Institution: The University of Edinburgh

Unit of Assessment: 1

Title of case study: I: Reducing blood transfusions in intensive care and surgery saves precious blood, reduces costs and decreases patient risk

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

Impact: Health and wellbeing; translation of a clear evidence base for reducing red blood cell use in intensive care and surgery into guidelines and changed clinical practice.

Significance: A 20% reduction in overall UK red blood cell usage between 2002–2012, saving the NHS approximately £100M annually; 7000 fewer patients are exposed to red cell transfusion annually, saving 500 lives.

Beneficiaries: Patients in intensive care units; the NHS and healthcare delivery agencies.

Attribution: Studies were led by Walsh at UoE with NHS and Canadian collaborators.

Reach: 7000 patients per year, UK-wide; incorporation into international guidelines.

2. Underpinning research (indicative maximum 500 words)

Professor Tim Walsh (Senior Lecturer; now Professor of Critical Care, UoE, 1999–present) established a research programme to define the relevance of Canadian pilot studies of transfusion in intensive care units (ICU) to UK practice. He established clear evidence for restricted transfusion use and, going further than other investigators, showed definitively that not only are outcomes not affected by restrictive transfusion practice, but also that mortality rates are almost certainly reduced.

During the late 1990s there was increasing interest in defining the risk (as opposed to assumed benefit) of red blood cell (RBC) transfusion in anaemic critically ill patients. Supported by awards from the National Institute for Health Research (£1.4M) and Chief Scientist Office (£182K), Walsh began to define current UK practice, explore persisting uncertainties among clinicians, quantify the risk of RBC transfusion and implement an evidence-based approach. Collaborations with the Scottish and English National Blood Transfusion Service and Canadian transfusion researchers aimed to quantify risk and reduce unnecessary patient exposure to blood transfusions, thereby conserving blood supplies.

Walsh developed methodology to describe ICU transfusion practice at Edinburgh Royal Infirmary in 1999–2000 [3.1]. He led a programme of education across all 25 Scottish ICUs, and completed a national cohort study of >1000 ICU patients in 2001; this was the first national benchmarking study of blood use in UK critical care [3.2] and highlighted areas where better evidence to define the risk of RBC transfusion was needed.

Severely unwell critically ill patients with heart disease. Walsh's observational studies of practice and national surveys (2001–8) demonstrated that existing evidence was insufficient to define best practice for patients with prolonged critical illness or heart disease [3.3, 3.4]. With funding from the Chief Scientist Office, Walsh and colleagues completed a multicentre feasibility trial (2009–11). This trial showed signals for harm from liberal use of RBCs even in the sickest ICU patients with multiple co-morbidities (absolute mortality difference over 6 months 18%; hazard ratio 0.54 (P = 0.061)), providing further evidence to support restricting RBC transfusion [3.5].

Storage age of the blood. The Edinburgh group associated the changes that occur during red cell storage with the evidence that RBC transfusions could have adverse effects (Br J Anaesth. 2002;89:537). Walsh is the UK lead on a large international randomised controlled trial, the Age of

Blood Evaluation study, which will report in 2014–15.

Persisting anaemia following critical illness. In a series of cohort studies (2005–8), Walsh and colleagues explored clinician concern that restrictive transfusion management and resultant ongoing anaemia might affect long-term health-related quality of life (HRQoL) among ICU survivors. These studies confirmed that anaemia was often prevalent for many months after ICU discharge and was associated with poor HRQoL, but that it could be an epiphenomenon [3.6]. The Walsh group's recent feasibility trial indicated no associations between restrictive RBC use and reduced patient survival, HRQoL, or disability over 6 months follow up [3.5]. Thus, Walsh and colleagues have demonstrated that restrictive transfusion practice should be used even among the sickest critically ill patients and will not result in adverse outcomes.

