Institution: University of Dundee		
Unit of Assessment: UoA 1 Clinical Medicine		
Title of case study: Faecal haemoglobin estimation in colorectal cancer screening and the triage of symptomatic populations		
Period when the underpinning research was undertaken: 2004 - 2019		
Details of staff conducting the underpinning research from the submitting unit:		
Name(s): Prof Robert J.C. **Steele**	**Role(s) (e.g. job title):** Research Professor; Consultant to Bowel Screening Unit	**Period(s) employed by submitting HEI:** 1996 to date
Period when the claimed impact occurred: 2013 to date		
Is this case study continued from a case study submitted in 2014? N		

1. Summary of the impact

Professor **Steele**'s recent work demonstrating the value of the faecal immunochemical test has greatly enhanced the already well-respected UK colorectal cancer screening programme, which continues to prevent some 2,000 deaths per year. The test, introduced for population screening in Scotland in 2017, was incorporated into NICE guidelines for investigation of symptomatic individuals in 2017 and adopted for this purpose in Scotland in 2020. Its use has facilitated the early diagnosis of neoplasia against a background of common symptoms which are usually associated with benign, self-limiting disease. This has reduced the need for colonoscopy, a costly, intrusive and often uninformative procedure.

2. Underpinning research

Population screening is currently the most effective means of detecting colorectal cancer while it can still be successfully treated. Previous research by **Steele**'s team, which formed the basis of a REF2014 impact case study, demonstrated the value of the faecal occult blood test in colorectal cancer screening and led to the introduction of national colorectal cancer screening programmes across the UK. This submission describes how that impact has been sustained and expanded by new work. A crucial factor in this research, which involved close collaboration between the University of Dundee and NHS Scotland, was the establishment of a Colorectal Screening Research Unit funded by a programme grant awarded to the University of Dundee by the Chief Scientist Office of the Scottish Government Health Department in 2005 and maintained by continuous project funding ever since.

Population screening can detect pre-malignant adenomas, allowing them to be treated before they progress and thus reducing both the incidence of colorectal cancer and mortality. The Scottish Bowel Screening Programme was rolled out by NHS Tayside, NHS Grampian and NHS Fife in June 2007; by December 2009 all NHS Boards in Scotland were participating in the programme. This in turn led to the introduction of national colorectal cancer (CRC) screening programmes across the UK. Over the last decade, according to bowel screening statistics, around 2,000 deaths have been prevented annually, contributing to a 13% reduction in UK bowel cancer mortality rates (12% in females and 15% in males).

Steele's team has scrutinised colorectal cancer incidence data, demonstrating a reduction in cancer incidence since roll-out of the Scottish Bowel Screening Programme for those over the age of 50 but increasing incidence in the pre-screening age range **[R1]**. The incidence reduction was restricted to screening participants, providing compelling evidence that screening reduces

colorectal cancer incidence against a background of increasing incidence in the unscreened population.

The faecal occult blood test used in the original UK screening programmes is an indirect measure of human haemoglobin in faeces whereas the faecal immunochemical test (FIT) specifically detects haemoglobin. Research by **Steele's** team demonstrated that use of the FIT to follow up a weakly positive occult blood test results in fewer false positive results being returned **[R2]**. Further research in 2010-2011 established that quantitative FIT is superior to faecal occult blood test in terms of both uptake and detection of neoplastic disease **[R3]**. In routine use, FIT has detected 20% more cancers and 40% more adenomas than the faecal occult blood test **[R4]**.

Despite screening, the majority of patients with CRC present with symptoms. In recent years there has been a marked escalation in demand for investigation of symptomatic patients, but this has had no impact on early detection. **Steele's** team therefore explored the use of FIT to assist decision-making as to which patients with large bowel symptoms should undergo colonoscopy. This trial, conducted between 2014 and 2016, received £2 million funding from Scottish Government. It demonstrated that FIT is a safe and effective "rule out" test (i.e. the absence of detectable haemoglobin in faeces is associated with a very low risk of disease) **[R5]**, and that implementation of this approach results in fewer referrals for invasive investigation without a negative impact on rates of diagnosis of serious disease **[R6]**.

