Global colorectal cancer screening - appropriate or practical?

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Outline

• WHO criteria to justify screening

• Appropriateness:
  - Global variation in incidence
  - Who is screening?
    • What test is used and how is it implemented?

• Practicality:
  - Context.
  - Constraints and expectations.
  - Screening program elements
  - Program philosophy - matching the test
WHO criteria for screening

**CRC itself:**
- must be an important problem **appropiate**
- have a suitable natural history, be accurately diagnosable and effectively treated in the early stages

**The test should:**
- Be shown in the absence of bias to reduce mortality (and incidence)
- Be cost-effective
- Be acceptable to the people being targeted

**The program:**
- Must be feasible within the health care system **practical**
  - Diagnosable, follow-up testing, reparticipation in screening
  - Benefit outweighs the down-side

(Watson and Junger WHO Public health Paper no 34, 1968)
An important problem? Incidence *cf* Screening Action

- Incidence of cancer in the colon and rectum in Asian populations compared with US and UK populations (1993-97)
- Data extracted from *Cancer Incidence in Five Continents* volumes I-VIII, IARC CancerBase number 7, Lyon, 2005.
- Sung JJY et al.
But incidence is not static!

Projections: 2008-2030

Japan

Australia

Malaysia

Singapore

Incidence in 2008
Demographic effect
Can we target subgroups?

- There are a range of options including simple case-finding strategies.
- It would be possible to undertake centrally organised screening if ASI <40/100,000, by inserting an additional risk profiling step.
  1. Various risk-algorithms are available.
  2. Why not pilot the use of an FOBT (FIT) and ascertain the PPV for colorectal neoplasia?
Global CRC screening programs (2008)

- 43 programs identified worldwide
  - 8 could not provide the requested data
- 35 programs from 24 countries

<table>
<thead>
<tr>
<th>Program type</th>
<th>Europe (n=20)</th>
<th>Americas (n=11)</th>
<th>Western Pacific (n=4)</th>
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<tbody>
<tr>
<td></td>
<td>FOBT</td>
<td>FS</td>
<td>TC</td>
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<tr>
<td>Full program</td>
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<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Pilot program</td>
<td>3</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

- Expectations are uncommonly explicitly stated in terms of outcomes or approach.

Vicky Benson, University of Oxford
1. Personal application of screening:
   • Goal: Minimise morbidity and/or avoid death
     - Issues: duty of care, individual choice, do what is best (cost is less important)
     - Colonoscopy is predominant test

2. Population application of screening:
   • Goal: Implement a program that reduces the burden to the community
     - Issues: cost, acceptability to majority, risks.
     - FIT is the predominant test
An accurate test must get done!

Engage subject

Screening test

Colonoscopy

Treatment

Follow-up/Surveillance
Dimensions of care; Australia NBCSP

- Invite subject
  - Perform test
    - pos^v
    - Development test
  - Develop test
    - Public Health
- Colonoscopy
  - Public Health
  - Primary care
- Treatment
  - Usual Care
- Follow-up/Surveillance

Earlier stage
Scenarios: Constraints and expectations

1. Limited colonoscopy resource with a need to constrain test positivity rate;
2. A priority for maximum colorectal neoplasia detection with little need to constrain colonoscopy workload;
3. An ‘adequate’ endoscopy resource that allows balancing the benefits of detection with the burden of service provision;
4. A need to maximize participation in screening.

Test options need matching to these scenarios

- Faecal occult blood test
  - guaiac-FOBT (gFOBT)
  - faecal immunochemical test (FIT) for haemoglobin
- Flexible sigmoidoscopy
- Colonoscopy
- Molecular tests of blood or faeces
A quantitative FIT is ideal.

Choose the FIT $[Hb]$ cut-off to suit the scenario.

