FIT SCREENING: GLOBAL PERSPECTIVE

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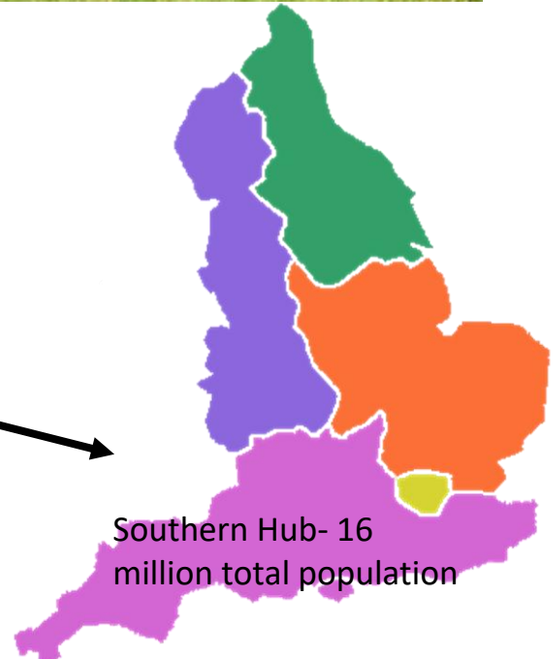

Diagnosis of Colorectal Cancer

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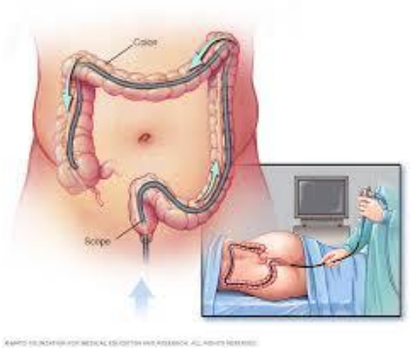
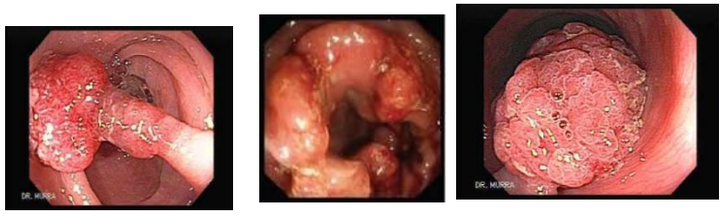
- Gold standard = colonoscopy
  - Capacity challenges and risk to patients



- CRC's and pre-cancerous lesions bleed



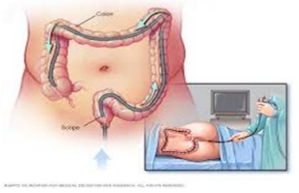
- Blood detected in faeces
  - faecal immunochemical Test for haemoglobin (FIT)

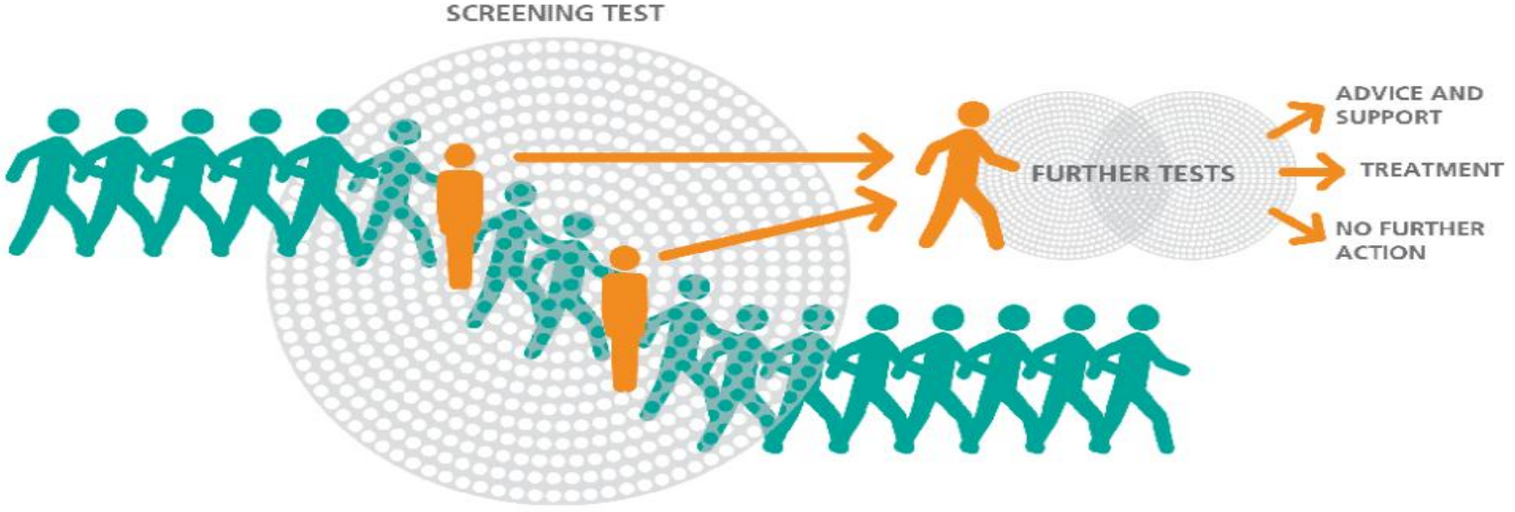
Faecal Immunochemical Test for haemoglobin (FIT)

Berkshire & Surrey Pathology Services

- Well established triage tool for **screening programmes** around the world

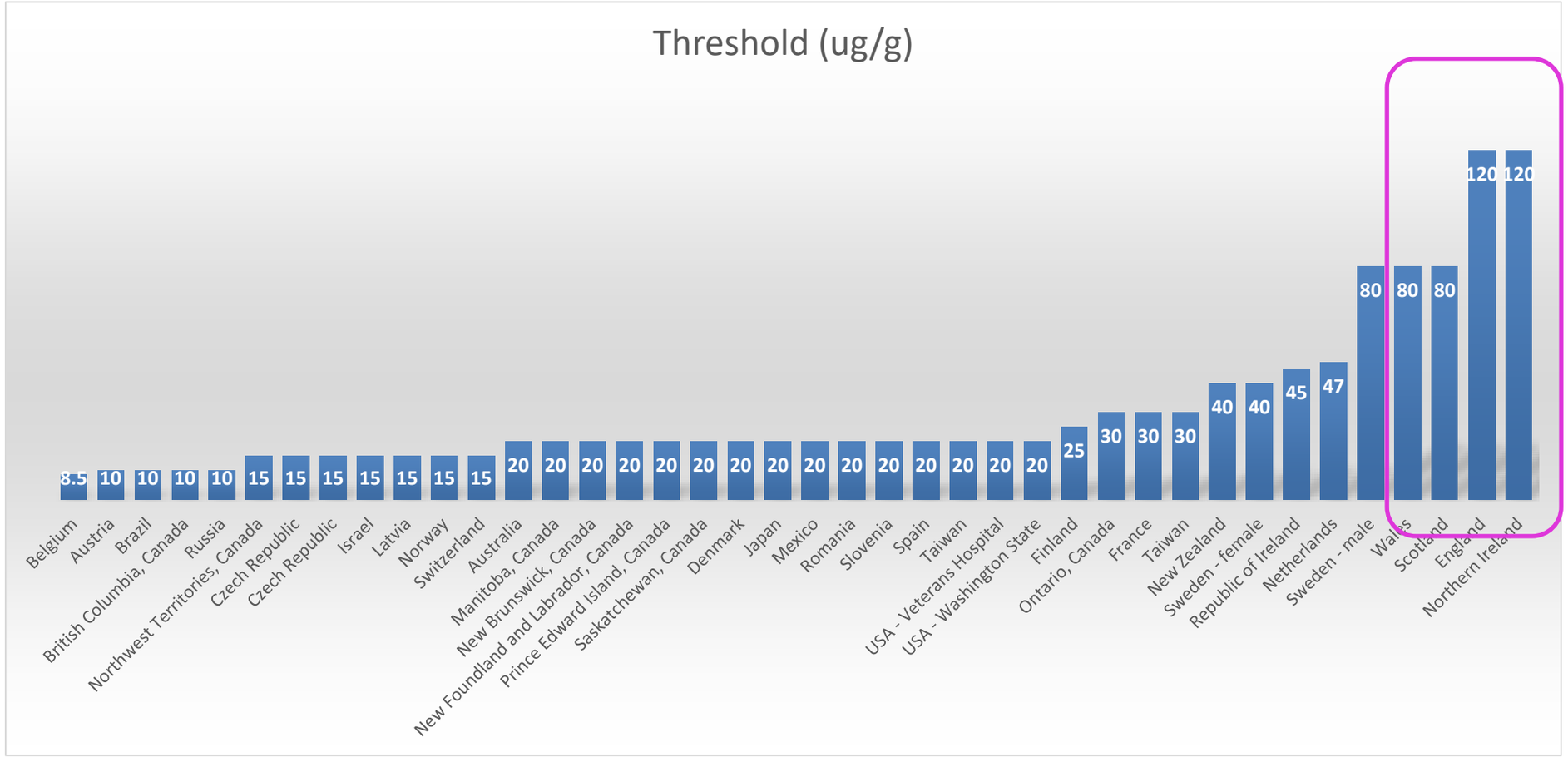
40-60 years
(programme/ country dependent)





Global Screening programme Thresholds

Berkshire & Surrey Pathology Services



Colonoscopy capacity challenges

Young GP, Benton SC, Bresalier RS, Chiu HM, Dekker E, Fraser CG, Frasa MAM, Halloran SP, Hoffmeister M, Parry S, Selby K, Senore C, Singh H, Symonds EL. **Fecal Immunochemical Test Positivity Thresholds: An International Survey of Population-Based Screening Programs**. Dig Dis Sci. 2025 May;70(5):1637-1645.