Cell salvage during surgery. Walsh, collaborating with the National Blood Transfusion Service, led a multicentre cohort study in 11 hospitals (210 cases), which indicated that cell salvage reduced RBC use in high-risk orthopaedic surgery (Br J Anaesth. 2012;108:63).

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

3.1 Chohan S, McArdle F, McClelland D, Mackenzie S, Walsh T. Red cell transfusion practice following the transfusion requirements in critical care (TRICC) study: prospective observational cohort study in a large UK intensive care unit. Vox Sang. 2003;84:211–8. DOI: 10.1046/j.1423-0410.2003.00284.x.

3.2 Walsh T, Garrioch M, Maciver C, et al.; Audit of Transfusion in Intensive Care in Scotland (ATICS) study group. Red cell requirements for intensive care units adhering to evidence-based transfusion guidelines. Transfusion. 2004:44:1405–11. DOI: 10.1111/j.1537-2995.2004.04085.x.

3.3 Walsh T, McClelland D, Lee R, et al.; ATICS Study Group. Prevalence of ischaemic heart disease at admission to intensive care and its influence on red cell transfusion thresholds: multicentre Scottish Study. Br J Anaesth. 2005;94:445–52. DOI: 10.1093/bja/aei073.

3.4 Walsh T, McIver C; Scottish Critical Care Trials Group and Scottish National Blood Transfusion Service Clinical Effectiveness Group. A clinical scenario-based survey of transfusion decisions for intensive care patients with delayed weaning from mechanical ventilation. Transfusion. 2009;49:2661–7. DOI: 10.1111/j.1537-2995.2009.02336.x.

3.5 Walsh T, Boyd J, Watson D, et al. Restrictive versus liberal transfusion strategies for older mechanically ventilated critically ill patients: a randomized pilot trial. Crit Care Med. 2013;41:2354–63. DOI: 10.1097/CCM.0b013e318291cce4.

3.6 Bateman A, McArdle F, Walsh T. Time course of anemia during six months follow up following intensive care discharge and factors associated with impaired recovery of erythropoiesis. Crit Care Med. 2009;37:1906–12. DOI: 10.1097/CCM.0b013e3181a000cf.

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

Pathways to impact

Walsh lead-authored a high-impact open-access clinical review (BMJ 341:doi:10.1136/bmj.c4408) authored/co-authored eight chapters/book contributions from 2001–12 and has spoken on this topic at >30 national and international meetings from 2003–12. He organised and hosted national educational meetings on blood transfusion in 2004 and 2009.

Impact on public policy

Walsh has worked closely with the Scottish National Blood Transfusion Service [5.1, 5.2] and Better Blood Transfusion Programmes (acting as expert advisor from 2003, a member of the National Transfusion Committee from 2005–12, and acting as Lothian Regional Lead 2004–8). He played key advisory roles (2005–10) in the development and implementation of the Scottish Transfusion Epidemiology Project that links national databases to report on blood use at regional, hospital and individual clinician level, and in national audit initiatives around major haemorrhage

management (2008–9).

Walsh chaired a British Committee for Safety in Haematology/UK Intensive Care Society evidence-based guideline group (2011–12), which completed the first evidence-based UK guideline for RBC transfusion practice in critical care [5.3]. Moreover, six of Walsh's papers are cited as part of the underpinning evidence for US/international guidelines on transfusion in critical care [5.4]. Walsh co-initiated the development of a National Institute for Health and Care Excellence Guideline for Transfusion and was selected as the UK critical care representative (first meeting 2013).

Impact on clinical practice and the economy

Impact on UK critical care: Walsh showed in 2001 that 40% of ICU patients were transfused, each receiving on average 1.9 RBC units. In comparison, his 2010 analysis [5.5] of 2006 data from 29 ICUs showed that transfusion rates had decreased to 33% of ICU admissions. Data calculated on the reduction in transfusion per admission over this period indicate that of the >100,000 patients treated annually in UK general ICUs, around 7000 fewer patients receive RBCs compared with in 2001, saving >40,000 RBCs/year. There have been substantial changes in practice among clinicians, and a major saving in precious blood supplies as donor numbers fall and production costs rise.

