patients will be accessed if they are under the care of the St Mark's Hospital Polyposis Registry and having endoscopic follow-up with our team. From a participant's perspective, it should not feel as if there is any difference from their current endoscopic surveillance (other than the application of dye spray, if they were randomised to this arm).

This is a randomised controlled trial that is both multicentre and international. This collaborative approach is the best way to get meaningful datasets in such a rare disease, particularly for a study looking at safety and effectiveness of aspects of endoscopic surveillance.

7 SAMPLE AND RECRUITMENT

7.1 Eligibility Criteria

Patients who are currently treated for FAP and are/will be planned for pouchoscopy in one of the participating centres will be eligible for this study.

7.1.1 Inclusion criteria

In order to be included in this study, a subject must meet all of the following criteria:

(1) Diagnosis of FAP i.e., at least one of following:

- Genetic diagnosis: proven *APC* germline mutation OR
- Clinical diagnosis: >100 colorectal adenomas in combination with a positive family history of FAP

(2) Have an ileal-pouch anal anastomosis (IPAA), either after primary proctocolectomy or secondary proctectomy after initial colectomy and ileorectal or ileosigmoidal anastomosis (IRA/ISA)

(3) Age ≥ 18 years

7.1.2 Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:

(1) Allergy to indigo carmine

(2) Unwilling or unable to give informed consent

7.2 Sampling

7.2.1 Size of sample

Due to the lack of prior studies comparing dye chromoendoscopy with virtual chromoendoscopy, the sample size calculation was performed using the available data. One study reported a pouch adenoma detection rate of 76% using dye chromoendoscopy and 58% using WLE (4), however, the study did not specify adenoma size and it is suspected that the adenoma detection rate may be higher with virtual chromoendoscopy compared to WLE. Considering the maximum number of patients that can be included, which is estimated to be 300, a sample size of 206 patients (103 per study arm) will be required to demonstrate a difference of 18% between dye-based chromoendoscopy (76%) and virtual chromoendoscopy (58%) in terms of adenoma detection rate. The sample size was calculated at a significance level of 0.05 and a power of 80% for a two-sided test. With an estimated drop-out rate of 10 patients (e.g., due to impaired bowel preparation), a total of 216 patients will be included in the study internationally.

7.2.2 Sampling technique

All eligible patients will be considered**.**

Patients will be identified from upcoming endoscopy lists by a research fellow working in the Polyposis registry. He will contact the patient by the Registry email and provide the patient PIS before their upcoming procedure. The patient will have the opportunity to read the PIS, ask questions/make contact

before their procedure. At their procedure if they would like to participate, they can sign the consent form and continue with the procedure as planned. If they choose not to participate, they undergo the procedure anyway.

7.3.1 Sample identification

Dr Latchford and/or Dr Zare (Research Fellow), who work in the Polyposis Registry and perform endoscopy on these patients, will identify patients from the endoscopy appointments system and approach those that are planned for endoscopy in 1-2 weeks' time.

They will be contacted using a secure NHS email, and via an email address that they have already provided to the Registry and which is held with the patient's prior agreement that it may be used as a means of contacting them. They will be sent a PIS by email at least 1 week before their planned procedure.

They will have the opportunity to further discuss the study when they attend their endoscopy and if wish to participate can consent then. Whether they wish to participate or not their surveillance procedure will go ahead as planned.

There is no payment involved for this study. They are receiving the surveillance that they would otherwise have had done, just with randomisation to either form of chromoendoscopy (both of which are considered acceptable within current standard of care and guideline recommendations).

7.3.2 Consent

Patients will have the opportunity to read the PIS, pose questions to contacts given in the PIS, as well as being given the opportunity to further discuss the study when they attend for their planned surveillance endoscopy.

Consent will be taken prior to the endoscopic procedure if they wish to participate in the study. If they do not consent to the study then their planned endoscopy will proceed unchanged, just in absence of the study randomisation.

If a patient lacks the capacity to consent, then they will not be approached for the study. Capacity will be reassessed on discussion with the patient, directly prior to undergoing their endoscopic procedure.

8 ETHICAL AND REGULATORY CONSIDERATIONS

The study will be conducted according to the principles of the Declaration of Helsinki. The Institutional Review Board (IRB) at the Amsterdam UMC (location AMC) has already assessed the study. It will be assessed at each participating site too and has been reviewed and approved by LNWH NHS trust RandD.

The procedures in this study are in line with the routine care of FAP patients.

8.1 Assessment and management of risk

This study is just assessing the relative efficacy of virtual and dye-based chromoendoscopy for detecting polyps in FAP patients with a pouch. Both of these methods already being employed at the centre, though the former with greater frequency currently, and therefore this study does not include anything which will expose patients to anything other than the risk they already are exposed to, during routine endoscopic surveillance.