Reasons for selecting positivity threshold

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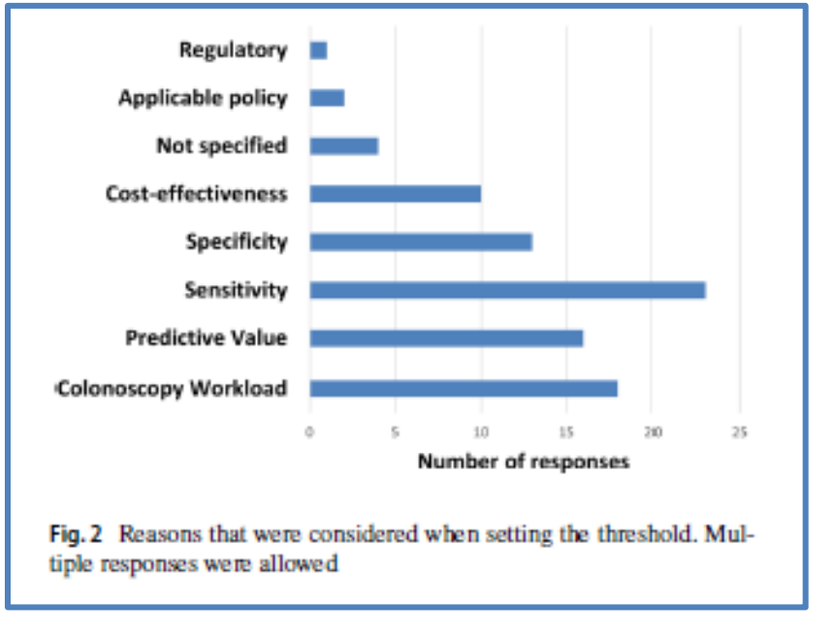

Fig. 2 Reasons that were considered when setting the threshold. Multiple responses were allowed

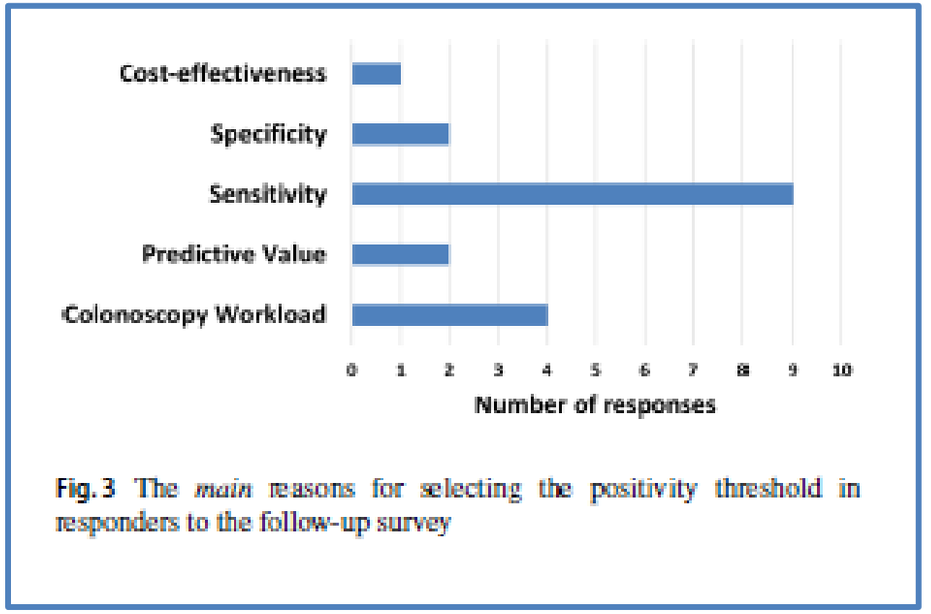

Fig. 3 The *main* reasons for selecting the positivity threshold in responders to the follow-up survey

- Majority of responses set threshold based on sensitivity
- Second most common reason was colonoscopy workload

Young GP, Benton SC, Bresalier RS, Chiu HM, Dekker E, Fraser CG, Frasa MAM, Halloran SP, Hoffmeister M, Parry S, Selby K, Senore C, Singh H, Symonds EL. **Fecal Immunochemical Test Positivity Thresholds: An International Survey of Population-Based Screening Programs**. Dig Dis Sci. 2025 May;70(5):1637-1645.

FIT Analyser use in screening programmes

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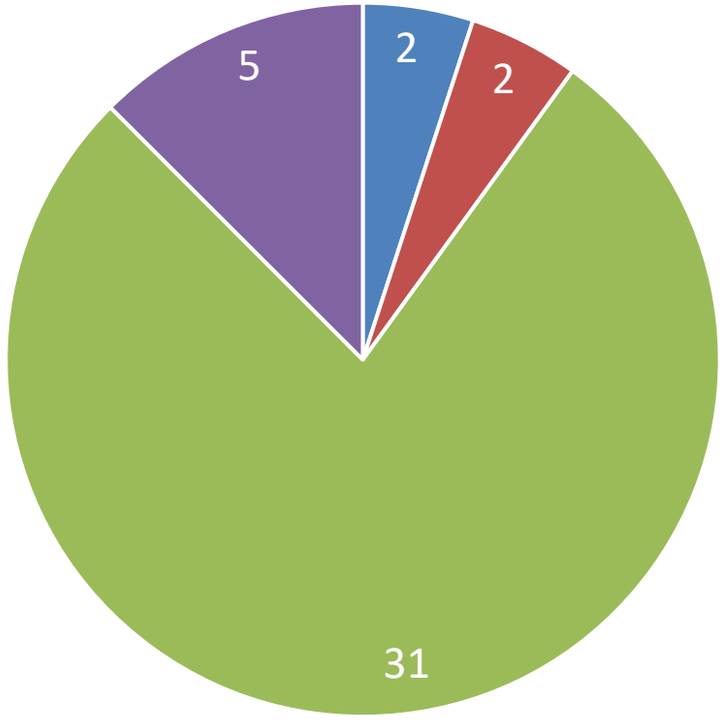


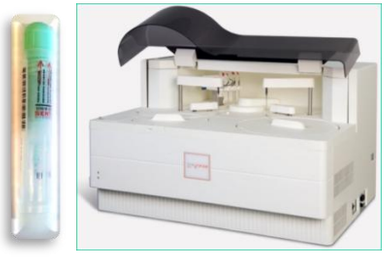
- NS-Prime, Alfresa Pharma
- HM-JACKarc, Minaris Medical
- OC-Sensor, Eiken Medical
- FOB gold, Sentinel

NS Prime

OC Sensor PLEDIA

HM-JACKarc

SentiFIT



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No standardisation of FIT methods

