Institution: University College London

Unit of Assessment: 2 - Public Health, Health Services and Primary Care

Title of case study: Inclusion of flexible sigmoidoscopy in the UK Bowel Cancer Screening Programme

1. Summary of the impact

Our evidence that a single flexible sigmoidoscopy (FS) dramatically reduced bowel cancer mortality and incidence, combined with evidence of high public acceptability in our pilot programme, led the Prime Minister to announce in late 2010 that once-only FS would be included in the UK National Bowel Cancer Screening Programme. The new FS screening programme started in March 2013 in six pilot centres, and is being progressively implemented nationally, with full roll-out expected by 2016. All eligible adults will be invited for screening around the time of their 55th birthday using the invitation and bowel preparation protocols developed for the trial. If uptake rates similar to those in the pilot are achieved, bowel cancer rates could be cut by a quarter, and deaths by a third, giving the UK the best colorectal cancer (CRC) outcomes in the world.

2. Underpinning research (indicative maximum 500 words)

Colorectal cancer (CRC) is the second most common cause of cancer death, and among the most feared cancers because of the effects of surgical treatment. Professor Jane Wardle from the Department of Epidemiology and Public Health at UCL has a long-standing collaboration with Professor Wendy Atkin (Imperial) to evaluate the potential of flexible sigmoidoscopy (FS) to prevent CRC through finding and removing pre-cancerous adenomas.

The natural history of CRC suggested that a single FS examination in the age range when adenomas are likely to have developed, but before CRC incidence starts to rise, could provide protection for 10-25 years. With Professor Atkin and colleagues, Professor Jane Wardle developed and piloted screening and pathology protocols, quality control procedures, patient management systems, patient information materials, and invitation protocols, which included pioneering the use of a mailed, self-administered enema to be carried out at home before the test. The trial team then carried out pilot studies of FS screening in asymptomatic 55-64 year olds in Welwyn Garden City and Leicester. The results demonstrated that FS could be safe and acceptable, and the yield of neoplasia suggested there would be a significant impact on CRC incidence **[1]**.

The success of the pilot studies led onto the main randomised controlled trial in which almost 400,000 adults around the UK were randomised either to be invited for FS screening at their local hospital or to usual care, using a novel, two-stage invitation procedure which allowed us to make a robust estimate of efficacy **[2]**. Baseline findings revealed high rates of pre-malignant adenomas, most of which were low risk and could be safely removed during FS. Rates of referral for colonoscopy were manageable (around 5%), with evidence that the risk of harm from the test was low **[3]**. Professor Wardle was responsible for the psychosocial elements of the trial and showed that uptake and acceptability were high in both men and women, and the psychological impact was favourable **[4]**. After 11 years of follow-up for cancer registrations and deaths, intention-to-treat analyses showed a 23% reduction in incidence and a 31% reduction in mortality, with per-protocol analyses (attenders vs controls) showing a 33% reduction in incidence and 43% reduction in mortality **[5]**. Incidence of distal colorectal cancer (rectum and sigmoid colon), the secondary outcome of the trial, was reduced by half. These were the best results ever reported in a cancer prevention trial, and the progressive divergence in incidence and mortality curves between screened and control groups indicates prolonged and continuing protection.

In the meantime, Professor Wardle had been commissioned by the National Cancer Screening Committee to set up a 'demonstration' study of an FS screening programme in a socio-

economically and ethnically diverse area of North London, with FS carried out by nurse endoscopists. In collaboration with Professor Atkin, she modified the trial procedures for a population programme, and concurrently evaluated a range of methods for promoting uptake. An uptake rate of 55% was achieved in the pilot programme **[6]**, and patient-reported outcomes were almost unanimously positive **[7]**. The Prime Minister announced in 2010 that FS screening would be added to the National Bowel Cancer Screening Programme. Starting in March 2013, a single FS screening test will be offered to all adults aged 55. Professor Wardle's group have been commissioned to monitor uptake and patient-reported outcomes using methods developed in the trial. She is also collaborating in the continued follow-up of the FS trial participants and they expect to publish 15 year outcomes in 2014.

