Institution: University of Dundee
Unit of Assessment: UoA2 Public Health, Health Services and Primary Care
Title of case study: Faecal Occult Blood screening and the prevention of deaths from colorectal cancer

1. Summary of the impact

The UK Faecal Occult Blood Test Screening Programme, based on Dundee-led research (**Steele**), offers bowel cancer screening through mailed test kits followed up with colonoscopy when faecal blood is detected. It is estimated to prevent about 2,000 UK deaths annually. **Steele**'s Screening Research Unit also trialled immunological faecal occult blood testing, which was subsequently incorporated into the Scottish screening algorithm. In addition to demonstrating a 27% reduction in bowel cancer deaths through participation in Faecal Occult Blood screening, the Unit has researched the incidence of interval cancers and the impact of repeated invitations, development of new tests, and strategies for increasing participation. All of these drive the National Screening Programme, and will further reduce mortality.

2. Underpinning research

Colorectal cancer is the third commonest cancer in the UK, with a lifetime incidence of ~5%, and is the second leading cause of cancer deaths; it caused over 16,000 deaths per year before routine screening was introduced. Cases often present clinically at an advanced stage of disease, with consequently poor outcome.

Single cohort randomised controlled trials carried out in Nottingham, England and Funen, Denmark and published in 1993 demonstrated that screening for colorectal cancer using Faecal Occult Blood testing reduced disease-specific mortality by up to 18%. On the advice of the National Screening Committee, the UK Departments of Health commissioned a demonstration pilot of faecal occult blood test screening to be carried out in two geographical areas, one in England and one in Scotland. The areas chosen, on the basis of competitive bids, were Tayside, Grampian and Fife in Scotland and Coventry and Warwick in England. The executive group established to oversee this exercise was chaired by **Steele** (Professor of Surgical Oncology, Ninewells Hospital and Medical School, Dundee). This group developed the pilot methodology and subsequently carried out the major piece of underpinning research, a demonstration pilot exercise in the two sites to test the effectiveness of the first round of a biennial screening programme. This ran between March 2000 and May 2003 and proved to be extremely successful, inviting 478,250 individuals aged 50-69 for faecal occult blood test screening over a two-year period and assessing key performance indicators against benchmarks set by the previous randomised controlled trials [i]. The results of this research were evaluated by an independent team and reported to the UK Departments of Health who acted on them by developing and introducing National Colorectal Screening Programmes [ii]. In Scotland, the demonstration pilot continued for two further biennial screening rounds. This provided information on the performance of both prevalence and incidence screening, allowing for more precise planning by the screening centres and NHS Boards [iii]. Subsequent research demonstrated that telephone communication with screen positive individuals increased the uptake of colonoscopy and that repeated invitations increased the overall uptake of screening [iv]. A further randomised controlled trial [v] to assess the impact of pre-notification for screening demonstrated a further significant increase in uptake. Additionally, research carried out at the Screening Centre and the Research Unit established that the use of a sensitive immunological faecal occult blood test in those with a weak positive guaiac faecal occult blood test provided a more accurate method of selecting screen-positive individuals for colonoscopy [vi].

Both the research work and the implementation of the screening programme involved close collaborations between the University of Dundee, NHS Boards and Government Health Departments. In order to analyse the data generated by the Scottish arm of the demonstration pilot and to support new developments, a Colorectal Screening Research Unit was established at the

Scottish Bowel Screening Centre in Dundee. This was funded by a programme grant awarded to the University of Dundee by the Chief Scientist Office of the Scottish Government Health Department, and led by Professor **Steele**. Other local researchers were Callum Fraser (Director, Scottish Bowel Screening Laboratory and Honorary Professor in Molecular and Cellular Pathology); Frank Carey (Pathology Lead for Colorectal Cancer Screening in Scotland and Honorary Professor of Pathology); and Gillian Libby (Research Statistician).

Finally, the Screening Research Unit obtained funding of £262,000 from TENOVUS to work with the College of Life Sciences, University of Dundee on the utilisation of advanced proteomics for the development of more sensitive and specific screening tests, and £1.55M from the MRC (through the National Prevention Research Initiative) with **Anderson** to study lifestyle interventions in individuals diagnosed with adenomas through the screening programme (the BeWEL study, which ran from January 2010 to July 2013).