8.2 Research Ethics Committee (REC) and other Regulatory review & reports

The project will meet the requirements and principles set by General Data Protection Regulations 2018 and the European Medicines Agency (GCP Guidelines).

No study activity will take place prior to all the approvals being in place from the relevant agencies, and permission to carry out the research has been received from the local R&D office.

The Investigators will obtain HRA and REC approval. The study will then seek the local R&D capacity and capability. The study will be conducted in accordance with the recommendations for physicians involved in research on human subjects adopted by the 18th World Medical Assembly, Helsinki 1964 (incl. later revisions) and any other relevant ethical guidance. On obtaining a favourable R&D approval and any subsequent changes to the study conduct, design or management will be notified to original approving R&D Department and any other relevant regulatory authority via a substantial amendment.

Regulatory Review & Compliance

The Chief Investigator will submit, and where necessary, obtain approval from the above parties for substantial amendments to the original approved documents. The Chief Investigator will produce the annual reports as required and notify the REC at the end of the study. An annual progress report (APR) will be submitted to the REC within 30 days of the anniversary date, on which the favourable opinion was given, and annually until the study is declared ended. If the study is ended prematurely, the Chief Investigator will notify the REC, including reasons for the premature termination. Within one year after the end of the study, the Chief Investigator will submit a final report with the results, including any publication/abstracts, to the REC. All correspondence with the REC will be retained and filed within the master site file.

Amendments

If there is any amendment to be made, this will not be instigated until it has been approved by the appropriate regulatory bodies, and confirmation has been received that their support is continued.

Notice of any amendments to the protocol will be submitted to the HRA, REC and local R&D office, following discussion within the team. Amendments to any documents will be clearly identified by the version number and date.

8.3 Peer review

The protocol has been drawn up by a group of European experts who are part of a consortium. It has not been peer reviewed. Given the study design and the nature of the study, peer review has not been sought other than review and approval by each site's RandD department and/or review by an Ethic Committee.

8.4 Patient & Public Involvement

This was not sought as this study is aiming to standardise surveillance undergone by patients, rather than exploring new treatments per se.

8.5 Protocol compliance

Accidental protocol deviations can occur and will be documented. Protocol compliance is monitored as part of the study.

Protocol deviation will either encompass the decision not to proceed with dye-based chromoendoscopy (despite randomisation to this arm) on the basis of suboptimal bowel preparation, or indeed removal of a polyp that was judged by the endoscopist to be required, as the endoscopist's clinical decision-making during the procedure remains paramount. The reasoning behind any deviation will be documented for the purposes of the study.

8.6 Data protection and patient confidentiality

The study will comply with the Data Protection Act 1998.

Only staff currently involved in the patient's care will have access to any of the patients record or any patient identifiable information.

Patients will be allocated a study number for anonymisation. The key for this will be held on an NHS computer drive, accessible to Dr Latchford. No patient identifiable information is transferred outside the Trust.

Site files will be held in a locked office in the Polyposis Registry on the hospital premises.

8.7 Indemnity

London North West University Healthcare NHS Trust holds negligent harm and non-negligent harm insurance policies which apply to this study.

8.8 Access to the final study dataset

Anonymised data are held centrally in Amsterdam. A data transfer agreement is in place. Access to full dataset can be requested by approaching the steering committee. The collated anonymised data are processed and analysed by the team in Amsterdam, working with Prof Evelien Dekker.

9 DISSEMINATION POLICY

9.1 Dissemination policy

It would be planned for the findings of this study to be disseminated by presenting at national/international meetings to the appropriate target audience, we would expect the work to be translated into a formal manuscript and submit to peer reviewed journals for publication.
St Mark's has an annual patient information day, and the outcomes would be presented there too, in the appropriate format for a lay audience.
If a participant wishes specifically to request results, then they can contact Dr Latchford or Dr Zare at the email address provided and once the results have been fully collected, analysed and published he can help provide the finalised manuscript and results, whilst complying with any copyright restrictions.
The final data are held by the consortium, which has a steering committee. There is a data transfer agreement already in place for data transfer between LNWH NHS Trust and the central team in Amsterdam.

9.2 Authorship eligibility guidelines and any intended use of professional writers

Authorship for any manuscript or presentation will be based upon and proportionate to their involvement in the study, as per the International Committee of Medical Journal Editors authorship criteria for manuscripts submitted for publication.

10 REFERENCES

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11. APPENDICIES

11.1 Appendix 1- Required documentation

- PIS v1
- Consent Form v1

11.2 Appendix 2 – Schedule of Procedures (Example)

N/A

13.3 Appendix 3 – Amendment History

Amendment No.	Protocol version no.	Date issued	Author(s) of changes	Details of changes made

List details of all protocol amendments here whenever a new version of the protocol is produced.

Protocol amendments must be submitted to the Sponsor for approval prior to submission to the REC.