Institution:
University of Cambridge

Unit of Assessment:
UoA2

Title of case study:
A major randomised trial of screening for abdominal aortic aneurysm, and initiation of a UK national screening programme.

1. Summary of the impact (indicative maximum 100 words)

Abdominal aortic aneurysm (AAA) is a major cause of death in older men, in the UK and elsewhere. A large UK trial led by the University of Cambridge evaluated the long-term benefits of ultrasound screening for AAA in men aged 65-74 years. This provided the basis for the introduction of a UK national AAA screening programme in men aged 65; this was announced in 2008, initiated in 2009, and achieved full coverage of England in 2013. Similar screening has started in Sweden, New Zealand and in parts of Italy, and is being actively discussed in Denmark, Norway and Finland.

2. Underpinning research (indicative maximum 500 words)

Key researchers: Since the year 2000, Professor Simon Thompson (Director, MRC Biostatistics Unit (2000-2011), Cambridge, and Professor of Biostatistics, Department of Public Health and Primary Care, University of Cambridge (2002-present) has been the lead statistician and co-principal investigator of the Multicentre Aneurysm Screening Study randomised trial, described below, and became the trial's principal investigator in 2005. Under his supervision, Dr Lois Kim (early career researcher 2001-07) undertook analyses of the accumulating data from the trial for its main publications, developed a detailed health economic model so that long-term cost-effectiveness could be estimated, and contributed to a variety of related projects. Thompson was the lead applicant on grants (funded by MRC) to extend the follow-up of the trial's participants from the initial 4 years to 13 years of follow-up. For the other studies mentioned below, Thompson was the lead statistician and co-investigator in the national trials of treatment of AAA (funded by MRC and NIHR HTA), and the principal investigator of the international RESCAN Collaboration which aimed to provide a better evidence-base for the choice of small AAA surveillance intervals (funded by NIHR HTA). In Cambridge, Thompson supervised Lu Gao, Anthony Brady and Dr Michael Sweeting for these studies.

Research undertaken: Uncertainty over the potential benefits of screening for AAA in the 1990s led to the initiation of the UK Multicentre Aneurysm Screening Study (MASS, started in 1997 with follow-up until 2013). This randomised trial recruited a population-based sample of 68,770 men aged 65-74, randomised to either invitation to ultrasound screening (with surveillance follow-up for small AAAs detected, and surgical intervention for large AAAs) or no invitation to screening. The University of Cambridge led the trial's protocol development, its randomisation, data management and patient recall systems, and supervision of statistical analyses. MASS remains the largest trial that has been conducted to date, and together with crucial long-term follow-up data has provided the majority of the worldwide randomised evidence on the benefit of AAA screening. Of the men invited, 80% attended screening, and 5% of these had a latent AAA detected. The early results at 4 years of follow-up showed that invitation to AAA screening led to a halving of AAA-related mortality (relative risk reduction 42% amongst those invited, 53% amongst those attending), as well as a halving of non-fatal AAA ruptures [research ref 1, Cambridge authors Day, Kim, Thompson, Walker]. This impressive reduction resulting from invitation to once-only screening was maintained in the longer term, despite some increase in the rate of AAA ruptures during the later years in those originally screened as normal [research ref 2, Cambridge authors Thompson, Gao]. In a linked health economic assessment, it was shown that offering AAA screening to 65-year old men was likely to be highly cost-effective in the long-term, with an estimated cost of £2970 per quality-adjusted year of life gained [research ref 3, Cambridge authors Kim, Thompson].

Additional research to optimise impact: To underpin policy on screening and treatment of AAA,

Thompson and colleagues conducted large nationally-based UK randomised trials to compare: (i) surveillance versus early surgery for small AAAs based on 1090 patients recruited in 1991-95 and followed up until 2005 [research ref 4, Cambridge authors Brady, Thompson], and (ii) open surgery versus endovascular aneurysm repair (EVAR) for large AAAs amongst 1252 patients recruited in 1999-2004 and followed up until 2009 [research ref 5, Cambridge author Thompson]. In the RESCAN Collaboration, Thompson and colleagues also collated individual longitudinal data on small AAA growth and rupture for 15,000 patients from 18 studies in different countries, with up to 8 years of follow-up, and undertook a detailed individual patient data meta-analysis in order to refine the choice of surveillance intervals [research ref 6, Cambridge authors Sweeting, Thompson].

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

1. Multicentre Aneurysm Screening Study Group (Scott RAP, Ashton HA, Buxton MJ, Day NE, Kim LG, Marteau TM, Thompson SG, Walker NM). The multicentre aneurysm screening study (MASS) into the effect of abdominal aortic aneurysm screening on mortality in men: a randomised controlled trial. *Lancet* 2002; **360**: 1531-1539. 440 citations.

2. Thompson SG, Ashton HA, Gao L, Scott RAP. Screening men for abdominal aortic aneurysm: 10 year mortality and cost effectiveness results from the randomised Multicentre Aneurysm Screening Study. *British Medical Journal* 2009; **338**: b2307. 77 citations.

3. Kim LG, Thompson SG, Briggs AH, Buxton MJ, Campbell HE. How cost-effective is screening for abdominal aortic aneurysms? *Journal of Medical Screening* 2007; **14**: 46-52. 18 citations

4. UK Small Aneurysm Trial Participants (Powell JT, Brady AR, Brown LC, Fowkes FGR, Greenhalgh RM, Ruckley CV, Thompson SG). Long-term outcomes of immediate repair compared with surveillance for small abdominal aortic aneurysms. *New England Journal of Medicine* 2002; **346**: 1445-1452. 249 citations

5. UK EVAR Trial Investigators (Greenhalgh RM, Brown LC, Powell JT, Thompson SG, Epstein D). Endovascular versus open repair of abdominal aortic aneurysm. *New England Journal of Medicine* 2010; **362**; 1863-1871. 253 citations

6. RESCAN Collaborators (Bown MJ, Sweeting MJ, Brown LC, Powell JT, Thompson SG). Surveillance intervals for small abdominal aortic aneurysms: a meta-analysis. *Journal of the American Medical Association* 2013; **309**: 806-813.