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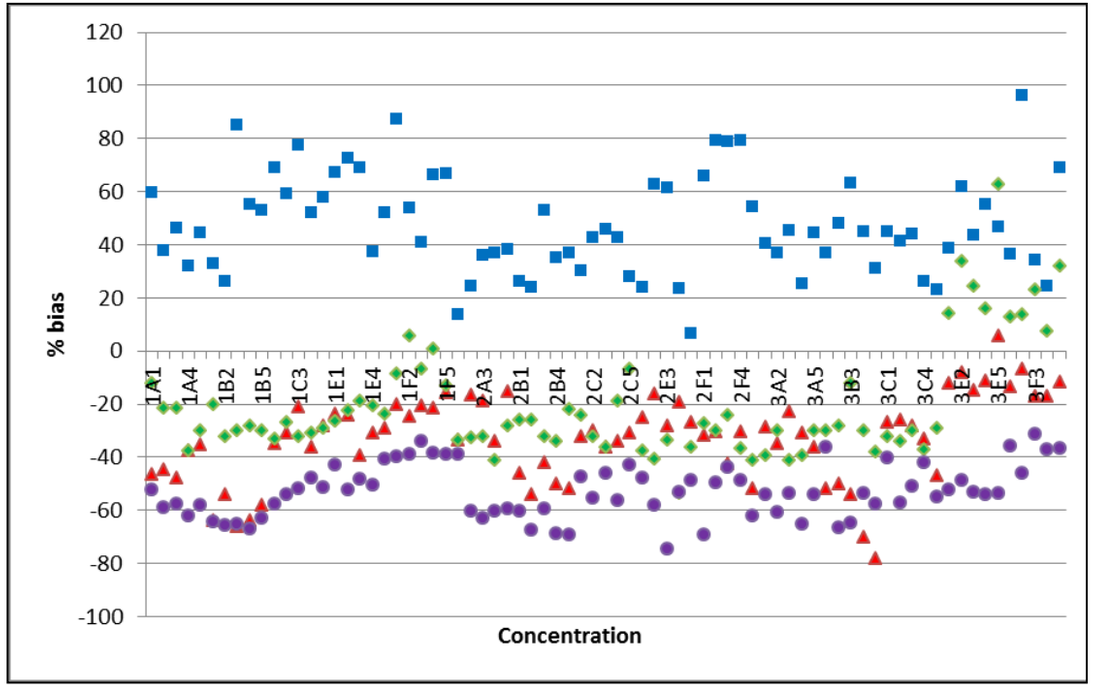
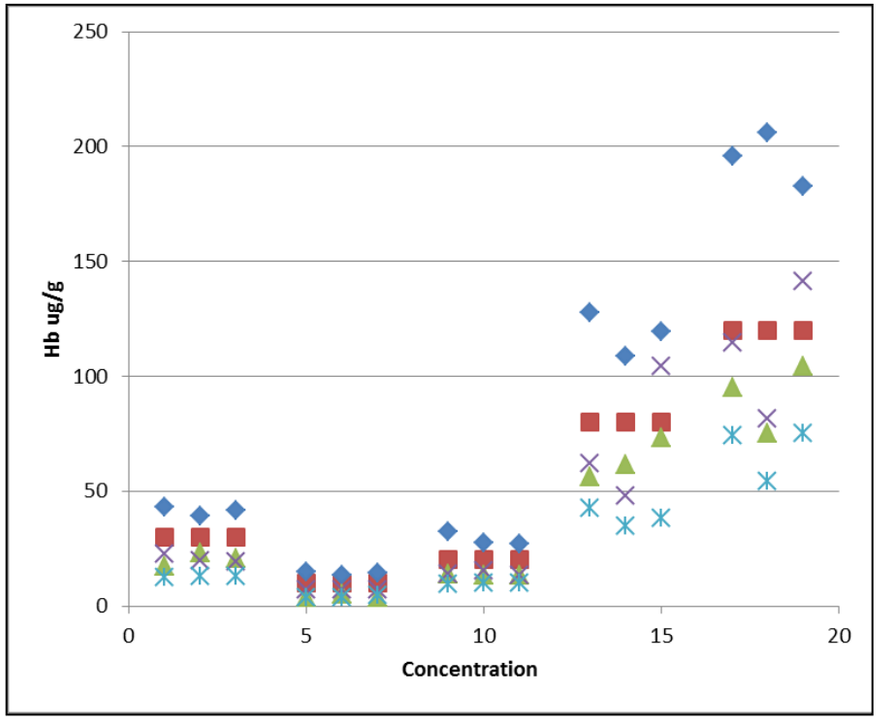
- No international standard for companies to calibrate methods against

- Different methods = different results





IFCC FIT working group established 2017

Canon CANON MEDICAL DIAGNOSTICS CORPORATION SENTINEL DIAGNOSTICS

EIKEN CHEMICAL CO.,LTD. alfresa Alfresa Pharma Corporation


Brussels 2018

ifcc International Federation of Clinical Chemistry and Laboratory Medicine


Vienna 2018


Barcelona 2019


Vienna 2024


Berlin 2025

Terms of Reference

- To harmonise and/or standardise analysis of haemoglobin in faecal samples by immunochemistry (FIT)
- To establish EQA and 3rd party IQC programmes
- To determine the feasibility of developing reference materials and/or commutable calibrators
- The IFCC FIT-WG can provide recommendations and guidance on preanalytical and analytical aspects of FIT

Photo Credit: Petr Kocna

Initial Summary statements from IFCC FIT working Group

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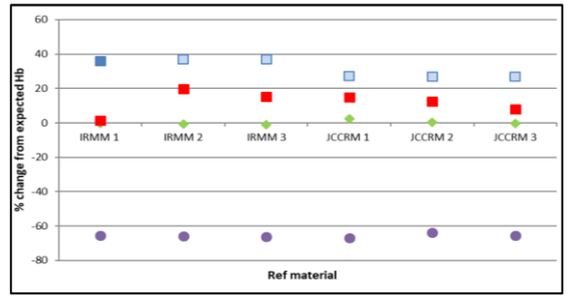
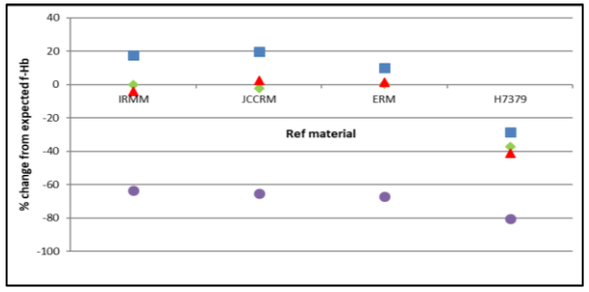
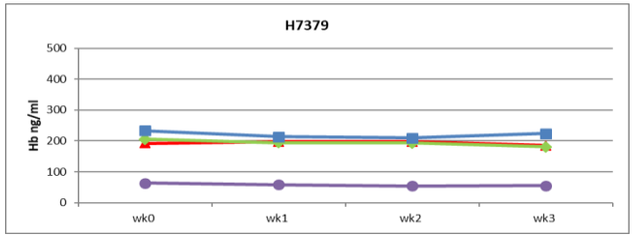
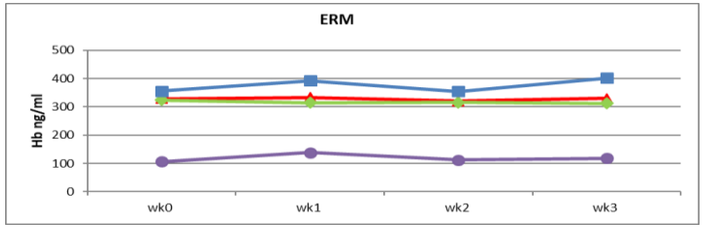
- Significant difference observed between quantitative results on different methods
- A common threshold cannot currently be applied
- We need to standardise methods
- Requires a common reference material to be identified for all manufacturers to calibrate method against









Standardisation – current status

Berkshire & Surrey Pathology Services

- Certified Reference Material (CRM) has been identified
- This should be available to purchase in the next 2 years
- Once CRM is available FIT manufacturers should re-calibrate their methods to the CRM
- **Currently - if moving from one FIT method to another important to ensure consider the impact on positivity/ referral rates**

Liesbet Deprez

European Commission
Joint Research Centre

Qualitative (Point of care) FIT

Berkshire & Surrey Pathology Services

- Lateral flow devices
- Marketed for public and/or healthcare use
- Manufacturer states a threshold for positivity
- Often this is based on a comparison to another lateral flow method
- No analytical evaluation carried out to assess thresholds quoted for positivity

Qualitative FIT

Berkshire & Surrey Pathology Services

Detect very low concentrations of f-Hb

Qualitative FOB product	Manufacturer LOD µg/g	Mean OC-Sensor Hb µg/g (each sample n=3)																
		0	0	1	2	3	4	5	6	6	7	7	8	10	20	27	82	82
		Results from qualitative FIT products																
Actim Fecal Blood	25	0	Fail*	0	0	0	0	0	0	100	0	100	100	100	100	100	100	100
Colonview	Not quoted	0	0	100	0	0	100	100	50	100	0	100	100	100	100	100	100	100
Colonview reader		**						100	0	**		100	**		100	**		
Diaquick FOB Cassette	5 supplier, 6 manufacturer	0	0	100	0	0	100	0	0	100	0	100	100	100	0	100	100	100
FOB Rapid Test	6	0	0	100	0	0	100	0	0	100	0	0	100	100	100	100	100	100
Hexagon OBTI	Not quoted	0	0	100	100	0	50	0	0	100	0	100	100	100	100	100	100	100
Nadal FOB	2	0	0	100	100	0	100	50	0	100	0	100	100	100	100	100	100	100
Nadal FOB75	3.75	0	0	100	0	0	50	0	0	100	0	100	100	100	0	100	100	100
Proflow Faecal Occult Blood	5	0	0	100	0	0	50	0	0	100	0	100	100	100	100	100	100	100

Clinically “safe” because no false reassurance

BUT

Will lead to excessive referrals

Southern Hub Research Team

Piggott C, John C, O'Driscoll S, Benton SC. Analytical evaluation of eight qualitative FIT for haemoglobin products, for professional use in the UK. Clin Chem Lab Med. 2024 Oct 9;63(3):572-580.

Qualitative FIT laboratory evaluation (2)

Berkshire & Surrey Pathology Services

	Non-frozen samples <6 µg/g			Non-frozen samples >6 µg/g		
Qualitative product	%Positive	%Borderline	%Negative	%Positive	%Borderline	%Negative
Supplier 1	25	6	69	100	0	0
Supplier 2	69	6	25	100	0	0
Supplier 3	69	13	19	100	0	0
Supplier 4	6	19	75	100	0	0
Supplier 5	19	19	63	100	0	0
Supplier 6	25	13	63	100	0	0
Supplier 7	63	19	19	100	0	0

Table 2. Positivity for f-Hb with qualitative FIT products using non-frozen samples, with the quantitative concentration determined by analysis of one OC-SENSOR sample prepared from homogenised faeces.

