Update on the NHS Bowel Cancer Screening Programme

...Focus on BS & FIT

Prof Stephen P. Halloran

Cancer Screening Programmes
World – **Top 20 Cancers**

**Incidence & Mortality (2012)**

**World – Colorectal Cancer**
- 3\(^{rd}\) commonest cancer
- 4\(^{nd}\) cause of Ca deaths

**Western Europe**
- 2\(^{nd}\) commonest cancer death
- 2\(^{nd}\) commonest cancer
- 1\(^{st}\) commonest cancer in non-smoking men?
Incidence & Mortality (2012)

W. Europe – Top 20 Cancers

Incidence & Mortality (2012)

World – Colorectal Cancer
- 3rd commonest cancer
- 4th cause of cancer deaths

Western Europe
- 3rd commonest cancer
- 2nd commonest cancer death
- 1st commonest cancer in non-smoking men?
<table>
<thead>
<tr>
<th>Region</th>
<th>Incidence</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Australia/New Zealand</td>
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<tr>
<td>Western Europe</td>
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<td>Southern Europe</td>
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<td>Northern Europe</td>
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<tr>
<td>More developed regions</td>
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<tr>
<td>Central and Eastern Europe</td>
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<tr>
<td>Northern America</td>
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<td>Micronesia</td>
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<td>Eastern Asia</td>
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<td>World</td>
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<td>Caribbean</td>
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<td>South America</td>
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<td>Western Asia</td>
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<tr>
<td>South-Eastern Asia</td>
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<tr>
<td>Less developed regions</td>
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<tr>
<td>Southern Africa</td>
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<td>Polynesia</td>
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<td>Melanesia</td>
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<td>Central America</td>
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<td>Northern Africa</td>
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<tr>
<td>Eastern Africa</td>
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<tr>
<td>South-Central Asia</td>
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<tr>
<td>Middle Africa</td>
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<tr>
<td>Western Africa</td>
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</tbody>
</table>

Estimated age-standardised rates/100,000

- Price we pay... for affluent lifestyle
- Pay a price... for cancer treatment

GLOBOCAN 2012 (IARC)

Trends in colorectal cancer mortality in Europe: retrospective analysis of the WHO mortality database

Ouakrim DA, Autier P et al BMJ 2015;351:h4970

Europe - 2012
Diagnosed - 447,000 p.a.
Died - 215,000 p.a.

Lifetime Risk
1 in 14 men
1 in 19 women
Predicted increase in the incidence of colorectal cancers in EU countries from 2012 to 2025
Alive - 5 years after treatment:
- 93% 77% 48% 7%

Case for Screening:

Screening Colonoscopy – 30 to 45 mins
- Look for cancers – remove by surgery
- Look for polyps – remove by polypectomy

>50 years old - 1 in 4 have polyps
1 in 10 change to invasive cancer

Polyp
How to Screen?

‘Screening is the process of identifying healthy people who may be at increased risk of disease’
Haem

$2H_2O_2 = 2H_2O + O_2$

Oxidised guaiaconic acid is **blue**
20-25 years ago...
Four Large Randomised Controlled Trials
gFOBT Bowel Cancer Screening

- Minnesota
- Nottingham
- Funen
- France

Overall
16% reduction in mortality

Amongst those who did the tests
23% reduction in mortality
Bowel Cancer Screening
England - July 2006

Screening Centres (18)

Colonoscopy Site

Clinic Sites

Bowel Cancer Screening in England - July 2006

Southern Hub (Guildford)

14.6 million
Screening Timeline

Start
2 yearly Screening Cycle

Day 1
Pre-Invitation
At Screening Due Date

Day 8
Invitation
Kit & Spatula
Return Envelope

Day 8
Kit
Read
(1 day)

<2 days

Day 8
Invitation
Kit
Returned

<2 days

Day 1
Kit
Returned

<2 days

<14 days

+ve Result
Patient & GP Letter

<14 days

SSP Clinic Appointment

<14 days

Screening Colonoscopy

<14 days

Reminder Letter

M3
No Response
GP Letter/E-Comms

D29

Surveillance Colonoscopy

2 Years

Next Pre-Invitation

Pre-Invitation
Patient letter & GP letter /e-message

Freephone Helpline
NHS BCSP News

Headline Statistics!
(July 2006 – March 31st 2017)