3. References to the research

i. **Steele** RJC for the UK Colorectal Cancer Screening Pilot Group (2004) Results of the first round of a demonstration pilot of screening for colorectal cancer in the United Kingdom. *Brit. Med. J.* **329**, 133-5 (DOI: 10.1136/bmj.38153.491887.7C).

ii. The UK CRC Screening Pilot Evaluation Team (2003) Evaluation of the UK Colorectal Cancer Screening Pilot Final Report; http://www.cancerscreening.nhs.uk/bowel/finalreport.pdf.

iii. **Steele** RJC, McClements PL, Libby G, Black R, Morton C, Birrell J, Mowat NAG, Wilson JA, Kenicer M, Carey FA, Fraser CG (2009) Results from the first three rounds of the Scottish Demonstration Pilot of FOBT Screening for Colorectal Cancer. *Gut* **58**, 530-5 (DOI: 10.1136/gut.2008.162883).

iv. **Steele** RJC, Kostourou I, McClements P, Watling C, Libby G, Weller D, Brewster DH, Black R, Carey FA, Fraser C (2010) Effect of repeated invitations on uptake of colorectal cancer screening using faecal occult blood testing; analysis of prevalence and incidence screening. *Brit. Med. J.* **341**:c5531 (DOI:10.1136/bmj.c5531).

v. Libby G, Bray J, Champion J, Colford L, Birrell J, Gorman D, Crighton E, Fraser C, **Steele** RJC (2011) Pre-notification increases uptake of colorectal cancer screening in all demographic groups; a randomised controlled trial. *J. Med. Screening*; **18**: 24-29 (DOI: 10.1258/jms.2011.011002)

vi. Fraser CG, Matthew CM, Mowat NAG, Wilson J, Carey FA, **Steele** RJC (2006) Immunochemical testing of individuals positive for guaiac faecal occult blood test in a screening programme for colorectal cancer: an observational study. *Lancet Oncol*. **7**, 127-131 (DOI:10.1016/S1470-2045(05)70473-3).

Funding

- **Steele** R (PI), Brewster D, Carey F, Kenicer M and Fraser C: Establishing a Bowel Screening Research Unit; Chief Scientist Office, Scotland (September 2007-August 2012) £546,227.

4. Details of the impact

This work produced by **Steele** and the Colorectal Screening Research Unit has contributed centrally to a complex programme that is currently having a major impact on cancer mortality rates. Their matched cohort study utilising the pilot data convincingly demonstrated a reduction of 27% in deaths from colorectal cancer among those participating in screening [1], vindicating the assumptions that had been made at the planning stage. National screening was developed from the pilot work and subsequent research led by **Steele**. It commenced in England in 2006, was followed by Scotland and Wales in 2007 and Northern Ireland in 2010 [2], and is already impacting on national mortality rates.

The impact of the group's research on repeated invitations [3] and on pre-notification [4] is reflected in demonstrated increases in the overall uptake of screening and of colonoscopy. For example, uptake of a first invitation for prevalence screening was 53%, and for a second and third invitation was 15% and 12% respectively, with a significant number proceeding to colonoscopy [3]; pre-notification with a letter (with or without an accompanying booklet) increased the uptake of screening from 54% to 59% [4]. Mortality figures are expected to continue to improve as this research, which has been incorporated into the national screening algorithm, leads to increased uptake and participation. As a result of the research into faecal occult blood testing methodology [vi], the screening algorithm in Scotland has also been changed to incorporate immunological testing. However, a study of interval cancers has demonstrated that the sensitivity of the screening Faecal Occult Blood test is only about 50% for cancer and that it is less sensitive in women than in men [5]. This set in train a piece of work funded by the Scottish Government (£130,241) that demonstrated the utility (improved efficiency, and age- and gender-specificity) and potential impact of improved faecal testing using quantitative faecal immunochemical testing as the first line test [6]. A business case for the introduction of this technology is currently being developed.

The demonstration pilot achieved similar short term outcomes to previous randomised trials, indicating that 30 colorectal cancer deaths per million of the total population per year will be avoided in the first instance. These figures will certainly continue to improve (a) as the proportion of the population participating in the screening programme increases; (b) with the implementation of more accurate testing methodologies such as immunological faecal occult blood testing (already partially implemented in Scotland) and the novel proteomics approaches that are currently under development in Dundee; and (c) as the uptake and impact of lifestyle interventions identified by the BeWEL study reduces the incidence of malignant tumours among those participating in screening. This work therefore demonstrates that the screening programme prevents around 2,000 UK colorectal cancer deaths each year, and will inevitably prevent many more in the future.

