Options to Manage Appropriate Use of Blood and Blood Products

For the Department of Health and Ageing

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Ian Haupt
Project Director
Executive Summary

This is one of several projects commissioned by the Department of Health and Ageing (DOHA) to help inform the financial management of the blood sector in Australia. The project involved the evaluation of strategies to ensure the appropriate use of blood and their impact on patient outcomes. The analysis covered the evidence base and strategies supporting appropriate use of blood, and the use of a range of strategies including, but not exclusively, clinical detailing, improved use of clinical data to support better practice, strategies to increase compliance with clinical guidelines, and the introduction of price signals in the supply chain.

The terms of reference (Appendix 1) required the consideration of price signalling to include a national model for price signalling and appropriate positioning in the supply chain, but excluding direct charging to patients, in accordance with the National Blood Agreement, 2003.

The project was undertaken in conjunction with the related project, Analysis of Cost Drivers and Trends in the Blood Sector. The projects were commissioned in the context of sustained increases in the costs to governments for the supply of blood and blood products. The aims of the projects included increasing the knowledge of the trends in the sector and identifying areas where governments may be able to act to manage more sustainably the growth in costs.

Many of the information sources were common to both projects, including much of the literature, data sources and stakeholders. The key findings and conclusions have consequently been drawn from both projects.

ACHIEVEMENTS IN THE AUSTRALIAN BLOOD SECTOR

The blood sector in Australia has seen significant progress over the last decade or so, particularly with the establishment of a national approach and cooperation among governments. The national approach gathered momentum with the creation of the Australian Red Cross Blood Service (the Blood Service) as a national body in 1995, the subsequent introduction of the Australian Health Ministers’ Advisory Council (AHMAC) Blood and Blood Products Standing Committee and, in 2003, the signing of National Blood Agreement among Australian governments and creation of the National Blood Authority (NBA).

The NBA’s achievements after its first five years of its operation (National Blood Authority, 2008) included establishment of:

- contract management arrangements that delivered significant cost savings to all Australian governments;
- a range of supply contingency provisions to prevent significant stock shortages;
- governance frameworks to integrate blood into overall health sector risk planning;
- effective relationships with key stakeholders;
- safety and quality products such as the recent Initial Australian Haemovigilance Report (2008) and the Criteria for the Clinical Use of Intravenous Immunoglobulin (IVIg) in Australia (2008).

The NBA has also progressed data capture and analysis as well with the development, for example, of:

- the Australian Bleeding Disorders Registry (ABDR), which allows for more accurate planning of supply requirements for people with haemophilia and other bleeding disorders;
• Integrated Data Management System (IDMS);
• the first Blood Measures Guide, which was a world first in establishing a nationally accepted set of measures on the use and effectiveness of fresh blood components;
• a national electronic ordering and receipting system (BloodNet), which is also planned to have enhanced data capture functions to assist sector planning and performance evaluation.

The current review of the clinical guidelines governing the use of blood components has been another significant development. While perhaps overdue, the resulting revised guidelines will provide the most contemporary evidence-based information on when and how to use fresh blood components.

Since the introduction of the National Blood Agreement, states and territories have also made progress, including promoting efficiency in use of blood and blood products, reducing wastage and promoting best practice management and use of blood products, blood related products and blood related services. The report on Options to Manage Appropriate Use of Blood and Blood Products provides information on the initiatives which the various jurisdictions have put in place. They have included:

• establishment of the Blood Watch program, with its many initiatives targeting clinicians, but also patient education, in NSW;
• establishment of BloodSafe in SA and Blood Matters in Victoria, again with multi-faceted initiatives;
• devolution of the state blood budget to public hospitals or Area Health Services, in NSW and Tasmania;
• concerted waste minimisation strategies in Queensland and Tasmania;
• development and implementation of the electronic ordering and receipting system (ORBS) in Queensland;
• development and commencement of a statewide Patient Blood Management Program (PBMP) in WA.

In terms of the safety record of the sector, the 2010 report of the Haemovigilance Advisory Committee (HAC) (2010) noted that “there is no evidence at this stage to suggest that the rate of transfusion errors in Australia is outside the range experienced in OECD countries.” (Ibid.) The report indicated that “[i]n common with other OECD countries, such as the United Kingdom, New Zealand, Sweden and Canada, the risks to the safety of transfused patients in Australia were predominantly in the hospital environment, arising from procedural errors.” (Ibid.) The 2008 report of the HAC had indicated that approximately 65 per cent of incidents reported in Australia had involved procedural errors and that this was “broadly compatible with (the results from) other OECD countries.” (Ibid.) The UK SHOT Annual Report 2008 (Serious Hazards of Transfusion, 2008) indicated that procedural errors represented 59 per cent of cumulative numbers of cases reviewed in the period 1996-2008.

**APPROPRIATE USE OF BLOOD AND BLOOD PRODUCTS**

‘Appropriate use’ of blood and blood products is defined in the reports as:

• adherence to current clinical practice guidelines;
• use which promotes safe and effective patient outcomes.
AUSTRALIAN USE

There is evidence of a degree of inappropriate use of blood and blood products in Australia, as assessed against the current guidelines. Evidence of a lack of compliance with current clinical guidelines relates mainly to the uses of blood components, with the bulk of evidence pointing to problems with red cell use.

The report refers to evidence indicating a wide variation in the levels of compliance with The National Health and Medical Research Council (NHMRC)/Australasian Society Of Blood Transfusion Incorporated (ASBT) Clinical Practice Guidelines on the use of Blood Components (‘the NHMRC/ASBT blood components guidelines) in relation to the clinical use of red cells. There is a similar, but smaller, amount of evidence that use of platelets and fresh frozen plasma (FFP) does not have a high level of compliance with the guidelines.

Evidence also points to clinicians being relatively unaware of the body of evidence about the appropriate uses of red cells and associated risks. For example, a joint NBA-NSW study in 2007 reported that many clinicians interviewed found it difficult to nominate the appropriate haemoglobin (hb) levels to justify transfusion (Eureka Strategic Report, 2007). As well, all doctors interviewed for that study indicated that they would typically prescribe a minimum of two units of red cells. This is despite the NHMRC/ASBT blood components guidelines indicating that red cells should be dispensed one unit at a time, so that the patient’s response can be assessed.

The reported uses of intravenous immunoglobulin (IVig) fall overwhelmingly within the published guidelines, according to information compiled by the Blood Service.

Other blood products are variously covered by clinical guidelines, with some not at all (for example, albumin). Apart from IVig, information on adherence to relevant guidelines was not found with regard to other blood products.

SAFETY AND EFFICACY

There have been significant gains made in Australia in securing the safety of the blood supply and in the handling and administration of blood and blood products. Notwithstanding this, there is a large and growing body of literature which questions the appropriateness of many common transfusion practices in terms of patient health outcomes. The main evidence relates to the use of red cells. The literature questions the efficacy of red cell transfusion in treating iron deficiency anaemia in surgical patients. Concerns have also been raised about dosage-dependent morbidity and mortality risks, and risks arising from the age of red cells at the time of transfusion.

For example, based on an exhaustive literature search on transfusion outcomes, the Scientific Committee of the 1st International Consensus Conference on Transfusion Outcomes (ICCTO) held in Phoenix, Arizona, in 2009 stated,

there is a paucity of evidence for benefit and a burgeoning literature demonstrating a strong association between transfusion and adverse outcomes (Society for the Advancement of Blood Management, 2009).

In a very recent article, Isbister, JP, et al. (2011) concluded that,

it is no longer acceptable to maintain a laissez faire approach and assume the benefits and accept the risks of allogeneic blood transfusion. Evidence has accumulated questioning RBC\(^1\) transfusion efficacy and establishing transfusion as a contributing risk

1 Red Blood Cell.
factor for adverse clinical outcomes in many clinical settings. Acknowledging that most available data are observational and that rigorous evidence to establish risks and benefits is needed, we should no longer accept transfusions as the default decision when there is clinical uncertainty.

The reports acknowledge that most of the evidence put forward is founded on observational studies, rather than randomised controlled trials (RCT). In this regard, Isbister et al. (2011) point out,

frequentist statisticians and clinicians demand evidence from RCTs; however, causation for the recognised serious hazards of allogeneic transfusion has never been established in this manner, and

the preponderance of evidence implicating RBC transfusions in adverse clinical outcomes ... from observational studies.

A large body of evidence concerns risks associated with the use of red cells for treatment of iron deficiency anaemia in surgical patients. The literature suggests that transfusion of red cells per se is a risk factor for increased mortality, intensive care unit (ICU) admission, increased length of hospital stay and morbidity, through increased incidence of infection and other adverse conditions.

The lack of evidence supporting the efficacy of use of red cells for treatment of iron deficiency anaemia is recognised in the recent NBA Patient Blood Management Guidelines: Module 2 - Perioperative (Pre-Public Consultation Draft version).

There is also evidence to show that these risks may not be well understood among clinicians. The 2007 NBA-NSW study referred to above included interviews with senior clinicians and registrars, from metropolitan and regional centres, within four main specialties—cardiac, orthopaedic, gastroenterology and anaesthetic. It found that while all doctors could name some of the risks associated with transfusion, very few could name all unprompted. The study concluded that,

senior doctors had a high personal confidence in prescribing habits, with a general assumption that they represent best practice. This is often incorrect, yet there is a reluctance to recognise this even when presented with the guidelines.

A recent Australia paper by Grey et al. (2008) revealed that marked variations in transfusion practice persist, highlighting poor clinician understanding of appropriate blood usage.

Consultations with stakeholders during the course of the project reinforced this finding about clinicians’ level of knowledge.

The problems of lack of knowledge and lack of understanding among clinicians of the risks associated with transfusion point, in part, to deficiencies with the information base. In some instances, the information is lacking and in other instances, the information is there, but inadequately transmitted to key decision makers. Gaps in the information base are taken up further below.

The report also refers to studies indicating that adverse patient outcomes may also be dose dependent, that is, the higher the volume of red cells transfused, the greater the risk of contracting infections and other conditions. They also refer to studies which have indicated that mortality and morbidity impacts associated with transfusion may be positively related to the age of red cells at transfusion.

**APPROPRIATE USE STRATEGIES**

Many strategies have been employed at the national and jurisdictional level in Australia to promote appropriate use of blood and blood products. On the whole, however, there was little information
available to assess the success or otherwise of these strategies. Some information was available from overseas experience.

**APPROPRIATE USE STRATEGIES IN AUSTRALIA**

National strategies to promote appropriate use of blood and blood products have been conducted mainly under the auspices of NBA. The NBA’s Blood Counts Program (National Blood Authority, 2008) aims to collaborate with jurisdictions, health professionals and other stakeholders to improve patient outcomes through the appropriate utilisation of blood and blood-related products. The Blood Counts Program comprises a number of projects divided into four streams as follows:

- development, implementation and promotion of best practice guidelines;
- facilitation of education, information sharing and practice improvement initiatives;
- improvements to systems;
- research, data and benchmarking to improve appropriate use of products.

The NBA is also developing a National Patient Blood Management Program (NPBMP) (National Blood Authority, 2010b) to facilitate the uptake of patient blood management best practice through the development and promotion of clearly defined national objectives. The program will build on existing state and local programs. The overarching aim will be to improve patient outcomes through national policies and drivers that support state and territory programs in the appropriate use of, and where possible the appropriate avoidance of the use of fresh components.

Significant efforts over the last decade in NSW to promote appropriate use of blood and blood products began with the Blood Transfusion Improvement Collaborative (BTIC) in 2002-03. That initiative focussed on appropriate use of red cells, based on the NHMRC/ASBT Blood Components guidelines. In 2005-06, the state blood budget was devolved to Area Health Services in NSW. This initiative extended a price signal to hospitals for the use of blood and blood products. A complementary program of interventions to promote appropriate use was begun with the establishment of the Blood Watch program, operated by NSW Clinical Excellence Commission (CEC), in 2006. Blood Watch aims to improve and promote the provision of world-class medicine practice and to reduce the costs of transfusion therapy. Its activities have included awareness and education of appropriate transfusion practices, development of educational materials and resource website, formation of transfusion committees in all Area Health Services (AHS), regular audit and feedback of red cell transfusion and platelet transfusion, implementation of restrictive transfusion thresholds in most facilities, academic detailing by Blood Watch Clinical Leads, development of policy and standards, research into prescribing behaviours of senior consultants, and an innovative communications strategy directed at senior clinicians including an on-line peer-to-peer debate around the emerging evidence of the inherent risks of transfusion.

In Victoria, appropriate use strategies have been implemented under the Blood Matters—Better Safer Transfusion (BeST)—program. This is a Victorian state government program for improving the quality and safety of hospital transfusion care to patients. As part of the Blood Matters project, the transfusion nurse role was installed into hospitals. To support those in the role, a Certificate in Transfusion course was developed. This has now been redeveloped into the *Graduate Certificate in Transfusion Practice* course at the University of Melbourne.

The Queensland Blood Management Program (QBMP) was established in July 2005 to ensure that the Queensland Government meets its obligations under the National Blood Agreement. Significant achievements in Queensland have been the development and implementation of ‘ORBS’—the electronic ordering and receipting system used to improve the efficiency of the supply of products from the Blood
Service. In recognition of its success, ORBS has since been assumed by the NBA for development into a system, which can be applied nationally in the sector.

The Queensland public sector has also made advances from recent initiatives to reduce red cell wastage levels, mainly involving the coordinated management inventory around the hospitals of the state. A further initiative will be the extension of price signals for blood and blood products with the devolution from 1 July 2011 of the state blood budget to public hospitals in Queensland.

South Australia has a well-established program of initiatives to promote appropriate use of blood and blood products, which operates under the banner of ‘BloodSafe’. BloodSafe partners include the South Australian Department of Health, the Blood Service and South Australian public and private hospitals and their transfusion service providers. The appointment of BloodSafe transfusion nurse consultants across the major public hospitals provided the driving force for achieving and sustaining improved practice in conjunction with doctors and scientists. The program was extended to country and private hospitals, and a dedicated nurse consultant for IV Ig has also been appointed.

BloodSafe has developed tools that have been adopted nationally, such as the BloodSafe information ‘flip’ chart the BloodSafe e-learning (online) program to help hospitals ensure staff competency in transfusion practice.

Western Australia has embarked upon a comprehensive Patient Blood Management Program (WAPBMP). It commenced in 2008 and will be implemented across the entire WA public health system over a five-year period. The WAPBMP has been developed on established and proven international models and will apply these across the health care system.

In Tasmania, initiatives have included state budget devolution, from 2008-09, to Area Health Services, employment of transfusion nurses at the four major hospitals to help coordinate education, haemovigilance activities and reporting and clinical audits of blood and blood product use. Tasmania has also had success in reducing wastage levels through concerted and collaborative efforts to manage expiry of red cells around the hospitals in the state.

The Australian Capital Territory (ACT) does not have an explicit blood management program. However, a fulltime Transfusion Nurse Consultant (TNC) since 2008 has coordinated initiatives in transfusion education, for both public and private sector health providers.

**Effectiveness of Australian appropriate use initiatives**

Information on the effectiveness of state and territory initiatives was limited, but generally showed that they have been productive.

NSW reported that the Blood Watch program had resulted in an overall 10 per cent reduction in usage of red cells within the inpatient cohort between 2007 and 2009 (NSW Health advice, 2011). The NSW CEC estimated that in the 12 month period July 2008 to June 2009, a possible 12,225 units of red cell transfusions were avoided. This equated to cost savings, in terms of both product supply and in-hospital costs, of around $8.6 million.

Queensland efforts to manage red cell wastage have resulted in average wastage levels falling from 6.5 to 7 per cent per annum prior to 2010, to just over 3 per cent by the end of November 2010. Queensland Health estimates that the annualised saving after five months is around $1.7 million when compared against historical wastage rates.

Initial BloodSafe audits of SA metropolitan teaching hospitals looking at red blood cell transfusions in stable patients in 2002 found that 18 per cent of these were outside the NHMRC guidelines. With development of practice improvement tools and education, this fell to 4 per cent and was maintained at less than one per cent five years on (SA Department of Health).
It is too early to conclude results from the in-hospital activities of the WAPBMP. However, between 2008-09 and 2009-10 there was a decline in demand of around 2,000 red blood cell units in WA. Although this indicator is encouraging, it pertains to a single year only and there may be other factors which have influenced the decline.

In Tasmania, the Department of Health and Human Services believes that a Memorandum of Understanding (MOU) between Tasmanian hospitals has been a key factor in reducing red cell use in Tasmania by around 20 per cent since 2002 to the current period and remaining below the national average.

As the NBA’s NPBMP is still under development, it is not possible to measure effectiveness. However, the general approach that NBA has taken in the design of the NPBMP takes best advantage of their central positioning in the sector. It will enable efficiencies to be gained among the jurisdictions, particularly the smaller jurisdictions, from the common use of materials, as well as the sharing of experience.

**OVERSEAS EXPERIENCE WITH APPROPRIATE USE STRATEGIES**

A number of studies highlighted the experience in Canada, the United States, Europe and the United Kingdom to promote appropriate transfusion practice.

For example, in Canada in 2002, the Ministry of Health and Long-term Care of Ontario developed a provincial blood conservation program. The investigators concluded that “implementation of the program represents important savings in costs associated with blood components, hospital stay and work in transfusion laboratories and nursing units, as well as enhancing patient satisfaction and safety.” The results included an overall reduction in the number of patients receiving red blood cell transfusion and annual savings of over eight times the cost of implementing the initiatives.

In the USA, there are reported to be over 200 programs to improve transfusion practice operating (Thomson, 2009). A number of US studies indicate positive outcomes for blood conservation programs such as reduced costs, lower lengths of stay, reduced blood product transfusion rates and improved patient outcomes.

The European experience of appropriate use strategies includes a number of successful examples, such as:

- from Austria—an estimated reduction in transfusion by 50 per cent flowing from appropriate preoperative management of anaemia in their patient population (reference);

- in Paris, a successful program to change practice and reduce blood transfusions and costs in elective orthopaedic surgery (Martinez and colleagues (2007)). The algorithmic approach used in the study resulted in fewer autologous, allogeneic and mixed blood transfusions;

- in Spain, the Hospital del Mar, Barcelona, a 67 per cent reduction in allogeneic blood transfusion in elective orthopaedic surgery patients enrolled in their blood conservation program (Lopez Soques, 2002);

- in Switzerland, a reduction in the transfusion rate in hip and knee replacement surgery from 35.0 per cent to 19.8 per cent in the University of Berne and the Winterthur Hospital after the introduction of a blood management algorithm and education program (Mulleret al., 2004).
LESSONS LEARNT FROM APPROPRIATE USE STRATEGIES

A NEW PARADIGM—PATIENT BLOOD MANAGEMENT

Many strategies have been built around the concept of ‘Patient Blood Management’ (PBM). PBM seeks to realign the transfusion paradigm to centre on patients, rather than the products. The primary focus is on conservation and appropriate management of the patient’s own blood by means of effective coordinated, multidisciplinary, multimodal clinical medicine.

The primary lesson from strategies in Australia and overseas is that PBM initiatives must engage clinicians. It is insufficient to rely on clinical guidelines to drive appropriate use of blood and blood products as uptake of the guidelines has been poor and is typically poor across the health sector. In 2007, Isbister (2007) remarked that “(t)he appropriateness of transfusion practices will only improve, not by expecting clinicians to be gatekeepers of the blood supply, but with better patient blood management”.

Appropriate use strategies need to take account of the fact that clinicians are influenced by a range of factors including: patient outcomes; peer practice; prescribing ‘culture’, particularly within individual institutions; education and training; and the evidence base and financial incentives.

The lessons from Australian and overseas experiences show that successful PBMPs incorporate the following features:

- a focus on culture change in transfusion practice—it is through culture change that change is most likely to be sustainable through time; program design should incorporate sentinel change management principles, including strong leadership, clinical championship and empowerment of a broad base of participants in the system (including patients);
- education and communication strategies tailored to the clinical groups in focus;
- effective data collection and monitoring systems to underpin education and communication strategies, and also to facilitate monitoring and evaluation, continuous improvement and risk management.

Successful programs have adopted coordinated and comprehensive education strategies, enabling all stakeholders—including patients and all clinical and non-clinical hospital staff—to be fully informed of current evidence on the risks and benefits of transfusion along with measures to minimise transfusion and utilise appropriate alternatives. They implement an integrated multidisciplinary, multimodal medical/surgical approach that has as its focus individualised advanced patient blood management with the view of improving patient care and outcomes (Goodnough, 2003a). The accumulating evidence demonstrates that these programs can dramatically reduce blood usage, at the same time reducing morbidity, mortality and length of hospital stay, as well as minimising costs.

Experience to date has also shown that more appropriate use of blood products is linked with data and information about costs and trends in order to achieve both improved patient outcomes and cost savings for health systems.

Successful PBM programs also focus on improving the uptake of clinical practice guidelines. In Australia, studies suggest that patient care and outcomes could be significantly improved if the knowledge gained from health research was better translated into practice. This situation is not unique to Australia and many overseas studies highlighted the similar issue.

The reasons why evidence is not translated well into practice include systemic barriers, such as financial or organisations systems level. For successful implementation of guidelines, it is necessary to devise a
strategy or plan for the project. A body of research has shown that successful implementation of clinical practice guidelines is not achieved by forcing physicians to obey ‘rules’, but rather by creating an environment in which they are given the skills, knowledge, attitudes and support systems to help them provide their patients with the best possible care, based on the best possible evidence.

**PRICE SIGNALLING**

The application of price signals in the blood sector is one particular strategy for promoting appropriate use of blood and blood products. Price signals, aligned to the cost of blood, can provide the right incentives for more efficient demand and supply outcomes throughout the blood supply chain.

In a blood and blood products context, price signals generally refer to the extent to which different consumption decision makers in the blood supply chain face prices and bear the budget consequences as part of their consumption choices. ‘Upstream’ parts of the supply chain relate to blood collection, processing and distribution. ‘Downstream’ parts of the supply chain relate to blood utilisation within hospitals and in clinical situations.

Price signals are generally applied across the ‘upstream’ supply chain with the exception of remunerating blood donations. There may be opportunities, however, to allow the price signal to work better to more accurately reflect consumer and supplier preferences and utilise market forces to make the system more efficient.

In relation to the ‘downstream’ supply chain, in most locations, blood products are provided at no charge to hospitals by states and territories. There is a lack of price signals applicable to many key decision makers affecting the volume of blood and blood products consumed, including laboratory managers and prescribing clinicians.

A ‘downstream’ price signal could take a number of forms. Given the current institutional arrangements for blood funding in Australia, one form often suggested has been the devolution of blood budgets beyond the centralised budget holder – for example, to health providers or administrative units of health providers.

Except in those states where state blood budgets have been devolved to Area Health Services (to date, NSW and Tasmania), blood and blood products are ‘free’ goods as far as public hospitals are concerned. Across Australia, blood and blood products are supplied free of charge to all private hospitals. Under present arrangements, the Australian Government, state and territory governments are generally the only ‘consumers’ in the system that see the prices of blood and blood products and bear the cost impact. However, these entities are remote from day to day consumption decisions.

**IMPACT OF PRICE SIGNALS IN THE SECTOR**

Lack of a ‘downstream’ price signal creates unaligned incentives because of a lack of transparency of costs to clinician and (in some cases) hospital buyers, and lack of moderating influence by government or insurance payers on consumption behaviour.

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2 The prices for blood products in Australia – for example, at a bulk level purchased by the NBA – are generally administered prices, determined on an annual basis in line with the institutional framework for blood product supply planning. They are not market-based or ‘free’. This does not change the fundamental concept of price signals as providing a general indicator of value and opportunity cost.

3 NSW and Tasmania are exceptions, where through budget devolution the price signal has been extended to the health provider administrative unit, but not necessarily at this stage to be transparent or accountable within the health provider.
For example, in the absence of a price signal for blood, and where there is a price signal for substitutes, there is a structural disincentive to adopting alternatives. There is a particular disincentive for large-scale, high-impact measures which can affect blood use over time such as auditing and education or capital investments such as information systems, when hospitals bear the cost for these measures but do not benefit from the consequent cost-reduction in blood use.

The impact of price on blood use depends on how responsive demand is to the level of or changes in price (the ‘price elasticity of demand’). Use of blood products, like most in-patient hospital services, is generally recognised as highly price inelastic. However, with technology change developing substitutes for blood use and greater clinical acceptance of these substitutes, blood use may be becoming more price responsive over time. To the extent that there is inappropriate or unnecessary use of blood and blood products in the system, there exists a level of ‘discretionary’ demand which could respond to a price signal.

‘Downstream’ price signals have been adopted as part of a broader approach to appropriate use in England and Wales, and the United States has a greater focus on pricing throughout the supply chain. The third largest public hospital in Austria (General Hospital Linz, AKH Linz) has recently introduced electronic price signalling to clinicians as part of a hospital wide PBMP. Clinicians can only order blood products through the hospital’s electronic ordering system and actual prices of all blood products or components are displayed on the screen as soon as the products are selected. The total amount payable is shown on the screen before the clinician makes a final ordering decision on the number of products and laboratory tests. The transfusion and blood utilisation rate in the General Hospital Linz is one of the lowest in the Federal Republic of Austria.

‘Downstream’ price signals have also been introduced in recent years within public hospitals in NSW and Tasmania, with the devolution of blood budgets. Queensland has taken the decision to devolve its State blood budget from July 2011. Advice from health authorities in NSW and Tasmania was that the creation of price signals, through the devolution of the budget, was alone insufficient to change clinicians’ use of blood and blood products. Initiatives under the NSW Blood Watch program, such as those targeted at clinician education, were required to bring about reductions in unnecessary red cell transfusions. However, both NSW and Tasmania remarked that budget devolution had provided the incentive for hospitals to support the implementation of patient blood management initiatives within their institutions.

**Options for ‘Downstream’ Price Signals**

Effective ‘downstream’ price signals for blood and blood products would meet the following principles:

- reflect the costs borne by governments for the provision of blood products;
- help to promulgate information on costs throughout the system, to support best use of available resources and financial and performance accountability for the use of resources;
- be devolved to the level of responsibility closest to the end use of the blood and blood product (in most cases, clinical directorates);
- be complementary to other actions to support appropriate use of blood products and better information on the use of blood products;
- have a level of administrative and compliance burden appropriate to the potential gain from its application;
- be able to be implemented in the short-to-medium term, and allow for adaptation to any special characteristics of individual jurisdictions;
• support other health reform and better practice for health administration;
• accord with the Australian Government-State relativities of blood product funding;
• accord with National Blood Agreement provisions;
• support hospital administrators gaining some level of benefit or carry some level of risk from a reduction or increase in blood product use relative to a situation where there is no price signal.

There is potential for further price signals to be nationally adopted in the ‘downstream’ elements of the supply chain – between state and territory governments and health providers, and then within health providers – in the broader context of various activities towards supporting appropriate use.

Options for ‘downstream’ price signals are to:
• incorporate the cost of blood and blood products into casemix funding;
• devolve the national blood budget to public hospitals and charge private hospitals for the costs of blood and blood products;
• introduce ‘soft’ price signals, that is, price visibility, to a range of decision makers in the system, including laboratory staff, clinicians and other clinical staff responsible for handling blood and blood products.

OPTIONS AND IMPACTS FOR ‘UPSTREAM’ PRICE SIGNALS

There may be strong efficiencies and price benefits for consumers from greater contestability around the various elements of collecting, manufacturing, testing, and storage and distribution. However, suppliers may also have economies of scale or scope associated with continued integrated provision or with providing the full Australian market which would reduce in a more competitive environment. Greater information and more specific analysis is probably required to identify potential benefits of more effective price signals in specific areas of the ‘upstream’ supply chain.

However, there are also ways to progressively make improvements in the ‘upstream’ supply chain – for example current work towards purchase recording being based on demand-based hospital ordering and receipt of blood product units, rather than supply-based delivery of units.

FUTURE TRENDS

There are several key influences over the trends in demand and cost into the future.

DEMOGRAPHIC FACTORS—THE AGEING POPULATION

As indicated above, blood and blood product use correlates positively with age. In large part, this is attributable to the positive correlation between ageing and the medical conditions associated with use of fresh blood and plasma derived products\(^4\). Several studies indicate that older age groups account for the greater proportion of red cell use. Haematological cancers, associated with over 20 per cent of IVlg use in Australia in 2009-10, are correlated with age. Taking ageing into account, the Blood Service projects IVlg demand to grow by an average 16 per cent per annum between 2010-11 and 2019-20. Another example is warfarin use, which influences the use of Prothrombinex-VF, is common in cases of atrial fibrillation, a condition which correlates positively with age.

\(^4\) The pattern of use of recombinant products responds to changes in the population of people with haemophilia
The general trend was also supported in the age-related analysis of hospital separations associated with transfusion, with the 40 to 70 year old age group accounting for the majority of separations involving transfusion of platelets, coagulation factors, IVIg and 'other serum' (including FFP and albumin) and the over 70 year age group for the greatest proportion of separations involving transfusion of red cells.

At the same time as an ageing population puts upward pressure on the demand for blood and blood products, it puts pressure on the available pool of donors for blood supply. At present, blood donations policy is founded on voluntary donation between the ages of 16 and 70. An ageing population will reduce the pool of potential donors.

The dual pressures placed upon the supply of blood and blood products are encapsulated in the concept of the Total Transfusion Dependency Ratio (TTDR) that is the ratio of the non-donating population to the donating population. Assuming continuation of current donations policy, the TTDR is predicted to rise steeply from 2010 onwards, for all jurisdictions in Australia. It is an international trend as well, with high human development index countries also experiencing ageing in their populations.

**FIGURE 1: PROJECTED TOTAL TRANSFUSION DEPENDENCY RATIOS, AUSTRALIAN STATES AND TERRITORIES, 1990 TO 2040**

Source: Sapere Research Group Limited projections using ABS catalogue 3222.0--Population Projections, Australia, 2006 to 2101, series B.

**PRESSURES ON PRODUCT DEMAND**

Further strong growth in demand for IVIg is already predicted, as indicated above. This could be enhanced by expanded clinical indications for use. There are a number of potential new indications for IVIg under active investigation, including Alzheimer’s Disease (AD) and Myocardial Infarction.

Australia already experiences a shortfall in plasma for fractionation to keep up with this level of demand and consequently imports finished product on an annual basis.

There are also risks presented by new and re-emerging pathogens, which would restrict the pool of donors in the absence of relevant tests.

There is also the risk of a possible shortening of the shelf life of red cells in response to recent research findings. A growing body of research is questioning impacts on patient outcomes related to the age of red cells older than 14 days at the time of transfusion. Data (albeit limited) from Pathology Queensland indicates that only 25 per cent of red cells might currently be released for transfusion by the age of 14 days.
**Blood Forecast Model**

Future demand and costs of blood and blood products are forecast using the Blood Forecast Model developed through this project. Within the model, cost is a function of price and volume. Price is indexed according to predicted price movements. (For the purposes of the forecasts contained in the report, price movements are assumed to continue at the rates built into the current forward estimates.)

Volume can be indexed in the model by a range of demand drivers, such as demographic factors, incidence of major blood-using medical conditions, impact of policy decisions, and changes in indicated uses.

For the purposes of the ‘baseline’ scenario demand and cost projections contained in the report, volume is indexed according to the population age profile of each state and territory, with an assumption made about the demographic usage rates of red cells. Estimates were able to be made of these factors on available data.

The total product cost of supply of blood products across all product groups (except diagnostic products) is estimated to be approximately $937 million in 2010-11. Under the assumptions of the model, this is expected to rise to $1.6 billion in 2020-21 and to reach $2.8 billion in 2030-31, and $3.6 billion in 2035-36 (the end of the forecast period). This represents an increase in total costs of over 70 per cent over the next ten years. Assuming current contribution rates, the Australian Government share of this expenditure would be 63 per cent, and the combined contribution of the jurisdictions 37 per cent.

The product cost of the national blood supply is forecast to grow in real terms, at an average of approximately 3 per cent per annum. Under the assumptions of the model, the real cost to Australian governments for the supply of blood and blood products is expected to nearly double in 25 years.

The model shows that the jurisdictions with the relatively younger age profiles will experience steeper rises in demand and costs over this time.

**Modelling of Future Demand Scenarios**

The terms of reference sought modelling of the impacts of price signalling options. The lack of information about the specific influence of price signalling means that these impacts cannot be modelled in isolation. First, there is a lack of data as there is no history of response to the price signals already in the supply chain that can be used to extrapolate information on the price elasticity of demand (that is, the demand responsiveness to price changes). Second, the impact of price on demand depends on a range of other factors, including who pays, whether substitutes are available and how much demand is discretionary. These factors in turn rely on the clinician being aware of alternative choices. In short, the impact of price signals in the blood sector depends on the impact of complementary actions such as patient blood management programs. This was the experience of NSW, where activities under the Blood Watch program were necessary to reinforce the impact of the devolution of the NSW blood budget.