- 33 million invitations
- 21 million gFOBt analysed
- 390,000 colonoscopies
  - 28,000 cancers
  - 91,000 advanced adenomas
England – July 2006

Phase 1 60 - 69 year olds
Phase 2 70 – 74
Phase 3 <60

Once in a lifetime flexisigmoidoscopy
Once in a lifetime flexisigmoidoscopy

Cumulative incidence distal cancer (%)

Outcome - Invited (participated)
- Incidence reduction 23% (33%)
- Mortality reduction 31% (43%)

Atkin et al.
Lancet. 2010;375: 1624-33
Bowel cancer screening
Flexible sigmoidoscopy
RCTs


<table>
<thead>
<tr>
<th>Reduction in...</th>
<th>UK</th>
<th>Italy</th>
<th>US</th>
<th>Norway</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence</td>
<td>23%</td>
<td>18%</td>
<td>21%</td>
<td>20%</td>
</tr>
<tr>
<td>Mortality</td>
<td>31%</td>
<td>22%</td>
<td>26%</td>
<td>27%</td>
</tr>
</tbody>
</table>
Works in Northern Italy?

- Invite to FS when **58 years old**
  - **19% uptake of FS**
- Invited to do FIT after 6 months
  - **23% uptake of FIT**
- Overall uptake @ 2 years...
  - **40 – 42% (FS and FIT)**
%Uptake in Taunton & Bristol 2013/4
%Uptake in Bristol 2013/4
FOBT kit return
First 2.6 million invitations in England

% Uptake - 3 Episodes (E1, E2 & E3)

Adherence to screening?

First Episode

1st Invitation

Second Episode

2nd Invitation

Third Episode

3rd Invitation

Adherence:

- Very Poor Adherence
- Poor Adherence
- Full Adherence

1 in 3

70%

2 in 3

61%

3 in 3

44%
NIHR Programme Grant for Applied Research

The ASCEND study:
Strategies to reduce the social gradient in bowel cancer screening uptake


Very small effect (0.7%) on...
- Uptake...
- Socioeconomic gradient
Blood in faeces
...still the best marker for population-based screening!
Faecal Immunochemical Test (FIT)

Hemoglobin

Haem

Globin (Human)
# FIT measure of Faecal Haemoglobin Concentration

*FIT Concentration relates to disease severity*

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Mean FIT Conc. ug Hb /g faeces</th>
<th>Positives at 20 ug /g Cut-off</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>10 (1-20)</td>
<td>6.9%</td>
</tr>
<tr>
<td>All adenoma</td>
<td>14 (4-28)</td>
<td>9.3%</td>
</tr>
<tr>
<td>Adv. adenoma</td>
<td>81 (37-125)</td>
<td>34.5%</td>
</tr>
<tr>
<td>Cancer</td>
<td>170 (89-252)</td>
<td>84.6%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Endoscopic Classification</th>
<th>Mean FIT Conc. ug Hb /g faeces</th>
<th>+ve at 20 ug /g Cut-off</th>
</tr>
</thead>
<tbody>
<tr>
<td>Histology</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LGD</td>
<td>27</td>
<td>14.1%</td>
</tr>
<tr>
<td>HGD</td>
<td>197</td>
<td>50.0%</td>
</tr>
<tr>
<td>Size</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 10 mm</td>
<td>12</td>
<td>9.0%</td>
</tr>
<tr>
<td>≥ 10 mm</td>
<td>99</td>
<td>36.4%</td>
</tr>
<tr>
<td>Number</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 3 adenoma</td>
<td>14</td>
<td>10.1%</td>
</tr>
<tr>
<td>≥ 3 adenoma</td>
<td>65</td>
<td>26.7%</td>
</tr>
</tbody>
</table>