Clinically “safe” because no false reassurance
BUT
Will lead to excessive referrals

**Unpublished data from Southern Hub Research Team*

Qualitative FIT

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- Analytical studies indicate that the tests are extremely sensitive.
- If being used in symptomatic patients this is clinically safe
- In screening programme likely to cause huge numbers of unnecessary / unwarranted referrals – huge positivity rate
- Caution should be taken if considering using in a screening programme

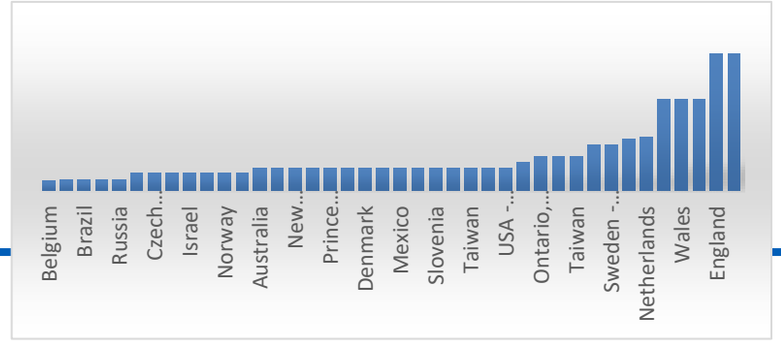
QuikRead Go – Quantitative Point of Care FIT

Berkshire & Surrey Pathology Services

- Suitable for use in clinic
- Evaluated analytically and clinically – good results
- 533 TWW patients included
- Sensitivity for CRC 92.9%
- Good agreement with laboratory FIT method
- Overall demonstrated good performance and suitable for clinical use

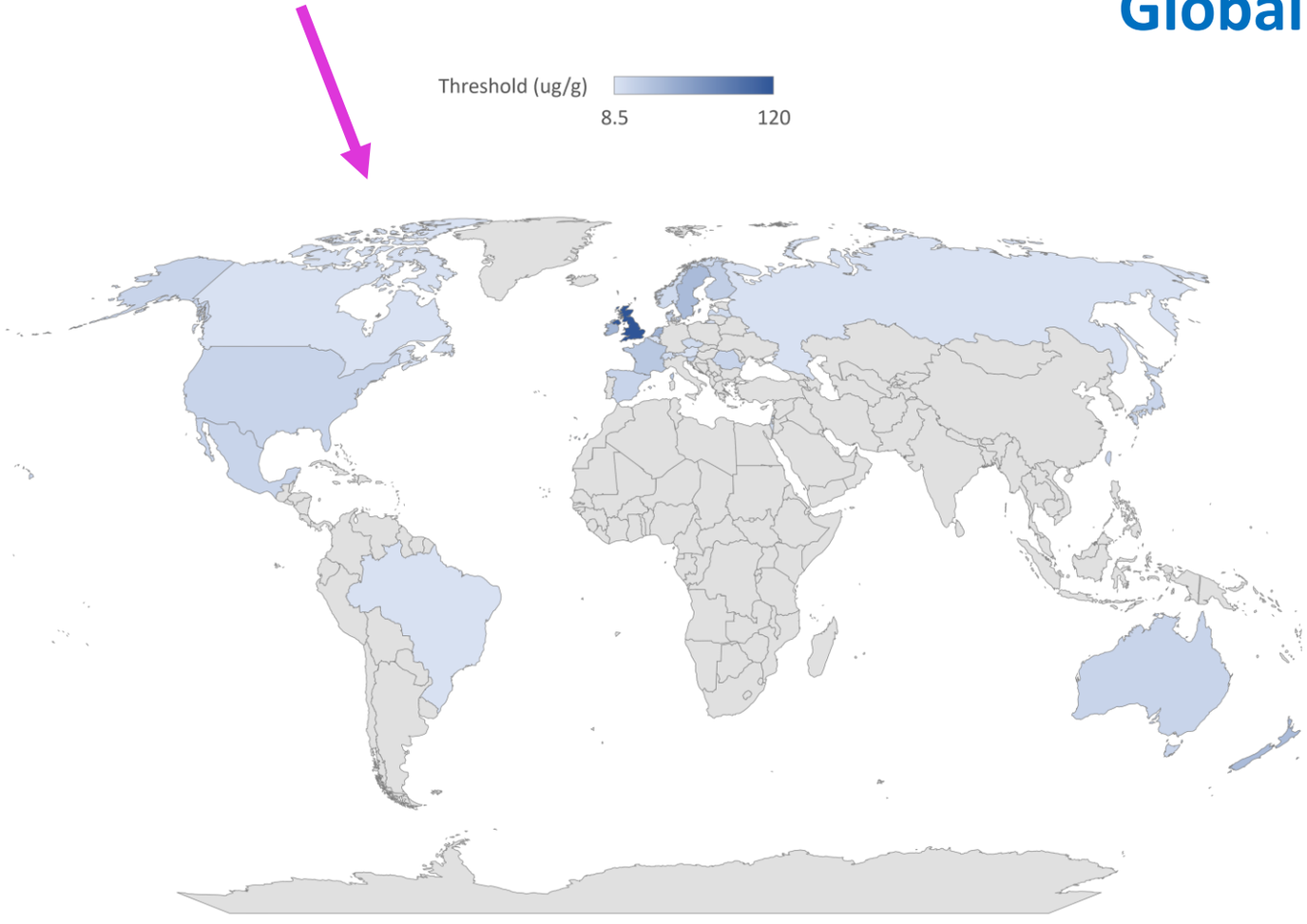
- Maclean W. Comparison of the QuikRead go® point-of-care faecal immunochemical test for haemoglobin with the FOB Gold Wide® laboratory analyser to diagnose colorectal cancer in symptomatic patients. Clin Chem Lab Med. 2021 Oct 25;60(1):101-108.
- Maclean W. Diagnostic accuracy of point of care faecal immunochemical testing using a portable high-speed quantitative analyser for diagnosis in 2-week wait patients. Colorectal Dis. 2021 Sep;23(9):2376-2386.

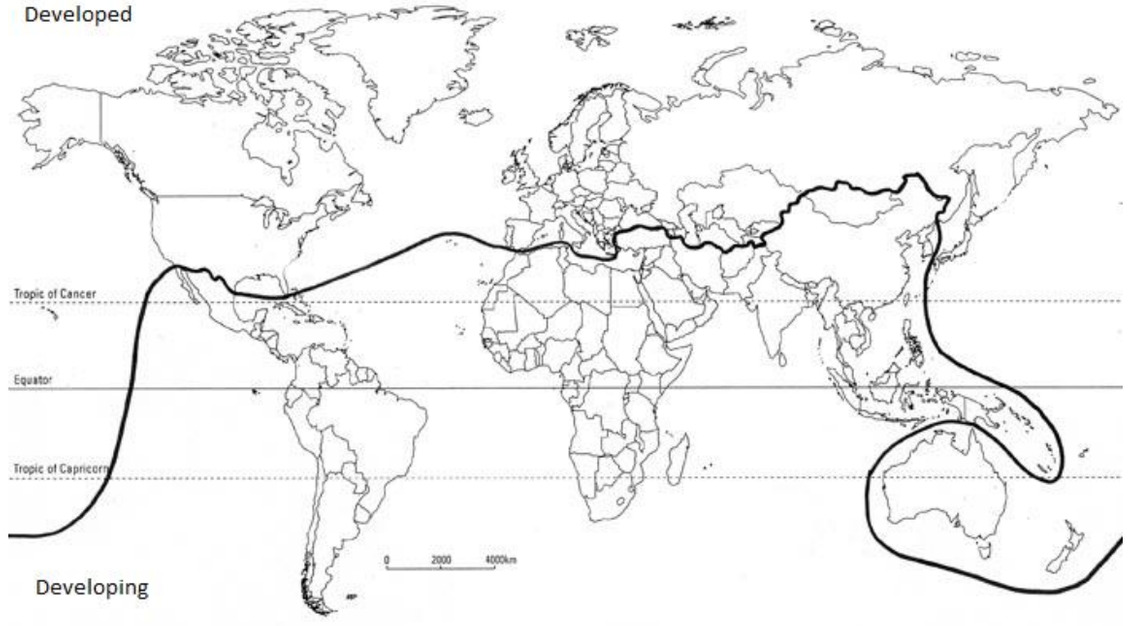
GLOBAL STATUS OF SCREENING PROGRAMMES



Berkshire & Surrey Pathology Services

Global Screening programmes





Young GP **Fecal Immunochemical Test Positivity Thresholds: An International Survey of Population-Based Screening Programs**. Dig Dis Sci. 2025 May;70(5):1637-1645.

Global Screening programmes

- Inequity

- Different challenges for different countries

Setting up a screening programme - challenging

Berkshire & Surrey Pathology Services

Programme Organisation
- National or regional
- Opportunistic of population based screening
- Local lab or Central lab

What FIT kit?

What threshold?

How are kits returned to lab?

How to get invitations and kits to the population?

General population	Educate and invite to screening	Sample Collection	Transport of sample	Receipt in lab	Analysis	Communicate result and refer for colonoscopy if required

Referral process if further test required?