As an alternative, the report puts forward a number of future blood demand scenarios for consideration and analysis. In addition to the baseline scenario referred to above, the scenarios include

- a scenario involving patient blood management approaches impacting on red cell use
- a scenario involving patient blood management approaches impacting on all blood components and products.

Table 1 summarises the nominal cost impacts of the three scenarios examined in this project.
### TABLE 1: SUMMARY OF SCENARIO OUTCOMES FOR PRODUCT COST OF BLOOD SUPPLY

<table>
<thead>
<tr>
<th>Scenario</th>
<th>2010-11</th>
<th>2015-16</th>
<th>2020-21</th>
<th>2025-26</th>
<th>2030-31</th>
<th>2035-36</th>
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<tr>
<td><strong>BASELINE SCENARIO</strong></td>
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<tr>
<td>Nominal Costs</td>
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<td><strong>PBM-RED CELLS SCENARIO</strong></td>
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<td><strong>PBM-ALL PRODUCT SCENARIO</strong></td>
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<td>$1,083</td>
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</table>

*Source: Sapere Research Group Limited model*

### KEY FINDINGS

Key findings were drawn from both the *Analysis of Cost Drivers and Trends in the Blood Sector* and *Options to Manage Appropriate Use of Blood and Blood Products*.

### SIGNIFICANT REFORMS ARE NEEDED

Notwithstanding the progress that has been made, significant reforms are needed to ensure sustainability of the blood sector in Australia.

The reasons for this include the level of risk that persists to patient safety and quality of care from some common transfusion practices; the fact that demand for blood products may well outstrip supply; and because existing governance and support systems do not promote efficiency and sustainability.

### Some common transfusion practices put patient wellbeing at risk

There is evidence indicating a degree of inappropriate use of blood and blood products in Australia, particularly in relation to the uses of blood components, with the bulk of evidence pointing to problems with red cell use. As well, there is a large and growing body of literature which questions the appropriateness of many common transfusion practices in terms of patient health outcomes, with the main evidence again relating to the use of red cells.

### Demand threatens to outstrip supply

Under current patterns of use, Australia’s ageing population will increase the demand for blood and blood products, while concomitantly decreasing the available pool of donors to maintain supply. This

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5 *Analysis of Cost Drivers and Trends in the Blood Sector* was a study undertaken in concert with *Options to Manage Appropriate Use of Blood and Blood Products* (see Project Methodology, p5).
situation may be exacerbated by other upward pressures on demand, such as the incidence of some diseases and expansion of indicated uses for certain blood products. Other factors, such as the emergence of new pathogens and the risk of a shortening of the shelf life of red cells due to health safety and quality issues, may add further pressures.

**Costs are likely to continue to rise**

As demand rises in the face of constrained supply, market forces will drive up prices. Competition for scarce resources in the economy, and lack of competition in the supply of commercially supplied blood products will contribute to the risk of price increases.

Expanded testing in the face of new pathogens will also increase unit prices. A shrinking donor pool may also put pressure on the costs of supply, for example through intensified marketing for donors; and/or a greater reliance on the (relatively more expensive) apheresis collection.

International demand for blood and blood products is also likely to rise as other developed economies experience ageing in their populations. This will create upward pressure on commercially supplied products.

**Current governance and support structures constrain efficiency or sustainability**

The information base in the sector is inadequate. It lacks routinely collected data on key aspects of blood and blood product usage, including, who uses it, how much is used, what is it used for (in a clinical sense) and levels of wastage. The level of usage attributable to the private and public sectors was not distinguishable. Hospitals and clinicians lack access to the data that would enable them to monitor their own performance against sector best practice. Data to enable adequate demand forecasting or benchmarking of appropriate use is also lacking.

Clinicians lack access to up to date information on best practice in transfusion. The NHMRC/ASBT Blood Components guidelines are under review, after ten years of operation. There was evidence of lack of awareness among clinicians of these guidelines.

Key pricing and funding arrangements present incentives, which impede efficient and sustainable growth. There is a lack of pricing signals to key consumption decision makers in the system. Blood and blood products are presented as ‘free’ goods to the majority of hospitals and clinicians in the system.

Payment arrangements for suppliers on the basis of product issued potentially create a bias towards oversupply of products. There is also a lack of emphasis on the assessment of cost effectiveness in the funding of products.

**THE WAY FORWARD**

**THE AUSTRALIAN BLOOD SECTOR REQUIRES SIGNIFICANT REFORM TO ENSURE SUSTAINABILITY**

The key requirements for the blood sector to ensure sustainability into the future are:

- for the sector to become more patient-centric;
- for the blood supply chain to be demand driven;
- for governance and support structures to promote sustainability.

**The Australian blood sector must become more patient-centric**

Some common transfusion practices carry unsustainable risks to the safety and quality of patient care. The patient blood management (PBM) approach needs to become embedded in the sector, such that
patients’ individual needs drive the decision regarding transfusion. PBM emphasises culture change and there will be substantial challenges in achieving this.

Patient Blood Management Programs (PBMPs) have typically been concerned primarily with the use of blood components. Their scope should be expanded to include all blood and blood products.

The four year, state-wide trial underway in WA since 2008, and the National Patient Blood Management Program (NPBMP) being developed by NBA to facilitate the uptake of PBM best practice, provide a good basis for entrenching PBM approaches within the sector. These and other projects demonstrate that successful PBMPs incorporate the following features:

- a focus on culture change in transfusion practice;
- education and communication strategies tailored to the clinical groups in focus;
- effective data collection and monitoring systems to underpin education and communication strategies, and also to facilitate monitoring and evaluation, continuous improvement and risk management.

As the majority funder of the budgetary cost of blood and blood products, it is in the Australian Government’s interest also to consider financial incentives for PBMPs to be implemented.

PBM needs also to be embedded in the private sector, which accounts for around one third of transfusion related separations nationally. This will require establishment of an information base on which to assess the extent of inappropriate use, and ultimately to design, implement and evaluate PBMPs. It will also require the creation of an appropriate incentive structure, such as the introduction of price signals.

Clinicians need a better understanding of the evidence base. The effectiveness of clinical guidelines needs to be improved and uptake should be encouraged within PBM settings. Patients should also be better informed of their risks and choices through informed consent processes and information campaigns.

**The blood supply chain must be demand driven**

Demand threatens to outstrip supply in the sector in the future. The supply chain needs to be driven by an efficient level of demand, one that truly reflects patient needs. While difficult to achieve across different jurisdictional cultures and administrative architectures, the move to a demand driven system is imperative if supply is going to meet future demand.

A demand driven system needs to be supported by price signals, which create the incentive for economical use of blood and blood products. Extending price signals in the system, particularly to hospitals, would establish the basic set of incentives needed to align demand with patient need. This would discourage inappropriate use and wasteful practices and would encourage hospitals to invest in PBM. Indeed, officials in NSW and Tasmania indicated in consultations that one of the tangible benefits that had arisen from blood budget devolution had been the interest it had engendered among hospital management to support appropriate use strategies.

The national blood budget should be incorporated into the hospital casemix funding system. The national blood budget should also be devolved to public hospitals and mechanisms to provide effective price signalling to private hospitals should be developed. There will be different considerations within the jurisdictions, which may affect that rate at which this initiative could be implemented. For example, NSW, Tasmania and, from 1 July 2011, Queensland, already have devolved state blood budgets. This may give them a lead on successful devolution of the national blood budget.
Price signals should also be extended to the private sector, given that this sector is responsible for around one-third of all transfused hospital separations. The incentive structures are different within the private sector and further consideration needs to be given to the best means for achieving the creation of appropriate price signals.

Suppliers should be paid by hospitals upon verified delivery against orders. This would remove the inherent incentive for oversupply. It would be efficient to transfer the responsibility for payment of suppliers from the NBA to hospitals.

The introduction of contestability into the supply chain should be considered. The high level of concentration of suppliers in the system may impede efficiency.

**Governance and support arrangements should be restructured**

The information base needs to be upgraded significantly to support patient care, as well as planning and management of demand and supply. Governments should require public and private hospitals to supply them with a minimum dataset that supports demand and supply management and evaluation of sector performance.

All jurisdictions should be required under the National Blood Agreement to generate a minimum dataset informed by the Guide to the Set of Standard Measures for the use of Fresh Blood Components in Australia, developed (in draft) by NBA and the Blood Service (2009). The information should be required to be provided in such a way as to feed into BloodNet’s central database (NBA’s ‘Big Red’). Using the power under the National Blood Authority Act, the NBA could require a similar minimum level of information from the private sector.

A demand driven system also needs to be supported by relevant information about blood and blood product use. Better communication of projected demand levels to inventory controllers and supply planners would drive greater efficiency.

Funding structures need to support sustainability. Against a background of rising costs to government for blood and blood products, it makes sense for governments to consider approaches that put a sharper focus on cost-effectiveness and appropriate use. Existing processes that could be applied to, or provide models for, the blood sector include the MBS Quality Framework and the Pharmaceutical Benefits Advisory Committee (PBAC) processes.

There are two ways in which these approaches could be adapted to the blood sector:

- assessing the cost-effectiveness of funding for high cost blood components; and
- regular reviews of funding and use of existing blood products.

Based on the evidence in this report, priority should be given to reviewing the use of Albumin as a substitute for saline; and to the use of red cells to treat iron deficiency anaemia. These approaches could also be applied to consideration of government funding for the use of IVIg, particularly where new application is proposed.

Given pressures on the pool of future blood donors, governments need to monitor the pressures on donations and keep under review the need for providing incentives to donors as a means of maintaining blood supply.

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Payment authority for suppliers should shift to hospitals and NBA’s role should shift more towards the coordination, analysis and dissemination of information, which supports appropriate use of blood and blood products and supply efficiency.

The provisions of the National Blood Agreement needs strengthening or revision in a number of areas, consequent upon the options discussed above. The main areas are:

- mandatory levels of information from jurisdictions to support system planning and management;
- changes in funding arrangements, including the extension of price signals through the supply chain;
- reconsideration of the policy aim of self sufficiency in the light of a demand driven system, and supply constraints.
Introduction

This project is one of several blood sector research projects to help inform Government considerations of how to fund and manage the Australian blood sector over the next decade.

The report has been commissioned in the context of the rising costs to government of blood and blood products. National expenditure on blood and blood products has increased on average at over 11 per cent per annum between 2003-04 and 2009-10. The project aims to determine what is driving these cost increases and to identify whether there are areas where governments could take action to reduce or contain costs. Governments’ ultimate aims are to increase the financial sustainability of the blood sector by containing costs but at the same time preserving the quality of patient outcomes.

The commissioning of the project reflects a desire on the part of governments for continuation of reform in the Australian blood sector. Following the Review of the Australian Blood Banking and Plasma Product Sector 2001, chaired by the Rt Hon Sir Ninian Stephen, a national partnership approach between the Australian Government and the states and territories was commenced. An intergovernmental agreement gave effect to changes to the sector including the establishment of the National Blood Authority (NBA) to undertake national supply planning and management of blood and blood products on behalf of Australian governments.

The Options to Manage Appropriate Use of Blood and Blood Products project aims to evaluate the appropriate use of blood and blood products in Australia and to identify strategies that might promote appropriate use. In promoting appropriate use, the Australian Government aims to maintain or improve the quality of patient outcomes while also increasing the financial sustainability of the blood sector.

It is not the purpose of this report to examine appropriate use from a clinical, medical, or scientific perspective. For example, it will not make recommendations on indications for use of blood and blood products from a clinical perspective. Rather, the focus of the report will be on the governance, management and economic aspects of the sector that support appropriate use.

The terms of reference for the project provide for an assessment of strategies including, among other things:

- clinical detailing;
- improved use of clinical data to support better practice;
- strategies to increase compliance with clinical guidelines;
- analysis of the introduction of price signals in the supply chain.

In relation to price signalling, blood and blood products in Australia are funded by Australian governments, but supplied ‘free of charge’ to hospitals and subsequently patients. As such, blood and blood products remain among the small number of health consumables where no explicit price impact is borne by the user. New South Wales (NSW) and Tasmania have introduced forms of price signalling with the devolution of blood budgets to area health services and/or hospitals. Queensland has taken a policy decision to do so in 2011. The report considers these price signalling mechanisms and assesses options for changing or extending price signals in the system to help drive appropriate use.

In terms of scope, ‘blood and blood products’ refers to:
all fresh, plasma-derived and recombinant blood products as purchased on behalf of Australian jurisdictions by the NBA under the National Blood Agreement; and

imported Intravenous Immunoglobulin (IVIg) where individual jurisdictions wish to purchase imported IVIg separately, under the Jurisdictional Direct Order arrangements under the Imported IVIg Standing Offer managed by the NBA.

The analysis in this report is limited to products or aspects of supply, demand and use where data are available. In terms of examining best practice or ‘appropriate use’ of these products, focus has been placed on products that are important in terms of overall costs, where information exists and where governments have scope for action. For example, the pattern of use of recombinant products is highly dependent upon the individual needs of relatively small patient groups. Recombinant products therefore receive less focus in the analysis than, for example, red cells. Red cells are used for a range of indications, across a varying patient cohort.

The main blood products included in this report’s analysis are described below. A brief introduction is given to the reasons for their inclusion in the report’s focus.

**FRESH BLOOD PRODUCTS**

Fresh blood products (also referred to as blood components) have traditionally accounted for more than half the national blood budget (around 53 per cent in 2009-10). In comparison to plasma-derived products, the fresh products, as they are less processed, bear the greatest level of risk to patients in terms of safety.

**RED CELLS**

Red cells (also referred to as red blood cells, RBCs and packed red blood cells) resuspended are given to increase the oxygen carrying capacity of the blood, for example, in patients with severe anaemia following major blood loss after trauma and surgery. Red cells are also used in elective settings to treat patients with severe anaemia—for example, patients with severe anaemia secondary to chronic disease, in the setting of chemotherapy and bone marrow transplantation and other causes (National Blood Authority, Undated – a).

Red cells account for the largest proportion of expenditure on fresh blood products (around 55 per cent in 2009-10) and account for the largest proportion of transfused separations (around 58 per cent in 2008-09). There is a large and growing body of literature questioning the efficacy and safety of some red cell transfusion practices.

**PLATELETS**

Platelets are indicated for treatment of patients with active bleeding due to severe thrombocytopenia (low platelet count) caused by decreased platelet production (for example, leukaemia) or increased platelet consumption. Platelets can be indicated in two clinical settings: when there is thrombocytopenia with bleeding or likely bleeding, or when there is an abnormality of platelet function with bleeding or likely bleeding.

Low platelet count can result from either of two main causes:

- reduced and inadequate production of platelets by the patient’s bone marrow; or
- normal production of platelets coupled with increased destruction of platelets by the patient’s circulation.
Abnormal platelet function can be inherited or acquired. The latter genesis is the more common and can be induced by certain medications, including aspirin. There is also a condition of the bone marrow, more common in the elderly, whereby the production of blood cells, including platelets, is both inefficient and disordered—myelodysplastic syndromes (National Blood Authority, Undated – a).

Platelets account for the next largest proportion of fresh blood product expenditure. The trend in growth in platelet demand has been variable over the period 2003-04 to 2009-10. However, platelet issues grew by over 8 per cent in 2009-10.

**FRESH FROZEN PLASMA**

FFP is plasma separated from whole blood and frozen within 18 hours. Its use is indicated for patients with a coagulopathy who are bleeding, or at risk of bleeding, where specific therapy (such as vitamin K or factor concentrate) is not appropriate or available. FFP may be used in massive transfusion, cardiac bypass, liver disease or acute disseminated intravascular coagulation (DIC) to replace labile coagulation factors. It may be indicated to correct warfarin overdose with life threatening bleeding in addition to Prothrombin Complex Concentrates (vitamin K dependent factor concentrates). FFP may be indicated for Thrombotic Thrombocytopenic Purpura (TTP) (National Blood Authority, Undated – c).

**PLASMA-DERIVED PRODUCTS**

**INTRAVENOUS IMMUNOGLOBULIN**

IVIg is an immunoglobulin preparation suitable for intravenous use. It can be used for replacing Immunoglobulin in both inherited and acquired immune deficiencies, modulate immunological/antibody mediated diseases (autoimmune diseases), either acutely (for example, thrombocytopenia) or chronically (for example, chronic inflammatory demyelinating polyneuropathy [CIDP]):

- replace immunoglobulins in a number of inherited primary immune deficiency conditions;
- treat acute and chronic autoimmune diseases; and
- treat rare or debilitating mainly neurological and immunological conditions.

In Australia, IVIg is used to treat more than 90 conditions, the vast majority of which fall within the three disciplines of haematology, immunology and neurology. Neurological use is the single main indication.

IVIg accounts for the greatest proportion of expenditure on plasma-derived products. IVIg is an expensive product for which demand has been growing strongly over the period 2003-04 to 2009-10 (at an average 12 per cent per annum). The collection of plasma for fractionation is driven by IVIg demand and, in Australia, the current supply is outstripped by demand. Australia imports IVIg finished product to fill the shortfall. Clinical trials are currently underway for a number of new indications, including myocardial infarction, and AD. Approval of IVIg for any of these indications would put significant upward pressure on the demand, and cost, of IVIg.

**ALBUMIN**

Albumin 20 per cent is indicated, mainly, in the management of critically ill patients with extremely low albumin or burns. Albumin 4 per cent is indicated, mainly, in the management of shock associated with significant hypoalbuminaemia, for fluids maintenance, therapeutic plasmapheresis and for ‘pump priming’ in cardiothoracic surgery (Australian Red Cross Blood Service, 2009).
Studies referred to in this report have indicated that, for many clinical applications, saline is a safe alternative to albumin. Saline is a cheaper product than albumin. However, because of the lack of price signals in the blood sector, albumin appears to most hospitals to be a free good.

**Prothrombinex-VF**

Prothrombinex-VF is a clotting factor concentrate, which contains clotting factors II, IX and X, and some other agents. Historically, there was a modest use of Prothrombinex-VF concentrate for haemophilia patients with inhibitors. This use has now been largely replaced by the use of rFVIIa and Factor Eight Inhibitor bypass Agent (FEIBA) therapy. The principal use in Australia is now for warfarin ‘reversal’ (National Blood Authority, 2010a).

Prothrombinex-VF accounts still for a relatively small proportion of the national blood budget. However, the rate of demand for the product has been growing very strongly, averaging close to 30 per cent per annum over the period 2003-04 to 2009-10.

Full terms of reference for the project are at Appendix 1.
Project Methodology

Sapere Research Group was contracted to undertake two blood sector related projects, namely *Analysis of Cost Drivers and Trends in the Blood Sector and Options to Manage Appropriate Use of Blood and Blood Products*. Except for the reporting stage, the two projects were undertaken in concert. Information and data gathering, including a literature review and consultations with key stakeholders, were undertaken to serve the purposes of both projects.

The projects were conducted by the same multidisciplinary project team. The team comprised expertise in health policy, financial and economic analysis, and public sector governance, as well as extensive knowledge in the clinical and managements aspects of the Australian blood sector. The team also contained extensive international experience of blood sector management and practice.

The main body of work of the projects was conducted over the period from July 2010 to March 2011. Literature and other information sources referenced within this report were current during that time period. In broad terms, the main steps in the conduct of the projects were to:

- obtain project inception briefings from the project management team and senior personnel in the DOHA;
- agree to a detailed project plan with DOHA;
- gather information and data;
- conduct consultations;
- analyse all project information;
- design and construct a model for forecasting blood usage;
- prepare project reports.

The main sources of information for the project were:

- an extensive literature review;
- information and data sourced from key organisations in the Australian blood sector;
- consultations with key stakeholders.

In addition, the project team received advice from a Blood Projects Reference Group. The Reference Group was chaired by DOHA and comprised members from:

- National Blood Authority (NBA);
- the Blood Service;
- nominated Jurisdictional Blood Committee (JBC) members (the representative from Queensland represented the larger States and South Australia the smaller jurisdictions).

The Reference Group’s role was to provide advice and information to the project team throughout the course of the projects. The Reference Group participants are provided in Appendix 2.
LITERATURE REVIEW

The literature review included material provided by the NBA, the Blood Service and DOHA. Some of the material was provided in confidence. Other literature, data and information were sourced from the public domain, including peer reviewed medical and scientific journals (principally from MEDLINE/PUBMED) and reviews and information available through the World Wide Web. MEDLINE covers over 20 million records of articles published in thousands of international journals in the fields of medicine and health. As a complementary interface for searching MEDLINE, PubMed (http://www.pubmed.gov) was chosen as the tool for our literature research on the given topics.

The MEDLINE/PubMed search found no peer reviewed medical and scientific journal articles specifically on ‘Price Signals and Appropriate Use’ and ‘Blood Costs and Trends’. Searches were conducted on the basis of other key words to lead to relevant material.

A search of literature and information from sources other than MEDLINE was undertaken to identify reputable sources of information relevant to the two projects.

In general, the literature search results obtained for allogeneic (fresh) blood products showed a strong focus in Australia and overseas over the last decade or so on patient blood management and the costs and patient (adverse) impacts rather than a focus on the administration of the products.

The results obtained from searching the ‘grey’7 literature also indicated a very strong focus in Australia over the last decade or so on patient blood management and the costs and patient (adverse) impacts rather than a focus on the administration of the products. In addition, the literature provided significant data and information on appropriate use, costs, trends, and pricing (including price signalling) for blood products (including plasma derived and recombinant products). The ‘grey’ literature also included many links to other relevant literature, data and information.

DATA

The majority of data were sourced from:

- NBA;
- the Blood Service;
- Australian Bureau of Statistics (ABS);
- DOHA.

Other data sources included the health authorities in each of the states and territories, and NSW CEC, and also Medicare Australia.

In addition, much data were sourced from the literature discovered through the literature review.

A list of data collected during the course of the review is at Appendix 3.

CONSULTATIONS

Consultations with key stakeholders were undertaken to:

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7 “Grey” literature refers to reports and articles not appearing in peer reviewed journals.
• inform analysis through the gathering of information, data and importantly ideas based on the knowledge and experience of stakeholders;

• refine and/or to test options developed through the projects.

Consultation for the two blood projects was targeted and involved organisations and individual experts in the Australian blood sector. Group meetings, interviews and teleconferences were used to conduct the consultations. The choice of means took into account the availability of individuals and timing considerations. Not all individuals contacted were available within the timeframe of the projects. Some key stakeholders presented alternative contacts for the team to consult. Some contacts that were unavailable to speak to were offered the opportunity to provide written comments.

Consultations were conducted in two stages.

The first stage primarily involved the general gathering of information, thoughts and ideas relevant to the aims and scope of the two projects. The information collected through this first stage of consultation was analysed along with data and other inputs into the two projects.

Stage 1 consultations were conducted over the period from late August to mid October 2010.

A second stage of targeted consultation sought additional information, for example, for the refinement of options. Second stage consultations also tested options with a select number of key organisations or individuals.

Stage 2 consultations were conducted in concert with the drafting of the reports.

Consultation was targeted. Nevertheless, the range and number of stakeholders consulted was large. The terms of reference for the project stipulated that the following key stakeholders be consulted:

• NBA;

• the Blood Service;

• DOHA;

• JBC;

• NHMRC; and

• other stakeholders as mutually agreed by the DOHA, as required and at the contractor’s discretion.

Organisations and persons consulted included State and Australian Government officials involved in the management and regulation of the blood sector, clinicians and professional colleges, blood product suppliers, pathology representatives, and health consumer/patient group representatives.

A full list of persons consulted is at Appendix 4.
Overview of Australian System

This section provides an overview of arrangements for the administration of the blood and blood product sector in Australia. It covers the governance structure of the Australian blood sector, recent government reviews of the sector, the national blood supply system, legislation, stakeholders and funding.

GOVERNANCE OF THE AUSTRALIAN BLOOD SECTOR

A Review of the Australian Blood Banking and Plasma Product Sector, chaired by the Rt Hon Sir Ninian Stephen, reported in March 2001. The major recommendations of the report were adoption of a national partnership approach between the Australian Government and the states and territories with an intergovernmental agreement giving effect to the proposed changes and the establishment of the National Blood Authority to undertake national supply planning and management of blood and blood products for Australia.

Following the Stephen Review, the Australian Government and the states and territories signed the National Blood Agreement in February 2003, which sets out a coordinated national approach to policy setting, governance and management for the Australian blood sector.

Governments agreed that the national approach should have the following key features:

(a) national agreement on the objectives of Governments for the Australian blood sector;
(b) a primary policy setting and governance role for Australian Government, State and Territory health Ministers, supported by a JBC of senior officials;
(c) a National Blood Authority (NBA), to manage the national blood supply;
(d) joint funding of the national blood supply by the Australian Government and the states and territories; and
(e) a nationally agreed framework for the management of safety and quality issues within the Australian blood sector.

The primary policy objectives for the Australian blood sector set out in the Agreement are:

(a) to provide an adequate, safe, secure and affordable supply of blood products, blood related products and blood related services in Australia; and
(b) to promote safe, high quality management and use of blood products, blood related products and blood related services in Australia.

In pursuing the primary policy objectives, the Agreement notes the Parties will have regard to a number of secondary policy aims. Among other things, these include:

(a) meeting international obligations and standards;
(b) maintaining reliance on voluntary, non-remunerated donations of whole blood and plasma;
(c) promoting national self-sufficiency;
(d) providing products to patients free of charge and based on clinical need and appropriate clinical practice;

(e) promoting optimal safety and quality in the supply, management and use of products, including through uniform national standards.

The Agreement allocates key responsibilities to the Australian Health Ministers’ Council (AHMC) including:

(a) the general oversight of the Australian blood sector;

(b) the determination of national policy;

(c) the oversight of coordination, cooperation and information exchange between bodies with safety and quality or national supply roles within the Australian blood sector;

(d) the oversight of the implementation of the Agreement.

The AHMC is also responsible for issuing policy principles to the NBA through the Commonwealth Minister in accordance with the NBA legislation. The AHMAC, a standing committee of senior officials, supports the AHMC.

The National Blood Authority (NBA) is an Australian Government statutory agency, established under the National Blood Authority Act 2003 to improve and enhance the management of the Australian blood and plasma product sector at a national level. The NBA represents the interests of the Australian, State and Territory governments and sits within the Australian Government’s Health and Ageing portfolio. It is subject to the Financial Management and Accountability Act 1997, Auditor General Act 1997 and the Public Service Act 1999.

The NBA manages the national planning and purchasing of blood in close co-operation with other stakeholders. Each year it is required to coordinate and produce, for approval by all Health Ministers, a National Product Price List and National Supply Plan and Budget for blood and blood products. It also negotiates and manages contracts on behalf of all states and territories, and the Australian government with suppliers of blood and blood products to enable the development of an agreed single national pricing schedule.

The NBA is jointly funded by all governments with the Australian Government contributing 63 per cent and the States 37 per cent.

The JBC is responsible for all jurisdictional issues relating to the national blood supply, including policy, demand, supply planning and product distribution, budgeting and evidence-based approaches to emerging products, services and technologies. It provides advice and support to the AHMC through the Clinical, Technical and Ethical Principal Committee (CTEPC) and the AHMAC.

The JBC is also responsible for considering advice from, and providing advice to, the NBA, on matters related to the national blood supply and overseeing the NBA’s role in relation to blood supply contracts. All Australian, State and Territory governments are represented on the JBC, which is the conduit between governments and the NBA.

CTEPC was established in 2006 to provide advice to the AHMAC on a range of issues in relation to clinical, technical and medico-ethical issues that affect the formulation of health care policy or delivery of health care services across multiple jurisdictions. It is responsible for eight subcommittees including the JBC.
The Therapeutic Goods Administration (TGA) was established under the *Therapeutic Goods Act 1989*. The TGA carries out a range of assessment and monitoring activities to ensure therapeutic goods available in Australia are of an acceptable standard with the aim of ensuring that the Australian community has access, within a reasonable time, to therapeutic advances. Among other things, it is responsible for regulating all blood, blood components and plasma derivatives supplied in Australia and for auditing supplies against good manufacturing practice.

A summary of the governance structure of the Australian blood sector is set out below.

**FIGURE 2: GOVERNANCE STRUCTURE OF THE AUSTRALIAN BLOOD SECTOR**

![Governance Structure Diagram]

*Source: National Blood Authority Australia – Annual Report 2009-10*

**RECENT REVIEWS OF NATIONAL BLOOD ARRANGEMENTS**

**Administrative Review of the National Blood Arrangements 2009 (the Webster Report)**

In 2009 an administrative review was undertaken, focusing on governance issues and implementation of the 2003 National Blood Agreement. The Review established that the 2003 arrangements, especially through their move to a national approach, have been a major improvement on the previous fragmented and inconsistent arrangements across the country. The Review concluded that radical changes to the Arrangements were not needed at this time.
However the Review proposed an increased strategic policy development role for the CTEPC of AHMAC. Among other things, this would include:

- taking the lead role in advancing strategic policy initiatives from AHMC and AHMAC and in advising AHMC/AHMAC of emerging policy issues and options;
- providing a formal problem solving and dispute resolution function for matters referred by the JBC;
- assisting the JBC and the NBA to develop a three year strategic plan, taking account of government initiatives in the broader health sector;
- convening a consultative forum, including the NBA and representatives of the Blood Service, CSL, other suppliers, consumer groups, hospitals and clinicians.

The JBC would continue to maintain a lead role in operational matters, including reviewing and submitting National Supply Plans and Budgets. The NBA should work with JBC and CTEPC to identify three-year priorities.

The Review concluded a multi-year supply planning and budgeting process should be introduced with plans covering a four-year timeframe, updated each year.

The Review also suggested a number of projects be undertaken, particularly in the areas of funding, sustainability and improved management of blood product use under the Agreement.

It is understood the conclusions in the report have been accepted.

**REVIEW OF AUSTRALIA’S PLASMA FRACTIONATION ARRANGEMENTS (THE FLOOD REVIEW)**

Australia’s plasma fractionation arrangements were reviewed in 2006 at the request of the then Minister for Health and Ageing by an independent committee chaired by Mr Philip Flood AO. The review was in line with commitments under the Australia-United States Free Trade Agreement. The Review recommended that overseas fractionation of Australian plasma was not an advantageous option for Australia. It further recommended that urgent action must be taken to increase plasma collection rates in view of prospective shortfalls in domestic supply collected by the Blood Service. Plasma products should be imported to address any shortfall. In March 2007 the Australian Government announced that the current arrangements whereby Australian plasma is processed in Australia would continue.

**NATIONAL BLOOD SUPPLY SYSTEM**

**Roles of Government**

Part 3 of the National Blood Agreement contains administrative arrangements for the national blood supply. It covers the establishment of the NBA as the manager of the national blood supply and specific roles for the AHMC, JBC, NBA and states and territories in the national blood supply.

The AHMC approves national supply and production planning and budgeting proposals from the NBA.

Together with the Australian Government, the states and territories are responsible for:

- establishing the policy framework and specific policies relating to the national blood supply;
- overseeing the NBA’s management of the blood supply arrangements;
• fostering the development and implementation of best-practice systems to promote efficient use and minimal wastage of blood and blood related products;

• providing information on demand for blood and blood related products;

• managing local issues.

The JBC refers national blood supply change proposals for evidence-based evaluation, participates in the supply planning and budgeting process and assists in oversight of the NBA’s role in management of the national blood supply.

The main functions of the NBA in relation to the blood supply system are to:

• gather information from State and Territory health authorities and other relevant organisations in relation to the demand for blood and blood products;

• develop, on a consultative basis, an annual supply plan and budget;

• negotiate and administer contracts for the collection, production and distribution of blood and blood products;

• develop the national price list for products, based on the annual supply plan and budget and on the contracts with suppliers.

SUPPLIERS OF BLOOD AND BLOOD PRODUCTS

To implement the annual National Supply Plan, the NBA has supply contracts with the following suppliers of blood and blood related products, which it manages closely to ensure that demand for product is always met:

The Australian Red Cross Blood Service (the Blood Service)

The Blood Service, a Division of the Australian Red Cross Society, collects fresh blood from voluntary donors in order to produce a variety of blood components. The Blood Service also collects plasma, which is provided to CSL Ltd for fractionation into a variety of products that are then purchased through the NBA contract with CSL. The Blood Service then distributes the blood components to hospitals.