OC-SENSA MICRO

Dong Il Park, MD\(^1\), Seungho Ryu, MD\(^2\), Young-Ho Kim, MD\(^3\), Suck-Ho Lee, MD\(^4\), Chang Kyun Lee, MD\(^4\), Chang Soo Eun, MD\(^5\) and Dong Soo Han, MD\(^5\)
Both Hubs
• Population 27.8 m
• gFOBT Kits = 1,126,087
• FIT Kits = 40,930

Southern Hub
Less Deprivation
• Population 14.7 m
• gFOBT Kits = 588,317
• FIT Kits = 21,641

Midlands & North West Hub
More Deprivation
• Population 13.1 m
• gFOBT Kits = 537,770
• FIT Kits = 19,289
Uptake at First Invitation
2014/5 South, Midlands, NW & London Pilots

1st invitation (mostly 60 year old subjects)

- Both: 10.9% Increase
- Southern: 9.7%
- London: 14.4% Increase
- Mid & NW: 12.2%

London: 38.6% in 2013, 52.4% in 2014,
Uptake at First Invitation 2014/5 South, Midland NW & London Pilots
Uptake in Prevalent Episodes
2014/5 South, Midlands, NW & London Pilots

1 – 5 invitations but no previous response

<table>
<thead>
<tr>
<th>Region</th>
<th>FIT</th>
<th>gFOBt</th>
</tr>
</thead>
<tbody>
<tr>
<td>Both</td>
<td>11.3%</td>
<td>11.6%</td>
</tr>
<tr>
<td>Southern</td>
<td>19.5%</td>
<td>11.8%</td>
</tr>
<tr>
<td>London</td>
<td>9.7%</td>
<td>9.8%</td>
</tr>
</tbody>
</table>

London: 9.7% uptake, 9.8% increase
Mid & NW: 11.3% uptake, 11.6% increase
Southern: 19.5% uptake, 11.8% increase
Uptake in Incident Episodes
2014/5 South, Midlands, NW & London Pilots

1 – 5 previous participation episodes

- **Both**: 4.2% Increase
- **Southern**: 4.1%
- **Mid & NW**: 4.3%

<table>
<thead>
<tr>
<th>Region</th>
<th>FIT</th>
<th>gFOBt</th>
</tr>
</thead>
<tbody>
<tr>
<td>82%</td>
<td></td>
<td></td>
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<tr>
<td>84%</td>
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<tr>
<td>86%</td>
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<tr>
<td>88%</td>
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<tr>
<td>90%</td>
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<tr>
<td>92%</td>
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</tbody>
</table>
Uptake & All Episodes
2014 South, Midlands, NW Pilot

0 – 5 previous screening invitations

- **Both**: 7.1% Increase
- **Southern**: 7.0%
- **Mid & NW**: 7.3%

290,000 Additional screens each year!
Impact on Colonoscopy & Pathology activity

Polypectomy rate increase >64% with... ...more polyps in each category

FIT 180

Cancer

High-risk Adenoma

Intermediate-risk Adenoma

Low-risk Adenoma

Abnormal

Colonoscopy

12.1%

10.6%

18.3%

18.6%
% Positivity & Deprivation

FIT Cut-off - 20 ug Hb/g Faeces
FIT Threshold and Positivity

(BCSP in England)

7.9%

1.7%

1.56%

ug Haemoglobin / g Faeces

FIT 20

FIT 40

FIT 100

FIT 150

FIT 180
Faecal Immunochemical Test (FIT) & Positivity

Thresholds adopted by National Bowel Cancer Screening Programmes
(1st October 2016)

