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COBIx: Multi-site validation study of the COBIx reporting tool

Submission date 30/11/2023	**Recruitment status** Recruiting	[_] Prospectively registered [X] Protocol
Registration date 20/02/2024	**Overall study status** Ongoing	[_] Statistical analysis plan [_] Results
Last Edited 02/05/2025	**Condition category** Digestive System	[_] Individual participant data [X] Record updated in last year

Plain English summary of protocol

Background and study aims

The diagnosis of serious large bowel diseases such as colitis, Crohn's disease and cancer, is done by examining tissue samples (biopsies) taken by endoscopic camera examination of the intestine. Large bowel biopsies of this type create a large volume of laboratory workload, comprising approximately 10% of all tissue requests. A significant percentage of these samples are normal (between 30-40%) and contain no evidence of disease. The samples are currently examined manually by a pathologist (a doctor trained to examine tissue), using a microscope. Recent investment means that more laboratories can now scan the microscope slides into a computer as a digital image. The COBIx algorithm takes advantage of digitisation by using computers to analyse biopsy image pixel data to find any irregularities that indicate the presence of disease. This project will fully optimize the COBIx algorithm to a design freeze and then test it more widely across more sites and with a greater number of cases. This is important because different labs have slightly different equipment, stain characteristics and patient populations; thus this study will ensure that the COBIx algorithm works equally well across different sites, despite these variations. Eleven NHS Hospital Trusts from England and Scotland have been chosen. Over the next 3 years, 11,000 large bowel biopsies will be examined from these centres, comparing the pathologists' reports with the results of the COBIx algorithm. The results will be compared and analysed statistically. The goal is to see if COBIx accurately separates normal large bowel biopsies from abnormal biopsies. This would enable normal biopsies to be solely reported by the computer program. Secondly, the study will see if the detection of serious disease by COBIx helps ensure cases containing diseases such as cancer or severe inflammation can be prioritised for urgent pathologist review.

Who can participate?

Identification will be done by NHS trust employees at each site who are part of the direct clinical care team. It will be done using a computer search (on each site's pathology reporting system) based on the tissue type (large bowel biopsy) and where specific diagnoses are required, using systemised nomenclature of medicine (SNOMED) codes apportioned to the cases. The cases will then be retrieved. The patient's NHS opt-in versus out status will be assessed by each site, and only those patients consenting to the use of their tissue in research will be included.

What does the study involve?
The study aims to recruit 10,000 patient samples from adults across 10 separate centres in the UK. All of the Haematoxylin and Eosin (H&E) stained slides (approximately 33,000 slides) from these samples will be scanned (or in some cases, have already been scanned) to digital whole slide images at the recruiting site using equipment used for routine diagnosis. Scanned images will be anonymised and transferred electronically to private cloud storage housed within the Tissue Image Analytics (TIA) Centre infrastructure. Once these digital slides have been transferred, they will be processed through the COBIx algorithm and classified into one of five categories. The results of the algorithm classification will be compared to the reference pathologist diagnosis.

What are the possible benefits and risks of participating?
There is no intervention which carries any risk physical or psychological to any patients or participants. As part of this study, there is a requirement to access patients' records to retrieve data on patient demographics, their clinical treatment and clinical outcomes. This will be carried out by staff at each NHS Trust who are part of the clinical care team who will access this data from the electronic records held on the trust's clinical results reporting system. This data will be uploaded to a secure web application with restricted access to protect patient confidentiality.