3. References to the research

[R1] Clark, G. R., Anderson, A. S., Godfrey, T. G., Strachan, J. A., Fraser, C. G. & **Steele**, R. J. (2020) Variation in changes in the incidence of colorectal cancer by age and association with screening uptake: an observational study. *BMJ Open,* 10**,** e037925; DOI: 10.1136/bmjopen-2020-037925.

[R2] Fraser, C. G., Matthew, C. M., Mowat, N. A., Wilson, J. A., Carey, F. A. & **Steele**, R. J. (2006) Immunochemical testing of individuals positive for guaiac faecal occult blood test in a screening programme for colorectal cancer: an observational study. *Lancet Oncology,* 7 (2)**,** pp. 127-131; DOI: 10.1016/s1470-2045(05)70473-3.

[R3] Steele, R. J., McDonald, P. J., Digby, J., Brownlee, L., Strachan, J. A., Libby, G., McClements, P. L., Birrell, J., Carey, F. A., Diament, R. H., Balsitis, M. & Fraser, C. G. (2013) Clinical outcomes using a faecal immunochemical test for haemoglobin as a first-line test in a national programme constrained by colonoscopy capacity. *United European Gastroenterology Journal,* 1 (3)**,** pp. 198-205; DOI: 10.1177/2050640613489281.

[R4] Clark, G., Strachan, J. A., Carey, F. A., Godfrey, T., Irvine, A., McPherson, A., Brand, J., Anderson, A. S., Fraser, C. G. & **Steele**, R. J. (2021*) Transition to quantitative faecal immunochemical testing from guaiac faecal occult blood testing in a fully rolled-out population-based national bowel screening programme. *Gut,* 70 (1)**,** pp. 106-113; DOI: 10.1136/gutjnl-2019-320297. [*First published 31 March 2020; Online publication 9 December 2020]

[R5] Mowat, C., Digby, J., Strachan, J. A., Wilson, R., Carey, F. A., Fraser, C. G. & **Steele**, R. J. (2016) Faecal haemoglobin and faecal calprotectin as indicators of bowel disease in patients presenting to primary care with bowel symptoms. *Gut,* 65 (9)**,** pp. 1463-1469; DOI: 10.1136/gutjnl-2015-309579.

[R6] Mowat, C., Digby, J., Strachan, J. A., McCann, R., Hall, C., Heather, D., Carey, F., Fraser, C. G. & **Steele**, R. J. C. (2019) Impact of introducing a faecal immunochemical test (FIT) for haemoglobin into primary care on the outcome of patients with new bowel symptoms: a prospective cohort study. *BMJ Open Gastroenterology,* 6 (1)**,** e000293; DOI: 10.1136/bmjgast-2019-000293.

Funding

Chief Scientist Office, Scotland (2014-2016): Can a Negative Faecal Immunochemical Test for Haemoglobin (FIT) Avoid the Need for Routine Surveillance Colonoscopy in Patients at Increased Risk of Colorectal Cancer, CZH/4/1032, £72,449 RJC **Steele**

Chief Scientist Office, Scotland; Stratified Medicine Call (2015-2017): Stratifying Risk of Colorectal Disease in Order to Direct the Use of Colonoscopy in Symptomatic Patients ASM/14/4, £319,200 RJC **Steele**

Chief Scientist Office, Scotland; Health Improvement, Protection and Services (2017-2020): Increasing Uptake of Bowel Cancer Screening: Development of a Planning Support Tool (joint with University of Glasgow and Stirling University), HIPS/17/23, £11,450 RJC **Steele**

4. Details of the impact

Colorectal cancer is the second commonest cause of cancer death in both sexes, killing ~1,600 people in Scotland each year. The Scottish Bowel Screening Programme, of which **Steele** has been Clinical Director since its implementation, started in 2007; between 2008 and 2018 colorectal cancer mortality in Scotland fell by 8%. By October 2018 ~6,000 colorectal cancers had been diagnosed through screening **[E1]**.