Predicted FIT positivity - % of participants referred for colonoscopy

<table>
<thead>
<tr>
<th>Country</th>
<th>Predicted FIT positivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>England (April 2018)</td>
<td>12%</td>
</tr>
<tr>
<td>Scotland (Dec. 2017)</td>
<td>7.8%</td>
</tr>
<tr>
<td>Netherlands</td>
<td>5.2%</td>
</tr>
<tr>
<td>Southern Ireland</td>
<td>2.9%</td>
</tr>
<tr>
<td>New Zealand</td>
<td>2.1%</td>
</tr>
<tr>
<td>Canada (Quebec)</td>
<td>1.7%</td>
</tr>
<tr>
<td>France</td>
<td>1.5%</td>
</tr>
<tr>
<td>Portugal</td>
<td>1.2%</td>
</tr>
<tr>
<td>Norway (pilot)</td>
<td>1.0%</td>
</tr>
<tr>
<td>Denmark</td>
<td>0.8%</td>
</tr>
<tr>
<td>Hungary</td>
<td>0.5%</td>
</tr>
<tr>
<td>Iceland (planned)</td>
<td>0.2%</td>
</tr>
<tr>
<td>Italy (North &lt;20)</td>
<td>0.1%</td>
</tr>
<tr>
<td>Korea</td>
<td>0.0%</td>
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<tr>
<td>Malta</td>
<td>0.0%</td>
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<tr>
<td>Singapore</td>
<td>0.0%</td>
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<tr>
<td>Slovenia</td>
<td>0.0%</td>
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<tr>
<td>Spain (Catalonia)&lt;20</td>
<td>0.0%</td>
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<tr>
<td>Taiwan</td>
<td>0.0%</td>
</tr>
<tr>
<td>Uruguay</td>
<td>0.0%</td>
</tr>
<tr>
<td>England (pilot)</td>
<td>0.0%</td>
</tr>
<tr>
<td>Australia</td>
<td>0.0%</td>
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<tr>
<td>Lithuania (pilot)</td>
<td>0.0%</td>
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<tr>
<td>Latvia (pilot)</td>
<td>0.0%</td>
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<tr>
<td>Belgium (Flanders)</td>
<td>0.0%</td>
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<tr>
<td>Switzerland (no t...)</td>
<td>0.0%</td>
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<tr>
<td>Netherlands (pilot)</td>
<td>0.0%</td>
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<tr>
<td>New Zealand (pilot)</td>
<td>0.0%</td>
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<tr>
<td>Israel</td>
<td>0.0%</td>
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<tr>
<td>Austria</td>
<td>0.0%</td>
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<tr>
<td>Sweden (pilot)</td>
<td>0.0%</td>
</tr>
</tbody>
</table>

Colonoscopy Capacity Problems

Threshold used in the FIT pilot in England

Faecal Immunochemical Test (FIT) threshold (ug haemoglobin /g faeces)

Challenge...
Screen Episode & FIT threshold – Cancer Detection Rate

- First Invitation (60 year olds)
- No response to previous invitations
- Participated previously

How to do it even better?

% Cancer Detection Rate

FIT 20 40 60 80 100 120 140 160 180 200 gFOBT
Screen Episode & FIT threshold – Cancer Detection Rate

- First Invitation (60 year olds)
- No response to previous invitations
- Participated previously

Benefits of low FIT threshold greatest in previous non-responders
Age & FIT Threshold – Cancer Detection Rate

Should age, incidence... or QALY (Quality-adjusted Life Years Gained) influence threshold?
Sex & FIT threshold – % Positivity

Positivity
Why a gender difference?
• More disease
• FIT more sensitive
The Power of **Quantitative** FIT
Multivariate Risk Scores

- **Quantitative** FIT concentration
  - Age & Sex
  - Screening history
  - Indices of Deprivation – Geodemographics *(Postcode)*
  - Medical History – IBD, Crohns, DM, etc
  - Family History – 1st and 2nd degree relatives
  - Life style – Smoking, exercise, diet, obesity

Multivariate Bowel Cancer Risk Score

Better *Personalised* Population-based Screening!
- Positive Predictive Values
- Cost Effectiveness
- Colonoscopy Referrals

How to do it even better!
FIT – An opportunity to **personalise** population-based screening?

Better Screening by -
...focusing on **individuals**...  
...as well as on **populations**?

‘**Personalising population-based screening’**

1. Intelligent use of FIT data *(variable cut-offs)*
2. Incorporate personal risk *in a Multivariate Risk Scores*
3. Personalised invitation *which is sensitive to sex & screening history*
Make MY screen the best for ME.

Screening needs to join the band wagon.

‘Personalised Medicine’ is just around the corner!