The NBA manages the relationship with the Blood Service—the sole supplier of fresh blood-related products in Australia—and is responsible for negotiating and managing the Blood Service Deed of Agreement.

The Agreement is structured around the Blood Service meeting State and Territory requirements for the supply of blood, blood products and associated services. Under the Agreement, the Blood Service collects, manufactures and distributes fresh blood products (also known as blood components) from voluntary donations. It also distributes plasma products and a number of imported blood products to hospitals and other end users in Australia. The Agreement brings together the needs of the Australian Government and the State and Territory governments in a single, national Agreement with the Blood Service.

The Australian Government provides 63 per cent of the funding for the Blood Service and the State and Territory Governments’ combined contribution is 37 per cent.
CSL Limited

Most plasma-derived products used in Australia are manufactured by CSL Limited from plasma collected by the Blood Service under the CSL Australian Fractionation Agreement. Materials for blood diagnostic purposes and some imported products are also sourced through CSL.

Other Pharmaceutical Companies

In 2009-10, the NBA held contracts for the provision of blood and blood related products under standing offer arrangements with:

- CSL Limited, Octapharma Australia Pty Ltd and Lateral Grifols Pty Ltd for the provision of overseas-sourced IVIg;
- Baxter Healthcare Pty Ltd, Wyeth Australia Pty Ltd and Novo Nordisk Pharmaceuticals Pty Ltd, for the provision of a range of imported plasma-derived and recombinant blood products;
- CSL Limited, Lateral Grifols Pty Ltd, Ortho-Clinical Diagnostics Inc (USA) and Abacus ALS (formerly Australian Laboratory Services), for the supply of diagnostic reagents.

Australia is totally reliant on an imported supply of plasma derived Factor XI and Factor XIII, anti-inhibitor coagulant complex concentrates, Protein C and a plasma-derived Rh(D) immunoglobulin product. These products are either not economical to manufacture in Australia or, as is the case for IVIg, the Australian system is unable to produce enough product to meet demand. IVIg is accordingly imported as a contingency to supplement domestic supply under a Standing Offer.

Table 2 below shows the value of blood and blood related products, purchased by supplier, in 2008-09 and 2009-10.

TABLE 2: BLOOD AND BLOOD RELATED PRODUCTS PURCHASED, BY SUPPLIER, 2008-09 AND 2009-10

<table>
<thead>
<tr>
<th>Supplier</th>
<th>Products purchased</th>
<th>2008–09 ($million)</th>
<th>2009–10 ($million)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CSL Ltd</td>
<td>Plasma Products</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• albumin products</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• immunoglobulin products (including IVIg and hyperimmune products)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• plasma-derived clotting factors</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Diagnostic reagent products</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• blood grouping sera</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• reagent red cell products</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Imported Blood Products</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Factors XI and XIII</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• IVIg standing offer</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Management of National Reserve</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Supplier</td>
<td>Products purchased</td>
<td>2008–09 ($million)</td>
<td>2009–10 ($million)</td>
</tr>
<tr>
<td>--------------------------------------------------</td>
<td>----------------------------------</td>
<td>--------------------</td>
<td>--------------------</td>
</tr>
<tr>
<td><strong>Australian Red Cross Blood Service</strong></td>
<td>Fresh Blood Products</td>
<td>432.62</td>
<td>456.12</td>
</tr>
<tr>
<td></td>
<td>• whole blood</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• red blood cells</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• platelets</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• clinical fresh frozen plasma</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• cryoprecipitate</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• plasma for fractionation</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Baxter Healthcare Pty Ltd</strong></td>
<td>Imported Blood Products</td>
<td>84.09</td>
<td>90.62</td>
</tr>
<tr>
<td></td>
<td>• Recombinant Factor VIII</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Protein C</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Factor VII concentrate</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Factor Eight Inhibitor Bypass Agent (FEIBA)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• WinRho</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Wyeth Australia Pty Ltd</strong></td>
<td>Imported Blood Products</td>
<td>48.65</td>
<td>48.94</td>
</tr>
<tr>
<td></td>
<td>• Recombinant Factor VIII</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Recombinant Factor IX</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Novo Nordisk Pharmaceuticals Pty Ltd</strong></td>
<td>Imported Blood Products</td>
<td>17.40</td>
<td>26.42</td>
</tr>
<tr>
<td></td>
<td>• Recombinant Factor VIIa</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Octapharma Pty Ltd</strong></td>
<td>Imported Blood Products</td>
<td>46.90</td>
<td>48.69</td>
</tr>
<tr>
<td></td>
<td>• IVIg Standing Offer</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Lateral Grifols Pty Ltd (formerly DiaMed Australia Pty Ltd)</strong></td>
<td>Diagnostic Reagent Products</td>
<td>0.92</td>
<td>0.81</td>
</tr>
<tr>
<td></td>
<td>• blood grouping sera</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• reagent red cell products</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Ortho-Clinical Diagnostics (Johnson &amp; Johnson Company)</strong></td>
<td>Diagnostic Reagent Products</td>
<td>0.47</td>
<td>0.43</td>
</tr>
<tr>
<td></td>
<td>• blood grouping sera</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• reagent red cell products</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Abacus ALS Pty Ltd</strong></td>
<td>Diagnostic Reagent Products</td>
<td>0.04</td>
<td>0.04</td>
</tr>
<tr>
<td>Supplier</td>
<td>Products purchased</td>
<td>2008–09 ($million)</td>
<td>2009–10 ($million)</td>
</tr>
<tr>
<td>-------------------</td>
<td>-----------------------------------------</td>
<td>--------------------</td>
<td>--------------------</td>
</tr>
<tr>
<td></td>
<td>• blood grouping sera</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• reagent red cell products</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TOTAL</td>
<td></td>
<td>793.18</td>
<td>858.23</td>
</tr>
</tbody>
</table>

Source: National Blood Authority Australia – Annual Report 2009-10

In relation to the above table, Lateral Grifols also have a standing offer for supply of IVIg with the NBA. Its primary purpose was to allow jurisdictions to buy product outside the NBA arrangements but NBA bought minor quantities for particular patients. In October 2011 Octapharma recalled Octagam and the NBA currently uses the Lateral Grifols contract to supply imported IVIg product for Australia.

**SUPPLY PLANNING PROCESS AND BLOOD SUPPLY CHAIN**

As indicated above, each year the NBA is required to coordinate and produce a National Product Price List and National Supply Plan and Budget for blood and blood products for approval by the Australian Health Ministers’ Conference. Supply planning commences twelve months prior to the next supply year and must be endorsed by the JBC, and AHMC to allow continued funding of blood and blood products to suppliers of blood and blood products. In addition, the NBA is responsible for the intensive management of products in short supply.

The NBA prepares initial Supply Plan estimates on the basis of information from the states and territories. This takes into account factors such as historical trends, policy decisions and predicted hospital workloads over the forward period. It then consults with the Blood Service on its ability to collect the blood and plasma for fractionation volumes required in the draft Plan. It also consults with other suppliers on their ability to provide the blood products required. Estimates are provided to each jurisdiction for consideration and sign off before final approval by the JBC and the AHMC.

The blood supply chain and payment flows from suppliers to end-users are described in Figure 3 on the following page.
FIGURE 3: BLOOD SUPPLY CHAIN

Source: National Blood Authority Australia – Annual Report 2009-10
The NBA is responsible for establishing blood and blood products supply Deeds (or Contracts), including for the imported recombinant products, with suppliers. The contracts provide for supply of products to the State and Territory health providers.

The Blood Service is the sole organisation in Australia responsible for collecting whole blood and blood components. All donations of blood are from voluntary and non-remunerated donors. Blood is collected either as whole blood, or through a process called apheresis, which can isolate and extract blood components, that is plasma and platelets.

The Blood Service is also the sole manufacturer of fresh blood products in Australia. From whole blood, the Blood Service produces a range of products, which fall into several main categories, namely:

- red cells (suspended);
- platelets;
- FFP;
- plasma for fractionation.

Plasma for fractionation is supplied free of charge to CSL Ltd for further processing into specific blood products. The main categories of plasma derived blood products are:

- immunoglobulins;
- hyperimmune products;
- clotting factors.

The NBA negotiates contracts with other pharmaceutical companies for the supply of plasma-derived and recombinant blood products. These include Abacus ALS, Baxter Healthcare Pty Ltd, Lateral Grifols Pty Ltd, Novo Nordisk Pharmaceuticals Pty Ltd, Octapharma Australia Pty Ltd, Ortho-Clinical Diagnostics Inc (USA) and Wyeth Australia Pty Ltd.

Contracts specify agreed products, supply and delivery arrangements, performance criteria and product prices. The Blood Service is required to deliver fresh blood products and plasma derived products manufactured by CSL to Approved Health Providers (AHPs). AHPs are almost all public and private hospitals. However, some blood products are delivered outside of hospital settings, for example, home deliveries for haemophilia treatment and some anti Rh(D) immunoglobulin are supplied to some recipients such as fertility and family planning clinics outside the hospital environment. Supply contracts with other pharmaceutical companies require delivery on the basis of orders from Approved Recipients (ARs) in accordance with the contract or as otherwise determined by the NBA under the contract.

There are jurisdictional differences in relation to inventory management of blood and blood products, but, typically, blood and blood products are receipted and held by a hospital’s internal blood bank or pathology unit (mostly for public hospitals), or another storage facility. For example, some private hospitals use off-site pathology laboratories to store their blood and blood products.

The product is released for use by the pathology unit, under request by the treating clinician. Different hospitals have different procedures for release of product. Release of IVIg and Recombinant Factor VIIa (rFVIIa) require approval by the Blood Service against indicated uses before release for use.

The internal arrangements within hospitals for the issue and use of blood and blood products vary widely. State and Territory guidelines emphasise that it is important during all stages of the supply process that appropriate documentation is obtained. It is a requirement of the National Association of
Testing Authorities (NATA) that laboratories record the fate of every fresh unit transfused with name, UR number, date of birth and probably location for look back purposes to identify any viral transmission. The clinical record of the hospital cannot be searched, as the donation number might be recorded but not really searchable. Units of blood are commonly searched for through pathology systems. However, data and information on exactly what happens with blood and blood products within hospitals are not routinely collated.

Before release from pathology for clinical use, fresh blood components are grouped to ensure blood type and Rh(D) compatibility with the recipient. Red cells are also cross matched with the prospective recipient. A single unit of red cells may be grouped and even cross matched many times without release, as the blood may not ultimately be required for use in a certain procedure. Increasingly, pathology performs the less expensive function of group match and hold, and completes the full cross match only if the blood is required to be released.

In the private setting, prescription of blood or blood products for transfusion by a clinician is eligible for a Medicare Benefits Schedule (MBS) rebate item, as are the pathology functions associated with the dispensing of blood and blood products.

**LEGISLATION, GUIDELINES AND STANDARDS**

The collection, storage, use and disclosure of information relating to blood and blood products are regulated by a mixture of legislation, guidelines and standards. These include:

- the legislative framework for the protection of information and health privacy based on the Privacy Act 1988 and similar state and territory legislation;

- State and Territory Human Tissue Acts, which regulate aspects of the removal of human tissue, including blood donations, as well as blood transfusions. Among other things, the legislation covers requirements for the consent to removal of blood;

- NHMRC/ASBT Blood Components guidelines;

- standards and guidelines released by the National Pathology Accreditation Advisory Council (NPAAC), which apply to pathology laboratories accredited in Australia. Laboratories that want to claim Medicare benefits must be accredited by the NATA to the appropriate standard. Laboratories can bill patients directly and avoid Medicare and NATA if desired;

- AHMC Criteria for the Clinical Use of IVlg in Australia (the ‘IVlg Criteria’);

- state and territory government health authority policies and guidelines which typically set out the obligations of a health care facility to ensure the safe and appropriate use of blood and blood products. The guidelines cover the obligations of clinicians (medical practitioners and nurses) for safe and effective transfusion therapy, transfusion verification procedures and transfusion equipment, hospital transfusion service staff for transportation, storage, inventory management and labelling and health service managers for reporting of infections and retention of records.

**STAKEHOLDERS**

The roles of Australian Government, state and territory governments have been described above in relation to the governance structure for the Australian blood sector and the supply planning process. The key roles of the NBA and other government agencies such as the TGA have been covered as well as the major suppliers of blood including the Blood Service, CSL Ltd and other pharmaceutical companies.
Other key stakeholders include a wide range of professional bodies representing doctors generally such as the Royal College of Physicians of Australasia (RACP), or specialist clinicians and scientists working in the blood sector such as the Australasian Society of Thrombosis and Haemostasis (ASTH) and Australian Haemophilia Centre Directors Organisation (AHDDO). There are some umbrella bodies representing a range of separate professional organisations. The Pathology Associations Council (PAC) brings together representatives of the various national organisations that are involved in pathology service delivery, with a particular emphasis on professional issues such as workforce, training, professional development, quality and safety. PAC aims to present a single voice to State and Federal governments on issues relating to pathology.9

Other groups of medical and other specialists working in the blood sector are represented through peak professional bodies such as the Royal College of Pathologists of Australasia (RCPA), the Australia and New Zealand Intensive Care Society (ANZICS), the Health Informatics Society of Australia Ltd (HISA), the Australasian Society of Clinical and Experimental Pharmacologists and Toxicologists (ASCEPT), the Australasian Society of Clinical Immunology and Allergy (ASCIA) and the Haematology Society of Australia and New Zealand (HSANZ). These organisations are primarily interested in training and support for their members, promotion of research, quality and safety issues and advocacy to governments.

Pathology practices are represented by the Australian Association of Pathology Practices (AAPP) which is the national peak body for private pathology in Australia covering both small specialized laboratories as well as large corporations with laboratories nationwide. AAPP aims to provide high quality, affordable, safe and accessible pathology services. Public pathology services are represented through the National Coalition of Public Pathology (NCOPP), which advocates advancing public pathology with the public, the medical profession and governments.

Other stakeholders include:

- hospitals and area health services;
- professional workers in the blood sector such as clinicians, pathologists, haematologists, researchers and nurses and associated unions such as the Australian Nursing Federation;
- the NHMRC;
- universities and medical research institutions;
- those working for the various State Emergency Medical Retrieval Services;
- health insurance companies who have strong interests in patient outcomes and costs.

Finally blood users also have a significant stake in Australia’s blood system. Some are represented through organisations such as the Haemophilia Foundation Australia (HFA), which represents people with haemophilia, von Willebrand disorder, and other related inherited bleeding disorders, and their families. HFA is committed to improving treatment and care through representation and advocacy,

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9 Professional societies or associations covered by the PAC include the Australasian Association of Clinical Biochemists (AACB), Australian Institute of Medical Scientists (AIMS), Australian Society of Cytology (ASC), Australian Society of Clinical Immunology and Allergy (ASCIA), Australian Society for Microbiology (ASM), Australian and New Zealand Society of Blood Transfusion (ANZSBT), Endocrine Society of Australia (ESA) and Human Genetics Society of Australasia (HGS)
education and the promotion of research. Immune Deficiency Foundation of Australia (IDFA) supports children, teenagers and adults with primary immune deficiency disorders.

**FUNDING**

Australia’s blood sector is government funded with cost-shared arrangements between the Australian, State and Territory governments. In general State and Territory governments contribute 37 per cent and the Australian Government 63 per cent. Funds provided to the NBA are used to purchase and manage blood, blood products and services from the Blood Service, CSL Limited and pharmaceutical companies as well as operational costs of the NBA.

In NSW and Tasmania, State Health authorities then pass this cost down to the Area Health Service level, and in some instances at least in Tasmania, further passed down to individual hospitals. In Tasmania, the apportionment is done on the basis of historical use that is the percentage of the hospital’s total use for the previous year.

Providers bill the NBA, on a monthly basis, for the volume of blood issues they deliver. On the basis of these invoices, NBA bills the Australian Government for 63 per cent and each State for 37 per cent of the cost.

The total cost of supply of blood and blood related products over the period 2003-04 to 2009-10 and for the operation of the NBA over the same period are shown in Table 3 and Table 4 respectively.

**TABLE 3: PRODUCT SUPPLY COST**(a) FOR BLOOD AND BLOOD RELATED PRODUCTS**(b)**, 2003–04 TO 2009–10

<table>
<thead>
<tr>
<th>Year</th>
<th>Amount ($million)</th>
<th>Growth</th>
</tr>
</thead>
<tbody>
<tr>
<td>2003–04</td>
<td>442.3</td>
<td>–</td>
</tr>
<tr>
<td>2004–05</td>
<td>492.6</td>
<td>11 %</td>
</tr>
<tr>
<td>2005–06</td>
<td>544.5</td>
<td>11 %</td>
</tr>
<tr>
<td>2006–07</td>
<td>615.2</td>
<td>13 %</td>
</tr>
<tr>
<td>2007–08</td>
<td>678.8</td>
<td>10 %</td>
</tr>
<tr>
<td>2008–09</td>
<td>771.4</td>
<td>14 %</td>
</tr>
<tr>
<td>2009–10</td>
<td>850.9</td>
<td>10 %</td>
</tr>
<tr>
<td>Average over period</td>
<td>12 %</td>
<td></td>
</tr>
</tbody>
</table>

*Source: National Supply Plan and Budget, 2003-04 to 2009-10, National Blood Authority*

(a) The ‘product supply cost’ refers to the cost to governments for the purchase of blood and blood products only. It does not include additional costs such as administrative expenses of health authorities and the NBA or the cost of the National Managed Fund.

(b) Excluding diagnostic blood products.
### TABLE 4: GOVERNMENT FUNDING FOR THE OPERATION OF THE NBA, 2003–04 TO 2009–10

<table>
<thead>
<tr>
<th>Year</th>
<th>Amount ($million)</th>
<th>Growth (per cent)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2003–04</td>
<td>7.4</td>
<td>–</td>
</tr>
<tr>
<td>2004–05</td>
<td>8.4</td>
<td>12.7</td>
</tr>
<tr>
<td>2005–06</td>
<td>10.4</td>
<td>24.1</td>
</tr>
<tr>
<td>2006–07</td>
<td>10.1</td>
<td>–2.6</td>
</tr>
<tr>
<td>2007–08</td>
<td>9.6</td>
<td>–4.8</td>
</tr>
<tr>
<td>2008–09</td>
<td>9.2</td>
<td>–4.9</td>
</tr>
<tr>
<td>2009–10</td>
<td>8.9</td>
<td>–3.3</td>
</tr>
</tbody>
</table>

*Source: National Blood Authority Australia – Annual Report 2009-10*

### APPROVAL PROCESSES

Under the National Blood Agreement, interested parties can make proposals for changes to products or services on the National Products and Supply List. Schedule 4 of the National Blood Agreement provides for evidence-based evaluation, information and advice to be provided to support decisions on these changes.

The NBA’s Multi-Criteria Analysis (MCA) Framework has been agreed by officials as the primary tool to assess applications in the following circumstances:

- changes to products currently supplied under the National Blood Arrangements; or
- proposed additions to the National Product and Services List (NPSL) of new blood products or services.

An assessment under the MCA framework can involve one or two cycles, depending on the complexity of the evaluation and information supplied. The Framework has been designed to ensure that assessment of new products or services addresses the primary and secondary policy objectives of the National Blood Agreement, as well as broader government policy objectives.

The objective of the first cycle is to identify whether there is sufficient evidence to support a change to blood products or services funded under the National Blood Arrangements. Following Cycle 1, if the JBC considers that further analysis or information is needed, this will be undertaken in Cycle 2.

New products cannot be submitted for listing on the NPSL unless they are registered with the TGA for supply in Australia.

The NPSL does not list specific products but rather a generic description of a product category. Just because a product is on the list, does not mean that government is committed to buy any particular quantity of the product at any particular time, nor are governments committed to any particular brand of a product. A decision to purchase a product is always subject to additional processes after completion of the MCA assessment.

The MCA framework applies to both ‘within category’ and ‘outside category’ change proposals.

‘Within category’ proposals are defined as changes to products already approved by Health Ministers and which are already listed on the NPSL. A ‘within category’ change will be assessed by the NBA
against the MCA Framework. A decision on whether to approve or not approve the change would usually be made by either the NBA or the JBC. In general, the NBA is able to approve the change if the MCA assessment shows that the change is either positive or neutral against all criteria. If the change is not neutral or positive against all of the MCA criteria, the proposal must be forwarded to the JBC for consideration. The JBC will assess the application and either approve/reject the proposal or require further analysis of the proposal via Cycle 2.

An ‘outside category’ proposal is a proposal for:

- a new product/service not already on the approved NPSL; or
- a change to a product on the NPSL that has altered the nature of that product to take it outside the definition of the listed product.

Examples may include:

- a new recombinant product;
- different route of administration;
- change in active ingredients; and
- an imported product, where the current category definition only includes product manufactured from Australian plasma.

All ‘outside category’ proposals are considered as Schedule 4 applications and must be considered by the JBC (Figure 4). JBC has three options:

- if there is sufficient information to make a decision, and the proposal is considered to be non-material (for example does not have a material effect on clinical care outcomes, production, supply or cost under the national blood supply), JBC can reject or approve the proposal;

- if there is sufficient information to make a decision, and the proposal is considered to be material (for example does have a material effect on clinical care outcomes, production, supply or cost under the national blood supply) JBC must refer the matter to AHMC for decision;

- if there is insufficient information to make a decision, then JBC can require further information for a more detailed Cycle 2 analysis.
ACHIEVEMENTS IN THE AUSTRALIAN BLOOD SECTOR

In the 1990s the world blood sector was undergoing change in response to a number of pressures, predominantly around cost and safety issues. In response to this, a number of countries undertook reviews of the organisation and management of their blood programs, leading to significant reorganisation and structural reforms. These reforms were based on rationalisation, consolidation and integration, as well as clarification of roles and responsibilities and system-wide approaches to achieving improved management, accountability and performance as part of risk management.

In Australia, the 1995 McKay Wells Review (McKay, 1995), recommended the formation of the Blood Service as a national blood service (rather than individual State-based services) providing the impetus for structural change. This, together with the establishment of the AHMAC Blood and Blood Products Standing Committee, provided the first steps towards a national approach to managing Australia’s blood sector.

The McKay Wells Review was followed in 2001 by the Review of the Australian Blood Banking and Plasma Product Sector, chaired by Sir Ninian Stephen (2001), as mentioned previously. The Stephen’s review had identified a number of shortcomings in the system, including that it was:

*Subject to any relevant procurement/contract provisions

Source: National Blood Authority
• fragmented and administratively costly and inefficient being driven by suppliers rather than clinical demand;

• lacking transparent evidence-based assessment mechanisms for new products and technologies;

• providing disincentives to achieving national economies of scale; and

• subject to rising cost pressures from the dynamic, changing nature of the blood sector.

NBA was established as a consequence, to address these shortcomings.

In an exceptionally short time and as an excellent example of cooperation between state and territory governments and the Australian Government, all parties accepted the recommendations of the Stephen Review, and the National Blood Agreement was signed by all Australian governments.

As indicated earlier, the National Blood Agreement also sets out the primary and secondary policy objectives of all governments in relation to the Australian blood sector. Major policy aims are the safe, secure, adequate and affordable supply of blood and blood products in Australia; and the highest quality, effectiveness and efficiency for the Australian blood sector. Supporting principles include a continued policy of national self-sufficiency in blood and blood products; voluntary, unpaid donations of blood and plasma; and the supply of such products free of charge to patients, based on clinical needs and appropriate clinical practice.

The role of the Australian Health Ministers’ Conference and establishment of the JBC are also set out in the National Blood Agreement. The Australian Health Ministers’ Conference is charged with a number of functions, including general oversight and determination of national policy for the Australian blood sector, and oversight of the implementation of the National Blood Agreement. As was indicated earlier, the JBC’s roles include providing advice to, and dealing with less significant issues under the authority of, the Australian Health Ministers’ Conference.

The JBC also has responsibilities in relation to the national blood supply. These include:

• referring proposed changes to the national blood supply to appropriate bodies for evidence-based evaluation;

• participating in the development of NBA supply and production planning and budgeting;

• considering advice from and advising the NBA on matters related to the national blood supply;

• monitoring developments in safety and quality; and

• overseeing the NBA’s role in relation to contracts.

The roles of the state and territory governments are aimed at better use of blood and blood products.

Together, the NBA Act and the National Blood Agreement form the foundations of the current arrangements within the Australian blood sector and the major achievements in the blood sector have been made through the NBA under its Act and the National Blood Agreement.

During 2003–04 (National Blood Authority, 2004) the NBA’s key priorities were focused, by necessity, on putting in place adequate operational infrastructure and identifying and minimising risks that might otherwise have prevented the supply system from responding in a crisis.

The mission set by the NBA in its establishment year was “To build a new national platform to achieve (our) vision while meeting current blood supply needs.” In that year the NBA fulfilled its primary function of meeting current blood supply needs. The refinement of the 2003–04 National Supply Plan
and Budget and the development of new ones for 2004–05 on behalf of the Australian Health Ministers’ Conference were particularly taxing tasks for the NBA, as governments had to base their demand estimates on unreliable past consumption data and had limited capacity to influence demand once their budgets had been set.

The NBA’s stocktake of achievements after the first five years of operation was impressive. The challenges in the first year were considerable — not the least being the task of creating an organisation from scratch and tackling the expectations arising from the National Blood Agreement. Other challenges for the NBA included:

• developing and managing new relationships at a national level;
• building confidence in the clinical and scientific communities about the roles and responsibilities of the new authority;
• demonstrating value for governments early in its existence.

Today, the NBA negotiates and manages contracts covering all the blood and blood-related products used in Australia. It also has a broad international network, coordinates a national approach to blood supply, usage and conservation, manages a diversity of stakeholder relationships, and has recently started work to drive improvements in transfusion appropriateness and blood sector performance analysis.

**Major National Achievements—2003-04 to 2008-09**

In the first five years of its operation the NBA:

• improved contract management, delivering significant cost savings to all Australian governments;
• implemented a diverse and innovative range of supply contingency provisions that have prevented significant stock shortages;
• established clear governance decision-making frameworks that integrate blood into the overall decision-making framework for health sector risk planning;
• built highly effective relationships with key stakeholders;
• delivered a range of safety and quality initiatives such as the recent *Initial Australian Haemovigilance Report (2008)* and the *Criteria for the Clinical Use of Intravenous Immunoglobulin (IVIg) in Australia (2008)*;
• began data collections on product issues and usage to assist in developing policies relating to appropriate use of products, and a rigorous analysis of future supply and demand; and
• implemented a range of strategies to reduce inappropriate use of blood products.

The achievements of the first five years of the NBA shown in Table 5 have been possible because of a commitment by the NBA to six principles, namely:

• detailed analysis of costs, options, international comparators and stakeholder concerns;
• meticulous planning of resources and activities against clear goals;
• seeking creative and innovative ways to achieve better outcomes;
• a high-level of stakeholder involvement and communication, both in the planning and designing phases, as well as implementation;

• careful management of cautious implementation;

• regular monitoring and review for all the projects undertaken.

**TABLE 5: FIVE YEARS OF AUSTRALIAN BLOOD SECTOR ACHIEVEMENTS, 2003–08**

<table>
<thead>
<tr>
<th>National Blood Authority Act Obligations</th>
<th>Achievement</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>To provide assistance:</td>
<td>Provided secretariat services to 53 JBC meetings.</td>
<td>Effective governance framework that supports consolidated policy decision-making and implementation across all jurisdictions.</td>
</tr>
<tr>
<td>in accordance with national blood</td>
<td>JBC focus evolved from strong operational concerns to strategic developmental focus.</td>
<td></td>
</tr>
<tr>
<td>arrangements to a committee referred to</td>
<td>Board directly engaged in informing strategic advice to the General Manager.</td>
<td></td>
</tr>
<tr>
<td>in those arrangements</td>
<td>Clinical Advisory Council established to provide detailed clinical advice and was instrumental in the development of the blood counts program.</td>
<td></td>
</tr>
<tr>
<td>to the Board</td>
<td>Suppliers provided with improved certainty and clarity of government supply requirements.</td>
<td></td>
</tr>
<tr>
<td>to the advisory committees (if any)</td>
<td>An improved level of accountability in blood expenditure.</td>
<td></td>
</tr>
<tr>
<td>To carry out national blood arrangements relating to annual plans and budgets for the production and supply of blood products and services.</td>
<td>National supply plan process created and implemented on an annual basis.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Presentation of plans delivered progressively earlier to Ministers each year.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Suppliers advised of indicative volumes more than six months before the commencement of plan.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mid-year reviews designed and implemented on a regular basis from 2004.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Verification procedures for ordering and receipting negotiated and implemented.</td>
<td></td>
</tr>
<tr>
<td>To enter and manage contracts and</td>
<td>New Deed with ARCBS negotiated and signed.</td>
<td></td>
</tr>
<tr>
<td>arrangements for the collection,</td>
<td>New Deed with CSL Ltd negotiated and signed.</td>
<td></td>
</tr>
<tr>
<td>production and distribution of the</td>
<td>New contractual arrangements for diagnostics implemented.</td>
<td></td>
</tr>
<tr>
<td>blood products and services necessary</td>
<td>New Standing Order arrangements for the importation and implementation of IVIg.</td>
<td></td>
</tr>
<tr>
<td>to ensure a sufficient supply of blood</td>
<td>New Deeds for imported plasma and</td>
<td></td>
</tr>
<tr>
<td>products and services in all the states</td>
<td></td>
<td></td>
</tr>
<tr>
<td>and covered territories.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>National Blood Authority Act Obligations</td>
<td>Achievement</td>
<td>Outcome</td>
</tr>
<tr>
<td>----------------------------------------</td>
<td>-------------</td>
<td>---------</td>
</tr>
<tr>
<td>recombinant products negotiated and signed.</td>
<td>Effective management of the development of:</td>
<td>High-quality, evidence-based guidelines for high cost products developed in consultation with the clinical community and published.</td>
</tr>
<tr>
<td>To carry out national blood arrangements to ensure that there is a sufficient supply of blood products and services in all the states and covered territories.</td>
<td>- Factor VIII and Factor IX Guidelines (2006) - Criteria for the Clinical Use of Intravenous Immunoglobulin (IVIg) in Australia (2008). - Guidelines on the prophylactic use on RhD immunoglobulin (anti-D) in obstetrics (2004). - Biostate shortage contingent supply management.</td>
<td></td>
</tr>
<tr>
<td>To carry out national blood arrangements relating to: (a) Safety and quality measures.</td>
<td>- ARCBS requests to governments for funding for increased levels of leucodepletion, bacterial contamination and sample archiving assessed. - Rolled out recombinant FVIII for all patients seeking this product. - Obtained funding for ARCBS to implement TGA requirement for changes to Hb tests. - Blood standard requirements integrated into hospital accreditation reform.</td>
<td>Product recipients have access to a selection of some of the world’s best products. Government approved 100 per cent leucodepletion and 100 per cent bacterial contamination testing of platelets.</td>
</tr>
<tr>
<td>To liaise with and gather information from governments, suppliers and others about matters relating to blood products and services.</td>
<td>- Ongoing horizon scanning project implemented. - Fresh Blood Products: Production Benchmarking and Demand Drivers released. - Strategic workshops initiated for JBC. - Created Blood Suppliers Forum, Professional and Community Forum and the Clinical Advisory Council. - Engaged stakeholders in specific</td>
<td>All contracts and major projects informed by international research, government, clinical and community needs.</td>
</tr>
<tr>
<td>National Blood Authority Act Obligations</td>
<td>Achievement</td>
<td>Outcome</td>
</tr>
<tr>
<td>-----------------------------------------</td>
<td>-------------</td>
<td>---------</td>
</tr>
</tbody>
</table>
|                                         | projects, for example ABDR redevelopment, NIMS and product tender processes.  
- Established Haemovigilance project working group.  
- Established an Expert Working Group to manage the review of guidelines for use of fresh blood components. |                         |                         |
| To provide information and advice to the Minister and the Ministerial Council about matters relating to blood products and services. | Approximately 20 papers have been submitted to AHMC for ministerial approval.  
- Recommended position on barcoding policy for blood products. | Ministers provided with consolidated strategic national policy and funding advice.  
Ministers provided with accurate and timely advice. |                         |
| To carry out national blood arrangements relating to the funding of the supply of blood products and services, and the NBA’s operations. | Established the NBA with independent infrastructure and services, including: IT systems; outsourcing of noncore business systems; appropriate and best practice governance arrangements; and key policies and processes to support the operation of the NBA.  
- Maintained an active recruitment program to address new functions.  
- Implemented an NBA Fellows program to ensure the NBA has access to high-quality advice.  
- Implemented Clinical Advisory Council to ensure the NBA has access to high level clinical advice to guide policy and program development  
- Recognition as high performing agency through:  
  - Prime Minister’s Silver Award for Excellence in Public Sector Management and  
  - Comcover Award for Excellence in Risk Initiatives. Highly Commended in the category of Risk Initiative. | NBA recognised for public service excellence.  
NBA recognised for high quality risk management procedures. |                         |
| Ensure that funding and supply contracts for the national blood supply include appropriate obligations on suppliers to meet safety and quality standards and to enforce those obligations. | All contracts comply with this requirement.  
- Requirement for additional pathogen inactivation steps in some CSL Ltd products in new Plasma Products | Australian supply contracts provide some of the world’s best products. |                         |
<table>
<thead>
<tr>
<th>National Blood Authority Act Obligations</th>
<th>Achievement</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Agreement.</td>
<td>Co-ordinated supply response for implementation of variant-Creutzfeldt-Jakob disease mitigation steps.</td>
<td></td>
</tr>
</tbody>
</table>
| Maintain a systematic approach to identify new developments and to provide a clearinghouse and coordination function for information in relation to new developments. | Framework for assessment of new technologies established.  
Supply contracts to provide information on new and emerging issues.  
Blood Sector Data Strategy. | Framework to ensure that the sector is informed and well poised for timely responses to new and emerging pressures.  
Standardised approach to information management and data systems development in the blood sector to be implemented. |
| Facilitate coordination, integration, cooperation and information exchange between the NBA and other bodies with a safety and quality role in the Australian blood sector, and between those other bodies. | Coordinated blood sector input to National Safety and Quality in Healthcare Commission accreditation reforms.  
Provided input to the Information Strategy for the National Safety and Quality in Healthcare Commission.  
Designed ABDR with input from National E-Health Transition Authority.  
Red Cell Utilisation Workshop sharing data between states.  
Co-sponsored support for market research on red cell prescribing behaviours of doctors (with NSW Government). | Blood issues integrated into health S&Q reform agenda. |
| Provide information and advice to the JBC and to the Ministerial Council (through the JBC). | Provided information on new and emerging products, technologies and procedures to JBC on a regular basis.  
Established strategic workshops for JBC.  
Prepared more than 500 papers to JBC. | Sound coverage and management of operational issues.  
Policy directions to be informed by careful consideration of emerging information. |
| Act on behalf of the JBC to purchase and organise activities under Clauses 34 (a), (b) and (c). | Started distribution review.  
Established a better practice fund to develop local ideas to national application. | Four projects commenced under this fund. |
<table>
<thead>
<tr>
<th>National Blood Authority Act Obligations</th>
<th>Achievement</th>
<th>Outcome</th>
</tr>
</thead>
</table>
| Facilitate the development of national information systems for safety and quality issues in relation to the Australian blood sector. | ▪ Haemovigilance reporting design requirements.  
▪ Australia’s first Haemovigilance report to guide sector reform.  
▪ ABDR redevelopment to provide improved demand data. | Awareness of transfusion-related reactions increased.  
Australia now meets best international practice in Haemovigilance.  
High-quality, evidence-based guidelines for high cost products developed in consultation with the clinical community and published. |

FIGURE 5: NATIONAL BLOOD AUTHORITY – FIRST FIVE YEARS HIGHLIGHTS

Since this major look back at achievements in the Australian blood sector significant improvement continues. The recent major achievements in the Australian blood sector are set out below in brief.