Steele is the Independent Chair of the UK National Screening Committee (UKNSC), which advises UK ministers and the NHS on population screening. In this role "he has been particularly helpful in navigating the policy positions in bowel screening… and facilitated an excellent and evidence-based outcome." **[E2]**.

The Scottish Bowel Screening Programme has been exemplary for similar programmes in other countries. The European Guidelines for Quality Assurance in Colorectal Cancer Screening and the International Agency for Research on Cancer (IARC) Handbook of Colorectal Cancer Screening **[E3]**, to both of which **Steele** made major contributions, drew heavily on experience gained in Scotland and the rest of the UK. **Steele**'s evidence contributed to the IARC conclusion "There is *sufficient evidence* that biennial screening with the faecal immunochemical test (FIT) reduces colorectal cancer mortality. …[and]… that the benefits of biennial screening with FIT outweigh the harms when the screening programme can be delivered with high quality." **[E3, p298]**. This evidence has been used to support use of the FIT in colorectal cancer screening programmes across the world.

Introduction of the FIT in Scotland and the UK

From 2007-2017 the FIT was used to follow up weak positive faecal occult blood test results in Scotland, Wales and Northern Ireland. In January 2016 the UKNSC recommended quantitative FIT as the primary method for colorectal cancer screening nationwide. The Scottish Bowel Screening Programme made this change in November 2017 **[E4]**; by the end of 2020 England, Wales and Northern Ireland had also adopted the FIT for their national bowel cancer screening programmes **[E5]**.

Uptake of screening invitations increased by ~10% in the year following introduction of quantitative FIT screening in Scotland. This was associated with a 64.8% increase in the detection rate for adenomas (1.02% *vs* 0.62% of the screening population with an adenoma) and a small increase in the detection rate for carcinomas (0.12% *vs* 0.11% of the screening population with a carcinoma) **[E1]**.

Contribution of the FIT to diagnosis in symptomatic patients

The presenting symptoms of colorectal cancer resemble those of numerous benign, self-limiting conditions. The challenge, therefore, is to achieve early diagnosis of neoplasia against this

background of non-cancerous disease, thus avoiding unnecessary investigation which can cause trauma and discomfort to patients, is a drain on resources and puts pressure on service providers.

Demand on colonoscopy services has recently increased enormously, driven by increasing awareness of these symptoms and waiting time targets. This has not, however, translated into improved early detection. Non-endoscopic methods which can identify all, but only, those patients who require full investigation are therefore essential. **Steele**'s group has demonstrated that quantitative FIT can be used to rule out colorectal neoplasia in symptomatic patients. This concept was incorporated into NICE guidelines in 2017 **[E6]**.

Research on this use of quantitative FIT demonstrated, over the first year of its implementation in NHS Tayside, a 20% reduction in colonoscopy referrals without appreciable failure to detect neoplasia. The quantitative FIT was added to the diagnostic process for symptomatic individuals across Scotland in July 2020 **[E7]**; this has been particularly valuable in reducing the need for face-to-face appointments during the COVID-19 pandemic.

Moving away from flexible sigmoidoscopy for colorectal cancer screening

Flexible sigmoidoscopy is an effective screening method for colorectal neoplasia. In England it used to be offered at age 55 before the faecal occult blood test (now replaced by the FIT) was offered at 60; however, significant uptake, delivery and quality issues were experienced. The benefits of population-based endoscopic screening were therefore questioned, especially given that the UKNSC now recommends FIT screening from age 50 (i.e. including the age at which endoscopy is offered) **[E8]**. A randomized trial by **Steele**'s group demonstrated that the benefits of flexible sigmoidoscopy as an adjunct to faecal occult blood test screening did not justify its introduction into the Scottish Bowel Screening Programme **[E9]**. Flexible sigmoidoscopy was not, therefore, adopted for screening in Scotland and in July 2020 the UKNSC recommended the permanent discontinuation of endoscopic screening in England **[E10]**.

