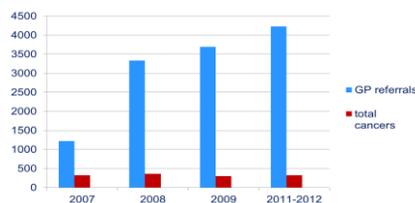


## A method to select FIT cut-off concentration

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## Colonoscopy 'crisis' in Scotland



- Recent escalation in primary care referrals placing huge demand of colonoscopy resource in Scotland
- Knock-on effect on Scottish Bowel Screening Programme, with positivity rate limited to ~2%



## 'FIT as a First-Line Test' evaluation

- 6 month evaluation of 'FIT as a First-Line Test' was carried out within the Scottish Bowel Screening Programme 2010/11



- Total of 66225 FIT kits
- 40125 returned to laboratory (61.1%)

- Automated result from analyser OC Sensor Diana within range of 0-200 µg Hb/g faeces
- Cut-off point for positive result set at 80 µg Hb/g faeces to give a positivity rate of 2.0% to be comparable with the current gFOBT/FIT two-tier reflex algorithm



## Outcomes of FIT evaluation

- Introduction of FIT as a first-line test in Scotland supported by:
  - Clinical outcomes being similar between the quantitative FIT and gFOBT/qualitative FIT screening strategies
  - Uptake and practicability of the FIT in colonoscopy limited settings
- Cost-Benefit analysis and business case for FIT was prepared:
  - **Change now approved by Scottish Government.**



## What is the best way to set the cut-off faecal haemoglobin concentration (f-Hb) in a colonoscopy limited country?

- **FIT evaluation gave a database of f-Hb recorded for 38,720 participants creating a resource for further research.**



## Positivity rate

- Cut-off f-Hb can be chosen simply according to number being referred to colonoscopy
  - using quantitative FIT as a binary, qualitative test
- Positivity independently associated with age, gender and deprivation, and negatively associated with previous screening. (Symonds *et al.*, J Med Screen, 2015)

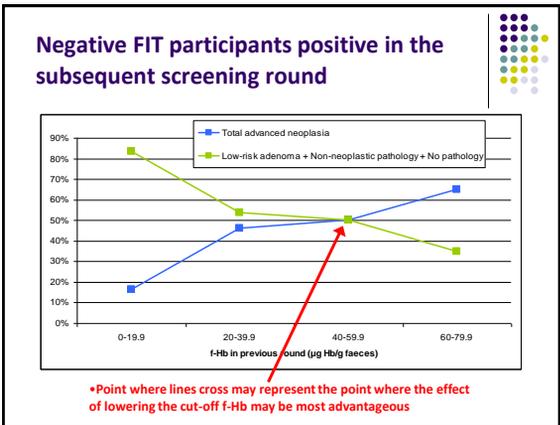
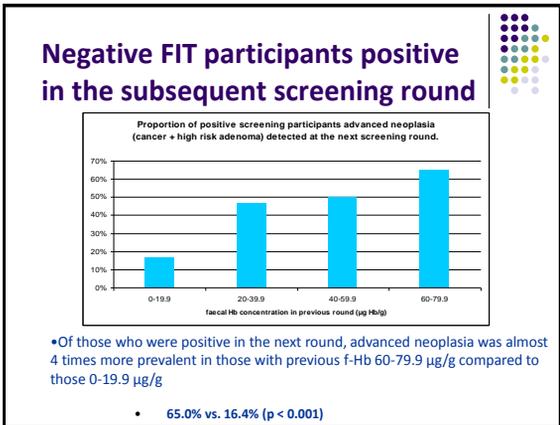
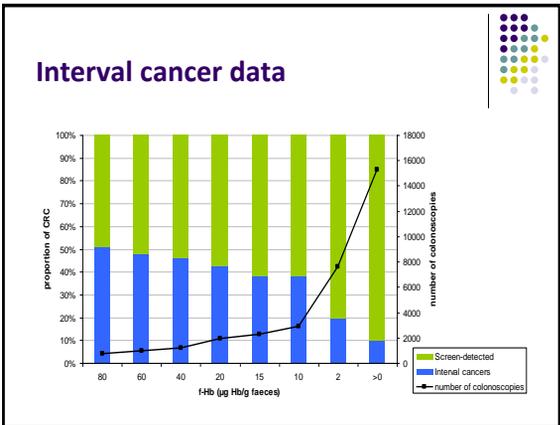


### Or...

- Should we take other data into account?
  - Interval cancers**
    - Effect on number of colonoscopies required and interval cancer proportion when lowering the cut-off f-Hb
  - Advanced neoplasia detected at subsequent screening round**
    - Effect on number colonoscopies required if looking to pick up *earlier* those with advanced neoplasia who had elevated f-Hb, but still below the cut-off.

### Interval cancer data

- 31 interval cancer cases detected in those with a negative FIT result in the 6 month evaluation
- Interval cancer proportion with FIT at high cut-off f-Hb of 80 µg/g was similar to gFOBT at 50.8%.
  - 48.4% in men, 53.3% in women.
- Those with f-Hb 60-79.9 µg/g were more likely to have an interval cancer compared with those with undetectable blood.
  - Adjusted odds ratio 24.70 (95% CI 4.89-124.64).



### Potential scenarios

- Compared with cut-off used of 80 µg Hb/g faeces:
  - Cut-off f-Hb of **60 µg Hb/g faeces could:**
    - detect **17.2% more colorectal cancer**
    - with **25.6% more colonoscopies**
  - Cut-off f-Hb of **40 µg Hb/g faeces could:**
    - detect **24.1% more colorectal cancer**
    - with **58.6% more colonoscopies**

## Recommendation



• Screening programmes introducing FIT should routinely collect data to aid decision making on which cut-off f-Hb to use

- Interval cancer data should be reviewed on a regular basis to calculate effect on detection rates and number of colonoscopies required at different cut-offs

- Initial f-Hb of participants positive in the subsequent screening round should also be assessed to allow estimation of yield of advanced neoplasia at different cut-off f-Hb

- Potential to monitor more closely those participants with consistently elevated f-Hb

- In larger cohorts, age and gender differences can also be assessed to determine if more tailored screening strategies are merited

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