Institution: The University of Edinburgh

Unit of Assessment: 4

Title of case study: C: Immediate computed tomography scanning in acute stroke improves outcomes for patients and is very cost effective, whereas arteriography and magnetic resonance scanning are not cost-effective in secondary prevention

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

Impact: Health and welfare; Wardlaw's work on diagnostic imaging in stroke prevention and treatment has effected changes to clinical guidelines worldwide, prevented thousands of strokes and decreased disability.

Significance: In the UK, changes in stroke treatment consequent upon effective imaging result in 6000 more quality-adjusted life-years and save ~£300M per year. Improved stroke prevention averts 1760 strokes and saves the NHS £30M per year.

Beneficiaries: Stroke patients, the NHS and healthcare providers in other countries

Attribution: The research took place entirely at UoE.

Reach: UK, Europe, N. America, Australasia.

2. Underpinning research (indicative maximum 500 words)

Professor Joanna Wardlaw (Professor of Applied Neuroimaging, UoE, 1994–present) undertook ground-breaking studies to demonstrate that immediate computerised tomography (CT) scanning in acute stroke was the most cost-effective imaging strategy.

Attitudes to stroke were generally nihilistic in the late 1990s, with poor access to imaging, often with long delays to diagnosis and in initiating treatment. Wardlaw and her group determined how best to use imaging in acute stroke diagnosis and prevention in three consecutive reports; the first report in 2004 on cost-effective imaging in acute stroke led to Wardlaw being commissioned, in open competition, to undertake two further health economic impact assessments: in 2005–2006 on cost-effective carotid imaging in stroke prevention and in 2010–2012 on cost-effective brain imaging in stroke prevention.

2.1. Acute stroke imaging diagnosis: Between 1998 and 2004, Wardlaw's group performed new primary studies and meta-analysed data on the accuracy of CT and magnetic resonance (MR) imaging; examined the effects of antithrombotic treatment given to patients with haemorrhagic stroke; calculated the costs of stroke care and of imaging; measured the effects of time-to-imaging after stroke on its accuracy; and devised health utility states for different stroke outcomes. Wardlaw's group built a health economics decision-tree model of stroke care and diagnosis, and performed Markov analysis to determine the effect of common imaging strategies on death and dependency after stroke and the cost-effectiveness of different approaches. The most cost-effective imaging strategy was to CT scan all patients admitted with acute stroke immediately [3.1–3.3].

2.2 Carotid imaging in stroke prevention: In secondary stroke prevention, carotid stenosis is an important treatable risk factor for stroke, but requires carotid imaging to diagnose the stenosis. Trials (also led by UoE) in the 1990s used intra-arterial angiography to diagnose carotid stenosis but this is time-consuming, carries significant risk of causing stroke and was only available in specialist centres. Between 20 and 30 patients present to stroke prevention services with suspected transient ischaemic attack (TIA) or minor stroke every week. Rapid access to accurate imaging is essential for rapid diagnosis and treatment. Wardlaw's group undertook a second health economics analysis between 2005 and 2007, meta-analysing existing data and

acquiring new data on the accuracy of non-invasive carotid imaging, gathering data on the costs of imaging, treatments and on the population risks of stroke. They constructed a time-series model of stroke prevention clinics, tested 18 different imaging strategies, and determined that intra-arterial angiography should be abandoned as it was less effective than rapid non-invasive imaging [3.4, 3.5].

2.3 MR brain imaging in stroke prevention: In 2010–2012, Wardlaw's group undertook a third analysis to determine if MR brain imaging (which is very sensitive to acute ischaemia) should be more widely used in stroke prevention. Following detailed analyses of all available literature and primary data, deterministic and probabilistic modelling, Wardlaw's group demonstrated that MR diffusion-weighted imaging was too insensitive and heterogeneous to differentiate stroke from TIA reliably, or to differentiate TIA from mimics, and was highly unlikely to be cost-effective in stroke prevention. Moreover, in some circumstances, a reliance on MR could lead to fewer strokes being prevented [3.6].

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

3.1 Wardlaw J, Keir S, Seymour J, et al. What is the best imaging strategy for acute stroke? NHS Health Technology Assessment Programme. 2004;8(1). http://www.hta.ac.uk/fullmono/mon801.pdf

3.2 Wardlaw J, Seymour J, Cairns J,… Keir S, Dennis M, Sandercock P. Immediate computed tomography scanning of acute stroke is cost effective and improves quality of life. Stroke. 2004;35:2477–83. DOI: 10.1161/01.STR.0000143453.78005.44.

3.3 Wardlaw J, Keir S, Bastin M, … Armitage P, Rana A. Is diffusion imaging appearance an independent predictor of outcome after ischemic stroke? Neurology. 2002;59:1381–7. DOI: 10.1212/01.WNL.0000032495.71720.C3.

3.4 Wardlaw J, Chappell F, Best J, … Wartolowska K, Berry E, on behalf of the NHS R & D Health Technology Assessment Carotid Stenosis Imaging Group. Non-invasive imaging compared with intra-arterial angiography in the diagnosis of symptomatic carotid stenosis: a meta-analysis. Lancet. 2006;367:1503–12. DOI: 10.1016/S0140-6736(06)68650-9.