1. Limited colonoscopy
2. Maximum detection
3. Balancing the benefits


**Figure 3** Age, gender, and fecal immunochemical test concentration in association with histological grade of colorectal tumor. A: Age; B: gender; C: FIT. The differences in age, gender, and FIT concentrations (Y-axis) in the different histological groups (X-axis). (Kruskal-Wallis test, all $P < 0.001$). FIT: fecal immunochemical test; O: Other; A: Adenoma; AA: Advanced adenoma; C: Cancer.
Conclusions

• Appropriateness
  - 40/100,000 ASI is the precedent set
  - But major subpopulations at such risk exist in countries with a lower overall incidence - they require some form of risk-profiling.

• Practicality
  - Contexts and approaches vary considerably.
  - The expectation needs to be set and the tool matched to that expectation.
  - Quantitative FIT provide the greatest adaptability
The test must be acceptable

- Without participation, detection is impossible!

- **Detection** of cancer in a *population* is not only related to accuracy

  \[
  \text{Detection} = \text{sensitivity} \times \text{participation}
  \]
Simple tests refine likelihood

- Likelihood Ratio (LR) expresses the chance that neoplasia is present when the test is positive relative to negative.

\[ LR = \frac{\text{Sensitivity}}{1 - \text{specificity}} \]

- For Danish RCT of Hemoccult (GFOBT) screening
  - \( 0.5/0.02 = \underline{25\text{-fold}} \) more likely to have neoplasia

- For Minnesota RCT (rehydrated Hemoccult)
  - \( 0.92/0.08 = \underline{12\text{-fold}} \) more likely to have neoplasia

Note: These sensitivities apply to programmatic (repeated) application
What is screening?

- Screening is the testing for presence of disease in apparently healthy people, where they have no recognised increase in risk for that disease.
- Screening concept proposed in 1968.
  - Colorectal cancer (CRC) screening was not proven to be effective until 1993.
- Key goal: To reduce the *community* burden of “dis-ease”
  - Targets the suffering caused by disease!
Outline

• Screening; definition and process
• WHO criteria justifying screening
  - Incidence
  - Screening process
  - Natural history of colorectal cancer (CRC)
  - Screening test options
  - The evidence for efficacy and effectiveness
  - Engaging the population (participation)
  - (Cost-effectiveness)
• Future perspectives
What is screening?

• “Screening” is testing for the presence of disease in apparently healthy people, where they have no recognised increase in risk for that disease.
  - “Surveillance” is applied to those at increased risk.

• Screening concept proposed in 1968.
  - Colorectal cancer (CRC) screening was not proven until 1993.

• Key goal: To reduce the community burden of “dis-ease”
  - Targets the suffering caused by disease!
Screening Provider Contexts Vary

• By Health care system
  - Is there a public health process?
• By doctors
• By whoever pays for screening. Models:
  1. User pays all costs (Singapore)
  2. Reimbursement by insurer (USA)
  3. Government takes responsibility for some program elements (Australia)
  4. Government takes responsibility for all program elements (UK)
FOBT Technologies

Faeces

Haemoglobin

Haem

Globin

Guaiac; peroxidase.

Interference by Meat, vegies, vitamin C, NSAIDs.

Detects bleeding from Stomach, small & large intestine.

gFOBT

Immunochemical.

NO Interference.

Detects bleeding from large intestine.

FIT
Test simplicity varies

- Colonoscopy
  - Requires bowel wash-out and *sedation*

- FS
  - Requires enema and per-anal examination
Why not straight to colonoscopy?

Status of colon in lifetime once reached age of 50 years

- Normal
- Adenoma
- Cancer

Stage

Everyone! Target
AVERSION - Novel stool sampling

guaiac-FOBT

Faecal immunochemical test - FIT

Hemoccult;
Needs diet for accuracy

InSure

OC-SENSOR
[Hb] rises with progression


Figure 3: Age, gender, and fecal immunochemical test concentration in association with histological grade of colorectal tumor. A: Age; B: gender; C: FIT. The differences in age, gender, and FIT concentrations (Y-axis) in the different histological groups (X-axis). (Kruskal-Wallis test, all P < 0.001). FIT: fecal immunochemical test; O: Other; A: Adenoma; AA: Advanced adenoma; C: Cancer.