3. References to the research (indicative maximum of six references)

[1] Atkin WS, Hart A, Edwards R, McIntyre P, Aubrey R, Wardle J, Sutton S, Cuzick J, Northover JM. Uptake, yield of neoplasia, and adverse effects of flexible sigmoidoscopy screening. Gut. 1998 Apr;42(4):560-5. http://dx.doi.org/10.1136/gut.42.4.560

[2] Atkin WS, Edwards R, Wardle J, Northover JM, Sutton S, Hart AR, Williams CB, Cuzick J. Design of a multicentre randomised trial to evaluate flexible sigmoidoscopy in colorectal cancer screening. Journal of Medical Screening. 2001;8(3):137-44. http://dx.doi.org/10.1136/jms.8.3.137

[3] Atkin WS, Cook CF, Cuzick J, Edwards R, Northover JM, Wardle J; UK Flexible Sigmoidoscopy Screening Trial Investigators. Single flexible sigmoidoscopy screening to prevent colorectal cancer: baseline findings of a UK multicentre randomised trial. *Lancet*. 2002;359:1291-300. http://dx.doi.org/10.1016/S0140-6736(02)08268-5

[4] Wardle J, Williamson S, Sutton S, Biran A, McCaffery K, Cuzick J, Atkin W. Psychological impact of colorectal cancer screening. Health Psychology. 2002 Apr 13;359(9314):1291-300. http://dx.doi.org/10.1037/0278-6133.22.1.54

[5] Atkin WS, Edwards R, Kralj-Hans I, Wooldrage K, Hart AR, Northover JM, Parkin DM, Wardle J, Duffy SW, Cuzick J; UK Flexible Sigmoidoscopy Trial Investigators. Once-only flexible sigmoidoscopy screening in prevention of colorectal cancer: a multicentre randomised controlled trial. Lancet. 2010 May 8;375(9726):1624-33. http://dx.doi.org/10.1016/S0140-6736(10)60551-X

[6] Robb K, Power E, Kralj-Hans I, Edwards R, Vance M, Atkin W, Wardle J. Flexible sigmoidoscopy screening for colorectal cancer: uptake in a population-based pilot programme. Journal of Medical Screening. 2010;17(2):75-8. http://dx.doi.org/10.1258/jms.2010.010055

[7] Robb K, Lo SH, Power E, Kralj-Hans I, Edwards R, Vance M, von Wagner C, Atkin W, Wardle J. Patient-reported outcomes following flexible sigmoidoscopy screening for colorectal cancer in a demonstration screening programme in the UK. Journal of Medical Screening. 2013 Sep 2. [Epub ahead of print] http://www.ncbi.nlm.nih.gov/pubmed/23417540

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4. Details of the impact (indicative maximum 750 words)

The major impact of the research has been the implementation of Flexible Sigmoidoscopy as a single examination at age 55 as part of the National Bowel Cancer Screening Programme. Following the publication of the trial outcomes in the Lancet in April 2010, and the results of the successful pilot programme in the Journal of Medical Screening in June 2010, the Prime Minister David Cameron announced in October 2010 that once-only FS screening would be included in the NHS National Bowel Cancer Screening Programme. £60m was pledged over the next four years to introduce this latest cancer screening technology, with estimates that flexible sigmoidoscopy could

save 3,000 lives a year **[a]**. Then Health Secretary, Andrew Lansley announced that pilot schemes for the new screening programme would begin in spring 2011 **[b]**, subject to approval by the UK National Screening Committee **[c]**.