Education and awareness

Requires
- Organised health system
- Resource
- Funding

Setting up a screening programme - challenging

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WEO
World Endoscopy Organization

WEO CRC Screening Committee: Colorectal Cancer Screening Committee
Task Force to Support the Implementation of CRC Screening Programs

https://www.worldendo.org/about-us/committees/colorectal-cancer-screening-committee

Developing screening programmes

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- South America
  - Brazil – FIT testing guided colonoscopy study successful
  - Chile – FIT trial “PRENEC” 2012. Endoscopy capacity limitations
  - Argentina – colonoscopy based trial

- Africa
  - Morocco, Nigeria and South Africa have carried out FIT based pilots and have plans to screen
  - Mauritius – recently set up a FIT CRC screening programme. Low uptake (24%)
  - Age considerations important – CRC seems to present younger in Africa

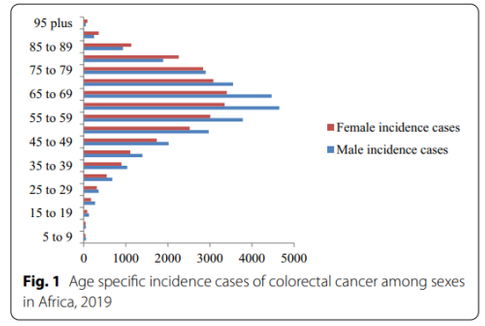

Fig. 1 Age specific incidence cases of colorectal cancer among sexes in Africa, 2019

- Asia
  - Philippines
  - Thailand

PARTICIPATION IS CRUCIAL FOR A SUCCESSFUL SCREENING PROGRAMME

UPTAKE

- The percentage of people offered a screening test who complete it

COVERAGE

- The percentage of eligible individuals in a population who have been adequately screened within a specified timeframe

Global Screening programme Thresholds

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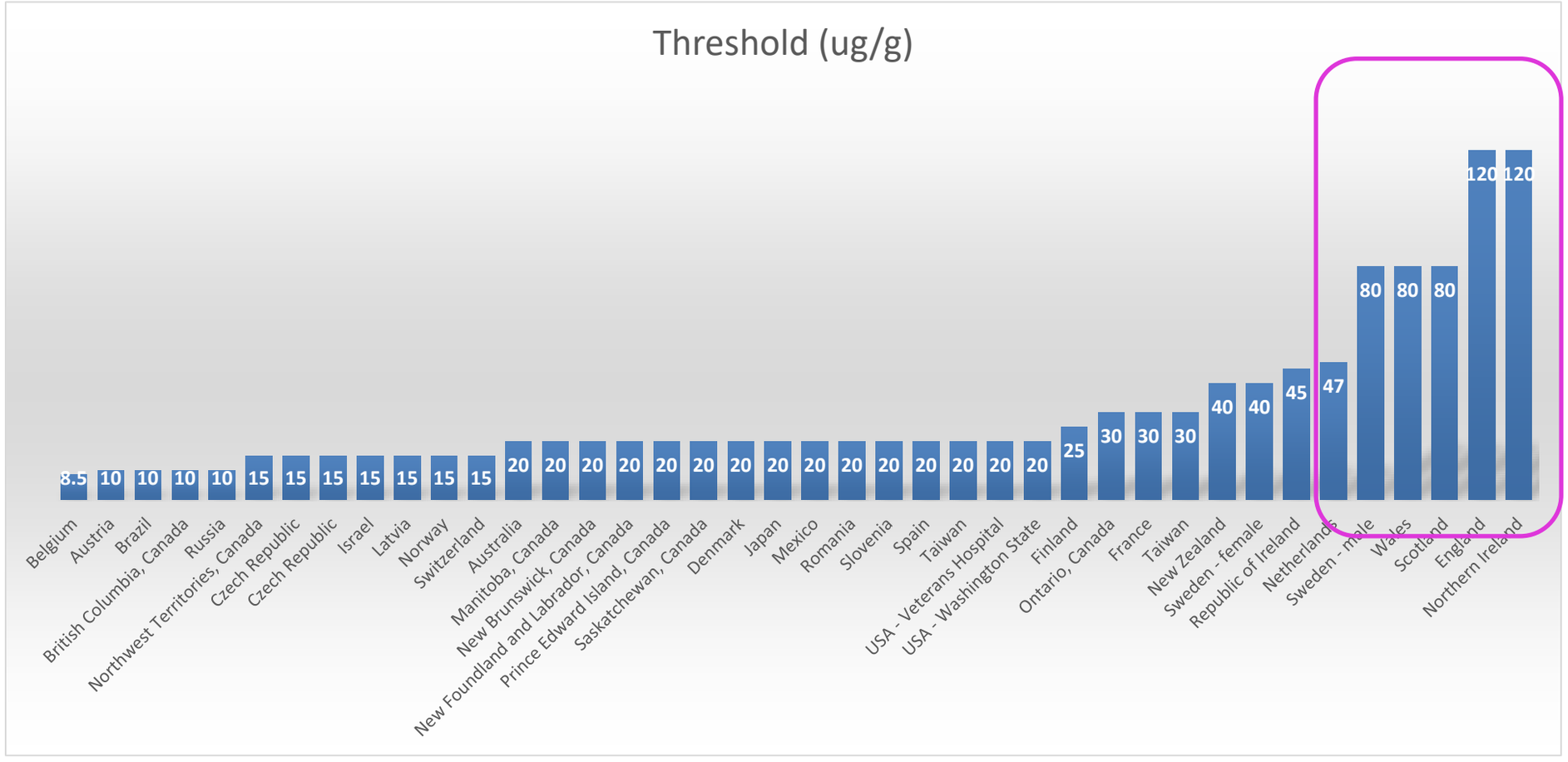

Colonoscopy capacity challenges

Young GP, Benton SC, Bresalier RS, Chiu HM, Dekker E, Fraser CG, Frasa MAM, Halloran SP, Hoffmeister M, Parry S, Selby K, Senore C, Singh H, Symonds EL. **Fecal Immunochemical Test Positivity Thresholds: An International Survey of Population-Based Screening Programs**. Dig Dis Sci. 2025 May;70(5):1637-1645.

Coverage

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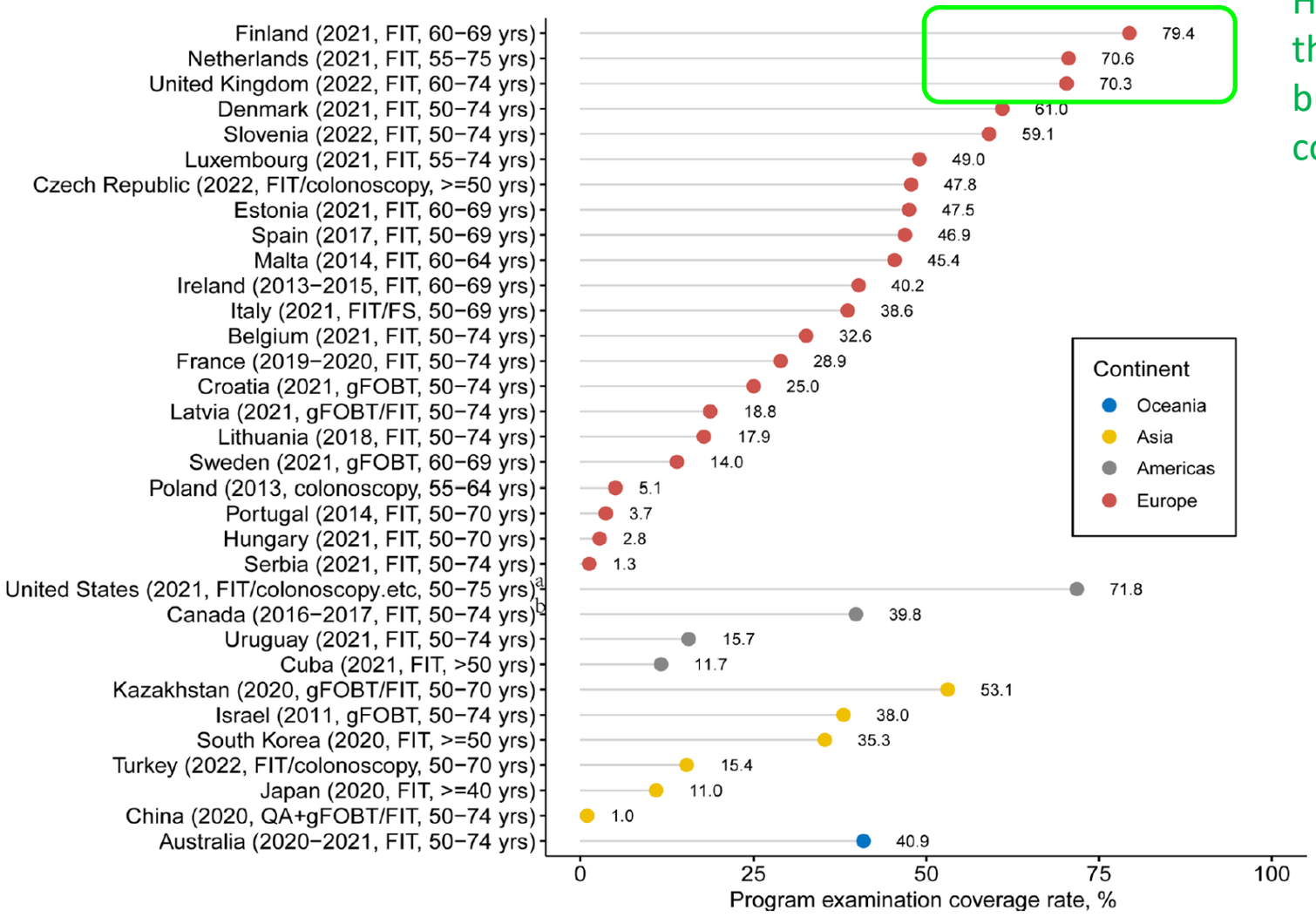
- The percentage of eligible individuals in a population who have been adequately screened within a specified timeframe