**MAJOR NATIONAL ACHIEVEMENTS SINCE 2008-09 (NATIONAL BLOOD AUTHORITY, 2009)**

Management and implementation of planning, funding and risk-management activities

Achievements have included:

- development of the National Supply Plan and Budget (NSPB) bringing together the best understanding of current and future demand and supply trends. Endorsement by Australian Government, and state and territory health ministers of the 2008–09 NSPB ensured the continued supply of a range of products required to meet clinical need. Expenditure on the blood supply was $789.9 million, which was 2.3 per cent less than the Commonwealth Budget estimate of $808.7 million (National Blood Authority, 2009). Most importantly, the NBA was able to ensure that products were available at all times to meet clinical need;

- the then Parliamentary Secretary, Senator the Hon Jan McLucas, launched the National Blood Supply Contingency Plan in November 2008. This plan establishes a clear decision-making framework for managing the blood supply in cases of supply shortage or demand surges and integrates with broader health emergency management arrangements. The plan was successfully activated from 22 August to 23 October during a shortage of red cells. Actions taken under the plan resulted in clinical practice not being compromised during this period:

  - three other incidents—the Victorian bushfires, the Ashmore Reef incident and the pandemic (H1N1) 2009 outbreak—had the potential to result in inadequate supply. While none of these incidents required activation of the National Blood Supply Contingency Plan, the NBA worked with governments and suppliers to closely monitor the supply situation;

  - understanding future risks—as well as opportunities—is a core activity within the NBA. Its horizon-scanning program continues to deliver early warning of possible future pressures and opportunities. In 2008–09 the NBA upgraded its reporting in the area;

  - the NBA established a meeting of international colleagues under the banner of the collaboration of National Plasma Products Supply Planners to exchange information and data on planning and risk-management activities.

**Enhanced data capture and analysis**

Improvement in the blood sector, in both supply chain management and clinical practice, is hampered by a lack of data and analysis. Along with jurisdictions and suppliers, the NBA is taking steps to redress this shortfall.

- In 2008–09 the NBA, on behalf of all governments, launched the redeveloped ABDR to provide to stakeholders information about patients with haemophilia and other bleeding disorders. The registry also allows for more reliable supply forecasting and planning.

- The NBA internal data warehouse capability also improved greatly with the rollout of the IDMS, which will assist in the further development of the National Supply Plan and Budget and the transition to multi-year budgeting and demand and supply planning.

- The release of the first Blood Measures Guide by the NBA was a world first in establishing a nationally accepted set of measures on the use and effectiveness of fresh blood components. It is
hoped that over time greater consistency in measurement will enable meaningful comparison of research results and lead to a better understanding of the use of fresh blood components.

Sector improvement projects

Progress on a number of projects continued to identify opportunities to improve the sector, especially in relation to value for money. In 2008–09 this included the following:

- development of a multi-criteria analysis framework for assessing new products or services (Schedule 4 of the National Blood Agreement) that aligns blood sector assessment methodology with that used in the Medical Benefits Scheme and the Pharmaceutical Benefits Scheme (PBS) and quantifies consideration of each of the objectives of the National Blood Agreement;

- completion of the first phase of the review of distribution arrangements for plasma and recombinant blood products;


Supply of blood and blood products

The NBA continues to place a high emphasis on being knowledgeable about the international blood sector, so that it can take a highly informed approach to development of the best-value contracts to deliver the blood products Australia needs. In 2008–09 their contract-management and negotiation activities made a key contribution to minimising increases in the overall cost and affordability of the blood supply for governments. Among the highlights were:

- prices for plasma and recombinant products were effectively restrained. NBA analyses demonstrate that during the past six years the collective effect of its activities is that there have been no increases in prices, despite global price rises;

- three contracts for imported plasma and recombinant products were successfully negotiated, with savings;

- all ministerial recommendations of the Blood Service business study progressed according to the agreed timetable, 32 per cent being fully implemented. This includes agreement to move towards a three-year rolling planning cycle and establishment of an output-based funding model;

- new contractual arrangements are in place with the Blood Service from 1 July 2009;

- the NBA progressed approvals through governments for the Blood Service’s new principal blood manufacturing sites in accordance with the time frames necessitated by the Blood Service’s project plans. This included managing the independent assessment of the Victoria and Tasmania principal site for the Australian Health Ministers Conference.

Monitoring and implementing the appropriate and safe use of products

Improving product and patient safety is a crucial element of the National Blood Agreement, and good progress in this regard was achieved in a number of projects during 2008–09. Highlights included:

- information on adverse effects from blood transfusions has been increased through the establishment of the ongoing Australian National Haemovigilance Program. Among other things, this involved finalising the definitions of the national minimum Haemovigilance data sets and developing a methodology for assessing the capability of jurisdictions to provide the required data;
the revised NHMRC’s guidelines for fresh blood will provide the most contemporary evidence-based information on when and how to use fresh blood components. In 2008–09, under the guidance of an expert working group of 27 clinicians, we began an extensive review of international research into blood-related guidelines. Evidence reports and associated recommendations for critical bleeding and peri-operative guidelines are due early 2010;

the availability and quality of education on blood administration have been improved through the establishment of a national framework for the continued development of the South Australian e-learning project;

information on where red cells are used has been improved as a result of the development of a draft minimum data set to guide further red cell use data-linkage activities.

In 2009-10 the NBA:

• won the 2010 United Nations Public Service Award in the category of Advancing Knowledge Management in Government;
• signed a new agreement with CSL Limited to maintain a safe, secure and affordable supply of domestically produced blood plasma products;
• won the Comcover Award for Excellence in Risk Management;
• implemented a pilot project for a national electronic Order and Receipting Blood System;
• completed a public consultation of the critical bleeding module on the PBM guideline designed to assist in the management of patients with life threatening bleeding;
• agreed to output based funding principles with the Blood Service, and a 12-month extension of the current Deed;
• developed a stewardship statement for use of blood and blood products by Approved Health Providers;
• commenced review of the Criteria for the Clinical Use of Intravenous Immunoglobulin In Australia;
• improved data capture and analysis to provide greater insight on the management, administration and use of blood and blood products;
• completed Stage 2 of the review of distribution arrangements of plasma and recombinant products;
• published the second Australian Haemovigilance Report 2010, which aims to increase the sector’s understanding of transfusion related adverse events.

The NBA has always believed that developing and maintaining the organisational capability to do its work well was a top priority, including having access to high-quality information so that it can be a well-informed purchaser and program manager. To that end, over the last six years the NBA has built a very effective private and civil network that provides it with the information it needs to maintain a high standard of work. It was therefore a very exciting day for NBA in June 2010 when the NBA’s work in this area was recognised by it winning the 2010 United Nations Public Service Award in the knowledge management category.
OTHER ACHIEVEMENTS IN 2009–10

Supply of blood and blood products

Among the NBA’s key functions are the development and management of the National Supply Plan and Budget and the management of contracts for blood and blood related products. In 2009–10, governments spent $872.8 million on blood and blood related products which are supplied free of charge to Australian patients (National Blood Authority, 2010a).

In 2009–10 current contracts with major suppliers CSL Limited and the Blood Service both expired. The NBA put a great deal of effort into negotiating the successful renewal of the contracts. In December 2009 a new agreement with CSL Limited was signed. Subject to a review in 2014, the agreement will run until 31 December 2017. Over that period this will ensure a secure supply of plasma products and services and provide improved value for money for governments.

Other major achievements in this area included:

- successfully ensuring that blood products were available at all times to meet clinical need;
- reaching agreement with the Australian Red Cross Society and the Blood Service on the principles of an output based funding model, to be implemented from 1 July 2010, and on the extension of the current Deed of Agreement for a further year;
- reaching agreement with Octapharma to extend the existing contract for the supply of imported IVIg until December 2011, with improved value for money;
- extending the contracts for diagnostic reagent products until June 2011;
- completing the 2010–11 National Supply Plan and Budget with a higher level of jurisdictional engagement on clinical demand than in previous years. The plan was approved by the JBC in December 2009 and received ministerial approval in April 2010; and
- achieving savings to governments of $22 million, compared to the prices that governments would have otherwise incurred before the establishment of the NBA.

Risk and sector improvement

The NBA continues to give high priority to its obligation to manage blood sector risks, especially those related to supply security. It does this by ensuring that responsibility and accountability lie with those best placed to manage risk. There were several highlights in this area during 2009-10:

- the NBA was awarded the 2009 Australian Government Comcover Award for Excellence in Risk Management for the National Blood Supply Contingency Plan;
- an annex to the National Blood Supply Contingency Plan, dealing with the management of transfusion-transmitted infections in the blood supply, was drafted;
- agreement was reached with the Blood Service on the need to standardise stock holdings for fresh blood components to assist in identifying appropriate trigger points for the National Blood Supply Contingency Plan and enabling improved reporting.

The NBA restructured its organisation in 2009 to enhance its capacity to capture and analyse data and provide insight into the management, administration and use of blood and blood products. NBA reported significant progress during 2009-10 on data capture that will allow the NBA to deliver more robust and accurate reports to jurisdictions on product use, the balance between supply and demand throughout the year, and intensive management of products in short supply where this is necessary.
Other projects are currently at various stages of progression within the NBA to improve the overall efficiency of the sector. These include:

- development, for national application, of an electronic ordering and receipting blood system for use by blood banks in ordering products from suppliers and enhancement of the system for additional data capture;
- review of the distribution of plasma and recombinant products;
- KPMG business review of the Blood Service;

**SAFETY OF SUPPLY**

In terms of the safety record of the sector, Australia appears to fare no worse than other countries. This was the conclusion of the 2010 report of the HAC (2010). That report noted that a number of OECD countries have national haemovigilance programs, and that some publish annual reports about the number and types of adverse events occurring in their hospitals. The 2010 HAC report concluded “there is no evidence at this stage to suggest that the rate of transfusion errors in Australia is outside the range experienced in OECD countries.” (Ibid.) The report indicated that “(i)n common with other OECD countries, such as the United Kingdom, New Zealand, Sweden and Canada, the risks to the safety of transfused patients in Australia were predominantly in the hospital environment, arising from procedural errors.” (Ibid.) For example, the 2008 report of the HAC had indicated that approximately 65 per cent of incidents reported in Australia had involved procedural errors and that this was “broadly compatible with (the results from) other OECD countries.” (Ibid.) For example, the UK Serious Hazards Of Transfusion Annual Report 2008 (Serious Hazards of Transfusion, 2008) indicated that procedural errors represented 59 per cent of cumulative numbers of cases reviewed in the period 1996-2008.

**ACHIEVEMENTS IN PROMOTING APPROPRIATE USE OF BLOOD AND BLOOD PRODUCTS**

There have been a number of achievements in this area through the efforts of the NBA as well as states and territories. These achievements are discussed below (Appropriate Use Strategies, p67).
Appropriate Use of Blood and Blood Products

This section considers appropriate use of blood and compares appropriate use of blood and blood products with the actual use of those products. It defines what is meant by appropriate use and assesses use in Australia against that definition.

The next section of the report (Appropriate Use Strategies) highlights achievements that have been made nationally and among the states and territories in terms of promoting appropriate use of blood and blood products in Australia. The analysis in this section, however, concentrates on identifying where current use might fall below appropriate levels. While the next section of the report acknowledges that there has been significant progress made towards appropriate use in some areas in Australia, the evidence presented below shows that inappropriate use remains an issue in the sector.

Because the balance of evidence lies in the area of the use of red cells, the discussion of appropriate use below devotes most attention to that product, however, the evidence, where available, of appropriate use of the other major blood products is also presented.

WHAT IS ‘APPROPRIATE USE’?

BACKGROUND

The WHO Handbook on the Clinical Use of Blood 2001 (Emmanuel, 2001) defines the appropriate use of blood as ‘the transfusion of safe blood products only to treat a condition leading to significant morbidity or mortality that cannot be prevented or managed effectively by other means’.

Since the publication of the WHO Handbook, appropriate use has become strongly associated with use of blood and blood products in accordance with published guidelines.

Australia followed the release of the Handbook with the promulgation of the NHMRC/ASBT Blood Components guidelines in 2001 (National Health and Medical Research Council, 2001b). Since then, Australia has been a leader in developing guidelines to support more appropriate use of blood and blood products.

The NHMRC/ASBT Blood Components guidelines, which cover the use of red cells, are the main guidelines used in Australia. The AHMC IV Ig Criteria were issued in December 2007, and are currently under review. The promulgation of the NHMRC/ASBT Blood Components guidelines (National Health and Medical Research Council, 2001b) prompted others, including the professional Colleges and Societies, to publish complementary guidelines and tools for use by their members to achieve increased appropriate use of blood products.
FIGURE 6: PRESCRIBING BLOOD COMPONENTS: CHECKLIST FOR CLINICIANS

<table>
<thead>
<tr>
<th>Prescribing blood components: checklist for clinicians</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decisions should be based on the NHMRC/ASBT Clinical Practice Guidelines for the Use of Blood Components, taking individual patient needs into account. Before prescribing red blood cells, ask yourself the following questions.</td>
</tr>
<tr>
<td>1. What improvement in the patient’s condition am I aiming to achieve?</td>
</tr>
<tr>
<td>2. Can I minimise blood loss to reduce the patient’s need for transfusion?</td>
</tr>
<tr>
<td>3. Are there any other treatments I should give before making the decision to transfuse?</td>
</tr>
<tr>
<td>4. Have cross-matching and any other relevant tests been carried out?</td>
</tr>
<tr>
<td>5. What are the specific clinical or laboratory indications for red blood cells for this patient?</td>
</tr>
<tr>
<td>6. What are the risks of transmitting infectious agents through the available blood products?*</td>
</tr>
<tr>
<td>7. Do the benefits of transfusion outweigh the risks for this particular patient?</td>
</tr>
<tr>
<td>8. Will a trained person monitor this patient and respond immediately if any acute transfusion reactions occur?</td>
</tr>
<tr>
<td>9. Have I recorded my decision to transfuse and reasons for transfusion on the patient’s chart and any documentation used in the ordering or administering of blood components?</td>
</tr>
<tr>
<td>10. Has the patient been given a clear explanation of the potential risks and benefits of blood component therapy in his or her particular case?</td>
</tr>
</tbody>
</table>

* Source: ASBT Clinical Practice Guidelines – Appropriate Use of Red Blood Cells – October 2001 (National Health and Medical Research Council, 2001a)
The WHO Clinical Use of Blood guidelines, although promulgated a year earlier than the Australian guidelines, have a more holistic and positive approach to specifying appropriate use by focussing more on patient outcomes through a patient-centred approach than on the use of fresh blood products. At the same time, they highlight the lack of evidence for transfusion and the risks of transfusion. The NHMRC/ASBT Blood Components guidelines have a strong products focus, concentrating more on the characteristics of inappropriate use, the lack of evidence for transfusion and the risks of transfusion.

In the Australian Council of Healthcare Standards Evaluation and Quality Improvement Program (EQuIP), the third clinical standard (in EQuIP 4 Standards and Criteria of the Australian Council of Healthcare Standards) is the appropriateness of care – more at www.achs.org.au/EQuIP4review. Here ‘appropriateness’ means to provide the ‘right treatment in the right way so that the desired outcome is achieved’.

Clearly the guideline documents have provided sound guidance to clinicians about appropriate use and the risks of transfusion. The EQuIP 4 Standard provides a more recent, patient-centred definition of appropriateness of care in transfusion practice.

**Definition of ‘Appropriate Use’**

In light of the above, this report interprets appropriate use to be adherence to the WHO definition of appropriate use above. This is to be measured by:

- compliance with published clinical guidelines;
- safety and quality of patient outcomes.

The WHO Handbook on the Clinical Use of Blood takes a cautious approach in relation to blood transfusions. The Handbook says that blood transfusion can be a life-saving intervention. However, like all treatments, it may result in acute or delayed complications and carries the risk of transfusion-transmissible infections. The safety and effectiveness of transfusion depend on two key factors:

- a supply of blood and blood products that are safe, accessible at reasonable cost and adequate to meet national needs; and
- the appropriate clinical use of blood and blood products.

Further, transfusion is often unnecessary for the following reasons:

- the need for transfusion can often be avoided or minimized by the prevention or early diagnosis and treatment of anaemia and conditions that cause anaemia;
- transfusions of whole blood, red cells or plasma are often given when other treatments, such as the infusion of normal saline or other intravenous replacement fluids would be safer, less expensive and equally effective for the treatment of acute blood loss;
- patients’ transfusion requirements can often be minimized by good anaesthetic and surgical management;
- if blood is given when it is not needed, the patient receives no benefit and is exposed to unnecessary risk;
- blood is an expensive, scarce resource. Unnecessary transfusions may cause a shortage of blood products for patients in real need.
IS USE ‘APPROPRIATE’ IN AUSTRALIA?

INTRODUCTION

There is a substantial degree of evidence in the literature indicating that many transfusion practices in Australia are inappropriate in terms of non-compliance with clinical guidelines, in terms of the risks that they pose to patients or because they are unnecessary for the patient’s wellbeing. Most of the studies referenced in this section of the report relates to the transfusion of red cells, as the greatest bank of evidence exists in this area. The section, however, also provides an assessment of evidence regarding appropriate use of other blood products where evidence was available.

The authors acknowledge that much of the evidence presented in this report which concerns risks associated with the transfusion of red cells, is drawn from observational studies, rather than RCTs. There is some controversy within the sector as to the acceptability of the evidence. In this regard, the authors highlight a recently released paper by Isbister, J.P., et al. (2011) in Transfusion Medicine Reviews, where the authors remark:

*The transfusion of allogeneic red blood cells (RBCs) and other blood components is ingrained in modern medical practice. The rationale for administering transfusions is based on key assumptions that efficacy is established and risks are acceptable and minimized. Despite the cliché that, ‘the blood supply is safer than ever,’ data about risks and lack of efficacy of RBC transfusions in several clinical settings have steadily accumulated. Frequentist statisticians and clinicians demand evidence from RCTs, however, causation for the recognised serious hazards of allogeneic transfusion has never been established in this manner. On the other hand, the preponderance of evidence implicating RBC transfusions in adverse clinical outcomes ... comes from observational studies, and a broad and critical analysis to evaluate causation is overdue.*

Isbister, J.P., et al. go on to point out that because of the already recognised serious hazards of allogeneic transfusion, the Precautionary Principle and ongoing evidence of inappropriate blood transfusion, causation, not the demand for RCTs should be what drives clinicians and researchers, including those that develop clinical practice guidelines for transfusion. Moreover, the challenge of establishing causation between transfusion and adverse outcomes, in the absence of or while awaiting evidence from large well-designed and conducted RCTs, is a central theme of their review. (The article contains more justification for the applicability of observational studies for guiding review of current transfusion practice. More details of this study are provided at Appendix 5.)

The next section makes an assessment of the appropriateness of use of blood and blood products in Australia, against the definition outlined above. That is, evidence is considered regarding:

- adherence to relevant clinical guidelines;
- the safety and quality of patient care as a result of transfusion practice.

DOES TRANSFUSION PRACTICE ADHERE TO CURRENT CLINICAL GUIDELINES?

Studies from both Australia and overseas indicate there is a significant gap between what is known from the best available research and what actually happens in clinical practice, including in transfusion practice. This section of the report looks at the evidence in relation to adherence in Australia and overseas to the various guidelines for clinical practice, particularly for the use of blood and blood products.

In Australia, the coverage of clinical guidelines is not comprehensive across all blood products. The relevant clinical guidelines for the administration of blood components are the NHMRC/ASBT Blood Components guidelines. Use of IVig is governed by the IVig Criteria. There are no specific national
clinical guidelines for the general use of Prothrombinex-VF. However, there are the Consensus guidelines for warfarin therapy which were issued in 2000 (Gallus, 2000) followed by a Position Statement: warfarin reversal: consensus guidelines, on behalf of the ASTH in 2004 (Baker, 2004). The Approved Product Information – Prothrombinex-VF also provides some guidance on use of the product (CSL Group, 2010). Albumin use is not subject to any clearly identifiable guidelines. However a number of recent studies have concerned its use in particular circumstances, as will be discussed below.

In general, the following discussion shows that there is evidence that a significant amount of red cell use in Australia contravenes the current guidelines, especially in relation to its use for iron deficiency anaemia. In terms of a measure against current guidelines, the level of IVig used inappropriately is very small. No other evidence exists concerning the appropriateness of use of the other blood products in focus in this report.

The reasons why adherence to clinical guidelines can falter are discussed later in this section.

Red cells

The NHMRC/ASBT Blood Components guidelines refer to studies estimating that between 16-50 per cent of red cell transfusions in Australia may be inappropriate (National Health and Medical Research Council, 2001b). It should be noted that these guidelines are being extensively reviewed and redeveloped (p137 below). A 2005 report referred to ‘a failure of contemporary Australian transfusion practices to align with recommended best practice.’ (Boyce, 2005) Other studies continue to show that, despite published guidelines, wide variations in transfusion practice exist between countries, institutions and between individual clinicians within the same institution (Bateman, 2008; Gombotz, 2007; Hutton, 2005; Karkouti, 2007; Rao, 2008; Shehata 2007; Snyder-Ramos 2008).

Most published guidelines, (Audet, 1992; Nuttall, 2006; Ferraris, 2007; Simon, 1998) including the NHMRC/ASBT Blood Components guidelines now recommend a transfusion trigger of around less than 60 to less than 70 g/L for haemodynamically stable patients. They also note that lower thresholds may be acceptable in some patients who are asymptomatic and/or where other specific therapy is available. Transfusing a patient with a Hb level greater than 70g/L may be appropriate if there is evidence of ischaemia, ongoing blood loss and/or other risk factors, however, the guidelines unanimously maintain that transfusion in patients with Hb levels greater than 100 g/L is not indicated.

The NSW CEC (Clinical Excellence Commission, Undated), through its Blood Watch teams conducted a comprehensive red cell audit within its major facilities. The combined audits included 323 transfusion episodes. Of these, 4 per cent of patients received red blood cell transfusion with Hbs over 100g/L, which is outside the NHMRC/ASBT Blood Components guidelines. 95 per cent of patients had post-operative red cell transfusion with Hb above 70g/L and, of those, 83 per cent received a transfusion without evidence in the medical record of clinical indication for transfusion.

An audit of WA transfusion practice in 2008 (Western Australian Department of Health, 2008) demonstrated that 53 per cent of transfusions in Perth metropolitan hospitals were administered to patients with a baseline Hb greater than 80g/L and 8 per cent to patients with Hb greater than 100g/L. A mean of 2.4 red cell units transfused and a mean post-transfusion Hb rise of 20 g/L suggest that the majority of transfusions were in non-bleeding patients. A total of 85 per cent of all transfusions resulted in post-transfusion Hb levels of more than 90 g/L.

Victoria’s BeST program (Victorian Government Department of Health, 2006a) analysed data from 20 Victorian and Tasmanian hospitals (15 public hospitals and five private hospitals) that performed relatively high numbers of elective orthopaedic surgery in 2005-06. The audit found blood conservation strategies were currently not commonly applied in elective orthopaedic surgery. Such strategies were relatively more commonly used in the private hospital sector. Intra-operative salvage of blood or post-operative salvage of blood was performed in 10 per cent of patients. Use of Cell Salvage was reported
by 11 of 20 participating hospitals (six of 15 public hospitals and all five private hospitals). There was a wide variation in the proportion of transfused patients within each procedural category between participating hospitals (transfusion rates reported at between 0 per cent and 100 per cent in each procedure category). Overall, in 79 per cent of transfusion episodes the ‘clinical triggers’ for transfusion were assessed as conforming to best practice guidelines. ‘Over-transfusion’ was deemed to have occurred in 12 per cent of patients and 10 per cent of transfusion episodes. Most instances of ‘over-transfusion’ occurred intra-operatively within a relatively small number of contributing hospitals.

**Platelets and fresh frozen plasma**

The Victorian Department of Human Services published a clinical audit of platelet use (Victorian Government Department of Health, 2008) in 25 Victorian and Tasmanian hospitals (19 public hospitals and 6 private hospitals) in 2007. Of 594 transfusions, 136 or 23 per cent did not align with the NHMRC/ASBT Blood Components guidelines. There was a large variation in range of alignment from hospital to hospital (33 to 100 per cent alignment). The most common reason for platelet transfusion was prophylaxis for bone marrow failure (54 per cent of aligned platelet transfusions) followed by prophylaxis for surgical or invasive procedures (16 per cent of aligned platelet transfusions). The audit highlighted a lack of adherence to documentation of indications for transfusion and reporting platelet counts. Of the 594 transfusions analysed, only 48 per cent complied with the clinical guidelines in these areas.

The NHMRC/ASBT Blood Components guidelines published in 2001 (National Health and Medical Research Council, 2001b) included recommendations for the appropriate use of FFP, as follows:

- patients with significant coagulopathy because of acquired deficiencies of multiple coagulation factors in whom serious bleeding has occurred or for whom emergency surgery or other procedures are planned;
- treatment of thrombotic thrombocytopenic purpura; and
- treatment of acquired single factor deficiencies where a product containing the specific factor is ineffective or unavailable.

An audit of FFP usage in Victoria and Tasmania conducted in 2005-06 (Victorian Government Department of Health, 2006b) showed that 66 per cent of the transfusion episodes were consistent with the proscribed clinical practice guidelines and were therefore considered “appropriate”.

Inappropriate FFP usage occurred when there was active bleeding, emergency surgery or preparation for major surgery or invasive procedures. In addition, those procedures in which no coagulation tests were determined were categorised as inappropriate. The dosage was deemed appropriate in 42 per cent of the cases examined, although of the remaining 58 per cent of cases, 23 per cent were classified as undetermined because of the absence of a recorded body weight. Dosage was deemed “effective” in 30 per cent of the cases, but in 35 per cent of the “ineffective” cases “the absence of a record of post-translational clinical or laboratory outcomes resulted in effectiveness being categorised as undetermined”.

In a similar audit conducted in South Australia (Hui, 2005) “more than 72 per cent FFP was “prescribed in an appropriate manner and the majority were monitored adequately”. In this case “reversal of warfarin ... emerged as the major indication to transfuse FFP (34 per cent)”.

The Victorian Department of Human Services published a clinical audit of FFP (Victorian Government Department of Health, 2009) in 25 hospitals (21 public and four private hospitals) in Victoria, Tasmania and the ACT in 2008. The use of FFP consistent with the clinical guidelines changed little from a previous audit in 2005 (66 per cent in 2005 versus 68 per cent in 2008). However some individual hospitals
showed considerable variance between the two audits. The majority (79 per cent) of aligned transfusions in the audit sample occurred for patients experiencing abnormal coagulation with active blood loss and/or an invasive procedure or surgery. Non-aligned FFP transfusions were most commonly prescribed to patients for bleeding and/or haemorrhage, as well as for plasma exchange. For aligned transfusion episodes, only 17 per cent were considered dose appropriate, 40 per cent were considered not dose appropriate and 43 per cent were ‘undetermined’ largely due to lack of data.

**Intravenous Immunoglobulin (IVIg)**

The IVIg Criteria are to be used by clinicians for the use of government subsidised IVIg, and are based on the strength of the evidence supporting the use of IVIg for certain clinical conditions. Within the IVIg Criteria: Section 5 conditions (conditions for which IVIg has an established therapeutic role) generally have a strong evidence base, and represent 83 per cent of product use; Section 6 conditions (Conditions for which IVIg has an emerging therapeutic role) have a lesser evidence base, and represent 14 per cent of usage; Section 7 conditions (conditions for which IVIg use is in exceptional circumstances only) have a poorer evidence base and IVIg is issued under Section 7 only in individual exceptional circumstances to treat mostly rare and debilitating conditions (these conditions represent approximately 2 per cent of product use). Subsidised IVIg is not available for Section 8 conditions. The IVIg Criteria are currently under review, including a literature review and an IVIg cost-effectiveness review.

The Blood Service Transfusion Medicine Team (TMT), in a ‘gatekeeper’ role, provides a consultancy service and issues IVIg based on clinical need. The TMT approves use of IVIg against the IVIg Criteria.

In Australia, there has been strong growth in IVIg supply to patients with a range of neurological, immunological and haematological indications, with an overall growth of 23.4 per cent between 2007-08 and 2009-10, and a Compound Annual Growth Rate of 7.3 per cent in this period.

Growth rates have differed between jurisdictions over this period. Queensland has experienced the highest rate of growth in absolute volumes of IVIg, with volume 108 per cent higher in 2009-10 over 2004-05. This was well above the national average of 81 per cent growth for the period. In fact, Queensland was the only jurisdiction with an aggregate growth rate above the national average. The next highest rate of growth was experienced in NSW, at 77 per cent over the 2004-05 base. Growth in Victoria was also relatively high at 69 per cent. The pattern in WA differs markedly from its fellow large States, with growth of 21 per cent in absolute volume of IVIg issued over the same period.

The use of IVIg in Australian jurisdictions varies considerably on a per population basis despite the IVIg Criteria being in place and despite the Blood Service playing a national gatekeeping role in accordance with the IVIg Criteria. In 2009-10, the national average usage of IVIg was 121.33 grams per 1000 population. Tasmania has consistently been the highest use jurisdiction of IVIg over the period 2003-04 to 2009-10. Use per 1000 population in 2009-10 was 156.83 grams in 2009-10. Queensland recorded the next highest use of IVIg per 1000 population in 2009-10, at 145.25 grams, which is also significantly above the national average. Queensland’s use of IVIg on a per population basis has consistently been above the national average over the period.

