

Impact case study (REF3b)

Institution: Imperial College London
Unit of Assessment: 01 Clinical Medicine
Title of case study: 20 Year Landmark Aortic Trials Produce National and International Guidelines and Alter Patient Management
<p>1. Summary of the impact (indicative maximum 100 words)</p> <p>Three national, multicentre randomised controlled trials and associated studies during a 20-year research programme on abdominal aortic aneurysm (AAA) led by Imperial College researchers have altered international practice. The United Kingdom Small Aneurysm Trial (UKSAT) set the threshold for intervention at 5.5cm to repair AAAs. Population screening programmes and guidelines in Europe (UK, Sweden and Europe as a whole), Australia and the United States are based on these data. The results from EndoVascular abdominal Aortic Repair (EVAR) trials have informed international audits, guidelines (including NICE) and task forces in the same countries.</p>
<p>2. Underpinning research (indicative maximum 500 words)</p> <p>Key Imperial College London researchers: Professor Roger Greenhalgh, Professor of Surgery (1979 – present) Professor Janet Powell, Professor of Vascular Biology (1994 - 2001), Visiting Professor (2001 – present) Professor Simon Thompson, Professor of Medical Statistics and Epidemiology (1996-1999)</p> <p>The programme of research at Imperial College (1993-present) has run under the leadership of Professor Greenhalgh supported by Professors Powell and Thompson both also of Imperial College (Thompson now moved to Cambridge).</p> <p>The United Kingdom Small Aneurysm Trial (UKSAT) (1991-1998; Principal Investigator [PI], Professor Greenhalgh) randomised over 1090 patients from all over the UK with small AAAs into surveillance and early surgery groups. This trial, for the first time confirmed that surveillance was the safe and therefore the preferred option for AAA up to a size of 5.5cm (1). This trial was later mimicked by the ADAM trial performed later with the Veteran's Affairs (VA) group in the US.</p> <p>The RESCAN study (2009-2012; PI, Professor Thompson) is an individual patient meta-analysis of small aneurysm growth and rupture rates, which uses UKSAT data, again, run from Imperial College. RESCAN has determined optimal time intervals for surveillance of patients with small aneurysms found at screening (2), 2-3 years, AAA 3.0-4.0cm, 1 year AAA 4.1-4.9cm and 6 months aneurysm > 5.0cm.</p> <p>The EndoVascular abdominal Aortic Repair (EVAR) trials (1999-funded to 2015; PI, Professor Greenhalgh) consist of the world's first major randomised controlled trial comparing EVAR and open AAA repair (EVAR-1) and a unique trial of EVAR versus best medical therapy (EVAR-2) in frail patients with AAA (3, 4, 5).</p> <p>The EVAR-1 trial provides the first clear picture of the benefits and drawbacks of a minimally invasive approach to AAA treatment. It showed that EVAR had a 3-fold lower operative mortality than open repair and that aneurysm related survival was greater for 6 years. However, there was no improvement in overall survival or quality of life beyond 2 years. Mean hospital costs were £3019 higher for patients in the EVAR group (4).</p> <p>With continued follow-up in this group, late aneurysm ruptures after EVAR eroded the early benefit of aneurysm related mortality (this has set the standard for 10-year follow-up of all EVAR patients). During the 10-year follow-up, 27 EVAR secondary sac ruptures occurred and follow-up CT scan audits have shown factors associated with those late ruptures (6). Investigations of patterns of sac growth are underway in follow-up investigations of 10-15 years to inform further endovascular stent</p>

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design and follow up strategies.

Results from the EVAR-2 trial highlighted considerable operative mortality in patients unfit for open repair (4), and led to the withdrawal of funding for EVAR in high-risk patients in the US. EVAR-2 randomised 404 patients who were not candidates for open repair to EVAR or no surgical intervention.