High thresholds but great coverage

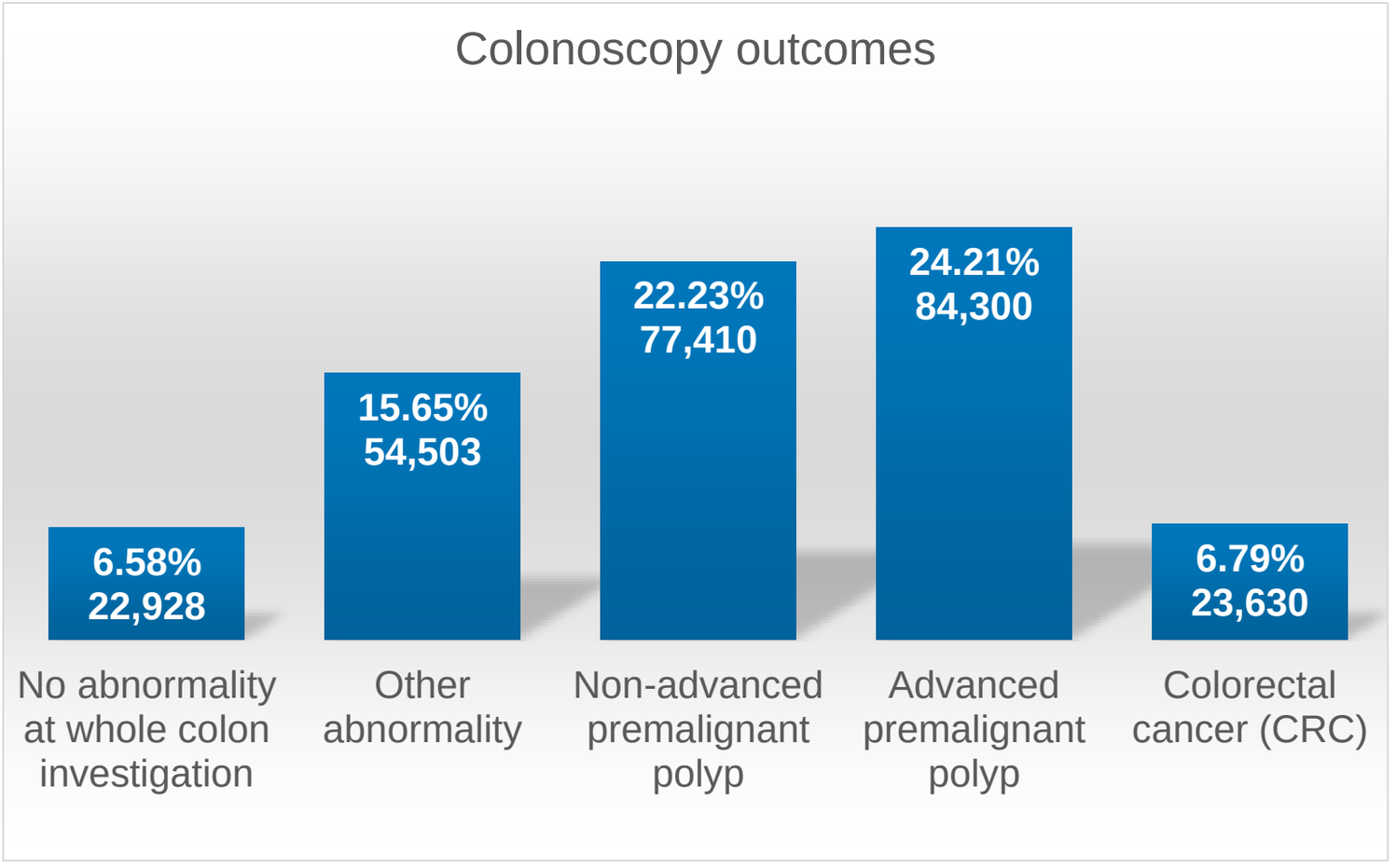
Chen Y et al. Global colorectal cancer screening programs and coverage rate estimation: an evidence synthesis. J Transl Med. 2025 Jul 22;23(1):811.

English Screening programme (2019 – 2024 – unpublished data)

Berkshire & Surrey Pathology Services

18,223,843 episodes*

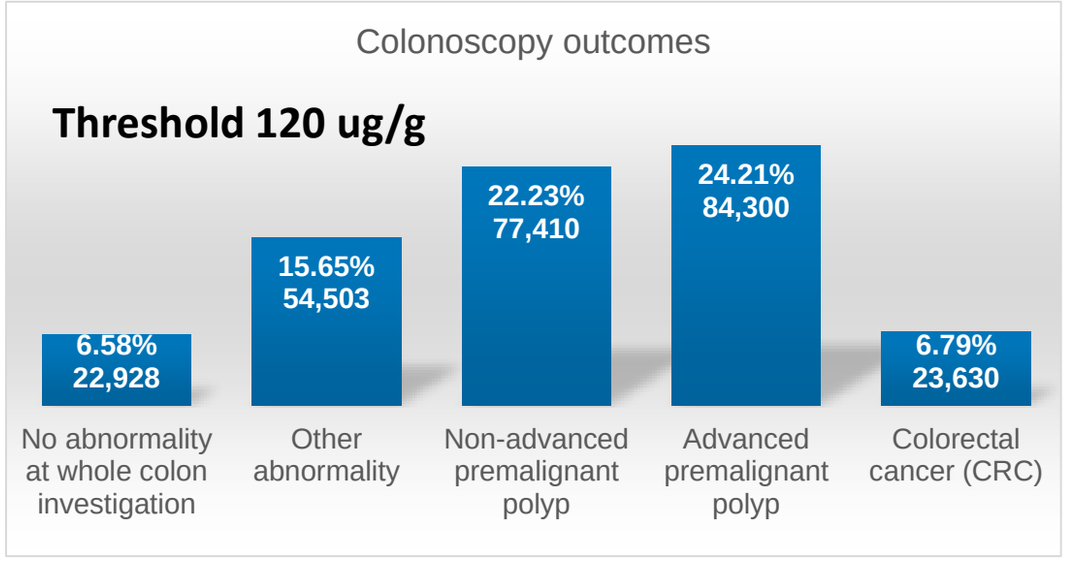
272,378 (1.49%) had further investigations



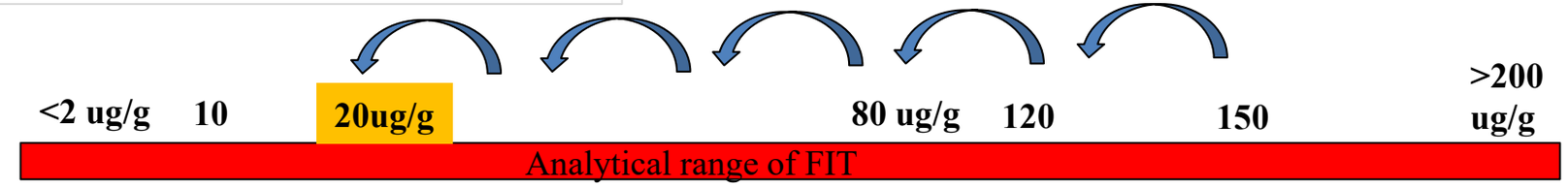
- Threshold 120 ug/g = too high.
- Number needed to Scope is good BUT we are missing cancers and pre-cancers

English Screening programme (2019 – 2024 – unpublished data)