Where is the study run from?
University Hospitals Coventry and Warwickshire NHS Trust; Warwick Clinical Trials Unit, University of Warwick; TIA (Tissue Image Analytics) Centre, University of Warwick (UK)

When is the study starting and how long is it expected to run for?
April 2023 to November 2025

Who is funding the study?
NIHR, Accelerated Access Collaborative

Who is the main contact?
Professor David Snead (Chief Investigator), David.Snead@uhcw.nhs.uk, David.Snead@pathlake.org

Contact information

Type(s)
Scientific, Principal Investigator

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Public

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
330776

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
DS631023, IRAS 330776, CPMS 59233

Study information

Scientific Title
COBIx: Multi-site validation study of the Colon and Rectal Endoscopic Biopsy (COBIx) reporting tool

Acronym
COBIx

Study objectives
The diagnosis of serious large bowel diseases such as colitis, Crohn’s disease and cancer, is done by examining tissue samples (biopsies) taken by endoscopic camera examination of the intestine. Large bowel biopsies of this type create a large volume of laboratory workload, comprising approximately 10% of all tissue requests. A significant percentage of these samples are normal (between 30-40%) and contain no evidence of disease. The samples are currently examined manually by a pathologist (a doctor trained to examine tissue), using a microscope.

Recent investment means that more laboratories can now scan the microscope slides into a computer as a digital image. The COBIx algorithm takes advantage of digitisation by using computers to analyse biopsy image pixel data to find any irregularities that indicate the presence of disease. This project will fully optimize the COBIx algorithm to a design freeze and then test it more widely across more sites and with a greater number of cases. This is important because different labs have slightly different equipment, stain characteristics and patient populations; we need to ensure that the COBIx algorithm works equally well across different sites, despite these variations. Eleven NHS Hospital Trusts from England and Scotland have been chosen. Over the next 3 years, we will examine 11,000 large bowel biopsies from these centres, comparing the pathologists' reports with the results of the COBIx algorithm. The results will be compared and analysed statistically. The goal is to see if COBIx accurately separates normal large bowel biopsies from abnormal biopsies. This would enable normal biopsies to be solely reported by the computer program. Secondly, we wish to see if the detection of serious disease by COBIx helps ensure cases containing diseases such as cancer or severe inflammation can be prioritised for urgent pathologist review.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 06/11/2023, Wales REC 5 (Health and Care Research Wales, Castlebridge 5, 15-19 Cowbridge Road East, Cardiff, CF11 9AB, United Kingdom; +44 (0)2922 940910; Wales.REC5@wales.nhs.uk), ref: 23/WA/0317

Study design
Multi-centre study

Primary study design
Observational

Secondary study design
Case series/case note review and laboratory study

Study setting(s)
Hospital, University/medical school/dental school

Study type(s)
Diagnostic, Screening, Efficacy

Participant information sheet
No participant information sheet available

Health condition(s) or problem(s) studied
Colon and rectal endoscopic biopsy

Interventions
Current interventions as of 02/05/2025:

The study aims to recruit 10,000 patient samples from adults across 10 separate centres in the UK.
All of the Haematoxylin and Eosin (H&E) stained slides (approximately 33,000 slides) from these

samples will be scanned (or in some cases, have already been scanned) to digital whole slide images at the recruiting site using equipment used for routine diagnosis.
Scanned images will be anonymised and transferred electronically to private cloud storage housed within the Tissue Image Analytics (TIA) Centre infrastructure.
Once these digital slides have been transferred, they will be processed through the COBIx algorithm and classified into one of five categories.
The results of the algorithm classification will be compared to the reference pathologist diagnosis.
Most cases (9000) will be from retrospective samples, while 1000 samples will be recruited prospectively. All except rare and unusual entities cases will be selected sequentially. Using retrospective cases is appropriate in this setting and ensures the volume of cases can be recruited and examined in the time available, it also ensures rare and unusual entities are included so we can explore how these are handled by the algorithm. Prospective cases allow the study to collect health economics data, including the time taken for pathologists to examine normal biopsy slides.