The existing NHS Bowel Cancer Screening Programme is based on biennial faecal occult blood testing using the guaiac-based test (gFOBT), with an immunochemical test (iFOBT) being piloted in 2014. An 'options appraisal' of colorectal cancer (CRC) screening modalities commissioned by the NHS Cancer Screening Programme in 2004 from SCHARR (University of Sheffield School of Health and Related Research) had used the baseline data from the FS trial, and concluded that FS screening was likely to be highly cost-effective compared with other methods because it reduced incidence of CRC and therefore the costs of the programme would be likely to be offset by a substantial reduction in the costs of treatment. SCHARR repeated the analysis in 2012 using the full FS trial outcome data and concluded that: '*For a strategy of one-off FS screening, the optimal effectiveness (QALYS) is achieved with a one-off FS screen in the age range 55-60. The most cost-effective strategy was FS at age 55 followed by biennial iFOBT screening for ages 56-74, irrespective of whether the comparator was the current screening programme of biennial gFOBT 60-74 or no screening. This strategy was associated with the greatest net monetary benefit and also the greatest reduction in CRC incidence, CRC mortality and CRC treatment costs*'. The report also concluded that '*it may be cost-effective to spend considerable resources on increasing screening awareness*' which has been a parallel focus of our research, with a particular emphasis on promoting awareness in order to reduce socioeconomic disparities in CRC screening uptake **[d]**. Professor Wardle now has programme grant funding from NIHR trial for a trial (ASCEND) of methods to reduce socioeconomic disparities in CRC screening uptake as Co-PI with Professor Rosalind Raine (also UCL).

In January 2011, the Department of Health's document *Improving Outcomes: A Strategy for Cancer* set out the plans for FS screening **[e]**. Implementation of the FS programme began in early 2011, with three 'pathfinder' screening sites set up to finalise the invitation and organisation procedures **[f]**. One of the centres explored a novel method of invitation, but the conclusion from the 4,022 invitations across the three sites was that the invitation system Wardle and her team had developed in the FS Trial and applied in the Demonstration Pilot (comprising a 'flyer' giving brief information about the programme, followed by a dated and timed invitation that could be confirmed, changed or cancelled, followed by a self-administered enema with detailed information about the test), was likely to be most successful.

Plans are now finalised for national implementation, and six sites began screening between March and July 2013 to finalise invitation procedures and patient information materials **[g]**. Professor Wardle's group has been commissioned to carry out real-time audits of uptake, patient-reported outcomes 24 hours after the test, and patient satisfaction at 12 weeks when any follow-up procedures should be completed, in the starter sites. This will allow rapid identification of any problems and make it possible to implement small modifications to optimise procedures in advance of the national rollout.

To the end of July, around 2,220 people had received FS screening between the pathfinder and starter sites. Data from the FS trial indicated that one colorectal cancer diagnosis is prevented for each 191 people screened. So even with the small number of people screened so far, it is likely that 11 of these terrible diagnoses have been prevented **[h]**.

5. Sources to corroborate the impact (indicative maximum of 10 references)

[a] BBC report of David Cameron's announcement: http://www.bbc.co.uk/news/uk-politics-11461495.

[b] BBC report of Lansley's interview about the outcomes of the 'Flexisig' trial and how cost-saving and pioneering the FS programme will be: http://www.bbc.co.uk/news/health-11463005.

[c] Mayor, S., *UK committee recommends flexible sigmoidoscopy to screen for bowel cancer*,

2011, which confirms that flexible sigmoidoscopy will be introduced to the national screening programme for bowel cancer. Available online: http://www.bmj.com/content/342/bmj.d2325.

[d] School of Health and Related Research (ScHARR), *Re-appraisal of the options for colorectal cancer screening,* Feb 2011, which re-evaluates the options for CRC screening in England using new data sources. New data is available from the England Bowel Cancer Screening Programme and a large randomised UK trial of FS. Document available online: http://www.cancerscreening.nhs.uk/bowel/scharr-full-report-summary-201202.pdf.

[e] Department of Health report, *Improving Outcomes: A Strategy for Cancer,* Jan 2011, which announces funding for FS screening based on the results of our trial. Document available online: http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/documents/digitalasset/dh_123394.pdf

[f] Department of Health report, *Bowel Cancer Screening Specification,* Apr 2013, which ensures that there is a consistent and equitable approach to the provision and monitoring of bowel cancer screening across England. Document available online: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/192977/26_Bowel_Cancer_Screening_service_specification__VARIATION_130422_-_NA.pdf

[g] NHS Cancer Screening Programme's announcement of FS screening, referring to our Lancet paper as the basis of the decision: http://www.cancerscreening.nhs.uk/bowel/flexible-sigmoidoscopy-screening.html. Document available online: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/215205/dh_132468.pdf.

[h] Numbers can be corroborated by audit lead, UCL. Contact details provided.