Risk Stratification in BowelCancer Screening Programmes

Presentation to NSC Horizon Scanning event 31st January 2024 David Weller, University of Edinburgh



Vision for extending risk-stratification:

A future in which stratification improves the benefits and reduces the harms of bowelcancer screening

Aspirations:

- More people are prevented from developing CRC
- People who develop CRC are diagnosed at the earliest possible stage
- Available resource is maximised, with efficiency and equity at the forefront

How to get there:

- Examine how use of CRC risk data on cancer <u>now</u> and cancer <u>in the</u> <u>future</u> can refine screening
- Understand the implications of stratified screening for society
- Design and run clinical studies to evaluate risk stratified screening

Current priorities:

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- To provide the evidence to guide bowel cancer screening programmes in potential transition to stratified screening
- To identify how stratified screening can detect more cancers within existing resource constraints through strategies which
 - are inclusive
 - don't exacerbate health inequalities
 - are widely acceptable in the UK population
- To explore acceptability of these approaches and their organisational & health economic implications
- To develop future research leaders in this field

What is stratified bowel cancer screening?

Genetic risk **Quantitative FIT** Non-genetic risk factors SNP **RISK FACTORS:** ACGI A POOR EXCESSIVE SEDENTARY GCA DIET AL COHOL LIFESTYLE GCGT G C A CGT Risk-**Risk-stratify** stratified screening screening participants Large bowsi (csten)protocols Colenceone • repeat FIT • alter FIT screening interval







Risk-stratified bowel screening: a CRUK priority

"

bringing flexible risk-adapted screening to the UK's national cancer screening programmes; through research, identify mechanisms to risk stratify the population (through genomic or other means) and then integrate clinically- and cost-effective risk stratification into existing national screening programmes to maximise appropriate ED&D "

It's imperative bowel screening continues to adapt

Key priorities:

- finite colonoscopy capacity for screening and symptomatic services
- lowering age limits and reducing FIT thresholds, while justifiable, lead to increased demands on colonoscopy, with lower PPV
- technical advances, eg liquid biopsies, multi-cancer early detection tests
- organisational changes within programmes
- screening effort needs to focus on those at higher risk with less-intensive screening in low-risk individuals
- there isn't a 'do nothing' option programmes need to adapt to changing demands and priorities



Bowel Cancer Screening Programme







Making better use of quantitative FIT

- numerous studies have demonstrated a correlation between fHb concentration and the presence of CRC and/or clinically significant adenomas.^[1]
- approaches which exploit the full range of FIT results could guide post-screening investigations,¹ and lead to more efficient and effective targeting of screening and associated resources. Growing data on changing existing screening algorithms - for example, lowering thresholds, repeat testing or reducing screening intervals.^{[2],[3]}
- these models need updating and refinement as more contemporary data become available they also need testing in 'real world' settings; trials of stratified screening have commenced in countries including the Netherlands^[4] and Italy.^[5]
- Interest in people with fHb levels just below threshold (more intense screening?) AND individuals with fHb levels in the range 0 - <10µg/g (less screening?)
 - 1. Navarro M, Hijos G, Ramirez T, Omella I, Carrera-Lasfuentes P and Lanas Á (2019) Fecal Hemoglobin Concentration, a Good Predictor of Risk of Advanced Colorectal Neoplasia in Symptomatic and Asymptomatic Patients. Front. Med. 6:91. doi: 10.3389/fmed.2019.00091
 - 2. Optimising Bowel Cancer Screening Phase 1: Optimising the cost effectiveness of repeated FIT screening and screening strategies combining bowel scope and FIT screening Sophie Whyte, Chloe Thomas, Ben Kearns, Mark Webster, Jim Chilcott. 25th June 2018 Prepared for: NATIONAL SCREENING COMMITTEE
 - 3. Shuping J, Seedher T, Sharples L et al. Impact of changes to the interscreening interval and faecal immunochemical test threshold in the national bowel cancer screening programme in England: results from the FIT pilot study British Journal of Cancer volume 127, pages1525–1533 (2022)
 - 4. Personalised colorectal cancer screening strategies: information needs of the target population Esther Toes-Zoutendijk International Cancer Screening Network (ICSN) Meeting June 21 June 23, 2023 Turin, Senore C. Trial of stratified bowel cancer screening in Reggio-Emilia. International Cancer Screening Network (ICSN) Meeting June 21 June 23, 2023 Turin, Italy

SHOULD WE USE PERSONAL BOWEL CANCER RISK INFORMATION?