3.5 Wardlaw J, Stevenson M, Chappell F, et al. Carotid artery imaging for secondary stroke prevention: both imaging modality and rapid access to imaging are important. Stroke. 2009;40:3511–7. DOI: 10.1161/STROKEAHA.109.557017.

3.6 Wardlaw J, Brazelli M, Chappell F, et al. An assessment of the cost effectiveness of magnetic resonance including diffusion-weighted imaging in patients with transient ischaemic attack and minor stroke. Health Technology Assessment. 2014, in press. *[Will appear on www.journalslibrary.nihr.ac.uk as a future publication in Oct/Nov 2013].*

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

Immediately following its publication in scientific journals, Wardlaw and colleagues' work was highlighted in many secondary commentaries by highly respected organisations that disseminate medical practice information; for example, the American College of Physicians Journal Club publications and, in the UK, the Database of Reviews of Effectiveness. The work was also included in a best-selling international textbook on stroke management [5.1].

Impact on public policy

The findings were cited by and led to changes to the guidelines on stroke management in the UK and internationally. The National Institute for Health and Care Excellence guidelines [5.2], European [5.3], Canadian [5.4], Australasian [5.5] and the American Heart Association [5.6] guidelines were changed in 2008 or subsequently. Wardlaw's recent survey of UK practice [3.6] revealed that intra-arterial angiography has been replaced rapidly and completely by non-

invasive imaging. Data from 2012 (see below) clearly indicate that, as a result of Wardlaw's research and these guidelines, a change in practice has occurred.

Wardlaw, with Chappell (CSO Health Services Research Fellow, UoE, 2002–present), Brazelli (CSO Health Services Research Fellows, UoE, 2010–2012) and Sandercock (UoE 1987–present; Professor of Medical Neurology; Head of Cochrane Stroke Group) were foundation members of the Cochrane Collaboration Diagnostic Tests Working Group, which is now publishing key systematic reviews of the accuracy of diagnostic tests [5.7], and important improvements in methodology. These increasingly underpin evidence on which tests should be used in clinical practice, particularly in the era of stratified medicine.

Impact on practitioners and services

A survey of UK stroke services by Wardlaw, published in 2008, showed that fewer patients were waiting more than 24 hours for CT brain imaging compared with a survey in 2000–2001 [5.8]. Wardlaw's Health Technology Assessment panel-commissioned survey of all stroke prevention services in the UK in 2012 [3.6] showed that no centres were using intra-arterial angiography, and 90%+ were using ultrasound, most on the day of referral, and had immediate access to CT brain imaging for stroke.

Impact on health and the economy

Performing immediate brain imaging in all patients with suspected acute stroke, compared with the less-effective strategies, for the 120,000 patients who have a stroke each year in the UK is calculated to have resulted in 6,000 more quality-adjusted life-years, and reduced the cost of stroke by between £156M and £312M per year in NHS costs.

Rapid non-invasive carotid imaging in patients with TIA, compared with the slow and more invasive carotid imaging methods, is calculated to have prevented about 1760 strokes per year in the UK and saved the NHS around £30M per year [3.5, 3.6].

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

5.1 Warlow C, van Gijn J, Dennis M, Wardlaw J,…Sandercock P, et al. Stroke: Practical Management, Third Edition. Blackwell Scientific Ltd, Oxford, 2008. ISBN 978-1-4051-2766-0. *[Available on request. Corroborates inclusion of the work in a best-selling textbook.]*

5.2 UK STROKE. National clinical guideline for diagnosis and initial management of acute stroke and transient ischaemic attack (TIA). NICE. 2008 http://www.nice.org.uk/nicemedia/live/12018/41363/41363.pdf. *[UK guidelines.]*

5.3 European Stroke Organization (ESO) Executive. Guidelines for Management of Ischaemic Stroke and Transient Ischaemic Attack 2008. Cerebrovasc Dis. 2008;25:457–507. http://www.eso-stroke.org/recommendations.php?cid=9. *[European guidelines.]*

5.4 Canadian Best Practice Recommendations for Stroke Care (May 2013 Update). http://strokebestpractices.ca/wp-content/uploads/2013/05/Ch3_SBP2013_Hyper-Acute-_23MAY13_EN_-FINAL4.pdf. *[Canadian guidelines.]*

5.5 The Australian National Stroke Foundation. Clinical Guidelines for Stroke Management 2010. http://strokefoundation.com.au/site/media/Clinical_Guidelines_Acute_Management_Recommendations_2010.pdf. *[Australasian guidelines.]*

5.6 Latchaw R, Alberts M, Lev M, et al. Recommendations for imaging of acute ischemic stroke: a scientific statement from the American Heart Association. Stroke. 2009;40:3646–78. DOI: 10.1161/STROKEAHA.108.192616. *[American Heart Association guidelines.]*

5.7 Brazzelli M, Sandercock P,…Wardlaw J, Deeks J. Magnetic resonance imaging versus computed tomography for detection of acute vascular lesions in patients presenting with stroke symptoms. Cochrane Database Sys Rev. 2008;4:CD007424. DOI: 10.1002/14651858.CD007424. *[Systematic review of diagnostic test accuracy.]*

5.8 Kane I, Whiteley W, Sandercock P, Wardlaw J. Availability of CT and MR for assessing patients with acute stroke. Cerebrovasc Dis. 2008;25:375–7. DOI: 10.1159/000120688. *[Corroborates change in clinical practice.]*