Impact on surgical practice: Evidence from critical care has been widely implemented in surgical and perioperative practice. The recognition that RBC transfusions should be avoided wherever possible has led to an increase in the use of blood conservation technologies, especially perioperative cell salvage. Walsh's study of cell salvage in orthopaedic surgery supported the widespread introduction of this technology, and Walsh initiated the Scotland-wide cell salvage programme, wrote the model business cases, and secured ongoing funding from 2005 for a Scottish coordinator to lead education, safety, and data management. Red cell salvage use has increased from 90 cases/million population (2005) to 650 cases/million population (2010), and the technology has been adopted across all health boards in Scotland undertaking major surgery.

Overall and economic impact: Data from the Scottish Transfusion Epidemiology Project indicate a reduction in annual RBC transfusions from 45.9 to 34.0 per 1000 population (2001 to 2012). Trends in England indicate similar reductions [5.6]. In Scotland, this represents a 50,000 units/year (22%) reduction in RBC use, at a cost reduction of approximately £6.5M/year (extrapolated to approximately £100M annually across the UK). In intensive care, around 7000 fewer patients are exposed to RBCs annually, saving 40,000 RBCs/year (annual cost saving approximately £5M).

Impact on health and welfare

Existing evidence suggests that restricting exposure to RBC transfusions improves patient outcome, so practice change is likely to have directly translated into saving lives. In critical care, reducing RBC use is associated with improved outcomes in many patient sub-groups [3.5]. A reasonable but conservative estimate of 1–2% mortality reduction in the UK over 10 years would indicate approximately 500 lives saved per year. Although attribution of direct causality is difficult in critical care populations, these changes are consistent with the progressive improvement in Standardised Mortality Ratios in Scottish ICUs over the past decade from 1.06 (2001) to 0.86 (2010) [5.7].

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

5.1 Letter from the Medical Director of the Scottish National Blood Transfusion Service. *[Available on request. Confirms the impact of the Walsh group's research]*.

5.2 Letter from the Professor of Blood Transfusion Medicine, University of Oxford *[Available on request. Confirms the impact of the Walsh group's research]*.

5.3 Retter A, Wyncoll D, Pearse R,…Walsh T. Guidelines on the management of anaemia and red cell transfusion in adult critically ill patients. Br J Haematol. 2013;160:445-64. DOI: 10.1111/bjh.12143. *[The first UK evidence-based guideline.]*

5.4 Napolitano L, Kurek S, Luchette F, et al.; American College of Critical Care Medicine of the

Society of Critical Care Medicine; Eastern Association for the Surgery of Trauma Practice Management Workgroup. Clinical practice guideline: Red blood cell transfusion in adult trauma and critical care. Crit Care Med. 2009;37:3124–57. DOI: 10.1097/CCM.0b013e3181b39f1b. *[International guidelines citing Walsh's work.]*

5.5 Seretny M. Red Blood Cell Transfusion in Intensive Care: A review of the Intensive Care Study of Coagulopathy (ISOC) dataset. Masters thesis, University of Edinburgh, 2010. *[Available on request. Provides evidence for decreased transfusion rates in UK critical care.]*

5.6 Tinegate H, Chattree S, Iqbal A, Plews D, Whitehead J, Wallis J; Northern Regional Transfusion Committee. Ten-year pattern of red blood cell use in the North of England. Transfusion. 2013;53:483–9. DOI: 10.1111/j.1537-2995.2012.03782.x. *[Provides evidence for decreased overall RBC use.]*

5.7 Audit of Critical Care in Scotland. Scottish Intensive Care Society Audit Group (2012). www.sicsag.scot.nhs.uk/Publications/web-SICSAG-report-2012-Final.pdf. *[Corroborates decrease in ICU mortality rates.]*