The use of IVIg in comparable countries overseas in 2010 (CSL Limited Presentation to Sapere Research Group), per 1000 head of population, is expected to be as follows:

- **USA** – around 127 grams;
- **Canada** – around 112 grams;
- **France** – around 73 grams;
- **UK** – around 50 grams;
• Germany – around 32 grams.

The use of IVIg in Australian jurisdictions varies considerably on a per population basis despite the IVIg Criteria being in place and despite the Blood Service playing a national gatekeeping role in accordance with the IVIg Criteria.

Given the increasing demand for IVIg, the Blood Service has undertaken a project to model and forecast future IVIg demand out to 2020 in order to shed light on the possible implications that an increasing demand for IVIg has on future plasma supply requirements. Based on the analysis conducted, the Blood Service currently estimates that IVIg demand will grow to 11,158 kg by 2019-20, which will require the supply of 1,430 tonnes of plasma for fractionation. This IVIg forecast takes the ageing of the Australian population into account, but does not incorporate future projections in relation to the possible use of IVIg to treat AD. Such estimates are useful in that they enable considerations around the future sustainability of the supply of IVIg in Australia.

The study by Pendergrast, J. M., et al. in Canada in times of shortages of IVIg seems to indicate that it is actual clinical practice in a country that drives use (with only a small effect from availability of product), with stricter adherence to evidence being the one possible way to get IVIg use to be more appropriate. More details of this study are included in Appendix 5.

**Prothrombinex-VF**

As noted above, there are no specific national clinical guidelines for the general use of Prothrombinex-VF. However, there are the Consensus guidelines for warfarin therapy which were issued in 2000 (Gallus, 2000) followed by a Position Statement: warfarin reversal: consensus guidelines, on behalf of the ASTH in 2004 (Baker, 2004). The Approved Product Information – Prothrombinex-VF also provides some guidance on use of the product (CSL Group, 2010).

The Warfarin Reversal Guidelines (Baker, 2004) were published by the Warfarin Reversal Consensus Group; these guidelines were promoted by CSL and the Blood Service, in association with the Australian Society for Thrombosis and Haemostasis (ASTH). The Warfarin Reversal Consensus Group said that, for most warfarin indications, the target maintenance international normalised ratio (INR) is 2-3. Risk factors for bleeding complications with warfarin use include age, history of past bleeding and specific co morbid conditions. To reverse the effects of warfarin, vitamin K₁ can be given. Immediate reversal is achieved with a prothrombin complex concentrate (PCC) and FFP. Vitamin K₁ is essential for sustaining the reversal achieved by PCC and FFP. When oral vitamin K₁ is used for warfarin reversal, the injectable formulation of vitamin K₁ is preferable to tablets because of its flexible dosing; this formulation can be given orally or injected. To temporarily reverse the effect of warfarin when there is a need to continue warfarin therapy, vitamin K₁ should be given in a dose that will quickly lower the INR to a safe, but not sub-therapeutic, range and will not cause resistance once warfarin is reinstated.

Prothrombinex-HT (now Prothrombinex-VF) is the only PCC approved in Australia and New Zealand for warfarin reversal. It contains factors II, IX and X, and low levels of Factor VII. FFP should be added to Prothrombinex-HT as a source of Factor VII when used for warfarin reversal. Simple dental or dermatological procedures may not require interruption to warfarin therapy. If necessary, warfarin therapy can be withheld 5 days before elective surgery, when the INR usually falls to below 1.5 and surgery can be conducted safely. Bridging anticoagulation therapy for patients at high risk for thromboembolism should be undertaken in consultation with the relevant experts. The management arrangements for this product under the National Blood Arrangements do not require authorisation on a named-patient basis. However, it is understood that the practice of the Blood Service is to require specific-patient information for Prothrombinex-VF release in some cases. Most large hospitals and large private pathology providers keep stocks of it in standard inventory.
Since January 2005 there have been some concerns raised about some of the use of Prothrombinex-VF, but it does not appear as though inappropriate use is common or widespread. For example, in connection with the devolution of the blood budget in NSW, the Blood Service said (Australian Red Cross Blood Service, 2010a), ‘Clinicians may be influenced to prescribe less expensive products where more expensive products may be more clinically appropriate, leading to suboptimal patient care and increased risk. Example is: Use of Fresh Frozen Plasma instead of Prothrombinex-VF for warfarin reversal’.

There is no doubt that use of Prothrombinex-VF has risen since the promulgation of the Consensus Guidelines, but there is no real evidence than any of the clinical use associated with that increase in use is inappropriate

**Recombinant Factor VIIa (rFVIIa)**

Clinical guidelines for the appropriate use of rFVIIa could not be identified for this report. The product is indicated (and approved) for the control of bleeding in patients with haemophilia with inhibitors and for patients with rare bleeding disorders (National Blood Authority, 2006). Novo Nordisk, the supplier must only accept an Order from an AR (as approved by the NBA under its supply Deed (contract) with Novo Nordisk. ARs for the Product are any hospital, where the Product is ordered specifically for the approved indications in the Deed and any other hospitals approved by the NBA, as notified by the NBA to Novo Nordisk from time to time.

Under the National Blood Agreement the use of rFVIIa (NovoSeven) (National Blood Authority, 2010) is funded to control bleeding episodes and to prevent excessive bleeding associated with surgery in patients who have:

- inhibitors to clotting factors VIII or IX; or
- congenital FVII deficiency; or
- Glanzmann’s Thrombasthenia, for whom platelet transfusion therapy is unsuitable.

Under the NBA arrangements, rFVIIa is not officially authorised on a named patient basis but does require confirmation of use for appropriate purpose (Ibid.). However, because of the cost of the product, some jurisdictions have authorisation arrangements, which do require this, to allow health departments to keep track of product issued under NBA funding.

In June 2006 the JBC was advised that there had been three cases of rare bleeding disorders requiring rFVIIa since the introduction of the new national blood arrangements. JBC agreed that the current AHMC approved policy on rFVIIa usage be slightly reworded to incorporate this very minor use. Members endorsed the following policy statement on the use of rFVIIa (Ibid.):

> That rFVIIa paid for under the National Supply Arrangement is able to be used for patients with haemophilia (including Acquired Haemophilia) with inhibitors, and patients with rare bleeding disorders like von Willebrand Disorder (with inhibitors), Glanzmann Thrombasthenia and FVII deficiency. Treatment may be for emergency or major bleeds, including haemorrhaging due to surgical procedures and for prophylaxis with planned surgery.

At that time, the JBC also agreed that the NBA re-negotiate the Novo Nordisk Deed to include the approved indication for rFVIIa as:

> The product is indicated for the control of bleeding in patients with haemophilia with inhibitors and for patients with rare bleeding disorders.
DOES CURRENT TRANSFUSION PRACTICE PROMOTE SAFETY AND QUALITY OF PATIENT CARE?

There is much evidence that calls into question the effect of blood products in terms of the safety and quality of patient outcomes. In general, this evidence relates most strongly to red cells and other blood components. However, there are also recent studies concerning safety and quality in the use of albumin. In this sense, there may be a significant degree of use of these products, which could be called inappropriate.

There was no evidence suggesting that other blood products present unacceptable risks to patient safety and quality of care.

The evidence presented in this section of the report comes from Australia and overseas.

The evidence base for use of red cells

Inappropriate and avoidable transfusions of allogeneic blood components continue despite an expanding and compelling literature suggesting that not only is there a lack of evidence for indications and benefit from transfusions, but concern that transfusion may be the cause of harm to patients. This section of the report presents a synopsis of Australian and overseas studies which highlight risks to patients in terms of increased mortality and morbidity from allogeneic blood transfusions. It presents evidence that some of these risks appear to be dose-dependent and some could also be associated with the age of red cells at the time of transfusion.

In addition to a burgeoning literature highlighting such risks, there exists by comparison very little evidence supporting the efficacy of the use of red cell transfusion, particularly in relation to treatment of iron deficiency anaemia. This fact has most recently been recognised in the NBA PBM Draft Perioperative Guidelines: Module 2 - Perioperative (Pre-Public Consultation Draft version) (National Blood Authority 2011c)\(^\text{10}\).

The NBA PBM Draft Perioperative Guidelines are based soundly on the evidence gathered in a systematic literature review, which was conducted to answer a set of research questions, and the review and analysis of that evidence which is presented in four Technical Reports (National Blood Authority 2011a; 2011b; 2011d; 2011e). The NHMRC definitions of evidence grades were employed to underpin the Recommendations for clinical practice and the Practice Points in the NBA PBM Draft Perioperative Guidelines. The NHMRC definitions of evidence grades for recommendations (National Health and Medical Research Council, 2009) are as follows:

- **Grade A** – Body of evidence can be trusted to guide practice
- **Grade B** – Body of evidence can be trusted to guide practice in most situations
- **Grade C** – Body of evidence provides some support for recommendation(s) but care should be taken in its application
- **Grade D** – Body of evidence is weak and recommendations must be applied with caution.

These evidence grades for recommendations are in turn based on the conventional levels of evidence used by the NHMRC, that is, Levels I, II, III-1, III-2, III-3 and IV (Ibid.). The evidence in the four NBA Perioperative PBM Technical Reports is then analysed and presented in accordance with the ‘NHMRC Evidence Statement’ approach for guidelines developers (Ibid.). In this approach the key research questions are examined, against five headings: evidence base; consistency; clinical impact; ability to be generalised; and applicability, to come up with a critical appraisal of individual studies included in the

\(^{10}\) Referred to in this report also as the NBA PBM Draft Perioperative Guidelines.
body of evidence compiled through the systematic literature review. For example, if ‘evidence base’ is the consideration for a particular research question, then the grades for recommendations, which can be derived, are:

- **Grade A** – One or more Level I studies with a low risk of bias or several level II studies with a low risk of bias
- **Grade B** – One or two Level II studies with a low risk of bias or Systematic Review/several Level III studies with a low risk of bias
- **Grade C** – One or two Level III studies with a low risk of bias or Level I or II studies with a moderate risk of bias
- **Grade D** – Level IV studies or Level I to III studies/Systematic Reviews with a high risk of bias.

In the NBA PBM Draft Perioperative Guidelines these levels of evidence and grades are then combined into:

- evidence-based recommendations, where the NBA reference group considered there was sufficient evidence\(^{11}\) available from the systematic literature review to support the recommendation; and

- ‘practice points’, where the NBA reference group considered there was insufficient evidence available from the systematic literature review, but where clinicians required guidance to ensure good clinical practice.

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\(^{11}\) The grade of evidence and the relevant section of the guidelines document are cited.
Examples are provided below:

Recommendations (National Blood Authority 2011c)

<table>
<thead>
<tr>
<th>No.</th>
<th>Grade</th>
<th>Recommendation</th>
<th>Relevant section of document</th>
</tr>
</thead>
<tbody>
<tr>
<td>R1</td>
<td>C</td>
<td>Health-care services should establish a multidisciplinary, multimodal perioperative patient blood management program (Grade C). This should include perioperative optimisation of red cell mass and coagulation status, meticulous attention to surgical haemostasis and minimisation of perioperative blood loss.</td>
<td>3.1</td>
</tr>
<tr>
<td>R2</td>
<td>B</td>
<td>In patients undergoing cardiac surgery, preoperative anaemia should be identified, evaluated and managed to minimise RBC transfusion, which is associated with an increased risk of morbidity (Grade B), mortality, ICU length of stay (LOS) and LOS (Grade C).</td>
<td>3.3</td>
</tr>
</tbody>
</table>

Practice Points (National Blood Authority 2011c)

<table>
<thead>
<tr>
<th>No.</th>
<th>Practice Point</th>
<th>Relevant section of document</th>
</tr>
</thead>
<tbody>
<tr>
<td>PP1</td>
<td>To implement the above recommendations, a multidisciplinary, multimodal perioperative patient blood management program is required. All surgical patients should be evaluated as early as possible to coordinate scheduling of surgery with optimisation of the patient’s Hb and iron stores.</td>
<td>3.3</td>
</tr>
<tr>
<td>PP2</td>
<td>RBC transfusion should not be dictated by a Hb ‘trigger’ alone, but should be based on an assessment of the patient’s clinical status. In the absence of acute myocardial or cerebrovascular ischaemia, postoperative transfusion is inappropriate for patients with a Hb level of &gt;70 g/L.</td>
<td>3.3</td>
</tr>
</tbody>
</table>

These NBA evidence-based PBM Perioperative guidelines take a step in addressing concerns regarding the lack of evidence for benefit of transfusion of blood components and that the current evidence is an imperfect guide to transfusion decisions. These concerns were raised, for example, in the 2001 NHMRC/ASBT Blood Components guidelines (National Health and Medical Research Council, 2001b), by the Society of Thoracic Surgeons and the Society of Cardiovascular Anaesthesiologists (SCA) (Ferraris, 2007) and Morton, J., et al. (2010).

The NBA evidence-based PBM Perioperative guidelines also introduce a paradigm shift in the practice of blood component transfusion, which has been urged by others in the sector. For example, J.P. Isbister (2007) in 2007, focused squarely on patient benefit, not on when, where and how to use certain blood and blood products.

However, in relation to ‘what’ evidence is collated and ‘how’ that evidence is weighted and rated to support recommendations for clinical practice, the NBA evidence-based PBM Perioperative guidelines, and, presumably, the other guidelines to follow, use the traditional approach to considering evidence. This is the approach required by the NHMRC. This traditional approach to the consideration of evidence to support transfusion has at its heart the principle that the evidence obtained from RCTs is the highest level of evidence (that is, Level I) to support practice. However, RCTs are unlikely to be appropriate or ethical in most transfusion settings. It must be said however, that the ‘practice points’ (where the NBA reference group considered there was insufficient evidence available from the systematic literature review, but where clinicians required guidance to ensure good clinical practice) in the NBA evidence-
based PBM Perioperative guidelines take a pragmatic approach to improving the appropriateness of transfusions where insufficient (traditional) evidence is available.

SAFETY AND QUALITY OF BLOOD COMPONENT TRANSFUSIONS

Although blood transfusion may be life-saving in the setting of critical bleeding, studies show it is also associated with significant risk (Sihler, 2009; 2010). The risk of known infectious agents such as human immunodeficiency virus (HIV), hepatitis C virus (HCV) and hepatitis B virus (HBV) has been reduced to very low levels, but the blood supply remains vulnerable to emerging infectious agents (Blajchman, 2006; Stramer, 2009; Wallis, 2009). Transfusion associated circulatory overload (TACO), transfusion-related acute lung injury (TRALI) (Gajic, 2007; Marik, 2008a) wrong blood component transfused, acute transfusion reactions and bacterial contamination of blood remain the leading causes of transfusion-related death and major morbidity in High Human Development Index (HLDI) countries.

Of increasing concern is the growing body of literature suggesting that transfusion per se is a risk factor for increased mortality, ICU admission, ICU and hospital LOS and morbidity including increased incidence of infection, septicaemia, ischaemic events (including stroke, myocardial infarction and renal impairment/failure), thromboembolism, multisystem organ failure, systemic inflammatory response syndrome and acute respiratory distress syndrome (ARDS) (Bateman, 2008; Bernard, 2009; Chaiwat, 2009; Corwin, 2004; Croce, 2005; Dunne, 2002; Engoren, 2008; Kim, 2007; Khorana, 2008; Kneyber, 2007; Koch, 2006a; 2006b; 2008; Leal-Noval, 2001; Malone, 2003; Marik, 2008b; Murphy, 2007; Rao, 2004; Shander, 2009; Surgenor, 2006; Taylor, 2006; Thomson, 2009; Vamvakas, 2010; Yang, 2005).

The Senior Vice President, Health Affairs and President, UF Shands Health System, in On the Same Page: ‘Saving blood, saving money, saving lives’, 1 October 2010 (Guzick, 2010) wrote to all his staff about the risks, costs, adverse events and benefits associated with transfusion. The article is compelling in relation to the need to change transfusion practice for the benefit of patients and health institutions. Accordingly, it is reproduced at Appendix 5 in full.

In a recent review Tinmouth et al. (2006) concluded ‘we have witnessed a ’dramatic paradigm shift’ whereby red blood cell transfusions, once regarded as ‘one of the great advances in modern medicine,’ are now considered harmful in some clinical situations.’ An editorial (Jackson, 2006) on the subject cautioned: ‘despite the robust evidence questioning its efficacy and safety, defiant liberalism of PRBC transfusion remains. If, like regimented headmasters or detached nihilists, we fail to objectively consider and reject the negative consequences of maintaining a once-accepted but clearly antiquated paradigm, we do so to the profound detriment of patients.’

In a clinical update in the Medical Journal of Australia in 2010, Saint-Ryan SP, et al. (2010) found that transfusion of red cells remains an overused treatment for iron deficiency anaemia (Grey, 2008), and that it is also expensive and potentially hazardous. In physiologically compensated patients, transfusion carries unnecessary risks and fails to replenish deficient iron stores. Adequate doses of oral iron can improve Hb concentrations within a few weeks, and IV iron can provide more rapid and predictable increases when clinically important. Transfusion is associated with adverse outcomes, including fluid overload (around 1 per cent of patients), and a range of immunological and infectious hazards. Hence, it should be reserved for immediate, targeted management in patients with severe anaemia compromising end-organ function (for example, angina pectoris or cardiac failure) or where iron deficiency anaemia is complicated by serious, acute ongoing bleeding. Iron therapy should always follow transfusion to replenish iron stores.

Based on an exhaustive literature search on transfusion outcomes, the Scientific Committee of the 1st ICCTO held in Phoenix, Arizona, 3-5 April 2009 stated: ‘There is a paucity of evidence for benefit and a burgeoning literature demonstrating a strong association between transfusion and adverse outcomes. Despite all available information and escalating costs of blood transfusion, practice remains essentially
unchanged. This would not be accepted or tolerated in any other field of medicine in the context of current safety and quality standards’ (Society for the Advancement of Blood Management, 2009).

In 2007 the Society of Thoracic Surgeons and the SCA joined forces to conduct an exhaustive review and produce clinical practice guidelines for perioperative blood transfusion and blood conservation (Ferraris, 2007). These societies emphasised again the lack of evidence for benefit of transfusion and that the current evidence is an imperfect guide to transfusion decisions. They suggest a postoperative transfusion trigger of a Hb value of less than 70 g/L. They also suggested that a higher Hb trigger may ‘not be unreasonable’ in certain patients with risk factors (for example, patients with critical non-cardiac end-organ ischemia). However, they qualify this recommendation stating that there is a need for more evidence to support it. The principle recommendation of this expert group was that clinicians employ all available blood conservation methods in patients at risk of blood transfusion. Two recent reviews by Vincent et al. and Klein et al. highlight the limited evidence for benefit in many clinical settings (Klein, 2007; Vincent, 2007).

The objective of a very large retrospective cohort study in 2004 in the US, Morton, et al. (2010), was to assess frequency and outcomes associated with blood products transfusion. Data from the 2004 Nationwide Inpatient Sample database were used. Length of stay, postoperative infections (PI), non-infectious transfusion-related complications, in-hospital mortality, and total charges were evaluated for transfused and non-transfused cohorts. The study found patient discharges in the transfused cohort were significantly more likely to have at least one comorbidity than discharges in the non-transfused cohort (54.5 per cent compared to 47.1 per cent). Of the estimated 38.66 million discharges in the United States in 2004, 5.8 per cent (2.33 million) were associated with blood products transfusion. Average LOS was 2.5 days longer, odds of death were 1.7 times higher, and odds of infection 1.9 times higher for the transfused cohort. More details of this study are included in Appendix 5.

Despite limitations, the Morton study shows that more than 2 million hospital admissions annually are associated with a blood products transfusion and that patients remain at risk of experiencing adverse clinical outcomes. The observation that transfusion recipients experience negative outcomes independent of age, sex, co morbidities, admission type, or DRG assignment warrants further investigation to better identify the appropriateness of current transfusion triggers and to develop and implement more effective approaches to reduce the non-emergent use of blood in hospitalized patients.

TRALI and incompatibility reactions were not reported for patients identified as transfusion recipients. This finding also warrants further investigation, given that the Joint Commission and the American Association of Blood Banks have established transfusion-specific performance improvement standards, blood use reviews, and reporting requirements for suspected transfusion-related adverse events. Finally, given that transfusion-related adverse clinical and health-related quality-of-life outcomes may persist after hospital discharge, additional prospective observational studies are needed to assess the long-term health status and quality of life of transfusion recipients. In conclusion, raising provider awareness and recognition of the frequency and potential negative clinical outcomes of blood products transfusion—as an independent predictor or surrogate for blood loss—may yield significant clinical and quality-of-life benefits at the individual patient level. Equally important is the need to encourage providers to adopt strategies and techniques that are more effective at controlling inadequate surgical haemostasis and that may reduce the frequency of blood products transfusions. More details of this study are included in Appendix 5.

Understanding of the clinical usage of red cells is limited despite its importance in transfusion practice improvement and planning for blood supply requirements. Previous studies have described red cell use based upon ICD and hospital discharge codes. However, such approaches are open to misclassification. The 2010 study by P. J. Barr, et al. (2010) addressed this limitation by undertaking an epidemiological analysis of red cell use using case note review. Patient, disease and contextual factors were extracted from the medical records of a randomly selected sample of hospital patients in Northern Ireland who
received a red cell transfusion during 2005 (n = 1474). Transfused patients received a total of 3804 units (median of two units per transfusion episode). Most transfusions occurred in a medical setting (71 per cent). Patients undergoing treatment for gastrointestinal conditions were responsible for the majority of the demand (29 per cent of transfusion episodes, 34 per cent of red cell units).

The presence of bleeding and abnormal tests of coagulation were associated with receiving larger transfusions (± 3 units), while patients undergoing orthopaedic surgery and those with a Hb level over 7 g/dl had the lowest risk of receiving ± 3 units in any one transfusion episode. Barr concluded that the majority of red cells are now prescribed in a medical setting. Barr concluded that with an ageing population and increasing therapeutic interventions, the demand for blood is likely to increase despite efforts to reduce usage by eliminating inappropriate transfusions through education and behaviour change. The post-transfusion target (and therefore the number of units to transfuse) for any given clinical situation as well as guidance on a ‘safe’ transfusion threshold should be considered in future guidelines.

A study conducted at a hospital in Brazil, is the first large randomized research effort among heart-surgery patients testing two blood-transfusion strategies. The study compared ordering a transfusion when the red-blood-cell count fell below 30 per cent against waiting until it was under 24 per cent. It found no significant difference in death and other major events within 30 days of surgery between an aggressive approach to transfusions and a restrictive one. In addition, patients who received a transfusion under either strategy had a 20 per cent higher risk of death or other complication from surgery than those who did not.

In two African RCTs, Holzer (1993) and Bojang (1997), children with severe malaria anaemia received either malarial treatment and whole blood transfusion or malaria treatment alone. There was no significant difference between the transfused and non-transfused groups although there were significantly more adverse events in the transfused group compared with the non-transfused group. More details of these studies are included in Appendix 5.

Apart from these two trials, RCTs in transfusion medicine have not evaluated the safety and efficacy of transfusion compared with no transfusion or with some other modality. They have been confined to comparing one transfusion strategy with another (that is a restrictive versus a liberal transfusion threshold with thresholds mostly based on a single Hb value). These studies have almost universally found no evidence for benefit from a liberal transfusion threshold. Many studies favour a restrictive policy with reduced transfusion and, in some cases, improved patient outcomes.

In a retrospective study of 1446 patients undergoing bowel surgery multivariate analysis identified perioperative red blood cell transfusion (transfused intraoperatively and up to 48 hours postoperatively), as independently associated with an increased risk of surgical site infections (SSI) (Walz, 2006). As well as the clinical implications of this study, there are possible financial implications as the authors refer to figures estimating that SSIs constitute 20 per cent of nosocomial infections (NI), which are reported to increase costs by approximately $2,000 to $4,500 per patient and extend hospital LOS by 7 to 10 days.

Taylor et al. (2006) identified transfusion being associated with an adjusted dose-dependent increased risk of NI, ICU and hospital LOS and mortality in 2085 surgical and medical ICU patients. Transfused patients were six times more likely to develop infection compared with non-transfused. The authors stated, ‘Transfused patients with a better prognosis had higher mortality rates, suggesting that transfusions may do more harm than good in ICU patients who have a reasonably good chance of survival.’ More details of this study are included in Appendix 5.

Zilberberg et al. (2007) conducted a sub-group analysis of the CRIT study (Anaemia and blood transfusion in the critically ill – Current clinical practice in the United States). They reported a strong
independent relationship between packed red blood cell transfusion and the development of ARDS in the ICU (adjusted odds ratio of 2.80). More details of this study are included in Appendix 5.

The improvement of renal allograft survival by pre-transplantation transfusions alerted the medical community to the potential detrimental effect of transfusions in patients being treated for cancer. Amato A, and Pescatori M (Amato, 2009), conducted a meta-analysis, which aimed to evaluate the role of perioperative blood transfusions (PBT) on colorectal cancer recurrence. This was accomplished by validating the results of a previously published meta-analysis (Amato 1998), and by updating it to December 2004. Amato and Pescatori concluded that the updated meta-analysis confirmed the previous findings. All analyses support the hypothesis that PBT have a detrimental effect on the recurrence of curable colorectal cancers. However, since heterogeneity was detected and conclusions on the effect of surgical technique could not be drawn, a causal relationship cannot still be claimed. Carefully restricted indications for PBT seem necessary. More details of this study are included in Appendix 5.

In a multi-centre prospective observational study of 8004 consecutive patients undergoing isolated coronary artery bypass graft (CABG) surgery the Northern New England Cardiovascular Disease Study Group (DeFoe, 2001) sought to address the question of whether the morbidity and mortality associated with haemodilution anaemia in CABG surgery with cardiopulmonary bypass is due to the anaemia or the red blood cell transfusions used to treat the anaemia. The authors conclude that haemodilution anaemia during cardiopulmonary bypass is associated with an increased risk of low-output heart failure; however, management of that anaemia with red blood cell transfusion is independently associated with an increased risk of low-output heart failure. More details of this study are included in Appendix 5.

In a prospective international multi-centre study of 5065 cardiac surgery patients, Kulier et al. (2007) found that overall, preoperative anaemia was associated with postoperative morbidity and mortality. Multiple logistic regression analysis revealed that preoperative anaemia was associated with non-cardiac but not cardiac adverse events. Cardiac adverse events were associated with a combination of preoperative anaemia and co morbidities. Red blood cell transfusion was independently associated in a dose-dependent manner with increased risk of cardiac and non-cardiac adverse events. Multivariate analysis revealed preoperative anaemia and red blood cell transfusion were independent but additive risk factors. Patients with low preoperative Hbs had higher rates of postoperative adverse events, but at the same Hb level the risks of adverse events increased with transfusion and the more units transfused the greater the incidence of adverse events.

Transfusion rates remain high in cardiac and orthopaedic surgery and differ widely across physician practices in spite of growing knowledge that allogeneic blood transfusion (ABT) is associated with a risk of PI. Very recently, and in view of the uncertainty regarding the health benefits of transfusion, the ICCTO was convened to rate the appropriateness of allogeneic red cell transfusion based on its impact on patients’ outcomes. ICCTO convened an international multidisciplinary panel of 15 experts which reviewed 494 published articles and used the RAND/UCLA Appropriateness Method to determine the appropriateness of allogeneic red cell transfusion based on its expected impact on outcomes of stable nonbleeding patients in 450 typical inpatient medical, surgical, or trauma scenarios. Panelists rated allogeneic red cell transfusion as appropriate in 53 of the scenarios (11.8 per cent), inappropriate in 267 (59.3 per cent), and uncertain in 130 (28.9 per cent). Red blood cell transfusion was most often rated appropriate (81 per cent) in scenarios featuring patients with Hb level 7.9 g/dL or less, associated comorbidities, and age older than 65 years. Red blood cell transfusion was rated inappropriate in all scenarios featuring patients with Hb level 10 g/dL or more and in 71.3 per cent of scenarios featuring patients with Hb level 8 to 9.9 g/dL. Conversely, no scenario with patient’s Hb level of 8 g/dL or more was rated as appropriate. Nearly one third of all scenarios were rated uncertain, indicating the need for more research. The observation that allogeneic red cell transfusions were rated as either inappropriate or uncertain in most scenarios in this study supports a more judicious transfusion strategy. In addition,
the large number of scenarios in which red cell transfusions were rated as uncertain can serve as a road map to identify areas in need of further investigation.

In 2006, more than 14 million units of allogeneic red blood cells were transfused in the United States alone (Whitaker, 2010). From 1997 to 2007, the hospital discharges in the United States in which patients' record indicated red cell transfusion increased from 5 per cent to 10.4 per cent, with blood transfusion becoming the most common inpatient hospital procedure (Levit, 2009). Red blood cell transfusion rates in other countries are variable but often comparably high (Cobain, 2007; Wallis, 2006; Yazer, 2007).

Although therapeutic modalities routinely undergo rigorous evaluation of their efficacy and safety before entering clinical practice, red cell transfusion has not been subjected to similar examination (Fernandes, 2001; Madjdpour, 2007; Napolitano, 2004; Vincent, 2007). In addition to the known transfusion complications (Vamvakas, 2009), a large (and increasing) number of studies indicate that red cell transfusion is associated with unfavourable general outcomes (Shander, 2009). Similarly, the available large RCTs (Carson, 2006; Hebert, 1999; 2001; Lacroix, 2007) and prospective observational studies (Corwin, 2004; Vincent, 2002) that have assessed the efficacy/effectiveness of allogeneic red cell transfusion have indicated that restricting red cell transfusions in nonhaemorrhaging patients has no significant negative effect on patient outcomes and may even improve outcomes in some populations.

Decisions to transfuse red cells are often based on unsubstantiated Hb level or haematocrit (Hct) “triggers” and are further complicated by regulatory constraints, fear of future litigation, and public expectations rather than on the clinical evidence (Vamvakas, 2004). Despite these limitations, rational red cell transfusion practices have still been sought, but in the absence of definitive answers, clinicians are often left with no option other than consensus guidelines (Napolitano, 2009).

The panel rated allogeneic red cell transfusion as inappropriate and unlikely to improve patient outcomes in most of the scenarios discussed in this study, which were based on hypothetical non–actively bleeding average (not extreme) patients with stable vital signs. These included all scenarios in which patients had an Hb level 10 g/dL or more as well as more than 70 per cent of scenarios featuring patients with an Hb level 8 to 9.9 g/dL and 6.7 per cent of scenarios with an Hb level 7.9 g/dL or less. In scenarios with an Hb level 8 to 9.9 g/dL, the main factor associated with transfusion being rated as inappropriate was absence of comorbidity. Similarly, scenarios with an Hb level 7.9 g/dL or less rated as inappropriate were predominantly concerning patients aged 64 years or younger and without comorbidity (Table 6).
TABLE 6: APPROPRIATENESS OF BLOOD TRANSFUSIONS ACCORDING TO THE PATIENT CHARACTERISTICS

<table>
<thead>
<tr>
<th>Age (y)</th>
<th>Comorbidity</th>
<th>Hb level (g/dL)</th>
<th>Inappropriate (1-3)</th>
<th>Uncertain (4-6)</th>
<th>Appropriate (7-9)</th>
<th>Median rating</th>
<th>IQR</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;65</td>
<td>Absent</td>
<td>≤7.9</td>
<td>8 (21.1%)</td>
<td>29 (76.3%)</td>
<td>1 (2.6%)</td>
<td>4 ± 1</td>
<td>2 ± 1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>≥10</td>
<td>38 (100%)</td>
<td>0</td>
<td>0</td>
<td>1 ± 0</td>
<td>0.5 ± 1</td>
</tr>
<tr>
<td></td>
<td>Present</td>
<td>≤7.9</td>
<td>1 (2.6%)</td>
<td>20 (52.6%)</td>
<td>17 (44.7%)</td>
<td>6 ± 1</td>
<td>2.5 ± 1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>≥10</td>
<td>30 (100%)</td>
<td>0</td>
<td>0</td>
<td>1 ± 0</td>
<td>1.001</td>
</tr>
<tr>
<td>≥65</td>
<td>Absent</td>
<td>≤7.9</td>
<td>1 (2.7%)</td>
<td>5 (13.5%)</td>
<td>5 (13.5%)</td>
<td>5 ± 1</td>
<td>2.5 ± 1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>≥10</td>
<td>30 (100%)</td>
<td>0</td>
<td>0</td>
<td>1 ± 0</td>
<td>1 ± 0.5</td>
</tr>
<tr>
<td></td>
<td>Present</td>
<td>≤7.9</td>
<td>0</td>
<td>0</td>
<td>3 (7.9%)</td>
<td>3 ± 1</td>
<td>2 ± 1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>≥10</td>
<td>1 (100%)</td>
<td>0</td>
<td>1 ± 0</td>
<td>1 ± 0.5</td>
<td>1.5 ± 1</td>
</tr>
</tbody>
</table>

NOTE: Median appropriateness ratings (on a scale of 1-9) and final appropriateness (1-3, inappropriate; 4-6, uncertain; and 7-9, appropriate) of the 450 scenarios according to patients’ characteristics.