In addition to informing the decision to introduce a national colorectal cancer screening programme, the research described here has had a significant impact on the testing modalities used in the screening programme and on the method of invitation. Furthermore, extremely valuable information has been gathered on the significance of interval cancers. In addition, £2m funding has also been made available from the Scottish Government in order to explore the introduction of flexible sigmoidoscopy as a primary screening modality, and a randomised evaluation is under development. Professor **Steele** chairs the Steering Group for this study.

The Screening Programme has attracted major national and international media attention [7], and has served as a model for the implementation of similar programmes in a number of other countries (most recently Ireland [8], with others under development in the Netherlands, Sweden, Croatia, Slovenia and Taiwan). The recently published European Guidelines for Quality Assurance in Colorectal Cancer Screening [9], to which Professor **Steele** made a major contribution [10], drew heavily on the experience gained in Scotland and the rest of the United Kingdom, and is a major influence on these programmes.

5. Sources to corroborate the impact

1. Libby G, Brewster DH, McClements PL, Carey FA, Black RJ, Birrell J Fraser CG, **Steele** RJC (2012) The impact of population based faecal occult blood test screening on colorectal cancer mortality: a matched cohort study. *Br. J. Cancer* **107**, 255-259 (DOI: 10.1038/bjc.2012.277).
2. NHS websites that describe the introduction and current status of the national bowel screening programmes in the UK:

   http://www.bowelscreening.scot.nhs.uk/

   http://www.cancerscreening.nhs.uk/bowel/

   http://www.wales.nhs.uk/sites3/home.cfm?orgid=747

   http://www.screening.nhs.uk/bowelcancer-northernireland

3. **Steele** RJC, Kostourou I, McClements P, Watling C, Libby G, Weller D, Brewster DH, Black R, Carey FA, Fraser C (2010) Effect of repeated invitations on uptake of colorectal cancer screening using faecal occult blood testing; analysis of prevalence and incidence screening. *Brit. Med. J.* **341**:c5531 (DOI:10.1136/bmj.c5531).
4. Libby G, Bray J, Champion J, Colford L, Birrell J, Gorman D, Crighton E, Fraser C, **Steele** RJC (2011) Pre-notification increases uptake of colorectal cancer screening in all demographic groups; a randomised controlled trial. *J. Med. Screening* **18**, 24-29 (DOI: 10.1258/jms.2011.011002).
5. **Steele** RJC, McClements P, Watling C, Libby G, Weller D, Brewster DH, Black R, Carey FA, Fraser CG (2012) Interval cancers in a FOBT-based colorectal cancer population screening programme: implications for stage, gender and tumour site. *Gut* **61**, 576-581 (DOI: 10.1136/gutjnl-2011-300535).
6. **Steele** RJC, McDonald PJ, Digby J, Brownlee L, Strachan JA, Libby G, McClements PL, Birrell J, Carey FA, Diament RH, Balsitis M, Fraser CG (2013) Clinical outcomes using a faecal immunochemical test for haemoglobin in a national colorectal cancer screening programme constrained by colonoscopy capacity. *UEG Journal* **1**, 198-205 (DOI: 10.1177/2050640613489281).
7. Examples of media reports (November 2011) of reduction in cancer deaths due to screening programme:

   Cancer Research UK press release: http://www.cancerresearchuk.org/cancer-info/news/archive/pressrelease/2011-10-09-Bowel-screening-reduces-cancer-deaths-by-more-than-25-per-cent.

   STV news report: http://news.stv.tv/scotland/278230-screening-cuts-bowel-cancer-deaths-by-a-quarter/.
8. National Cancer Screening Service (Ireland). Implementing Ireland's First National Population-based Colorectal Cancer Screening Programme (2009) www.cancerscreening.ie/publications/ImplementingColorectalProgramme.pdf, based on **Steele**'s Scottish, UK and European models, and to which Professor **Steele** contributed directly (page 9)
9. Segnan N, Patnick J and von Karsa L (eds) (2011) European Guidelines for Quality Assurance in Colorectal Cancer Screening and Diagnosis. First Edition. European Commission (DOI:10.2772/15379; electronic version) http://www.pathologie-guetersloh.de/informationen/leitlinien-empfehlungen-und/prostata-leitlinien-und-emp/crc_guidelines_publication.pdf.
10. Corroborating statement from the Director, NHS Cancer Screening Programmes, Directorate of Health and Wellbeing, Public Health England (impact on UK screening programmes and European guidelines).