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

The initial clinical and cost-effectiveness results from the MASS trial were presented to the UK National Screening Committee (NSC) in 2003-04 who consequently recommended, in 2005, the introduction of a national AAA screening programme for men aged 65 [impact ref 1]. Work was then undertaken to raise the profile of AAA screening as a matter for public debate, and in particular to increase awareness amongst policy makers and politicians. Also during 2006-07 Thompson and Kim refined the estimates of the long-term cost-effectiveness of an AAA screening programme in the UK, made the NSC aware of this work, and worked with health economic modellers at the Department of Health to answer questions about the health service impacts of such a programme. In January 2008, the prime minister Gordon Brown announced the introduction of a national AAA screening programme, in line with the NSC's original recommendation [impact ref 2].

As a result, the NHS AAA Screening Programme (NAAASP) was initiated in 2009, in four geographical centres in England [impact ref 3]. On the basis of the research findings, Thompson and colleagues provided advice on issues including: training and quality control monitoring of ultrasonographers; deployment of surgical services necessary to accommodate the anticipated increased numbers of elective AAA repairs undertaken; and content of the core data needed to audit and control the programme as it rolled out. An issue crucial to the success of NAAASP in terms of delivering the anticipated reduction in AAA-related mortality was that the mortality from elective AAA operations was kept as low possible, as had been achieved in the MASS trial. For

this purpose, and after much debate, it was decided that AAA surgery should be concentrated into larger centres where surgical experience would be greater, excellence could be more easily achieved, and monitoring could be more effective [impact ref 4].

NAAASP currently (August 2013) covers the whole of England [impact ref 3], with identical programmes being initiated in the devolved jurisdictions of Wales, Scotland, and Northern Ireland [impact refs 5,6]. It is anticipated that full UK-wide coverage will be achieved in 2015. The uptake of the screening invitation in NAAASP has been 75%, only slightly lower than the 80% achieved in the MASS trial, and the elective surgical mortality rate for large AAAs has been kept low (<2%) [3]. Surveillance for small AAAs follows the protocol and intervals developed for the Cambridge-led MASS trial, but may be slightly relaxed in the future in response to the publication [research ref 6] from the RESCAN Collaboration on the effects and cost-effectiveness of alternative surveillance intervals.

AAA screening leads to improved patient outcomes through the monitoring of those at risk with a small AAA, and by offering elective surgery to those with a large AAA. Based on the MASS trial and the three other smaller randomised trials of AAA screening that are available internationally, it is anticipated that mortality from AAA should be reduced by about a half in men aged over 65 through the introduction of NAAASP. Given current mortality rates, this corresponds to 1300 deaths prevented per year in the UK [impact ref 3].

At international meetings in London (2012) and Budapest (2013), representatives from 12 different countries worldwide compared their prospects for initiating AAA screening programmes. Outside the UK, screening programmes have started in Sweden [impact ref 7], New Zealand and parts of Italy, while initiation is being actively discussed in Denmark, Norway and Finland [impact refs 8,9]; in the USA, ultrasound AAA screening is now recommended for all men aged over 65 who have ever smoked [impact ref 10]. These changes in international policy have been driven by the results from the MASS trial, as well as the early experience of NAAASP in the UK.

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

1. UK National Screening Committee statement on AAA screening: AAA policy review summary, November 2005: http://www.screening.nhs.uk/aaa [accessed 2 Sept 2013] The screening committee's guidance (see "Related documents AAA policy review summary" on this website cites the work described above as the 'major MRC sponsored trial of screening')

2. BBC News website: Men to get aneurysm screening, 5 January 2008: http://news.bbc.co.uk/1/hi/health/7172094.stm [accessed 14 Aug 2013]

3. NHS Abdominal Aortic Aneurysm Screening Programme (NAAASP) main website: http://www.aaa.screening.nhs.uk, and most recent progress report for 2011-12 (Summary and Data): http://aaa.screening.nhs.uk/annualreport [accessed 14 Aug 2013]

4. Statement on NHS AAA Screening Programme's quality criteria for elective surgery, June 2010. http://aaa.screening.nhs.uk/publications [accessed 14 Aug 2013]

5. Wales Abdominal Aortic Aneurysm Screening Programme: http://www.aaascreening.wales.nhs.uk/home [accessed 14 Aug 2013]

6. Scottish Abdominal Aortic Aneurysm Screening Programme: http://www.scotland.gov.uk/Topics/Health/Services/Screening/Abdominal-Aortic-Aneurysm [accessed 14 Aug 2013]

7. Screening for Abdominal Aortic Aneurysm in Sweden, September 2008: http://www.sbu.se/en/Published/Alert/Screening-for-Abdominal-Aortic-Aneurysm [accessed 14 Aug 2013]

8. International progress on AAA screening: http://aaa.screening.nhs.uk/international-research

[accessed 14 Aug 2013]

9. Stather PW, Dattani N, Bown MJ, Earnshaw JJ, Lees TA. International variations in AAA screening. *Eur J Vasc Endovasc Surg* 2013; **45**: 231-234.
10. US Preventive Services Task Force. Screening for abdominal aortic aneurysm: recommendation statement. *Ann Intern Med* 2005; **142**: 198–202.