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

- (1) The UKSAT participants. (1998). Mortality results for randomised controlled trial of early elective surgery or ultrasonographic surveillance for small abdominal aortic aneurysms. *Lancet*, 352 (9141), 1649-1655. [DOI](#). Times cited: 491 (as at 8th November 2013 on ISI Web of Science). Journal Impact Factor: 39.06
- (2) RESCAN Collaborators. (2013). Surveillance intervals for small abdominal aortic aneurysms – A Meta-analysis. *JAMA*, 309 (8), 806-813. [DOI](#). Times cited: 3 (as at 8th November 2013 on ISI Web of Science). Journal Impact Factor: 29.97
- (3) Greenhalgh, R.M., Brown, L.C., Kwong, G.P.S., Powell, J.T., Thompson, S.G. (2004). Comparison of endovascular aneurysm repair with open repair in patients with abdominal aortic aneurysm (EVAR trial 1), 30-day operative mortality results: randomised controlled trial. *Lancet*, 364, 843-848. [DOI](#). Times cited: 757 (as at 8th November 2013 on ISI Web of Science). Journal Impact Factor: 39.06
- (4) EVAR trial participants. (2010). Endovascular Repair of Aortic Aneurysm in Patients Physically Ineligible for Open Repair. *New England Journal of Medicine*, 362, 1872-1880. [DOI](#). Times cited: 73 (as at 8th November 2013 on ISI Web of Science). Journal Impact Factor: 51.65
- (5) EVAR trial participants. (2010). Endovascular versus Open Repair of Abdominal Aortic Aneurysm. *New England Journal of Medicine*, 362, 1863-1871. [DOI](#). Times cited: 266 (as at 8th November 2013 on ISI Web of Science). Journal Impact Factor: 51.65
- (6) Wyss, T.R., Brown, L.C., Powell, J.T., Greenhalgh, R.M. (2010). Rate and predictability of graft rupture after endovascular and open abdominal aortic aneurysm repair: data from the EVAR Trials. *Ann Surg.*, 252, 805-812. [DOI](#). Times cited: 44 (as at 8th November 2013 on ISI Web of Science). Journal Impact Factor: 6.32

Key funding:

- Medical Research Council (MRC; 1991-1995; £285,396), PI R. Greenhalgh, UK Small Aneurysms trial: early surgery or observation for small AAA.
- MRC (1991-1995; £107,882), PI R. Greenhalgh, UK Small Aneurysms trial: economic evaluation in UKSAT.
- MRC (1996-1998; £196,212), PI R. Greenhalgh, UK Small Aneurysms Trial extension.
- British Heart Foundation (1991-1998; £122,950), PI J. Powell, UK Small Aneurysms trial: growth and management of small AAA.
- Health Technology Assessment (HTA; 1999-2003; £543,320), PI R. Greenhalgh, Endovascular Aortic Aneurysm Repair (EVAR) trials.
- HTA (2003-2005; £209,093), PI R. Greenhalgh, EVAR 1&2 Extension 1.
- HTA (2005-2010; £866,996), PI R. Greenhalgh, EVAR 1&2 Extension 2.
- HTA (2012-2015; £377,058), PI R. Greenhalgh, Late aneurysm-related mortality up to years, secondary endovascular repair late sac rupture risk and cost-effectiveness implications.
- HTA (2009-2012; £259,976), PI S. Thompson, RESCAN – individual patient meta-analysis of small aneurysms growth and rupture rates.

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

Impacts include: health and welfare, public policy and services, practitioners and services
 Main beneficiaries include: patients, practitioners, NICE, European Society, Society of Interventional Radiology

For many years, there was no evidence at what diameter it would benefit the patient to undergo elective surgery for AAA to reduce the rupture risk and hence death rate. Many patients were

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receiving intervention at an early stage (with small aneurysms) without evidence to support this practice. The UKSAT provided those data to set intervention at 5.5cm, by proving a surveillance strategy was safe for patients below this size. UKSAT, alongside a second UK aneurysm screening study (MASS), UKSAT informed the treatment strategy for population screening for AAA after the research showed that the number of death from burst aneurysms could be reduced by up to 50%, and as a consequence a National UK screening initiative has recently been instituted [1]. The Swedish Council on Technology Assessment in Health Care (2008) also identified screening for AAA in men [2].