The panel rated transfusions likely to improve patients’ outcomes in less than 12 per cent of the scenarios. These scenarios were concerning patients who invariably had an Hb level 7.9 g/dL or less, and most (88 per cent) had comorbidity. Clinical settings were not found to be significant determinants of the ratings; rather, patient characteristics were significant. Of the patient characteristics evaluated in this study (age, comorbidity, and Hb level), the Hb level was the most significant determinant of the panel rating. Haemoglobin level is the most commonly used parameter to make red cell transfusion decisions in the clinic and is commonly considered in transfusion indications in various red cell transfusion guidelines (Carless, 2010; Carson, 2002b). It is generally accepted that during escalating haemodilution/anaemia, oxygen consumption is not adversely affected unless tissue oxygenation becomes supply-dependent and a so-called critical Hb level concentration is reached.

Studies indicate the dismal consequences of profound anaemia (Hb levels b5-6 g/dL), as evidenced by a steep increase in mortality rate in surgical and trauma patients (Carson 1996; 1998; 2002a; Knottenbelt, 1991; Spence, 1992). However, most patients who are routinely transfused with red cells do not have (or are not at imminent risk of having) Hb levels anywhere near these critically low concentrations (Napolitano, 2004). The scenarios were constructed with the assumption that the patients were stable, not extreme cases, and not actively bleeding. Thus, even patients belonging to the Hb level 7.9 g/dL or less group are most likely to have Hb level values near the upper limit (7.9 g/dL) and not in the extremely low ranges. As such, an Hb level 7.9 g/dL or less was not necessarily rated to be an indicator of transfusion being likely to improve patients’ outcomes. In fact, only 35 per cent (53/150) of the scenarios concerning patients with Hb level 7.9 g/dL or less were rated appropriate and deemed likely to improve the outcomes based on available literature.

Nonetheless, this level is an often-cited trigger for recommending red cell transfusion in several guidelines (Carson, 2002b). Although the relentless search for transfusion Hb level triggers has driven a considerable part of red cell transfusion investigation, in this study, the Panel attempted to establish a different approach for one of the most difficult clinical decisions by focusing on the impact of red cell transfusion on patients’ outcomes. The lack of definitive information regarding the outcomes of red cell transfusions in the available literature can be inferred from the fact that the ICCTO panel rated 29 per cent of the total clinical scenarios reviewed to be of uncertain appropriateness. Scenarios rated as uncertain all occurred at Hb level values of less than 10 g/dL and were equally divided among younger and older patients. Most scenarios concerning patients with an Hb level 7.9 g/dL or less (58 per cent) were rated to be of uncertain benefit by the panel, another indicator that the commonly held thresholds
for red cell transfusion are arbitrary numbers and likely to be irrelevant to the outcomes in many patients. A similar paucity of robust outcomes data for guiding red cell transfusion policy was noted in an earlier review of transfusion thresholds (Carless, 2010). Future clinical research to determine the effectiveness of red cell transfusion in scenarios rated as uncertain in this study should be given a priority. In the absence of additional data, red cell transfusion should be withheld or given with caution in these clinical scenarios. Other important future directions include the role of patients' age and co morbidities on outcomes of red cell transfusion, given the paucity of evidence currently available regarding these factors.

The findings of the ICCTO panel suggest that clinical situations in which allogeneic red cell transfusion has demonstrated unequivocal benefit based on available data are uncommon. In the most rated scenarios, red cell transfusions are not deemed likely to improve outcomes and, in fact, may lead to harm. In a substantial number of cases, the impact of red cell transfusion on outcomes still remains uncertain and in need of further investigation. These observations, in combination with data indicating that red cell transfusion is associated with adverse events in a wide variety of clinical settings, provide a rationale for more judicious use of allogeneic red cell transfusion in many patients who are routinely transfused.

In a prospective observational study Shander, A., et al. (2009) compared the timing and incidence of ABT-associated PIs in 1,489 orthopaedic or cardiac surgery patients at nine hospitals. Of 455 cardiovascular and 1,034 orthopaedic surgery patients, 415 (55.6 per cent of the cardiovascular patients and 15.7 per cent of the orthopaedic patients) were given ABT. The overall rate of PI during hospitalization was 5.8 per cent. The relative risk of PI was 3.6-fold greater after ABT (50 patients; 12.1 per cent) than in patients not having ABT (36 patients; 3.4 per cent; 95 per cent confidence interval 2.4, 5.4; p=0.001). Postoperative infections appeared both during hospitalization (n=86) and within four weeks after discharge (n=81). Shander, A., et al. concluded that patients should be followed for as long as four weeks after discharge to determine the true incidence and risk of ABT-associated post operative infection.

Transfusion practices in hospitalised patients are being re-evaluated, in part due to studies indicating adverse effects in patients receiving large quantities of stored blood. Concomitant with this re-examination have been reports showing variability in the use of specific blood components. Rogers (2009) assessed hospital variation in blood use and outcomes in cardiac surgery patients. They concluded that allogeneic blood transfusion was associated with an increased risk of infection at multiple sites, suggesting a system-wide immune response. Hospital variation in transfusion practices after CABG was considerable indicating that quality efforts may be able to influence practice and improve outcomes. More details of this study are included in Appendix 5.

Wu (2001) assessed the benefit of transfusion in anaemic elderly patients with myocardial infarction by analysing a United States Medicare/Medicaid database of 234,769 patients. Univariate analysis demonstrated that transfusion was associated with decreased 30-day mortality in patients admitted with a Hb value less than or equal to 100 g/L, and a trend toward improved survival up to a Hb value of 110 g/L. However, patients transfused with a Hb value greater than 110 g/L had an increased mortality. No multivariate or propensity score matching was performed and the less than 100 g/dL group had twice the number of do-not-resuscitate (DNR) orders, more diabetes and fewer aggressive cardiology and cardiac surgery interventions compared with the higher Hb groups, resulting in considerable debate over the relevance of the findings of this study. More details of this study are included in Appendix 5.

A study subsequent to Wu (2001) of patients with myocardial infarction came to a different conclusion. Rao (2004) analysed data from three large international RCTs involving 24,111 patients with acute coronary syndrome. After multivariate and propensity analysis, adjusting for timing of events, bleeding, type of infarction, nadir Hb and procedure, blood transfusion was associated with a 3.94 times increased risk for 30-day mortality. When examined by Hb levels, the investigators found an association between
transfusion and increased 30-day mortality at a mean Hb >greater than 83 g/L. The adjusted increased hazard (odds ratio) for death was 168.64 for a mean Hb level of 100 g/L and 291.64 for mean nadir Hb of 117 g/L. They found no association between transfusion and increased mortality and, conversely, no benefit in patients with a mean Hb less than 83 g/L. More details of this study are included in Appendix 5.

Others have sought to evaluate the effects of anaemia and transfusion on tissue or organ hypoxia by looking at their effects on renal function. Swaminathan and colleagues from Duke University examined renal failure in relationship to the lowest Hct level on bypass (Swaminathan, 2003). They found a direct correlation between the lowest Hct level and postoperative rise in serum creatinine value after heart surgery. However, transfusion did not mitigate this adverse outcome, rather transfusion worsened renal function. Habib and colleagues (Habib, 2005), similarly found that in 1700 patients undergoing coronary artery bypass surgery low Hct level was an accurate predictor of which patients would experience adverse renal function. However the use of transfusion made it worse.

A study, led by Elliott Bennett-Guerrero (2010), a researcher at Duke University’s Duke Clinical Research Institute, found wide variation in transfusion practices at 798 U.S. hospitals, involving 100,000 people receiving coronary-artery bypass surgery in 2008. Some hospitals gave transfusions to fewer than 10 per cent of their patients, while at others transfusion rates topped 90 per cent. Researchers found that only about 20 per cent of the variation was explained by how sick the patients were. They also found no link between a hospital’s use of transfusions and death rates.

A recent editorial in Critical Care Medicine referred to “the burgeoning literature relentlessly establishing the deleterious effects of blood transfusion in the critically ill.” (Jackson, 2005) Numerous studies have demonstrated a strong association between allogeneic transfusion and adverse outcomes including increased short- mid- and long-term mortality, morbidity, ICU admission, and ICU and hospital LOS (Croce, 2005; Dunne, 2004; Engoren, 2002; Kneyber, 2007; Koch, 2006a; 2006c; 2006d; Kuduvalli, 2005; Malone, 2003; Rogers, 2006; Taylor, 2006; Yamada, 2005).

These studies are retrospective and prospective observational studies and thus, individually, need to be interpreted with caution as there may be unknown confounders not identified by the statistical analysis. However, in recent times the value of large observational studies has been acknowledged as an important tool in identifying safety issues.

Vincent et al. (2002) in an international epidemiologic prospective observational trial of 3534 patients from 146 European ICUs found that the risk of death was increased 33 per cent in transfused patients compared with propensity score matched patients not transfused (28-day mortality 22.7 per cent compared with 17.1 per cent; P less than 0.02). Transfused had higher ICU mortality (18.5 per cent compared with 10.1 per cent; P less than 0.001) and overall mortality (29.0 compared with 14.9 per cent; P less than 0.001) compared with non-transfused patients. The investigators also found that transfused patients had an increased length of ICU stay (7.2 days compared with 2.6 days) and a significant increase in diminished organ function.

Malone et al. (2003) in a trauma registry database study prospectively collected data on 15,534 patients admitted to a Level I Trauma Centre over a three-year period. Patients were stratified by age, gender, race, Glasgow Coma Scale (GCS) score, and Injury Severity Score (ISS). After controlling for confounding variables (ISS, GCS score, age, race) and all shock variables (lactate, base deficit, and shock index) blood transfusion was a strong independent predictor of mortality, ICU admission, ICU LOS and hospital LOS. Transfused patients were almost three times more likely to die and greater than three times more likely to be admitted to the ICU. Linear regression analysis demonstrated that patients who received blood within the first 24 hours spent greater than four more days in the ICU than non-transfused and greater than six more hospital days than non-transfused. The investigators also identified a dose-response
relationship with increased mortality. Of interest, admission anaemia was identified as an independent predictor of ICU admission, ICU LOS, and hospital LOS, but not mortality.

In an effort to minimise the confounding contribution of injury and shock to outcome, Croce (2005) evaluated the association between delayed transfusion and serious respiratory complications in a cohort of ICU patients with less severe blunt trauma who received no transfusion within the initial 48 hours after admission. They found blood transfusion was still an independent predictor of serious adverse outcome. The authors concluded, “This study demonstrates that transfusions are not innocuous and that aggressive pursuit of transfusion substitutes is warranted.” More details of this study are included in Appendix 5.

Dunne (2004) in a study of 9539 trauma patients found that blood transfusion within the first 24 hours was an independent predictor of systemic inflammatory response syndrome (SIRS) as well as mortality, ICU admission, and ICU LOS. Patients who received blood transfusion in the first 24 hours after trauma had a significantly increased risk of SIRS compared to those not transfused. More details of this study are included in Appendix 5.

Engoren (2002) in a prospective observational cohort study of 1915 patients undergoing CABG surgery used multivariate analysis and propensity score matching to compare transfused versus non-transfused patients. Patients were followed up for five years. Transfusion was associated with a significantly increased early and late (5-year) mortality. After adjusting for co morbidities and other factors, transfusion was associated with a 70 per cent increase in mortality.

Two large observational cohort studies (11,963 and 10,289 patients) conducted by the Cleveland Clinic Foundation found that, after adjustment for multiple risk factors, perioperative red blood cell transfusion was associated with a significantly increased early and late hazard for death (p less than 0.0001) in patients undergoing isolated CABG surgery (Koch, 2006a; 2006d). The first study, looking at in-hospital morbidity and mortality, found that after adjusting for variables known to contribute to a sicker patient profile there was a dose-dependent relationship between each red blood cell unit transfused and postoperative mortality. Receiving just one unit of red cells had a 77 per cent increased adjusted odds for postoperative mortality, which escalated rapidly after 5 units. Red blood cell transfusion was also associated with a risk-adjusted increased risk for every postoperative morbid event (renal failure, prolonged ventilatory support, serious PI, cardiac complications and neurologic events).

The second study identified a dose-dependent relationship between increasing units of red cells transfused peri-operatively and an incremental decrement in mid- to long-term survival. After controlling for the confounding effects of demographics, co morbidities, operative factors and early hazard for death, survival was significantly reduced (p less than 0.0001) among transfused patients compared with non-transfused patients up to 6 months (94 per cent vs.99 per cent), at 5 years (80 per cent vs.90 per cent) and at 10 years (63 per cent vs.80 per cent). Transfusion with as little as one unit was associated with decreased 10-year survival. The authors concluded, ‘Blood conservation methods should be implemented and enforced, and more restrictive transfusion guidelines based on RCTs must be put in place to assure a more judicious use of red cells.’

Two subsequent studies by the Cleveland Clinic Group found an association between transfusion and increased risk of postoperative atrial fibrillation and a worse 6 to 12-month postoperative functional recovery. This study also identified a dose-dependent relationship, with each unit transfused being associated with incrementally poorer functional recovery. From their data they suggest that a 4-unit red blood cell transfusion has an equivalent effect on postoperative functional recovery as a PI or neurologic morbid event, and a 2-unit red blood cell transfusion has an equivalent effect to a preoperative history of chronic obstructive pulmonary disease.
Given the greater postoperative mortality rate in women compared to men following CABG surgery, Rogers and colleagues investigated whether the higher transfusion rate in women may contribute to the gender-different mortality (Rogers, 2006). They found women were 3.4 times more likely to be transfused than men and received a significantly greater number of units. Women were 1.5 times more likely to die within 100 days of surgery than men. However, when adjusted for blood transfusion, there was no longer a significant difference in the mortality between men and women – suggesting blood transfusion being a risk factor for mortality. The authors conclude that this study suggests the increased mortality in women following CABG surgery is likely due to their increased receipt of blood transfusion. More details of this study are included in Appendix 5.

For some patients, blood transfusion is a necessary and life-saving intervention, however, many transfusion medicine experts deem blood transfusion an imperfect solution to manage blood loss. Although advances in surgical and anaesthetic techniques have reduced transfusion requirements for some surgical procedures, intraoperative and early postoperative bleeding can be difficult to manage because of anatomy, tissue condition, patient factors, and, at times, surgical technique. Regardless of why it happens, the inability to achieve haemostasis or the inadequacy of rapid surgical haemostasis can contribute to prolonged intensive care time and postoperative morbidity and mortality. Not surprisingly, studies evaluating clinical outcomes among surgical patients have repeatedly reported negative clinical outcomes associated with blood transfusion including higher PI rates, non-infectious complications such as TRALI, poor postoperative functional recovery, and reduced long-term survival.

Murphy (2007) aimed to quantify associations of transfusion with clinical outcomes and cost in patients having cardiac surgery. They concluded that red blood cell transfusion in patients having cardiac surgery is strongly associated with infection and ischemic postoperative morbidity, hospital stay, increased early and late mortality, and hospital costs. More details of this study are included in Appendix 5.

Adverse effects of transfusion have also been observed in children. In a study of 295 children admitted to the paediatric ICU (PICU) the mortality rate was 16.4 per cent in the transfused compared with 2.6 per cent in the non-transfused (P less than 0.001) (Koch, 2006d). Of interest, the investigators found no association between pre-transfusion Hb levels and mortality. However, they did identify a dose-dependent relationship between the number of transfusions and increased mortality. Compared with non-transfused, transfused children had increased duration of ventilatory support (3.2 compared with 11.1 days), vaso-active agents infused (2.8 compared with 8.2) and PICU stay (3.2 compared with 13.0). After adjusting for confounding factors, the authors found a strong independent association between red blood cell transfusion and increased mortality, ventilatory support, use of vaso-active agents and PICU stay. Disturbingly, in transfused patients the investigators found an ‘excess mortality’ among less severely ill children. The authors note that an interesting aspect of their study’s finding is that, in contrast to some other recent studies, this study found these adverse associations despite leucodepleted blood being used. Additionally, a dose-dependent increase in mortality was observed.

Dr Jacque Lacroix and colleagues (Lacroix, 2007) report on their 2007 international multicentre Transfusion Requirements in the Paediatric Intensive Care Unit (TRIPICU) Study, a trial, described by the authors of the accompanying editorial, as having implications for understanding the role of such transfusions in all critically ill patients. The investigators compared a liberal versus a restrictive transfusion threshold in stable critically ill children. Results showed that the restrictive transfusion threshold resulted in a 44 per cent reduction in the number of red blood cell transfusions and a 96 per cent reduction in the number of patients exposed to any transfusion when compared with the liberal threshold. This was achieved without any increase in measured adverse outcomes. The authors conclude that a restrictive transfusion threshold in stable critically ill children in ICU can be used safely to reduce transfusion exposure. They caution, however, on applying this finding to other patient groups. After commenting on this trial and reviewing the results of three other randomized trials evaluating transfusion triggers, Drs Howard Corwin and Jeffery Carson in their editorial conclude that the overall evidence does not support liberal use of transfusion in critically ill patients. They state, ‘Red-
cell transfusion should no longer be regarded as “may help, will not hurt” but, rather, should be approached as “first do no harm.” More details of this study are included in Appendix 5.

**Dose-dependent risks**

Data also suggest the existence of a dose-dependent relationship between units transfused and the risk of experiencing negative outcomes. The inherent risks and adverse outcomes associated with blood transfusion necessitate ongoing efforts to raise awareness of the frequency and clinical impact of blood transfusion in hospitalized patients, to reduce perioperative blood loss and optimize its management, and to minimize the use of blood transfusion. To date, the association of blood transfusion with negative clinical outcomes has primarily been demonstrated in subgroups of surgical patients including CABG, hip and knee replacement, trauma, and colorectal surgery patients.

The NHMRC/ASBT Blood Components guidelines refer to evidence-based practice guidelines recommending that, when the decision is made to transfuse, ‘blood should be transfused one unit at a time, followed by an assessment of benefit and further need.’ This recommendation is consistent with the recently published Clinical practice guideline: Red blood cell transfusion in adult trauma and critical care (Napolitano, 2009) and data from a large number of recent studies demonstrating that the adverse outcomes associated with transfusion are dose-dependent, with the risk increasing with each unit given (Banbury, 2006; Basran, 2006; Beattie, 2009; Bernard, 2009; Bochicchio, 2008; Bursi, 2009; Carson, 1999; Chaivat, 2009; Chang, 2000; Corwin, 2004; Croce, 2005; Dunne, 2002; Gong, 2005; Ho, 2007; Jagoditsch, 2006; Karkouti, 2008; Kneyber, 2007; Koch, 2006a; Koch 2006b; Kulier, 2007; Leal-Noval, 2001; Malone, 2003; Murphy, 2007; Palmieri, 2006; Rogers, 2006; Rogers, 2007; Salim, 2008; Scott, 2008; Shorr, 2005; Taylor, 2002; Zilberberg, 2007).

The 2004 CRIT study (Corwin, 2004) enrolling 4892 critically ill patients in 284 ICUs similarly found that red blood cell transfusions are independently associated in a dose-dependent manner (the more blood the patient received, the worse the outcome) with longer ICU and hospital LOS and increased mortality. The number of red blood cell units transfused was significantly associated with increased ICU and hospital LOS compared with patients who did not receive transfusions. Patients with a transfusion amount of 1–2, 3–4, and 4 units had a corresponding increase in median ICU LOS of 2.1, 3.8, and 10.1 days, respectively, and an increase in median hospital LOS of 3.5, 6.7, and 16.6 days, respectively, compared with the median ICU LOS of 4.6 days and hospital LOS of 11.0 days observed in the patients who did not receive transfusions.

The objective of a study by Corwin (ibid.) was to quantify the incidence of anaemia and red cell transfusion practice in critically ill patients and to examine the relationship of anaemia and red cell transfusion to clinical outcomes. It was a prospective, multiple centre, observational cohort study of ICU patients in the United States. Enrolment period was from August 2000 to April 2001. Patients were enrolled within 48 hours of ICU admission. Patient follow-up was for 30 days, hospital discharge, or death, whichever occurred first. A total of 284 ICUs (medical, surgical, or medical-surgical) in 213 hospitals participated in the study, and a total of 4,892 patients were enrolled in the study. The main findings were as follows:

- the mean Hb level at baseline was 11.0 +/- 2.4 g/dL. Haemoglobin level decreased throughout the duration of the study. Overall, 44 per cent of patients received one or more RBC units while in the ICU (mean 4.6 +/- 4.9 units). The mean pre-transfusion Hb was 8.6 +/- 1.7 g/dL. The mean time to first ICU transfusion was 2.3 +/- 3.7 days;

- more RBC transfusions were given in study week 1. However, in subsequent weeks, subjects received one to two RBC units per week while in the ICU;

- the number of RBC transfusions a patient received during the study was independently associated with longer ICU and hospital lengths of stay and an increase in mortality;
• patients who received transfusions also had more total complications and were more likely to experience a complication;

• baseline Hb was related to the number of RBC transfusions, but it was not an independent predictor of LOS or mortality. However, a nadir Hb level of less than 9 g/dL was a predictor of increased mortality and LOS.

Corwin, H.L., et al. concluded that anaemia is common in the critically ill and results in a large number of red cell transfusions. Transfusion practice has changed little during the past decade, and the number of red cell units transfused is an independent predictor of worse clinical outcome.

Zilberberg et al. (2007) also identified an adjusted dose-response relationship between increasing red cells transfused and increased risk of ARDS. Receiving 1 to 2 units of red cells was associated with a greater than twofold increase in ARDS, 3 to 4 units with an almost threefold increase, and greater than 4 units with a greater than fivefold increase, compared with patients not exposed to any red cell transfusions. More details of this study are included in Appendix 5.

Perioperative red cell transfusion is commonly used to address anaemia, an independent risk factor for morbidity and mortality after cardiac operations. The objective of the 2010 Transfusion Requirements After Cardiac Surgery (TRACS) study by Hajjar, Ludmila A., et al. (2010) was to define whether a restrictive perioperative red blood cell transfusion strategy was as safe as a liberal strategy in patients undergoing elective cardiac surgery. The study found that, independent of transfusion strategy, the number of transfused red blood cell units was an independent risk factor for clinical complications or death at 30 days. The authors concluded that, among patients undergoing cardiac surgery, the use of a restrictive perioperative transfusion strategy compared with a more liberal strategy resulted in non-inferior rates of the combined outcome of 30-day all-cause mortality and severe morbidity. More details of this study are included in Appendix 5.

In a recent article Marik, P.E., and Corwin (2008a), reviewed and analysed the evidence with the aim of expanding the definition of Acute Lung Injury (ALI) following transfusion. The classic TRALI syndrome is an uncommon condition characterized by the abrupt onset of respiratory failure within hours of the transfusion of a blood product. It is usually caused by antileucocyte antibodies, resolves rapidly, and has a low mortality. A single unit of red cells or blood component product is usually implicated in initiating this syndrome. It has, however, recently been recognized that the transfusion of blood products in critically ill or injured patients increases the risk (OR of 2.13; 95 per cent CI, 1.75–2.52) of the development of the ARDS, 6–72 hours after the transfusion. This ‘Delayed TRALI Syndrome’ is common, occurring in up to 25 per cent of critically ill patients receiving a blood transfusion and is associated with a mortality of up to 40 per cent. Although the delayed TRALI syndrome can develop after the transfusion of a single unit, the risk increases as the number of transfused blood products increase. The management of both the classic and delayed transfusion related acute lung injury syndromes are essentially supportive.

A multicentre study of 666 major burn injury patients found an adjusted association between the number of red blood cell units transfused and infection and mortality (Palmieri, 2004; 2006). Heavily transfused patients had a tenfold increase in sepsis, 3-fold increase in wound infection, fourfold increase in urinary tract infections and a sevenfold increase in ventilator associated pneumonia. There was a 13 per cent increased risk of infection with each unit transfused. Of interest, the authors report that there was wide variation in clinicians’ transfusion thresholds and these actual thresholds varied from their stated thresholds in an earlier survey. The accompanying editorial suggests blood conservation strategies be used to reduce transfusions and calls for further research into methods to reduce blood loss, indications for transfusion and their relationship to patient outcomes (Jeschke, 2006).
Jeschke and colleagues investigated the association between allogeneic blood transfusion and infection and mortality in severely burned paediatric patients (Jeschke, 2007). Even after adjusting for the known effects of increased total body surface area burn and inhalation injury on sepsis, the authors conclude that receiving >20 units of red cells significantly increased the risk of sepsis. Of interest the investigators included weight as a covariate and report that it appears that the total amount of red cells transfused determined the risk, not the relative amount, that is, red cells given per kilogram. More details of this study are included in Appendix 5.

In all of the articles presented above there is a question that must be asked: to what extent did the transfusion practice that caused the infections described vary from guidelines, evidence and the appropriate use of blood products. Some of the articles (Taylor 2006; Rogers 2009; Corwin 2008a; Palmieri 2004; 2006; Jeschke 2007), show transfusion rates remain high to very high in surgery and differ widely across physician practices and between hospitals in spite of growing knowledge that allogeneic blood transfusion (ABT) is associated with a risk of PI which are all clear examples of practice varying from appropriate use.

**Risks associated with the age of red cells**

Evidence is emerging that the age of blood at transfusion is probably not neutral or unworthy of consideration as may have been the case to date.

Allogeneic packed red cells suppress immunity and influence outcomes, and the influence of blood on the risk of infection and death may be related to the duration of storage. Hassan (2011) sought to determine whether blood storage duration was associated with infection or death in a large cohort of injury victims. They reviewed a cohort of trauma patients transfused at least 1 Unit of red cells within 24 hours of admission to a level 1 trauma centre.

The outcomes of interest were complicated sepsis and mortality. Hassan compared the amount of older blood (>14 days storage) given to patients who did or did not develop the outcomes of interest using univariate and multivariate methods. A total of 820 patients were included. Patients who died (n = 117) received more units of older blood than those who lived (5 Units [inter quartile range {IQR}, 2-9] vs. 3 Units [IQR, 2-6]; P < 0.001). Patients with complicated sepsis (n = 244) received a greater volume of older blood than those without complicated sepsis (6 Units [IQR, 2-10] vs. 3 Units [IQR, 1-5]; P < 0.001).

After adjusting for clinical factors, including the total amount of blood transfused, patients receiving greater than or equal to 7 Units of older blood had a higher risk of complicated sepsis than patients receiving 1 or fewer units (odds ratio, 1.9; P = 0.03). The risk for complicated sepsis and death in trauma victims who are transfused blood is high. The amount of older blood transfused is associated with complicated sepsis. Although the best strategy to minimize the effects of allogeneic blood is to avoid unnecessary transfusions, it may be particularly important to avoid transfusing multiple units of older blood.

A new US study (Koch, 2008) found that cardiac surgery patients who received transfusions of blood that had been stored for 2 weeks or less had lower rates of complications and death than those who received blood that was older. The study was the work of researchers (Koch, Colleen Gorman, Li, Liang, Sessler, Daniel I., Figueroa, Priscilla, Hoeltge, Gerald A., Mihaljevic, Tomislav, Blackstone, and Eugene H) based at the Cleveland Clinic Foundation, Cleveland, Ohio.

In this large observational study, Kock et al. compared 2,872 cardiac surgery patients who received transfusion blood that had been donated within the previous 2 weeks with 3,130 cardiac surgery patients who received transfusion blood that had been donated more than 2 weeks earlier. They found that the patients who were given older blood had a higher risk of dying in hospital than their newer blood counterparts (2.8 versus 1.7 per cent), and they were significantly more likely to need prolonged
ventilation support, have kidney failure, sepsis (inflammation affecting the whole body), or multiple organ failure.

The Cleveland Clinic investigators also discovered a direct ‘dose response’ relationship between days of storage and the chances of a combination of serious complications or adverse events. After eliminating potential confounding factors, an analysis revealed that patients who had received older blood had a significantly higher rate of combined serious adverse events than those who received newer blood. Also, they found that patients who received newer blood had a higher chance of surviving the first year after surgery than those who received older blood (92.6 versus 89.0 per cent).

Editor in chief of Journal Watch (published by NEJM), Dr Harlan M. Krumholz said that the study raised important questions about usage of old blood in cardiac surgery transfusions. The study findings are likely to be true throughout the US, said Krumholz, adding that: ‘with a blood supply in constant demand, finding a solution to this problem will not be easy. For now, it seems reasonable to try to ensure that patients needing transfusions who are at the highest risk for adverse events receive blood that is as fresh as possible.’

Marik (1993) conducted a prospective, controlled, interventional study in 1993 to determine the effect of red blood cell transfusion on gastrointestinal and whole-body oxygen uptake in a multidisciplinary ICU of a tertiary care teaching hospital. They concluded that they had failed to demonstrate a beneficial effect of red blood cell transfusion on measured systemic oxygen uptake in patients with sepsis. Patients receiving old transfused red cells developed evidence of splanchnic ischemia. They postulated that the poorly deformable transfused red cells cause microcirculatory occlusion in some organs, which may lead to tissue ischemia in some organs. More details of this study are included in Appendix 5.

Stored red cells undergo progressive structural and functional changes over time. Koch (2008) tested the hypothesis that serious complications and mortality after cardiac surgery are increased when transfused red cells are stored for more than two weeks. They concluded that, in patients undergoing cardiac surgery, transfusion of red cells that had been stored for more than two weeks was associated with a significantly increased risk of postoperative complications as well as reduced short-term and long-term survival. More details of this study are included in Appendix 5.

Tsai (2010) reviewed the experimental evidence showing systemic and microvascular effects of blood transfusions instituted to support the organism in extreme haemodilution and haemorrhagic shock, focusing on the use of fresh versus stored blood as a variable. The question: ‘What does a blood transfusion remedy?’ was analysed in experimental models addressing systemic and microvascular effects showing that oxygen delivery is not the only function that must be addressed. Tsai concluded that fresh blood is intrinsically a better resuscitation fluid than older, stored blood in the animal model systems in which it has been carefully studied.

Tsai also concluded that it is apparent that blood transfusions are called for to restore oxygen carrying capacity, while one of the major problems is deficient microvascular perfusion and function. Further, that it is in fact questionable whether a blood transfusion is the optimal remedy for re-establishing tissue perfusion in an organism subjected to haemodilution and haemorrhage, or both. A precise understanding of the mechanisms involved in blood transfusion may be intrinsically impossible, because blood composition per se is a moving target. Distinguishing between ‘fresh’ and ‘old’ red cells overlooks that the distribution of red cell age in the circulation is presumed to be approximately Gaussian, with an average centred at their circulatory half-life, therefore even ‘fresh’ blood has a fraction of red cells at the end of their cycle.

Tsai also commented that experimental studies in transfusion provide only a preliminary answer to: what is the problem that must be remedied when a blood transfusion is called for? Tsai proposed that oxygen is only one part of the problem, and that microscopic perfusion was the other component, with
their relative importance not yet established. However, Tsai remarked that there was evidence that adequate restoration of microvascular perfusion deficiency in anaemia and haemorrhagic resuscitation may be as efficacious as restoring oxygen carrying capacity, therefore potentially significantly reducing the use of blood. More details of the Tsai study are included in Appendix 5.

An abstract entitled Blood Transfusion Increases Hospital Acquired Septicaemia by O’Mara, from the Hunter New England Health Service, Australia was presented at the 52nd ASH Annual Meeting and Exposition, December 4-7, 2010, Orlando, Florida (O’Mara, 2010). The abstract said the study showed there was a statistically significant increase in septicaemia following red cell transfusion. The null hypothesis was rejected. The database was examined by the age of red cells transfused and its effect on nosocomial septicaemia. There was a statistically significant effect of older blood on the rate of septicaemia. The study received some publicity in the Australian press in November 2010. A copy of the abstract is at Appendix 5.