Berkshire & Surrey Pathology Services



UK National Screening Committee



Increase sensitivity and decrease specificity

Decrease sensitivity and increase specificity

Impact of dropping threshold on Colonoscopy referrals in England

NHS
Berkshire & Surrey Pathology Services

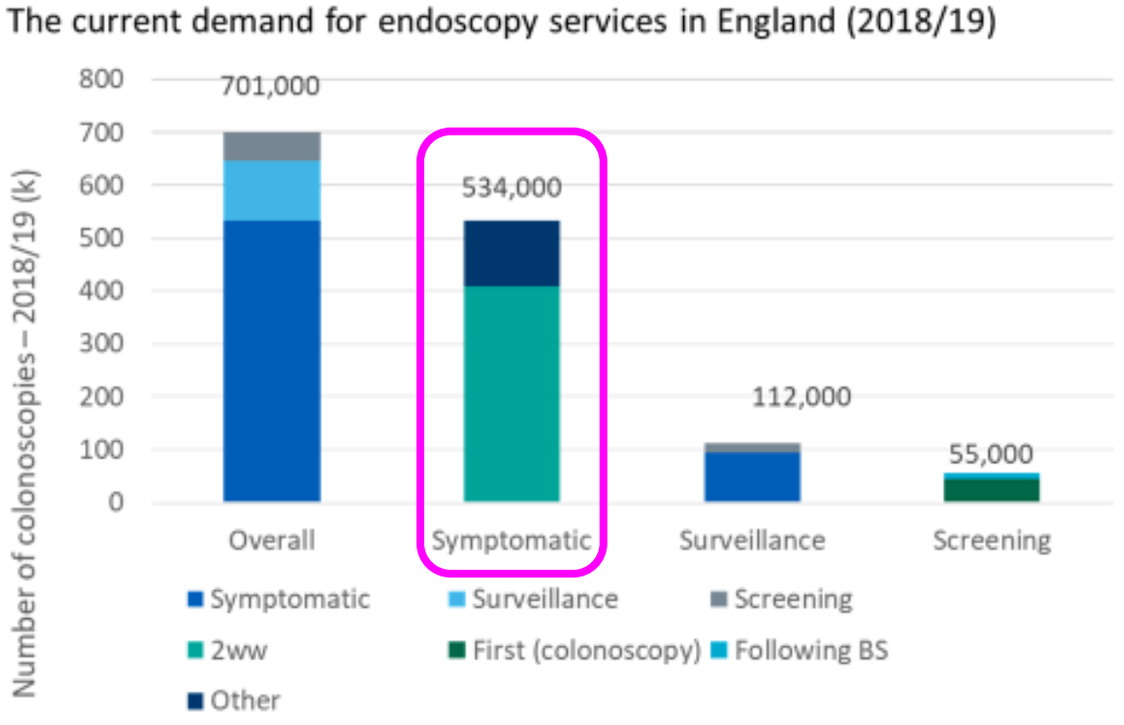
FIT threshold (µg/g)	Number of positives	Positivity (%)	Percent increase in the number of FIT positive episodes compared to the 120 µg/g threshold
120	348,218	1.9	0
110	373,041	2.1	7.1
100	402,559	2.2	15.6
90	437,442	2.4	25.6
80	479,427	2.7	37.7
70	531,554	3	52.7
60	598,847	3.3	72
50	690,453	3.8	98.3
40	828,088	4.6	137.8
30	1,053,999	5.9	202.7
20	1,415,720	7.9	306.6
10	2,144,423	11.9	515.8

300% increase in endoscopy requirement

Unpublished data from English Screening Programme (2019-2024)

Symptomatic Risk stratification to free up screening colonoscopy capacity

Berkshire & Surrey Pathology Services



NHS England and NHS Improvement

FIT use in symptomatic pathways

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- In England FIT used to triage symptomatic patients for colonoscopy
- Threshold of 10 ug Hb/g faeces
- High sensitivity, poor specificity

NICE National Institute for Health and Care Excellence

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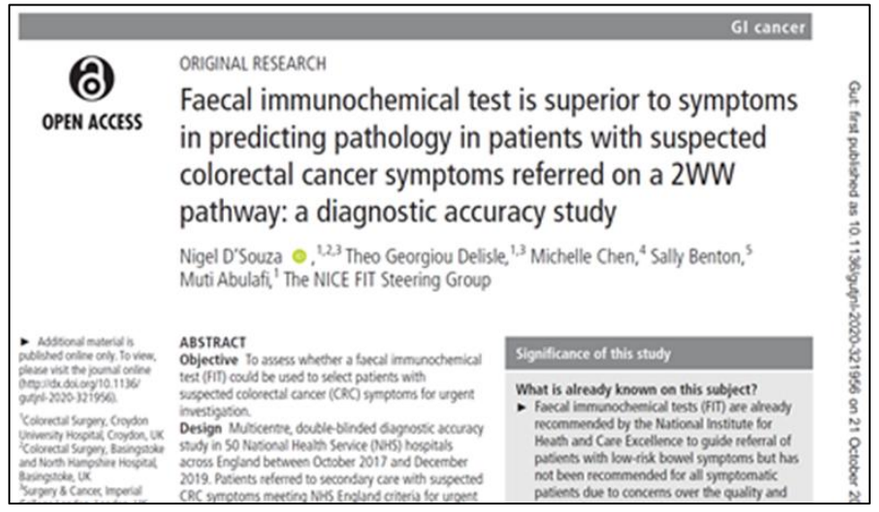
Quantitative faecal immunochemical testing to guide colorectal cancer pathway referral in primary care

Diagnostics guidance [DG56]
Published: 24 August 2023 Register as a stakeholder



GI cancer

OPEN ACCESS

ORIGINAL RESEARCH

Faecal immunochemical test is superior to symptoms in predicting pathology in patients with suspected colorectal cancer symptoms referred on a 2WW pathway: a diagnostic accuracy study

Nigel D'Souza, Theo Georgiou Delisle, Michelle Chen, Sally Benton, Muti Abulafi, The NICE FIT Steering Group

ABSTRACT

Objective To assess whether a faecal immunochemical test (FIT) could be used to select patients with suspected colorectal cancer (CRC) symptoms for urgent investigation.

Design Multicentre, double-blinded diagnostic accuracy study in 50 National Health Service (NHS) hospitals across England between October 2017 and December 2019. Patients referred to secondary care with suspected CRC symptoms meeting NHS England criteria for urgent

Significance of this study

What is already known on this subject?

- Faecal immunochemical tests (FIT) are already recommended by the National Institute for Heath and Care Excellence to guide referral of patients with low-risk bowel symptoms but has not been recommended for all symptomatic patients due to concerns over the quality and

Gut: first published as 10.1136/gutjnl-2020-321956 on 21 October 20

Nigel D'Souza et al. Gut doi:10.1136/gutjnl-2020-321956

RISK STRATIFICATION

Risk stratification in Symptomatic FIT pathways; "COLOFIT"

Nottingham Colorectal Service

Prof David Humes

- Risk algorithm being implemented in England for symptomatic patients

- Input Factors
  - Gender
  - Age
  - Full Blood Count (MCV, Platelets)
  - f-Hb

$$92014) \begin{pmatrix} +1.6685765\left(\frac{AGE}{100}\right)^3 - 13.9435406\left(\frac{AGE}{100}\right)^3 \cdot \ln \\ -\frac{1.9965475}{\sqrt{\left(\frac{FIT}{100}\right)}} - \frac{0.2657153}{\sqrt{\left(\frac{FIT}{100}\right)}} \cdot \ln\left(\frac{FIT}{100}\right) \\ +0.9208493 \cdot \ln\left(\frac{PLATELETS}{100}\right) \\ -\frac{3.9007829 \cdot MCV}{100} \\ +0.4543275 \cdot male \end{pmatrix}$$

Ref: COLOFIT: Development and internal-external validation of models using age, sex, faecal immunochemical and blood tests to optimise diagnosis of colorectal cancer in symptomatic patients. CJ Crooks, J West, J Jones, W Hamilton, SER Bailey, G Abel, A Banerjea, CJ Rees, A Tamm, BD Nicholson, SC Benton, COLOFIT Research Group, DJ Humes. medRxiv 2024.03.01.24303196;

ColoFIT – impact and outcomes

Extrapolating true and false positive and negative rates from Cox model to 100,000 FITs in the validation cohort. (First FIT per patient only, 95% confidence intervals derived through bootstrapping [*n* = 1000]). All numbers rounded to the nearest integer.
Developed model with MCV, platelet count, f-Hb, age and sex