At the time of UKSAT, the only well recognised treatment option was open repair of AAAs. AAA prevalence in 65 year old men in 2012 was 1.8% of the population. Now >75% in the US and >50% patients in Western Europe receive EVAR. Data collected by Biba MedTech Insights for the European Vascular and Endovascular Monitor (originally set up by Professor Greenhalgh) shows the growth in the use of EVAR as compared with open repair (which has decreased) [3]. This growth correlates with the publication of mortality results from the Imperial group after 30 days, 5 and 10 years follow up. The mortality data provided the evidence clinicians needed to be convinced of the safety of using EVAR.

2010 Guidelines from the European Society [4] and the Society of Interventional Radiology [5] support the expansion in use of EVAR, including the intervention threshold described above (5.5cm), drawing evidence from the trials and studies of this Imperial research program. Guidelines for the use of EVAR have been drawn up for the treatment of AAA in two separate populations: Those fit for open repair (EVAR-1) and those unfit (EVAR-2).

As well as influencing guidelines across the world, this research shaped the NICE guidelines "Endovascular stent-grafts for the treatment of abdominal aortic aneurysms" (February 2009) [6]. Professor Greenhalgh was also invited to inform the Guideline Development Group's discussions as a clinical specialist. The NICE guidelines state that:

1. Endovascular stent-grafts are recommended as a treatment option for patients with unruptured infra-renal AAAs, for whom surgical intervention (open surgical repair or endovascular aneurysm repair) is considered appropriate (see page 1, point 1.1)
2. The decision on whether EVAR is preferred over open surgical repair should be made jointly by the patient and their clinician after assessment of a number of factors (see page 1, point 1.2)

The Model of Care document for AAA in Australia also recommends Endovascular stent grafts as one of two treatment options in the repair of aneurysms [7; see page 21]. This document justifies intervention by either open or endovascular repair for aneurysms > 5.5cm referencing UKSAT. The EVAR trials 30 day mortality results (2004), 5 years results (2005) and 10 year results (2010) impacted on the use of EVAR preferentially to open repair.

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

[1] UK NHS National AAA Screening Programme <http://aaa.screening.nhs.uk/aaascreening>. Archived on 24th October 2013.

[2] Swedish Council on Technology Assessment in Health Care http://www.sbu.se/upload/Publikationer/Content0/3/Screening_Abdominal_Aortic_Aneurysm_2008_04.pdf. Archived on 24th October 2013.

[3] Data from the [European Vascular and Endovascular Monitor](#)

[4] Management of Abdominal Aortic Aneurysms – Clinical Practice Guidelines of the European Society for Vascular Surgery (2010) <http://www.lfb.lv/files/ESVS-AAA-guidelines.pdf>. (see pages S11 and S14). Archived on 24th October 2013.

[5] Clinical Practice Guidelines for the Endovascular Abdominal Aortic Aneurysm Repair: Written

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by the Standards of Practice Committee for the Society of Interventional Radiology (SIR, USA) and Endorsed by the Cardiovascular and Interventional Radiology Society of Europe (CIRSE) and the Canadian Interventional Radiology Association (2010) <http://www.sirweb.org/clinical/cpg/Q112.pdf>.
[Archived](#) on 24th October 2013.

[6] NICE guidelines for Abdominal Aortic Aneurysm – Endovascular Stent Graphs
<http://guidance.nice.org.uk/TA167/Guidance/pdf/English>. [Archived](#) on 24th October 2013.

[7] Cardiovascular Health Network – Abdominal Aortic Aneurysm Model of Care
Department of Health, State of Western Australia, 2008
http://www.healthnetworks.health.wa.gov.au/modelsofcare/docs/AAA_Model_of_Care.pdf.
[Archived](#) on 24th October 2013.