The functional quality and efficacy of labile blood components has also been questioned (Hogman, 2006). Storage age of transfused blood appears to play a role, because longer storage time of blood (albeit still within the range acceptable by regulators) correlates with higher mortality rates, especially when larger volumes are transfused (Koch, 2008; Weinberg, 2008). The clinical significance, in terms of adverse clinical outcomes, of storage time of blood is thus currently a topic of heated debate and ongoing research, with the issue of ‘aged blood’ being causative for adverse clinical outcome remaining subjudice and a topic of ongoing research and RCTs (Hess, 2010; Tinmouth, 2006). A wealth of supporting in vitro experimental data and animal studies also suggest that storage-induced changes in labile blood components may render transfused Red cells less efficacious than assumed, and this can further support the link between transfusion and adverse clinical consequences (Cabrales, 2007; Frenzel, 2009; Isbister, 2003; Solheim, 2004).

QUESTIONS REGARDING THE BENEFITS OF RED CELL TRANSFUSION

A study, led by Elliott Bennett-Guerrero (2010), a researcher at Duke University’s Duke Clinical Research Institute, found wide variation in transfusion practices at 798 U.S. hospitals, involving 100,000 people receiving coronary-artery bypass surgery in 2008. Some hospitals gave transfusions to fewer than 10 per cent of their patients, while at others transfusion rates topped 90 per cent. Researchers found that only about 20 per cent of the variation was explained by how sick the patients were. They also found there wasn’t any link between a hospital’s use of transfusions and death rates.

More than half of open-heart-surgery patients receive blood transfusions to reduce the risk of complications, but new studies suggest that many of the transfusions provide little benefit (Figure 7)(Winslow, 2010).

Cardiologists warn that unnecessary transfusions incur higher costs, deplete supplies of donated blood and can increase a patient’s risk of infection and other serious problems. Several hundred thousand Americans undergo open-heart surgery each year but there has been little rigorous research to help guide doctors on whether a transfusion is beneficial.
FIGURE 7: RED STATES - REDUCING THE NUMBER OF BLOOD TRANSFUSIONS DURING SURGERY

Source: WSJ research; Society of Thoracic Surgeons
Based on a systematic review and analysis of all literature published over 13 years on transfusion and outcomes, the 2009 ICCTO (Simon, 1998), using the RAND/UCLA Appropriateness Method to determine appropriateness of allogeneic red cell transfusion in 450 clinical scenarios of non-bleeding relatively stable patients found no evidence to support a clinical benefit from transfusion in any scenario where the Hb level was greater or equal to 80 g/L. Based on the available published evidence, the 15-member international multidisciplinary expert panel concluded that in only 12 per cent of the 450 scenarios was transfusion likely to improve the patient’s health outcome.

SAFETY AND QUALITY OF ALBUMIN USE

The Saline versus Albumin Fluid Evaluation (SAFE) study, which was published in May 2004 (Finfer, 2004; Safe, 2004) looked at the use of albumin. The SAFE Investigators issued a subsequent report in 2007 (Myburgh, 2007) of a post hoc follow-up study of patients with TBI who were enrolled in the SAFE study. The study was a collaboration of the Australian and New Zealand Intensive Care Society (ANZICS) Clinical Trials Group, the Blood Service, and The George Institute for International Health. The SAFE Investigators concluded that, in patients in the ICU, use of either 4 per cent albumin or normal saline for fluid resuscitation results in similar outcomes at 28 days. Following the conduct of a post hoc follow-up study in 2007 of patients with TBI who were enrolled in the study, they concluded that fluid resuscitation with albumin was associated with higher mortality rates than was resuscitation with saline. More details of these studies are included in Appendix 5.

In June 2009, an Access Economics report (Access Economics, 2009) to the Victorian Government stated that routine use of saline to resuscitate individuals with TBI as opposed to albumin would significantly reduce mortality associated with brain injury in Australia. The authors noted that their findings were exactly the same as the results of the SAFE Investigators subsequent report in 2007 (Myburgh, 2007). Further, Access Economics noted that the lower mortality rate with the use of saline as compared to albumin would save costs such as productivity losses and burden of diseases due to premature death. They undertook a cost effectiveness analysis based on economic modelling which estimated that the total Disability Adjusted Life-Years averted was 17,915 with a net benefit of $687.7 million (in net present value terms), and a benefit/cost ratio of 10.52.

It is particularly noteworthy that:

- neither the authors of an Editorial in the Medical Journal of Australia in September 2004 (Finfer, 2004) which noted that the recent publication of the SAFE study brings certainty to the issue of albumin’s safety in a heterogeneous population of adult ICU patients, nor any other appropriate individuals, organisations or professional associations in Australia or New Zealand provided commentary or opinion in the public domain, including in peer-reviewed journals on the significant findings of either the SAFE Investigators subsequent report in 2007 (Myburgh, 2007) or the Access Economics report of 2009 (Access Economics, 2009);

- these two reports were published in a period when use of albumin (including 4 per cent albumin) was on the rise in Australia; and

- following the publication of the 1998 Cochrane Injuries Group Albumin Reviewers systematic review (Cochrane, 1998) the use of albumin fell dramatically in Australia, and elsewhere, to reach an all-time low in 2003-04 (growth in the use of albumin then commenced to rise steadily from 2004-05 the year following the SAFE Investigators SAFE study in May 2004 (Safe, 2004) and the Editorial in the Medical Journal of Australia in September 2004 (Finfer, 2004).

SAFETY AND QUALITY OF INTRAVENOUS IMMUNOGLOBULIN USE

No direct evidence was found to suggest that IVIg posed unacceptable risks to safety and quality of care. However, the availability of IVIg in Australia relative to clinical need and demand has been reviewed
repeatedly since at least the early 1990s. Three approaches have been used to ensure that IVIg is available for the patients who need it most:

- aligning the use of IVIg with conditions for which there is evidence of benefit;
- increasing the manufacture of IVIg in Australia; and
- importing IVIg from overseas suppliers.

Despite much published clinical research on IVIg, evidence for its efficacy and effectiveness in the treatment of many different conditions remains uncertain. This is due to:

- the difficulty of conducting rigorous evaluative studies of treatments for rare and complex medical conditions that are often accompanied by equally complex co morbidities;
- the difficulty of evaluating outcomes where IVIg is used as a treatment of last resort (as is sometimes the case) after other therapies have failed; and
- a lack of monitoring data from all parts of the world on the use and outcomes of IVIg therapy.

Given the variable extent and quality of evidence for IVIg use, successive reviews and guidelines since 1992 have recommended that indications should be categorised according to the quality of the available evidence and whether or not it showed that IVIg was beneficial.

**SAFETY AND QUALITY OF RECOMBINANT FACTOR VIIA USE**

The AHCDO Guidelines review (2008) reports that recombinant rFVIIa has been widely used in Australia and has proved to be highly effective in the management of bleeding episodes in patients with inhibitors to FVIII or FIX (Australian Health Ministers’ Advisory Council (AHMAC) 2006). Evidence in the literature suggests that it is effective in 79-92 per cent of such episodes. One study demonstrated that it was effective in over 90 per cent of surgical cases. Apart from the registered and funded use of rFVIIa for the treatment of episodes of active bleeding in haemophilia patients with inhibitors, in Australia and internationally there is a growing use of this agent as prophylaxis - aimed at the primary and secondary prevention of bleeding episodes or the amelioration of those episodes. In these patients the number, frequency and severity of bleeding episodes is monitored on the prophylactic regimen, to determine its efficacy and to guide adjustment of the prophylactic dose size and frequency. Since its release and TGA registration in Australia there has been a steady take-up of rFVIIa treatment for haemophilia patients with high titre inhibitors.
Appropriate Use Strategies

This section of the report provides information on the main strategies that have been employed in Australia, over the last decade and presents some information on the effectiveness of these various strategies (where information was available to the project). The information has been sourced predominantly from health authorities in the states and territories, including their websites and public documentation.

The section also draws together lessons learnt regarding strategies for promoting appropriate use of blood and blood products, including a discussion of ways to improve the uptake of clinical guidelines.

APPROPRIATE USE STRATEGIES IN AUSTRALIA JURISDICTIONS

The following section provides information, and some limited assessment of effectiveness where information was available, for various strategies implemented in Australia over the last several years.

NATIONAL STRATEGIES—NATIONAL BLOOD AUTHORITY

Blood counts

National strategies to promote appropriate use of blood and blood products are mainly conducted under the auspices of NBA. The NBA’s Blood Counts Program (National Blood Authority, 2008) aims to collaborate with jurisdictions, health professionals and other stakeholders to improve patient outcomes through the appropriate utilisation of blood and blood-related products. The Blood Counts Program comprises a number of projects divided into streams that reflect the safety and quality intent of the National Blood Agreement. Specific projects have been selected after consideration by the NBA Clinical Advisory Council, the professional and community forum, JBC priorities and other key stakeholders.

STREAM 1 — DEVELOPMENT, IMPLEMENTATION AND PROMOTION OF BEST PRACTICE GUIDELINES AND STANDARDS

This stream has involved the development of the IVIg Criteria, for the clinical use of IVIg in Australia and, currently, a review of the NHMRC/ASBT Blood Components guidelines.

For the current review of the NHMRC/ASBT Blood Components guidelines, the NBA has facilitated the formulation of a Steering Committee, Expert Working Group, and Clinical/Consumer Reference Groups. A distinguishing feature of the review is that it is supported by a comprehensive systematic literature review so that all of the available evidence is collected and analysed to form the foundations of the clinical practice espoused in the new set of guidelines.

The review will result in the production of six modules as part of a comprehensive, evidence-based, PBM Guideline in three phases as follows:

- Phase 1: Module 1 - Critical Bleeding/Massive Transfusion and Module 2 - Perioperative
- Phase 2: Medical and Intensive Care
- Phase 3: Obstetric and Paediatric / Neonates

Each module of the PBM Guideline will be subject to NHMRC approval, (including methodological and peer review) and an independent ‘AGREE II assessment’ (http://www.agreetrust.org/).
Module 1—Critical Bleeding/Massive Transfusion was submitted to the NHMRC for approval in early August 2010. The approval process has been completed and the module will now undergo graphic design for publication and release in March 2011. The module has undergone an independent AGREE II assessment.

Module 2—Peri-operative Clinical/Consumer Reference Group (CRG) members have been reviewing the technical report and will be refining the evidence statements, recommendations and practice points. The module content and clinical guidance is currently being drafted. Public consultation was scheduled to commence in early 2011.

Phase 2

The Medical and Critical Care Research Protocol has been finalised and the systematic review is underway.

STREAM 2 — FACILITATION OF EDUCATION, INFORMATION SHARING AND PRACTICE IMPROVEMENT INITIATIVES

A major initiative within this stream has been the development of the South Australian e-learning package as a national tool. In 2006 the South Australia Department of Health funded the development of an online education package (e-learning) for clinical staff involved with the transfusion chain, including medical officers, nurses and midwives, and courier or porter staff that transport blood products. Other jurisdictions expressed interest in this e-learning tool following its successful use within South Australia. This led the NBA to work with South Australia Health to develop appropriate governance arrangements for the tool to become a sustainable national tool.

STREAM 3 — IMPROVEMENTS TO SYSTEMS

An important initiative has been the establishment of the National Haemovigilance Project. Publication of the Initial Australian Haemovigilance Report was achieved in February 2008. The report outlined jurisdictional progress towards achieving improvements in transfusion safety through increased systems of vigilance and improved transfusion safety practices. The report also provided a synopsis of available jurisdictional and national data. A key observation relating to the more than 600 transfusion-related incidents reported over the past 3–5 years in Australia was that approximately 65 per cent of reports involved procedural errors. These included patient misidentification, labelling errors, wrong blood in tube, prescription and dispensing errors, incorrect blood component transfused and ABO incompatibilities.

The first report recommended that governments support the establishment of an enduring national haemovigilance program and that states and territories continue to align their reporting systems with the agreed dataset to create a comprehensive national minimum dataset.

In recognition of the prevalence of procedural errors, the report recommended that state and territory governments consider:

- facilitating standardised training, development and proficiency testing;
- performing procedural audits of near-patient activities;
- actively encouraging compliance with universal specimen-labelling standards and patient identification standards;
- that governments work collaboratively with clinical colleges and the Blood Service to scope, assess and, where appropriate, promote a stronger awareness and adoption of comprehensive patient blood management strategies to reduce risks associated with exposure to unnecessary transfusions.
A major milestone was reached in 2010 with the completion of Australia’s second national Haemovigilance Report. The report is a valuable resource that aims to increase the understanding of the risks associated with transfusion.

**STREAM 4 — RESEARCH, DATA AND BENCHMARKING TO IMPROVE APPROPRIATE USE OF PRODUCTS**

There have been several significant initiatives in this area:

*Red cell usage analysis linkage project:* The purpose of this initiative is to provide for more detailed analysis of red cell usage data through state- and territory-based data linkage projects.

This will provide data on the appropriateness of the use of red cell products in Australia by:

- providing a nationally consistent data set of (and ultimately a national report on) red cell use in Australia;
- making available data that could be used to drive and influence clinical practice via peer-based review.

The NBA is collaborating with the Australian Institute of Health and Welfare to develop a proposal for a nationally facilitated data linkage project. The Department of Health in South Australia and the CEC in New South Wales are also contributing research and data to the project.

The challenge for the NBA is to devise a methodology that will allow the disparate data collection systems within each jurisdiction to provide information against the proposed minimum data set. There is potential to advance the project’s aims with a proposed national roll out of an enhanced electronic ordering and receipting blood system (known as ‘BloodNet’).12

*Market research into red cell prescribing practices for haemodynamically stable patients:* The NBA and the CEC in New South Wales jointly funded market research to inform the development of state and national communications strategies (Eureka Strategic Report, 2007).

**Blood Measures:** This is a collaborative project between the National Blood Authority and the Blood Service, which aims to achieve widespread use by those involved in the collection of blood use data by:

- a set of standard parameters that are indicators of appropriate blood and blood-related product use across a range of clinical scenarios;
- consistent data management techniques that will enable the data collected on the use of blood and blood-related products to be used to promote best practice and provide data for registry and research purposes.

The release of the first Blood Measures Guide by the NBA was a world first in establishing a nationally accepted set of measures on the use and effectiveness of fresh blood components.

**National Patient Blood Management Program (NPBMP)**

NBA is currently developing a national PBM program (referred to as the NPBMP) (National Blood Authority, 2010c). The aim of the program will be to facilitate the uptake of patient blood management best practice through the development and promotion of clearly defined national objectives. The

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program will build on existing state and local programs. The goal is to improve patient outcomes through national policies and drivers that support state and territory programs in the appropriate use of, and where possible the appropriate avoidance of the use of fresh components.

A NPBMP Steering Committee has been established to assist the NBA in the development and implementation of a NPBMP in Australia. The Steering Committee will provide expert advice, influence the uptake of patient blood management, and oversee research to support the program’s design and delivery. The Steering Committee aims to increase awareness and uptake of contemporary patient blood management practices by providing advice on:

- potential or desirable national objectives and targets for PBM;
- prioritisation and oversight of program initiatives;
- the direction for the NPBMP including implementation strategies;
- how to evaluate policy changes and progression toward meeting national PBM objectives (and targets).

The Steering Committee has proposed that the NPBMP be built on a range of infrastructure and materials that will support the states and territories in performing appropriate use activities as described in the National Blood Arrangements. This infrastructure and materials will consist of:

- national PBM outcome and performance measures;
- a national network of jurisdictional PBM managers;
- development of a PBM tool kit/materials to support local PBM initiatives;
- PBM information/education;
- promulgation and implementation of the PBM Guideline;
- creation of linkages with other national safety and quality initiatives.

**NATIONAL PBM OUTCOME AND PERFORMANCE MEASURES.**

NBA has developed a set of National PBM Outcome and Performance Measures (O&PMs) (Figure 8 below) designed to complement sector wide accreditation and standards (for example EQuIP and Australian Commission on Quality and Safety in Health Care Blood and Blood Product Standard). It is planned that the PBM O&PMs set the goals for the NPBMP and provide direction for investment of time and resources within jurisdictions. Should jurisdictions choose to participate in the NPBMP, they will be expected to monitor and report against these measures.

The Steering Committee has also agreed to two other measures being developed to align with the national Haemovigilance program and red cell data linkage initiatives.

**Opt-in arrangements for Jurisdictional Based PBM Program Managers**

The current proposal is for funds to be made available to jurisdictions opting into the program, to employ a PBM program manager. The network of PBM managers will be expected to coordinate and report against the National PBM O&PMs and provide support for reporting for other national programs (for example Haemovigilance).
PBM gap analysis and review

The jurisdictional-based PBM program managers would also be responsible for assessing the gaps in the jurisdictions’ ability to report against the National PBM O&PMs and Haemovigilance and red cell data linkage O&PMs. The assessment would include identification of strategies and resources for addressing these gaps.

NATIONAL NETWORK TO SUPPORT THE SHARING OF SUCCESS INITIATIVES AND IDEAS

A national network consisting of the jurisdictional-based PBM program managers would be established by the NBA to support information sharing and communication between jurisdictions and assist with the rapid uptake of ‘good ideas’. To facilitate fertilisation and uptake of quality PBM improvement strategies that ‘work’, the network will meet two times a year and have access to a web-based information-sharing hub.

DEVELOPMENT OF A PBM TOOLKIT/MATERIALS TO SUPPORT LOCAL PBM INITIATIVES

A key element of the program is expected to be the development of a PBM tool kit, containing a range of materials to support the development and introduction of local PBM initiatives. Some examples of the types of materials that may be developed include:

- describing the elements of effective PBM initiatives for example who needs to be involved, how to set it up and what roles are critical to success;
- examples of PBM audits and a guide on how to conduct an effective audit and provide feedback;
- describing the key components of a blood order form/prescription to support decision making;
- materials on assessing the effectiveness of a PBM Program (that is what data/information should be collected and how should information be presented and to whom?);
- examples of care pathways that incorporate PBM (for example for orthopaedic surgery).

ENSURING AVAILABILITY OF PBM INFORMATION/EDUCATION

Ongoing education of the clinical community and patients is considered to be a key element in supporting changes in clinical practice. A national approach to PBM education will focus on:

- training of health workers and health care administrators in how to implement and support patient blood management initiatives;
- increasing knowledge of patient blood management practices in all health care professionals where transfusion is commonly practiced; and
- informing consumers of patient blood management initiatives.

A communications strategy is also planned. It is anticipated to include education and information activities such as:

- a ‘Tired all the time’ campaign and patient poster and flyers;
- a patient checklist for clinicians and patients on ‘what should I know about blood management and appropriate alternatives to transfusion?’;
• existing educational offerings (for example BloodSafe e-Learning, Victorian Graduate Certificate in transfusion practice and university nursing and doctor curricular), if appropriate, may be encouraged to incorporate PBM concepts (particularly anaemia management).

**PROMULGATION AND IMPLEMENTATION OF THE PBM GUIDELINE**

The proposal is for the NPBMP to support the publication, promulgation and implementation of the six, evidence-based PBM Modules (Critical Bleeding/Massive Transfusion, Peri-operative, Medical, Critical Care, Obstetrics and Paediatrics/Neonates). The focus would include:

• designing and making the guidelines available in a format that will support clinical uptake;

• including in the PBM toolkit doctor and patient materials designed to support the uptake of the PBM guideline;

• providing support, through the jurisdictional based PBM program Managers, to investigate ways to enhance coordinated patient centred care to embed PBM practices.

**CREATING LINKAGES WITH OTHER NATIONAL SAFETY AND QUALITY INITIATIVES**

The NBA advised that it will continue to investigate and capitalise on opportunities to enhance safe and appropriate practices, including appropriate avoidance of transfusions of blood components using PBM practices. For example, the NBA obtained a commitment from the ACSQHC to develop a Blood and Blood Product Standard as one of only ten mandatory standards to be implemented nationally.
### FIGURE 8: DRAFT PBM NATIONAL OUTCOMES AND PERFORMANCE MEASURES

<table>
<thead>
<tr>
<th>No. 1</th>
<th><strong>Outcome</strong></th>
<th>Every hospital that offers elective surgery has arrangements for pre-operative anaemia screening, agreed levels for triggering referral and appropriate referral pathways if anaemia is identified.</th>
<th><strong>Rationale:</strong></th>
<th>Optimising the patient’s red cell mass prior to surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>Numerator:</strong></td>
<td>Number of hospitals that comply with an appropriate policy</td>
<td><strong>Denominator:</strong></td>
<td>Number of hospitals offering elective surgery</td>
</tr>
<tr>
<td></td>
<td><strong>Potential Source:</strong></td>
<td>Hospital Survey</td>
<td><strong>Potential Source:</strong></td>
<td></td>
</tr>
<tr>
<td>No. 2</td>
<td><strong>Outcome</strong></td>
<td>All patients undergoing elective or planned surgery have had a pre-operative anaemia assessment and are treated and managed to correct anaemia before surgery.</td>
<td><strong>Rationale:</strong></td>
<td>Optimising the patient’s red cell mass</td>
</tr>
<tr>
<td></td>
<td><strong>Numerator:</strong></td>
<td>Total number of patients that have had pre-operative anaemia assessment (4 to 12 weeks prior to surgery)</td>
<td><strong>Denominator:</strong></td>
<td>Total number of elective surgery patients</td>
</tr>
<tr>
<td></td>
<td><strong>Potential Source:</strong></td>
<td>Audits</td>
<td><strong>Potential Source:</strong></td>
<td></td>
</tr>
<tr>
<td>No. 3</td>
<td><strong>Outcome</strong></td>
<td>As part of the pre-operative consent process all patients receive information about treatment options for managing blood loss anaemia including the likelihood of, and the potential benefits and complications of transfusion.</td>
<td><strong>Rationale:</strong></td>
<td>Harnessing and optimising the tolerance of anaemia</td>
</tr>
<tr>
<td></td>
<td><strong>Numerator:</strong></td>
<td>Number of patients who received relevant information</td>
<td><strong>Denominator:</strong></td>
<td>Number of elective surgical patients</td>
</tr>
<tr>
<td></td>
<td><strong>Potential Source:</strong></td>
<td>Patient Survey</td>
<td><strong>Potential Source:</strong></td>
<td></td>
</tr>
<tr>
<td>No. 4</td>
<td><strong>Outcome</strong></td>
<td>All hospitals review transfusion in all elective procedures.</td>
<td><strong>Rationale:</strong></td>
<td>Harnessing and optimising the tolerance of anaemia</td>
</tr>
<tr>
<td></td>
<td><strong>Numerator:</strong></td>
<td>Number of hospitals that have a review process in place</td>
<td><strong>Denominator:</strong></td>
<td>Number of hospitals offering elective surgery</td>
</tr>
<tr>
<td></td>
<td><strong>Potential Source:</strong></td>
<td>Hospital Survey</td>
<td><strong>Potential Source:</strong></td>
<td></td>
</tr>
</tbody>
</table>

**Source:** National Blood Authority, 2010

**TIMEFRAME FOR NPBMP IMPLEMENTATION**

Draft implementation timelines for the NPBMP provided by the NBA are reproduced in Figure 9. These are indicative only.
EFFECTIVENESS OF NATIONAL MEASURES TO PROMOTE APPROPRIATE USE

As the measures described above have not been implemented, it is not possible to comment on their effectiveness. However, some comments are provided below regarding the strengths and/or shortcomings in the design of these measures.

The general approach that NBA has taken in the design of the NPBMP takes best advantage of its central positioning in the sector. That is to say, NBA is well placed to provide national leadership and guidance on issues of common interest like PBM among the jurisdictions. This role appropriately includes the development and management of national governance and management frameworks like the NPBMP, development and promulgation of appropriate use guidelines like the PBM clinical practice guidelines being developed and promulgated under the auspices of the NHMRC within the NPBMP framework, provision of instructional and educational materials that have common purpose (such as clinician or patient information brochures or posters), collection, collation and provision of data and other information, facilitating the sharing of data, information and experience among the jurisdictions and feedback on best practice and lessons learned through the production of standards and other guidance materials.

As is detailed below, this project looked at the experience of states and territories in promoting appropriate use of blood and blood products. It was evident from this analysis that efficiencies could be gained among the jurisdictions from the common and consistent use of guidelines and other materials, as well as the sharing of experience. The small jurisdictions in particular struggle to be able to produce the informational materials, for example, for their clinicians or patient groups, given the small number of staff directly involved the administration of the sector. The ACT, for example, relies heavily upon the efforts of a single transfusion nurse to provide education on appropriate transfusion and implementation of sector initiatives (p92).

It is also valuable that NBA proposes to place on its agenda the promulgation of the new clinical guidelines once they have been approved. As will be taken up further below (Improving the Uptake of Clinical Guidelines, p109), the translation of clinical guidelines into practice after the production of guidelines is an area of endeavour that, according to the available evidence, stills requires significant attention and work to achieve even satisfactory results. Guidelines do not implement themselves and carefully designed promulgation and clinician education, training, engagement and sustainable support resources and services are required to ensure effective translation into clinical practice.
### FIGURE 9: DRAFT INDICATIVE IMPLEMENTATION TIMELINE

<table>
<thead>
<tr>
<th>Event</th>
<th>Timeline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Draft Tool Kit developed</td>
<td>Jul - Oct 2011</td>
</tr>
<tr>
<td>PBM tool kit released</td>
<td>Jul 2012 onwards</td>
</tr>
<tr>
<td>National network arrangements established</td>
<td>Jul – Aug 2011</td>
</tr>
<tr>
<td>Implementation Communication Strategy</td>
<td>Jul 2012 onwards</td>
</tr>
<tr>
<td>Implementation of strategies to address gaps analysis</td>
<td>Aug - Oct 2011</td>
</tr>
<tr>
<td>Implementation of strategies to address gaps analysis</td>
<td>Nov 2011</td>
</tr>
<tr>
<td>Implementation Communication Strategy</td>
<td>Nov 2012</td>
</tr>
<tr>
<td>1st network meeting</td>
<td>Nov 2012</td>
</tr>
<tr>
<td>3rd Network meeting</td>
<td>Nov 2013</td>
</tr>
<tr>
<td>5th Network meeting</td>
<td>Nov 2013</td>
</tr>
<tr>
<td>PBMP approval</td>
<td>Dec 2010</td>
</tr>
<tr>
<td>2011-12</td>
<td>2012-13</td>
</tr>
<tr>
<td>2012-13</td>
<td>2013-14</td>
</tr>
<tr>
<td>Opt-in Jurisdictional-Based Program Managers</td>
<td>Feb – Jun 2011</td>
</tr>
<tr>
<td>Gaps Analysis Reports</td>
<td>Feb 2012</td>
</tr>
<tr>
<td>Implementation Communication Strategy</td>
<td>Feb–May 2012</td>
</tr>
<tr>
<td>Implementation of strategies to address gaps analysis</td>
<td>Feb–May 2012</td>
</tr>
<tr>
<td>Implementation Communication Strategy</td>
<td>Jun 2012</td>
</tr>
<tr>
<td>1st NO&amp;PM Reports</td>
<td>Jun 2013</td>
</tr>
<tr>
<td>2nd NO&amp;PM’s Reports</td>
<td>Jun 2014</td>
</tr>
<tr>
<td>3rd NO&amp;PM Reports</td>
<td>Jun 2014</td>
</tr>
<tr>
<td>Commence PBM O&amp;PM reporting framework</td>
<td>May – Jun 2011</td>
</tr>
<tr>
<td>2nd Network meeting</td>
<td>Jun 2012</td>
</tr>
<tr>
<td>Jun 2013</td>
<td>Jun 2013</td>
</tr>
<tr>
<td>4th Network meeting</td>
<td>Jun 2013</td>
</tr>
<tr>
<td>6th Network meeting</td>
<td>Jun 2014</td>
</tr>
</tbody>
</table>

*Source: National Blood Authority, 2010*
New South Wales (NSW)

Significant efforts over the last decade in NSW to promote appropriate use of blood and blood products began with the BTIC in 2002-03. The initiative followed a study (Rubin, 2001) by the NSW Council on the Quality of Health Care which demonstrated that 30 per cent of red cell transfusions in NSW failed evidence for appropriateness of transfusion in haemodynamically stable patients. This group of patients accounted for approximately 70 per cent of red cell usage in the state at the time.

The BTIC focussed on appropriate use of red cells, based on the NHMRC/ASBT Blood Components guidelines. The initiative involved seventeen volunteer clinical teams from both public and private hospitals, covering eleven Area Health Services in metropolitan, regional and rural areas, from surgical and medical disciplines. The teams varied from single clinical teams to whole hospitals.

The BTIC used the Institute for Healthcare Improvement Breakthrough Methodology (Berwick, 2003) as its approach to reduce inappropriate and cell transfusion. The methodology relied on collaboration across multiple sites in the testing of redesign and change strategies to make improvement. Teams share experiences using learning sessions, teleconferencing and web based discussion forums. The teams are required to measure key performance indicators as developed by the collaborative.

BTIC reported (Harrison, 2003) achieving its aim of reducing inappropriate use of red cells in elective transfusions in clinically stable patients by 50 per cent in 12 months in the collaborative sites. The report noted that the results achieved by the top five sites in the collaborative represented ‘almost total elimination of ‘inappropriate’ transfusions at those sites’ (Ibid.).

The BTIC Final Project Report also made a number of recommendations aimed at spreading and sustaining the initiative’s achievements in NSW. These are discussed below (Lessons Learnt from Appropriate Use, p99).

Two further significant initiatives established in NSW have been:

- the Blood Watch program of the NSW CEC; and
- devolution of the state blood budget to Area Health Services.

**THE NSW CLINICAL EXCELLENCE COMMISSION BLOOD WATCH PROGRAM**

The NSW Blood Watch program was established within the NSW CEC in 2006. The program’s objectives are:

- to improve and promote the provision of world-class transfusion medicine practice in NSW specifically in regards to fresh blood products including, red cells, and FFP, cryoprecipitate and platelets;
- to reduce the costs associated with transfusion therapy by reducing the number of inappropriate red cell transfusions, as well as inappropriate usage of platelets and FFP and more effective management of inventory based on improved clinical practice.

The Blood Watch program was developed in consultation with key stakeholders. Its priorities are to address the key performance areas originally identified in 2004 by NSW Health’s Fresh Products Advisory Committee (FPAC, 2004):

- appropriateness of transfusion of fresh products;
• appropriate clinical governance including the requirement for Area Health Service Transfusion Committees, if not already in place;

• the requirement for education and development of strategies to disseminate key resources through existing professional and educational bodies;

• the requirement for reporting of adverse events through IIMS, so as to identify transfusion related errors to enable the development of strategies to help eliminate such errors;

• the requirement for good communication between Area Health Services, NSW Department of Health, the Blood Service and the National Blood Authority;

• the development of accurate costing models for the direct and indirect costs of transfusion medicine.

The following quality improvement principles relating to bringing about change in an organization underpin the organisational design of the program:

• improvement is always local;

• to improve at the local level there has to be change in process and roles;

• it is the individuals in the work place who have the profound knowledge of the core processes – why they fail and how they can be improved; and

• local ownership and leadership support is critical.

The program is run and coordinated centrally at the CEC by a Program Manager. During the two-year establishment phase of the program, advice and support was provided by a Steering Committee known as the Transfusion Medicine Advisory Committee (TMAC). The oversight role of the TMAC has been superseded and there was a requirement for a Committee to provide advice of a more direct clinical nature, particularly in relation to the use and appropriateness of the full range of fresh blood products, not just red cells. Because of the overlap of the required new functions of the Blood Watch Committee and those of the existing NSW Health Fresh Blood Products Advisory Committee, the two Committees were combined in early 2009 to form the NSW Health/ CEC Blood Clinical and Scientific Advisory Committee (BCSAC).

The CEC has used clinical practice improvement methodology and created a collaborative network between Blood Watch improvement teams in a similar vein to IHI Breakthrough methodology. The Blood Watch program is implemented at the local Area Health Service (AHS) level by AHS Project Officers and project teams drawn together by clinical leads (Haematologists) nominated by their respective AHS. The project teams comprise representatives from local pathology providers and blood banks in addition to other key clinical and governance staff.

In the first five years of the program, emphasis was placed on promoting appropriate red cell transfusion in haemodynamically stable patients with normal bone marrow, with ‘appropriateness’ being that defined by the NHMRC/ASBT Blood Components guidelines. In 2007 the NSW CEC funded nine project officer positions for 12 months – the majority of which were Clinical Nurse Consultants in Transfusion Medicine (Transfusion Nurses).