- based on a range of potential parameters, including age, sex, previous FIT screening results, genetics (polygenic risk scores, PRS), familial and lifestyle factors: potential to refine and improve risk stratification based on fHb level alone
- PRS major focus of CRC risk assessment research; modelling studies have illustrated their potential
 - reasonable acceptability of incorporating PRS into cancer screening programmes
 - impact on health outcomes and resource use is yet to be examined in 'real world' settings
 - concerns that PRS contribution to bowel cancer risk may be 'overwhelmed' by other factors (eg FIT level).
 - genetic testing may be expensive and difficult to implement at a population level
 - complex ethical challenges associated with widespread testing, and concerns around equality, particularly amongst non-white European populations.
- family history and lifestyle factors: also significant impact on CRC risk for example better detection of advanced colorectal neoplasia when used in conjunction with FIT

PRS, lifestyle, previous screening history and bowel cancer screening

- we know both PRS and lifestyle add <u>something</u>
- evidence that previous screening history is significant
- feasibility of collecting/using this information within screening programmes
- vital that cancer screening programmes are at the vanguard of risk stratification based on personal bowel cancer risk





RESEARCH ARTICLES | JULY 01 2022

Evaluating the Potential of Polygenic Risk Score to Improve Colorectal Cancer Screening

Coral Amau-Colleli : Anna Diez-Villanueva 🎯 ; Beatriz Beliosillo 🗣 ; Josep M. Augé 🗣 ; Jenifer Muñoz 🗣 ; Elisabet Guinó; Leticia Moreira 🗣 ; Anna Serradesanferm; Angels Pozo; Isabel Tora-Rocamora; Lala Bonjoch 🖗 ; Germa Ibañez-Sanz 🖗 Mirela Obon-Santasana 🗣 ; Ferra Moratalia-Navarro; Rebeca Sanz-Pamolona; Carmen Márquez Marquez; Rebeca Rueda Miret 🗣 . Rocio Pérez Bertegal; Gabriel Flquer Velasco 😜 ; Antoni Castella 🗣 ; Josep M. Borràs 🍣 ; Cristina Hernandez Rodriguez; CRIPREV consortium" Jaume Grau 🛇 ; Antoni Castella 🗣 ; Josep M. Borràs 🍣 ; Xaver Bessa 🍽 ; Victor Voreno 🖆 ; Serg (Castelivi-Bei 📽 🍵

Clinical and Translational GASTROENTEROLOGY

Clin Transi Gastroenterol, 2022 Mar; 13(3): e00458. Published online 2022 Jan 19. doi: 10.14309/cjq.00000000000458 PMCID: PMC8963839 PMID: 35060941

Variation of Positive Predictive Values of Fecal Immunochemical Tests by Polygenic Risk Score in a Large Screening Cohort

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Sally Benton





Ian Tomlinson



CRUKEarly Diagnosis Programme Grant on Stratified

Bowel Cancer Screening, commencing May 2024

Max Agnew



Christian Von Wagner



Malcolm Dunlop



Juliet Usher-Smith

Stephen

Sophie Whyte

Duffy



Rhian Gabe





Peter Hall



A multi-institutional, multi-disciplinary collaboration



Our programme of work

Integrated WPs, running concurrently



Health economics of stratified screening

Aims

To model the cost-effectiveness of using risk-stratified screening protocols in UK bowel screening programmes

To determine which model parameters contribute most to uncertainty and us this to inform the design of our cohort study

To evaluate how risk-stratified screening might impact socioeconomic inequalities in CRC incidence and mortality over the long term

Research questions

- Using microsimulation modelling what are the predicted long term impacts of risk stratified screening? (such as impact on late stage incidence, CRC mortality, QALYs, endoscopy capacity etc.)
- 2. What is the predicted impact of risk stratified screening on health inequalities?

Informed choice and patient experience

- how acceptable are stratified approaches to CRC screening (either fHb-driven or incorporating personal risk information) to the UK population?
- how can we best ensure that stratified approaches don't exacerbate existing health inequalities?
- what might be the psychological impact of stratified CRC screening approaches in the population?

Stratified screening and NHS impact

Aims

To build a comprehensive picture of the impact of adopting risk-stratified approaches in UK bowel screening

To produce operationalised recommendations for key stakeholders in UK colorectal screening programmes on transitioning to risk-stratified approaches

Research questions

- 1. How will moving to stratified approaches impact on UK bowel cancer screening programmes?
- What are the key organisational and IT changes required to accommodate stratified approaches to bowel screening
- 3. What are the essential elements of recommendations for NHS bowel screening stakeholders to assist in transitioning to stratified screening?

International Collaboration – and impact



The changing bowelscreening environment: some key implications for risk-based approaches

- colonoscopy capacity: (for example, could greater use of FIT release some extra capacity for screening?)
- existing programme change plans (eg to age ranges, FIT cut-off levels)
- new screening tests (and follow-up investigations such as colon capsule)
- the advent of multi-cancer early detection (MCED) tests
- wider availability of genetic/lifestyle information (eg initiatives such as Our Future Health)
- broader societal issues: ethical considerations (eg offering LESS screening to some), equality and diversity/impact on health inequalities

Risk Stratification in BowelCancer Screening Programmes

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