In summary, **Steele** and his team have driven improvements in colorectal cancer screening in Scotland and across the UK. They championed the FIT, which is easier to use and more sensitive than the faecal occult blood test, enabling signs of colorectal cancer to be detected earlier, saving more lives. They have also provided evidence against the need for endoscopy in screening and early diagnosis; as well as avoiding the need for an intrusive and often uninformative procedure, this could "save the NHS millions, as each colonoscopy costs the NHS £372 compared to about £5 for the FIT test" (2017 figures) **[E11]**.

5. Sources to corroborate the impact

[E1] Public Health Scotland. (2020) *Scottish Bowel Screening Programme* [Online]. Available: https://www.isdscotland.org/Health-Topics/Cancer/Bowel-Screening/ [Accessed 30th December 2020]. The pdf printout includes the front page of the website and the Excel spreadsheets for the May 2019 data submission.

[E2] Director of Programmes UK National Screening Programme 2021. To whom it may concern. Letter of Support, 11th January 2021.

[E3] International Agency for Research on Cancer (2019) Colorectal Cancer Screening. IARC Handbooks of Cancer Prevention, Volume 17. Available: https://publications.iarc.fr/Book-And-Report-Series/Iarc-Handbooks-Of-Cancer-Prevention/Colorectal-Cancer-Screening-2019 [Accessed 12th February 2021]. **Steele** is identified as a panel member on p4 and as primary author or a co-author of six of the publications cited.

[E4] Chief Medical Officer Scotland 2017. Changes to the Bowel Screening Programme. Open Letter, 7th November 2017. Chief Medical Officer Directorate.

[E5] NHS England, Public Health Wales & Public Health Agency NI. (2020) *Bowel Cancer Screening* [Online]. Available: https://www.nhs.uk/conditions/bowel-cancer-screening/; https://phw.nhs.wales/services-and-teams/screening/bowel-screening/about-screening/frequently-asked-questions/; https://www.publichealth.hscni.net/directorate-public-health/service-development-and-screening/bowel-cancer-screening [Accessed 19th January 2021].

[E6] NICE (2017). Quantitative faecal immunochemical tests to guide referral for colorectal cancer in primary care. *Diagnostics Guidance.* Available: https://www.nice.org.uk/guidance/dg30 [Accessed 12th February 2021]. National Institute for Health and Care Excellence.

[E7] Scottish Government. 2020. *Coronavirus (Covid-19): Guidance for use of FIT testing for patients with colorectal symptoms* [Online]. Available: https://www.gov.scot/publications/coronavirus-covid-19-guidance-for-use-of-fit-testing-for-patients-with-colorectal-symptoms/ [Accessed 31st December 2020].

[E8] UK National Screening Committee (2016) Screening in the UK: Making effective recommendations 2015 to 2016. Available: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/733227/Screening_in_the_UK___making_effective_recommendations_2015_to_2016.pdf [Accessed 12th February 2021]. **Steele** wrote the Foreword as Incoming Chair of the UK National Screening Committee.

[E9] Steele, R. J., Carey, F. A., Stanners, G., Lang, J., Brand, J., Brownlee, L. A., Crichton, E. M., Winter, J. W., Phull, P. S., **Mowat**, C., Strachan, J. A., Digan, A. M. & Fraser, C. G. (2020) Randomized Controlled Trial: Flexible sigmoidoscopy as an adjunct to faecal occult blood testing in population screening. *Journal of Medical Screening,* 27 (2)**,** pp. 59-67; DOI: 10.1177/0969141319879955.

[E10] UK National Screening Committee. (2020) *The UK NSC Recommendation on bowel cancer screening in adults* [Online]. Available: https://legacyscreening.phe.org.uk/bowelcancer [Accessed 31st December 2020].

[E11] Bowel Cancer UK. (2017). *New NHS study expected to almost halve number of endoscopies by 2020* [Online]. Available: https://www.bowelcanceruk.org.uk/news-and-blogs/news/nhs-study-finds-new-screening-test-could-almost-halve-endoscopy-procedures-by-2020/ [Accessed 19th January 2021].