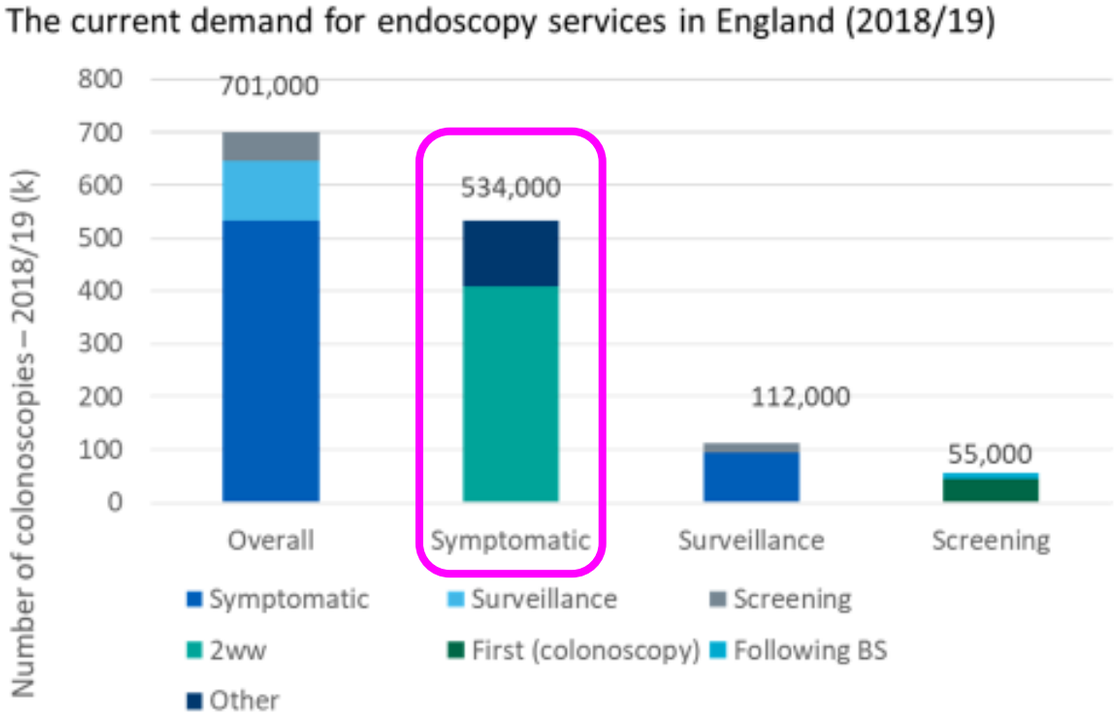
Selected cut off for referral for further investigations	**Derivation. FITs November 1 2016–November 30 2021**			
Cancer risk threshold (1-survival predicted from model)	**Colonoscopies performed for patients above predicted threshold**	**Detected cancer cases (true positives)**	**Missed cancer cases (false negatives)**	**Normal colonoscopies (false positives)**
0%	100,000	1515	0	98,485
0.6%	21,383	1388	127	19,994
1%	17,033	1349	166	15,684
2%	12,472	1287	228	11,185
3%	10,001	1239	276	8762

Symptomatic Risk stratification to free up screening colonoscopy capacity

Berkshire & Surrey Pathology Services

NHS England:

- A national change to FIT@80ug/gm in the BCSP would require 33,000 more colonoscopies to be delivered.
- It is expected this change will result in ~500 more cancers being diagnosed per year and 3000 HRA's.



NHS England and NHS Improvement

- 35,000 FIT kits sent out/ per day in England
- ~68% uptake
- Not possible to get blood sample on this number of people

- Colofit cannot be used in screening programme because no blood results

UK Risk stratification in Screening

Berkshire & Surrey Pathology Services

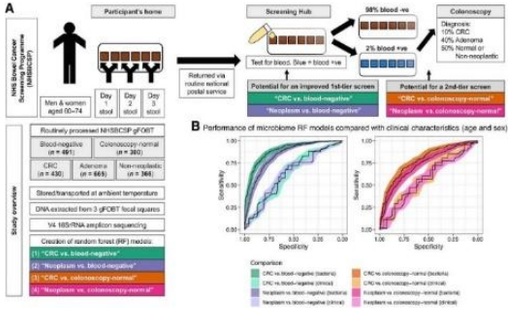
BOWEL STAR STUDY

- £2.5m CRUK grant
- Scotland and England

CANCER RESEARCH UK

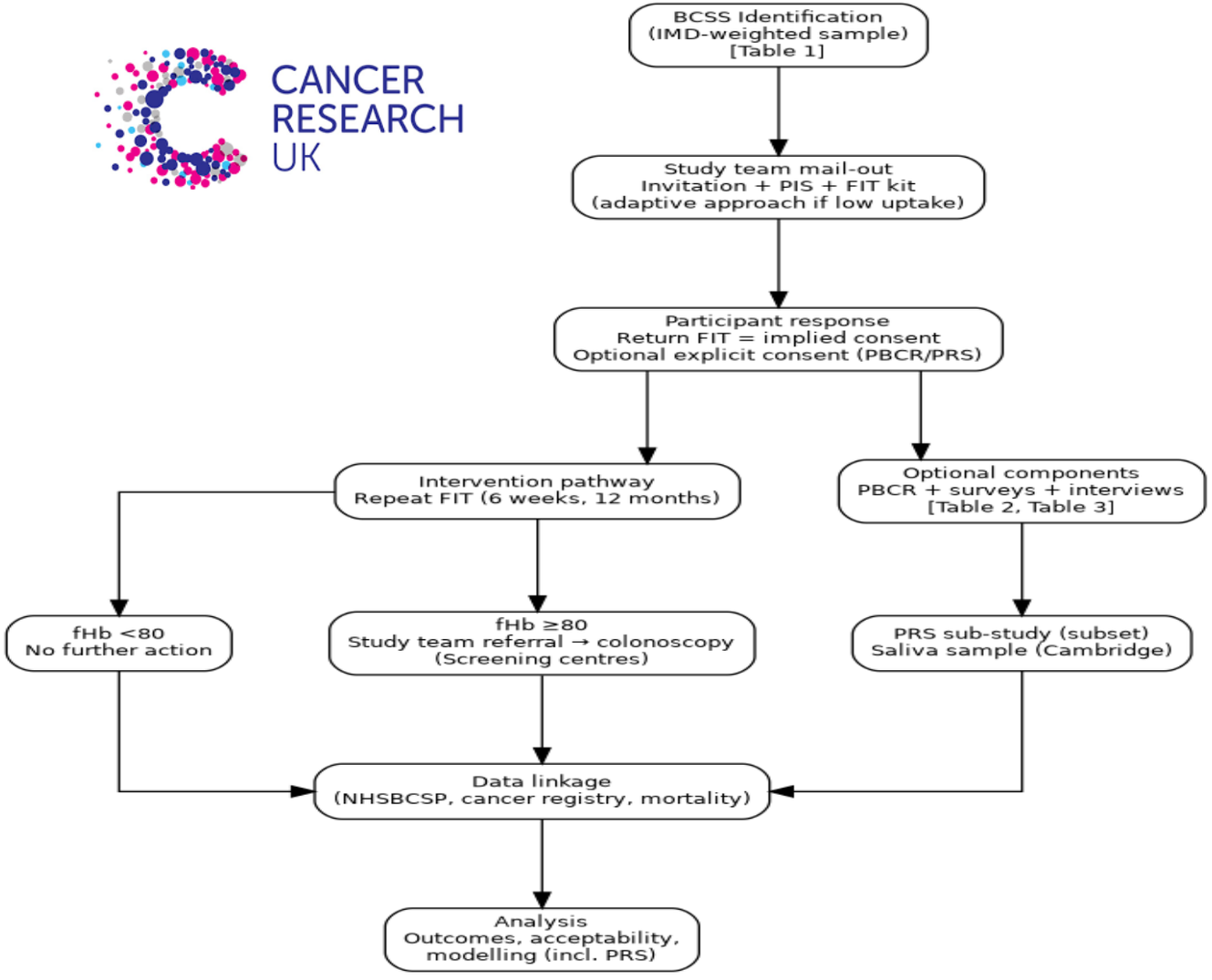
MICROBIOME

CANCER RESEARCH UK



UK Bowel Star Study

Berkshire & Surrey Pathology Services



- £2.5 million pound grant
- Lead by Profs David Weller and Peter Sasieni
- Intervention study = additional FIT at 6 weeks and 12 months
- England and Scotland
- Huge challenges getting the study approved to be run as part of the screening programme in both nations

Risk stratification

- Lots of discussion over a number of years

- Huge numbers of publications modelling and proposing risk stratification strategies
  - Using age and sex alongside f-Hb
  - Different screening intervals based on f-Hb concentration
  - Introduction of new biomarkers alongside FIT
  - Utilising data already available eg artificial intelligence

- Finland and Sweden implemented sex specific thresholds
  - Sweden - Women 40ug/g; Men 80 ug/g
  - Finland piloted different thresholds but now have single threshold

- Taiwan - 4P based CRC screening – not yet implemented
- Netherlands – Perfect Study – RCT in progress

Risk stratification

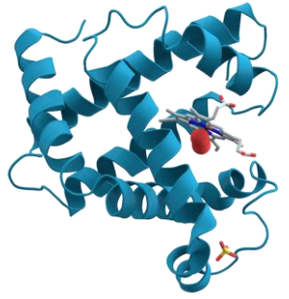
Berkshire & Surrey Pathology Services

- Implementation of risk stratification/ personalised screening is challenging
- Destabilises current screening programmes already established
- How do we move from modelling to implementation?

Novel Biomarkers

Berkshire & Surrey Pathology Services

- Lots of interest in this and developments on-going from diagnostic companies
- Circulating tumour DNA and protein based biomarkers in blood
- Faecal microbiome



Two stage triage/ biomarker testing ?

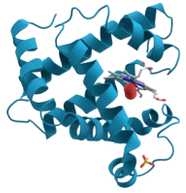
Berkshire & Surrey Pathology Services

- Low threshold FIT has high sensitivity and poor specificity for CRC and pre-cancerous lesions

- Need to improve specificity without losing sensitivity

- 1st line test FIT (sensitive) → 2nd test (specific) → Colonoscopy



Summary

NHS
Berkshire & Surrey Pathology Services

- FIT screening programmes are well established in the developed world and evolving in other countries
- Work towards harmonising FIT methods is on-going and making good progress
- Caution urged with use of qualitative FIT in screening programmes
- Risk stratification continues to be a topic of discussion and interest and appears to remain a challenge for full implementation

Southern Hub Research Team