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Previous interventions:

The study aims to recruit 11,000 patient samples from adults across 10 separate centres in the UK.
All of the Haematoxylin and Eosin (H&E) stained slides (approximately 33,000 slides) from these samples will be scanned (or in some cases, have already been scanned) to digital whole slide images at the recruiting site using equipment used for routine diagnosis.
Scanned images will be anonymised and transferred electronically to private cloud storage housed within the Tissue Image Analytics (TIA) Centre infrastructure.
Once these digital slides have been transferred, they will be processed through the COBIx algorithm and classified into one of five categories.
The results of the algorithm classification will be compared to the reference pathologist diagnosis.
Most cases (9900) will be from retrospective samples, while 1100 samples will be recruited prospectively. All except rare and unusual entities cases will be selected sequentially. Using retrospective cases is appropriate in this setting and ensures the volume of cases can be recruited and examined in the time available, it also ensures rare and unusual entities are included so we can explore how these are handled by the algorithm. Prospective cases allow the study to collect health economics data, including the time taken for pathologists to examine normal biopsy slides.

Intervention Type
Other

Primary outcome measure
The effectiveness of the COBIX algorithm compared with the original pathologist diagnosis (e.g. sensitivity, specificity, AUC-ROC, false negative rate, false positive rate, PPV, NPV) measured using a range of statistical measures at one timepoint

Secondary outcome measures
The effectiveness of the COBIX algorithm at separating samples into different diagnostic categories compared with the original pathologist diagnosis measured using a range of statistical measures at one timepoint

Overall study start date
04/04/2023

Completion date
30/11/2025

Eligibility

Key inclusion criteria
Large bowel biopsies taken from adult patients at an endoscopic examination

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
10,000

Key exclusion criteria
1. All other types of GI biopsies e.g. small bowel
2. Other types of large bowel specimens e.g. resections
3. Biopsies from children and young persons (under 18 years)

Date of first enrolment
01/12/2023

Date of final enrolment
30/09/2025

Locations

Countries of recruitment
England

Scotland

United Kingdom

Study participating centre

University Hospital Southampton NHS Foundation Trust
Southampton General Hospital
Tremona Road
Southampton
United Kingdom
SO16 6YD

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

Study participating centre
Cambridge University Hospitals NHS Foundation Trust
Cambridge Biomedical Campus
Hills Road
Cambridge
United Kingdom
CB2 0QQ

Study participating centre
The Royal Wolverhampton NHS Trust
New Cross Hospital
Wolverhampton Road
Heath Town
Wolverhampton
United Kingdom
WV10 0QP

Study participating centre
Greater Glasgow and Clyde
Gartnavel Royal Hospital
1055 Great Western Road
Glasgow
United Kingdom
G12 0XH

Study participating centre
Darlington Memorial Hospital
Hollyhurst Road
Darlington
United Kingdom
DL3 6HX

Study participating centre
North Tees and Hartlepool NHS Foundation Trust
University Hospital of Hartlepool
Holdforth Road
Hartlepool
United Kingdom
TS24 9AH

Study participating centre
University Hospitals Coventry and Warwickshire NHS Trust
Walsgrave General Hospital
Clifford Bridge Road
Coventry
United Kingdom
CV2 2DX

Study participating centre
Sheffield Teaching Hospitals NHS Foundation Trust
Northern General Hospital
Herries Road
Sheffield
United Kingdom
S5 7AU

Study participating centre
University Hospitals Birmingham NHS Foundation Trust
Queen Elizabeth Hospital
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Sponsor information

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Sponsor type
Hospital/treatment centre

Website
https://www.uhcw.nhs.uk/

ROR
https://ror.org/025n38288

Funder(s)

Funder type
Government

Funder Name
National Institute for Health and Care 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

Planned publication in a high-impact peer-reviewed journal. All efforts will be made to ensure that the results arising from the study are published in a timely fashion, in established peer-reviewed journals. Results will be disseminated via internal and external conferences and seminars, newsletters, and via interested groups, including local healthcare commissioning groups.

Intention to publish date

30/09/2025

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are/will be available upon request

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file	version 1.0	12/10/2023	04/12/2023	No	No