A range of strategic interventions and solutions has been put in place by Blood Watch project teams. It includes:

• formation of an Area-based Transfusion Committee in all Area Health Services (AHSs);
• regular audit and feedback of red cell transfusion and platelet transfusion;
• implementation of restrictive transfusion thresholds in most facilities;
• dissemination of Blood Service Lanyard cards (with red cell guidelines) to all facilities;
• academic detailing by Blood Watch Clinical Leads;
• a series of Blood Myths Posters developed in consultation with transfusion experts and disseminated across the State. The purpose of the posters is to debunk some common myths about transfusion, based on the fact that blood is a living tissue transplant and the safety considerations of this are significant yet seriously underestimated;
• dissemination of Blood Service / BloodSafe Flippin’ Blood booklets to all AHSs;
• development of Area-wide transfusion administration forms within some AHSs;
• development of Area Standard of Practice for transfusion;
• development of Area-wide policy for blood and blood component transfusion in most Area Health Services;
• improvement training and communications training for clinical leads and program officers;
• the CEC commissioned market research to determine the prescribing behaviours of senior consultants - surgeons, anaesthetists and physicians - who treat haemodynamically stable patients with normal bone marrow. This research informed a strategic communications initiative;
• an innovative communications strategy directed at senior clinicians including a direct marketing campaign, provocative advertisements, a resource website and an on-line peer-to-peer debate around the emerging evidence of the inherent risks of transfusion.

**Effectiveness**

A series of interventions rolled out within NSW public hospitals as part of the Blood Watch program has resulted in an overall 10 per cent reduction in usage of red cells within the inpatient cohort between 2007 and 2009 (NSW Health advice, 2011).

Furthermore, the CEC has undertaken an in-depth analysis of the clinical groups where these reductions have occurred and has found that a significant number of blood transfusions were avoided between July 2008 and June 2009 within the elective surgical groups targeted by the Blood Watch program. The CEC estimated that around 12,225 units of blood were possibly avoided in this period, against the predicted rate of transfusion extrapolated from historical trends. CEC estimated that this may have represented cost savings, in terms of product supply and in-hospital costs, of around $8.6 million. The results of this CEC study are expected to be published in 2011. The only identifiable change to account for this reduction during this period was the implementation of a number of Blood Watch interventions within NSW public hospitals.

**Blood budget devolution**

NSW devolved its blood budget to AHSs in 2005, with the aim of providing the incentive for practice change in blood use. The budget devolution makes AHSs, and ultimately hospitals, responsible for the financial management of the costs of blood and blood products. It sends a price signal for the
efficient management and appropriate use of these products. The budget devolution is discussed in more detail in the next section Price Signalling.

**Effectiveness**

NSW officials interviewed during the project indicated that no changes on the patterns of blood use occurred following the devolution of blood budgets between 2004-2007. However, they did remark that budget devolution had been a positive force in gaining support among hospital senior management for the implementation of appropriate use initiatives. This experience appears to demonstrate that improving blood usage involves multi-modal intervention strategies.

It is not possible to discern from the National Supply Plan and Budget data whether budget devolution in NSW has had an impact on blood and blood product usage in that State. However, the following observations are made:

- the rate of red cell use per 1000 population declined in 2006-07 and has remained relatively flat since then;
- NSW records the lowest rate of red cell use per population, among the larger States (34.8 units in 2009-10, against 38.4 and 38.2 in Queensland and Victoria respectively);
- the per population rates for platelet, albumin and Prothrombinex-VF use are similarly lower:
  - Prothrombinex-VF use per population in NSW is equally lowest (with NT) among all jurisdictions;
- however, this pattern does not hold for use of FFP or IVIg use:
  - IVIg use per population in Victoria is significantly lower than in NSW.

Many stakeholders, including NBA (National Blood Authority, Undated – c), indicated that there is a trend in NSW to use FFP rather than Prothrombinex-VF for warfarin reversal and that this could be a choice influenced by the price signal given through budget devolution (FFP being a less expensive blood product). Victoria, conversely, has a relatively low rate of FFP use per population and a very high rate of Prothrombinex use.

There are several observations that can also be made from hospital separations data (Department of Health and Ageing). The national trend over the period 2003-04 to 2008-09 was for separations involving transfusion to grow more than total separations (26.5 per cent as opposed to 19.1 per cent). NSW, however, went against this trend with transfused separations growing by a lesser degree than total separations (Figure 10).
FIGURE 10: PERCENTAGE CHANGES IN TRANSFUSED AND TOTAL SEPARATIONS BY JURISDICTION, 2003-04 TO 2008-09

Source: National Admitted Patient Care Collection, Department of Health and Ageing

In addition, the rates of transfused separations per population in NSW for red cells, platelets and IVIg were significantly lower than in the other large jurisdictions in 2008-09 (Figure 11). The rate for Other Serum is slightly higher than that in Queensland (but lower than Victoria) and may be influenced by the relatively high use of FFP per population in NSW (Sapere Research Group 2011 unpublished).

FIGURE 11: TRANSFUSED SEPARATIONS PER 1000 POPULATION AS RATIO OF NATIONAL AVERAGE, SELECTED BLOOD PRODUCTS BY JURISDICTION, 2008-09

Source: National Admitted Patient Care Collection, Department of Health and Ageing

VICTORIA

The Blood Matters, BeST, program is a Victorian state government program for improving the quality and safety of hospital transfusion care to patients. The work of the Blood Matters program is
supported by the Blood Matters Advisory Committee, Secretariat, working groups and through collaboration with the Blood Service.

The Blood Matters Advisory Committee has been established to improve outcomes in patients requiring blood product transfusion in Victorian hospitals by enhancing the safety and appropriateness of blood and blood product use.

The Blood Matters project commenced in April 2002 with the formation of a consortium of three organisations. This consortium developed and tested tools and processes to improve transfusion practice in hospitals. The Blood Matters project was expanded in 2003 to include an additional 12 public hospitals in a Blood Matters Breakthrough Collaborative project, a project methodology developed by the Institute for Healthcare Improvement (IHI) in the United States. These hospitals further tested and developed transfusion interventions over an 18-month period. The interventions included:

- improvement of clinician and patient awareness and knowledge of blood product use;
- improvement of clinical decision making;
- enhancement of the blood administration process by making all successful practical strategies for improvement available to other hospitals in Victoria and Tasmania.

As part of the Blood Matters project, the transfusion nurse role was installed into hospitals. To support those in the role, a Certificate in Transfusion course was developed as part of the Blood Matters Consortium project. A list of Victorian, Blood Service, Tasmanian, Northern Territory, and ACT transfusion nurse contacts is on the Blood Matters website. There would appear there could be much to gain in the larger jurisdictions assisting the smaller States where possible, particularly in relation to the sharing of information, education and promotional materials.

The Blood Matters Advisory Committee has established three key results areas as follows:

- Clinical governance: To promote the implementation of clinical governance frameworks within Victoria that support delivery of the highest possible standards of clinical transfusion practice within Victorian hospitals.

- Blood management: To promote best practice in patient blood management, including implementation of strategies that minimise the need for blood product use and those that help ensure safe and appropriate transfusion practices: and to derive recommendations for improvements for better, safer transfusion practice for the monitoring of serious transfusion incidents (including adverse events and near misses) during blood and blood product utilization in Victoria, and to disseminate these to Victorian hospitals and health services.

- Communications: To share knowledge and promote collaboration with relevant stakeholder groups locally, nationally and internationally for the achievement of better and safer transfusion practice.

A Transfusion Interest Group Discussion Forum has been formed and is publicised on the Blood Matters website. The Forum aims to provide an avenue for Transfusion practitioners to privately discuss current issues and clinical views in transfusion to inform and support transfusion practice improvements.

The website also includes transfusion tools covering awareness, implementation, evaluation, excellence and leadership and examples of policy and procedures used in Victorian health services to promote good transfusion practice and blood management.
Blood Matters also involves the private sector in its activities. The Victorian Department of Human Services reported that engagement in the private sector has improved when there has been a champion within the private organisation or group, for the promotion of Blood Matters activities and blood management practices. This is no different with the public health services.

Blood Matters has invited private health sector as members of Blood Matters committees; this has helped drive key messages. For example, the incident reporting group has representation from Cabrini health care group and Melbourne Pathology. The PBM group has an anaesthetist whose practice is largely private organisations. This is a key driver for both these working groups to engage their organisations/groups to be involved.

Blood Matters has always invited private organisations to participate in any of its activities, clinical audits, surveys and Serious Transfusion Incident Reporting (STIR). Victorian Department of Human Services estimates that private sector organisations would make up 10-20 per cent of hospital involvements in any given audit and within STIR.

There has also been interest over the years in looking at transfusion nurse positions, with St John of God (SJOG) Pathology thus far the only private organisation to fund a part time position that covers the Geelong hospital and a consultant to all other Victorian SJOG health services. The Victorian Department of Human Services believes, however, that many of the public transfusion nurses would have some involvement in private organisations that are in close physical proximity (for example co-located) to their health service and that involvement may assist with a clinical risk issue such as mislabelling specimens, education of nurse graduates and/or clinical staff and in policy development. Involvement is often enhanced when there are shared pathology services/consultant haematologists.

**Graduate Certificate in Transfusion Practice**

In February 2009, the JBC agreed to provide funds additional to those already committed by the Victorian Department of Human Services to support the redevelopment of the Graduate Certificate in Transfusion Practice course material for delivery through the University of Melbourne in the 2010 academic year. This is the only formal transfusion-specific tertiary qualification in Australia especially intended for transfusion improvement practitioners. The NBA administers the funds approved for this purpose by the JBC.

The redeveloped course includes modules on transfusion patient safety, clinical transfusion practice and quality requirements. It has also provided an opportunity to incorporate national input into the curriculum’s content, in consultation with the Australian and New Zealand Society of Blood Transfusion (ANZSBT), the Blood Service, the Royal College of Nursing and the University of Melbourne.

During the latter half of 2009 and in 2010 the course material for both semesters was reviewed and updated using authors from across Australia, and was evaluated by a small expert panel. Topics were developed or altered to align with national direction, and there is a particular focus on patient blood management.

The first student intake of the redeveloped course is proceeding well, with the initial informal evaluation positive for content, delivery and support. Semester 2 topics are in preparation for the latter half of 2010.

**Effectiveness**

There was no information on the effectiveness of the Victorian Blood Matters activities made available to this project.
QUEENSLAND

The QBMP was established in July 2005 to ensure that that the Queensland Government meets its obligations under the National Blood Agreement. The specific objectives of the QBMP are to:

- manage the escalating costs of the Queensland blood supply;
- establish and improve communication, lines of accountability and reporting relationships between all elements in the blood transfusion service;
- improve the accuracy of the supply planning process so as to better predict demand, future cost and budgeting;
- develop and implement a quality and safety program for transfusion services in Queensland to ‘improve patient outcomes’, ensure appropriate usage of blood and blood products and to reduce adverse events and improve patient outcomes;
- take responsibility for clinical leadership and appropriate access to blood products under the National Blood Agreement;
- ensure Queensland’s effective participation in policy formation and decision making under the terms of National Blood Agreement;
- ensure effective and accountable management of the Queensland blood budget.

Initiatives

Work was undertaken throughout 2010 to focus on reductions in red cell waste due to expiry. At a workshop conducted early May 2010 involving all pathology providers (public and private), the NBA and Blood Service, a statewide target of 5 per cent wastage was agreed. Reduction in wastage has been achieved (see below) through a combination of modifying inventory levels in hospital blood banks, and increasing the cycling of units from lower use sites as they approach expiry. Some additional freight costs have been incurred, but these are minimal compared with the savings. Blood was actively moved around hospitals, especially from lower use centres to high use institutions like Royal Brisbane Hospital.

A pilot project is beginning at the Royal Brisbane and Women’s Hospital to trial innovations relating to effective blood use. Clinicians will be engaged in the design phase to develop initiatives under this pilot.

It is intended that the blood budget in Queensland will be devolved to public sector health networks from 1 July 2011. The budget devolution will be supported by a toolkit aimed at reducing inappropriate use and providing clinical decision support and analysis tools to help to identify and address inappropriate use. Queensland is in the early stages of developing these resources with South Australia and NSW assisting in the development of data linkage and analysis tools.

Effectiveness

The initiative to reduce red cell wastage in Queensland has had great success, as it indicated by Figure 12 (the dotted red line indicates the wastage target of 5 per cent). Prior to the intervention in 2101, wastage had averaged 6.5 per cent to 7 per cent over a significant period of time, with the majority of this due to expiry. Since the workshop, the monthly wastage rates from May to November 2010 were consistently below the 5 per cent target, and had fallen to just over 3 per cent by the end of that period.
FIGURE 12: RED CELL DISCARDS, QUEENSLAND 2007 TO 2010

Source: Queensland Blood Management Program
Queensland Health estimate that the annualised saving after five months is around $1.7 million when compared against historical wastage rates.

**SOUTH AUSTRALIA**

The BloodSafe Collaborative, funded by the South Australian Department of Health, commenced as a pilot project in 2002. Over the past eight years BloodSafe has evolved into a successful and ongoing blood transfusion safety and quality improvement collaboration between the South Australian Department of Health, Transfusion Medicine Services of the Blood Service and South Australian public and private hospitals and their transfusion service providers. The BloodSafe mission is to coordinate a safety and quality framework for all steps of blood transfusion practice to improve patient outcomes and ensure sufficiency of the blood supply. BloodSafe staffing and projects include:

- transfusion nurse consultants in the major public teaching hospitals in the Adelaide metropolitan area;
- a transfusion nurse consultant to work with private hospitals;
- a transfusion nurse consultant to work with country hospitals;
- a transfusion nurse consultant to ensure effective and efficient use of IVIg in SA;
- a nurse educator employed by the Blood Service, to assist with education, resource development and administration/management;
- a clinical haematologist; and
- pathology staff engaged to work on cold chain management issues.

The appointment of BloodSafe transfusion nurse consultants (senior nurses with experience in blood transfusion) across the major public hospitals provided the driving force for achieving and sustaining improved practice in conjunction with doctors and scientists. The program was extended to country and private hospitals, and many of the tools developed to improve practice have been adopted nationally and internationally.

A dedicated nurse consultant for IVIg has been appointed (Figure 13). This was presented at the HSANZ/ANZSBT/ASTH Annual Scientific Meeting in Hobart in October 2006.
FIGURE 13: (ANZSBT POSTERS): ‘AN AUSTRALIAN FIRST’: A DEDICATED NURSE CONSULTANT FOR INTRAVENOUS IMMUNOGLOBULIN (IVIG) USE IN SOUTH AUSTRALIA

POSTER
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Background
Nationally the use of IVIg increased by sixteen per cent over two years and in response to this the Blood Service IVIg User group developed dosage guidelines and approached the Department of Health to fund an IVIg Project Nurse within the ‘BloodSafe’ Program. ‘BloodSafe’ is focused on improved safety and appropriateness of transfusion practice.

Some of the major objectives of the role are:

- ensure efficient and effective use of IVIg in consultation with key stakeholders;
- develop comprehensive state-wide management plan;
- promote safety and quality of IVIg administration by:
  - participating in dedicated review clinics;
  - facilitating patient reviews;
  - supporting any changes following reviews;
  - assisting with dosage issues;
  - educating patients and staff and; and
  - improving inventory management.

Achievements to date
In collaboration with consultant Immunologists:

- dedicated Immunodeficiency clinics have been established and reviewed 80 per cent of patients across SA receiving IVIg, resulting in dosage adjustments in 36 per cent of patients (10 per cent increase and 26 per cent decrease in dose);

- potential savings related to dosage adjustments of 1,400gms IVIg for 12 months if adjustments remain constant. Equating to potential savings of:
  - $140,000 for IVIg if an estimated price of $100 / gram is used;
$44,000 for infusion related costs; and

at least 350 hours of donor time;

- immunodeficiency clinical management database has been established and now functioning at 3 sites across S;

- adverse event investigation and follow-up;

- development of statewide home subcutaneous (S/C) immunoglobulin therapy program;

- IVIg product education including safe administration practice;

- development of education material.

**Conclusion**

A coordinated approach across SA has resulted in:

- improved patient care;

- improved safety and quality related to use and administration of IVIg;

- dosage adjustments and subsequent product and infusion cost savings resulting in the role being cost effective;

- enhanced knowledge of IVIg use and administration.

*Source: HSANZ/ANZSBT/ASTH Annual Scientific Meeting, Hobart, Tasmania, Australia, 15-18 October, 2006*

SA has found that the NHMRC guidelines for the use of blood transfusions alone do not improve practice. BloodSafe has facilitated the dissemination and implementation of best practice through activities such as clinical audit, education, development of tools for use at the bedside and re-designing hospital systems. BloodSafe has focused strongly on appropriate use – with a view that the safest transfusion is the one that can be avoided when not warranted.

BloodSafe has championed improvements in patient identification including simple measures such as always checking a patient’s name/date of birth (asking them to state it rather than using closed questions that require yes/no) and checking their wristband. This is essential to ensure that patients receive the care that is intended for them whether it be the right blood, medication, test or treatment.

In 2006 the SA BloodSafe Program was funded by NBA to review its experience with transfusion incident reporting because of its advanced work in the use of systems across the entire state public health sector. This review provided a basis for further work on a national reporting scheme.

BloodSafe has developed tools that have been adopted nationally such as the BloodSafe flip chart, Flippin’ Blood, which gives step-by-step illustrated instructions on how to safely give a patient each different type of blood product.

BloodSafe also developed an e-learning (online) program to help hospitals ensure staff competency in transfusion practice. The e-learning program is freely available for anyone to view or use (at www.bloodsafelearning.org.au). It is a highly interactive, multi-media rich program that is engaging,
practical and recreates the hospital experience for staff with a built-in assessment component. Developed initially for South Australia it has subsequently been adopted by all states and territories. Since its release it has been used by more than 70,000 health professionals, and has received $1.1 million of national funding for its ongoing maintenance and development.

BloodSafe project activities are currently focussed on using the South Australian red cell data linkage results to help target areas for audit and facilitate engagement with clinicians. By developing tailored reports on blood usage patterns by specialty, the program is raising awareness of the potential impact patient blood management strategies could have. Supporting this, a new patient blood management governance framework has recently been endorsed by the Department of Health and will be implemented during 2011.

BloodSafe activities are overseen by the BloodSafe Steering Committee, a group of representatives from the Department of Health, the Blood Service and other BloodSafe Program partners, which in turn reports to the South Australian Department of Health’s Blood Sector Advisory Committee (SABSAC). The BloodSafe Steering Committee reports to the SABSAC. Several combined Department of Health-Blood Service User groups report to SABSAC (the Clinical User Group, IVIG User Group and the Coagulation User Advisory Group) to provide advice and assist in priority setting for the South Australian BloodSafe program.

The nurse educator employed by the Blood Service provides day-to-day coordination and support to the nurses’ network. The haematologist employed by the Blood Service provides high-level medical expertise to the program and mentoring to the BloodSafe nurses.

BloodSafe staff use a free clinical audit tool called Auditmaker; this has been developed by the Australian Centre for Evidence Based Clinical Practice. This tool allows audit data to be collected and analysed by clinical staff.

The BloodSafe website provides access to documents, tools and resources developed by or for the BloodSafe Program. Included on the website are:

- Publications – presentations, policies and reports related to the BloodSafe Program;
- Education and Standards:
  - BloodSafe e-Learning;
  - Practice Guidelines and Standards;
- Resources for clinicians:
  - Blood Specimen Collection;
  - Prescribing Blood & Blood Products;
  - Administration of Blood & Blood Components;
  - Anaemia and PBM;
- Resources for Health Services:
  - Storage and Transport;
  - Blood Product Registers;
• Consumer information.

**The BloodSafe e-learning project**

In 2006 the South Australian Department of Health funded the development of an online education package for clinical staff involved in the transfusion chain, including medical officers, nurses, midwives and courier or porter staff, who transport blood products. The BloodSafe e-Learning tool has been very successful throughout Australia and in 2008–09 the JBC agreed to provide national support for three years.

The website continues to be popular, with new registrations averaging around 2,500 per month; in June 2010 it reached a significant milestone when the user registration number hit 50,000. The project is highly regarded; in 2009 the program received two South Australian awards and was a finalist for the South Australian Premier’s Award.

During 2009–10, governance arrangements for the project were established with the creation of a National e-Learning Transfusion Advisory Committee. Additional material was added to the website, including promotional print documents, a promotional DVD and reporting functionality, and discussions commenced with the database developers on changes needed for additional content. The committee agreed that the program for the next 12 months would focus on:

• review of existing content and update as needed to conform to current practice and policy (using the new patient blood management guideline if available);
• completion of the post-partum haemorrhage module;
• expansion of the existing assessment database and formats;
• development of an anaemia management module with an initial emphasis on iron deficiency anaemia;
• development of a blood cold chain management/inventory module (particularly for hospitals with no on-site pathology laboratory).

**Effectiveness**

Initial BloodSafe audits of SA metropolitan teaching hospitals looking at red blood cell transfusions in stable patients in 2002 found that 18 per cent of these were outside the NHMRC guidelines. With development of practice improvement tools and education, this fell to 4 per cent and was maintained at less than 1 per cent five years on (SA Department of Health).

In addition to improvements in appropriate use, there were significant and parallel improvements in documentation of patient consent, the two person patient/blood bedside checking procedure transfusions given over more than 4 hours (increasing the risk of bacterial growth in the bag) and blood specimen collection (ensuring blood tubes for blood group testing are labelled with the correct patient details).

The BloodSafe e-Learning project has also had a high rate of participation, as indicated above.

**Western Australia**

**Initiatives**

WA has embarked upon a comprehensive PBM Program, WAPBMP. It commenced in 2008 and will be implemented across the entire WA public health system over a five-year period.
The WAPBMP has been developed on established and proven international models and will apply these across the health care system.

The WAPBMP is an evidence-based, patient-focused concept encompassing a philosophy that realigns the transfusion paradigm from the traditional product focus to a patient focus. PBM involves an integrated multidisciplinary multimodal team approach built around the three pillars of patient blood management:

- optimising the patient’s red cell mass well before surgical or medical intervention;
- minimising the patient’s blood loss throughout the patient’s treatment; and
- optimising recovery by harnessing and optimising patient-specific physiological tolerance of anaemia.

The WAPBM Program has commenced at Fremantle Hospital and Health Service with the appointment of a PBM Program Clinical Director and a PBM Nurse Coordinator. Equivalent statewide appointments are being negotiated. The program also proposes to expand by:

- placing medical staff and PBM clinical nurse consultants in each tertiary hospital and ultimately these resources will be available to each Area Health Service in Western Australia;
- establishing effective data collection and monitoring systems to facilitate evaluation, safety and quality improvement and outcomes research;
- building a strong guiding coalition of champions to change the paradigm and realign institutional culture;
- developing and implementing PBM clinical policies, procedures and guidelines--including the development of an anaemia / iron deficiency identification and management program;
- developing multiple education and communication strategies;
- benchmarking locally and with international centres of excellence.

Although the WAPBMP is state based, it is structured to allow and encourage partnerships and collaborations across the state and outside WA.

A Clinical Reference Group (CRG) has been established and is continuing to be expanded to provide senior clinical leadership and facilitate communication between the Steering Committee and multidisciplinary teams being established within tertiary health services. The CRG will participate in:

- key working parties to develop protocols, algorithms and training programs;
- developing research projects; and
- facilitating and integrating PBM as the standard of care through effective communication, information sharing, and scientific understanding.

Links have also been established with the Medical Society for Blood Management [www.bloodmanagement.org](http://www.bloodmanagement.org) and the Society for the Advancement of Blood Management [www.sabm.org](http://www.sabm.org).

Local, national and international experts in the field of PBM have contributed to an education program to familiarise doctors, nurses, scientists and other allied health professionals with this new standard of care.
In 2010, WAPBM was introduced formally into one tertiary public hospital. In other hospitals, in both the public and private sector, there has been increased interest in reviewing and updating current protocols. Hospitals with high levels of surgical activity are working to raise the profile of pre-admission clinics and to encourage attendance in a time frame that will enable anaemia to be detected and treated. General Practitioners also are being encouraged to identify and manage anaemia in their patients.

An intranet website has been established and this provides access to information and other resources. The range of these resources, including fact sheets will be increased as the program develops.

Data analyses using the WA data linkage system have commenced, as has the development of information and ordering systems that support appropriate ordering and decision making consistent with PBM principles.

As the WAPBM expands throughout the public sector it is expected that it will become so integrated into practice improvement activities as to become self-sustaining.

**Effectiveness**

NBA National Supply Plan and Budget figures show an absolute decline between 2008-09 and 2009-10 of around 2,000 red blood cell units in WA. While this broad indicator is encouraging, it must be noted that it pertains to a single year only. There may be a range of other factors which have influenced the decline in red cell use in WA in a single year, as the volume of red cells has not followed a uniform trend over the period 2003-04 to 2009-10.

**TASMANIA**

The Department of Health and Human Services has introduced a range of initiatives in Tasmania as part of a blood management program.

- A MOU is in place to provide for the distribution of fresh blood products between hospitals.
- The Tasmanian Supply Plan budget was devolved to Area Health Services in 2008, with the proportional share of payments made to the NBA calculated on AHS utilisation.
- There is transfusion laboratory and clinician participation in the supply planning and review, which promotes understanding of demand drivers.
- Transfusion nurses are employed at the four major hospitals and coordinate education, Haemovigilance and audits.
- Policies and procedures are maintained and are available on intranet. E-learning is rolled out across all public hospitals.
- An accreditation program has been implemented for rural facilities for use of blood and blood products.
- Regular reviews of patients receiving IVlg in Tasmania are conducted by the Blood Service transfusion team in conjunction with the treating clinicians, to promote optimal patient care and best use of IVlg.
- Tasmania is participating in the proof of concept trial for ORBS with all public and private sector laboratories now operating with ORBS.
• Tasmanian utilisation data is reported at Approved Health Provider level and provided to Area Health Services.

• Tasmanian hospitals are active participants in the Blood Matters collaborative.

• Adverse events are reported to the statewide EIMS system. SAC1 and SAC2 are referred to the serious incident panel. Significant blood product incidents are reported to the STIR regional haemovigilance program and Tasmanian clinicians participate on the STIR Expert Working Group.

Effectiveness

The Department of Health and Human Services believes that the MOU between Tasmanian hospitals, referred to above, has been a key factor in red cell use in Tasmania decreasing by around 20 per cent since 2002 to the current period and remaining below the national average.

AUSTRALIAN CAPITAL TERRITORY

The ACT does not have an explicit blood management program. However, ACT Health has had a fulltime TNC since 2008. The TNC works operationally within The Canberra Hospital (TCH), and is administratively supported by the Senior Policy Officer – Blood and Blood Products, Population Health Division under the authority of the ACT Chief Health Officer.

The TNC’s immediate clinical supervisor is the Director Haematology/Transfusion at TCH and she works closely with him in supporting the work of the TCH Transfusion Committee.

The role, responsibilities and duties of the Transfusion Nurse includes:

• clinical education relating to the appropriate use of blood and blood products:

  : some sessions are provided as scheduled ward in-services and others are provided as part of Clinical Staff Orientation programs or on an ad-hoc basis as requested or required. Awareness raising sessions, focussed on nurses, were held in 2009 and 2010, with public and private participation;

• development and promulgation of blood product related policy and standard operating procedures:

  : two recent examples of policies that have been developed primarily by the Transfusion Nurse are Blood and Fresh Blood Products Administration and Intravenous Immunoglobulin Approval and Administration;

• preparation and promulgation of ACT Health Patient Information Brochures, available on the TCH Intranet;

• response to and reporting of Blood Related Adverse Events at each of the local, jurisdictional and national reporting forums;

• collaboration with Blood Matters STIR;

• local Champion for the territory wide adoption of the SA BloodSafe e-learning program, which is now part of mandatory clinical training for both public and private hospitals.

Particular initiatives have been two Transfusion Specific full day forums over the past two years:
• the first Transfusion Forum in 2009 was used to launch a new local initiative in the ACT called the ACT Transfusion Champions program. This program regularly brings together clinical staff from across the ACT and is used to promulgate efficiently and effectively blood and blood product information such as blood policy updates across all relevant treating areas, both public and private;

• the second Transfusion Champions Forum was held in 2010 at Red Cross House. Participants (primarily nurses from across ACT) were given tours of the blood donor collection and production facility as well as a tour the transfusion laboratory at TCH. The program also included a series of workshops that focused on four topics, namely Transfusion Reactions, Massive Transfusion, Haemophilia and IV Ig Approval and administration. The Forum was also used to promote the ‘NO BAND – NO BLOOD’ campaign designed by the Transfusion Nurse.

The Population Health Division of ACT Health hosts the quarterly meetings of the Appropriate Use Of Blood Reference Group (AUBRG). AUBRG has stakeholder representation from all of the ACT hospitals (public and private), the Blood Service and the National Blood Authority. The role of AUBRG is to provide strategic direction and leadership in the safe and high quality use of blood and blood products in ACT health care settings.

Effectiveness

ACT Health advises that the governance arrangements for the TNC have been very beneficial in broadening her role and activities across all hospitals in the ACT – both public and private.

ACT Health advised that private sector nurses have welcomed the awareness raising activities and at least one private hospital has distributed information material prepared in the public sector.

NORTHERN TERRITORY

No information was made available to the project in regard to NT initiatives.

OVERSEAS EXPERIENCE WITH APPROPRIATE USE STRATEGIES

A number of studies were available which highlighted the experience of some other countries to promote appropriate transfusion practice.

CANADA

The Ontario Government of Canada in its 2000 budget committed ‘$21 million over three years for projects supporting blood conservation and bloodless surgery techniques.’ In 2002 the Ministry of Health and Long-term Care of Ontario developed a provincial blood conservation program. A medical director and a project administrator were appointed, along with program nurse coordinators in 23 hospitals. The focus was on three targeted procedures. Initial results at 12 months demonstrated an overall 24 per cent reduction in blood use in total knee arthroplasty (TKA), 14 per cent reduction in abdominal aortic aneurysm, and a 23 per cent in CABG surgery. Additionally, patients who were transfused received fewer units. Non-transfused had lower PI rates (p<0.05) and LOS (p<0.0001) and multivariate analysis showed transfusion as an independent predictor of increased LOS. The investigators concluded: ‘Implementation of the program represents important savings in costs associated with blood components, hospital stay and work in transfusion laboratories and nursing units, as well as enhancing patient satisfaction and safety.’ In an updated report published in 2007 (Freedman, 2007) data showed at 18 months and 24 months there was an overall reduction in the number of patients receiving red blood cell transfusion. The
authors stated that the annual cost of running the program was $1,800,000, and the total estimated savings were $14,950,000.

Wong (2007) randomised 30 hospitals in Canada to either a blood conservation algorithm (BCA) or usual care (UC) in patients undergoing total hip replacement surgery and found that the BCA resulted in a significant overall 10.4 per cent reduction in the allogeneic blood transfusion rate. More details of this study are at Appendix 5.

The optimum strategy for reducing allogeneic blood transfusion in patients undergoing total hip joint arthroplasty (THJA) is unknown. The effectiveness of a comprehensive BCA was evaluated by means of a cluster randomization trial by Wong (Ibid.). Thirty hospitals performing primary THJA were randomly assigned to implement the algorithm or to continue with UC. Subsequently, the institutional rate of allogeneic transfusion was determined for 60 consecutive patients who underwent surgery at each site. The BCA consisted of patient and provider education, Hb-based recommendations for specific blood conservation strategies (recombinant human erythropoietin [rHuEPO] or autologous blood donation [ABD]) and transfusion guidelines. The main outcome measure was the institutional allogeneic transfusion rate.

One hospital withdrew consent after randomization, resulting in 14 hospitals assigned to BCA and 15 to UC. In the BCA arm, the institutional rates of rHuEPO use and ABD participation were 20.1 and 27.1 per cent compared to 0.6 and 25.8 per cent, respectively, in the UC arm. The allogeneic transfusion rate was substantially reduced in hospitals assigned to the BCA group (p = 0.02; absolute risk reduction, 9.6 per cent [26.1 per cent UC vs. 16.5 per cent BCA]). Multivariate analysis of patient-level data showed that assignment to the UC arm was an independent risk factor for allogeneic transfusion (p = 0.037; odds ratio, 1.8; 95 per cent confidence interval, 1.0-3.1) when adjusted for other prognostic factors. No differences were observed in the use of autologous blood.

Wong concluded that a comprehensive approach to blood conservation was superior to Usual Care for reducing allogeneic transfusion in patients undergoing THJA.

University Health Network, a consortium of 3 teaching hospitals in Ontario, published their initial data looking at the contribution of blood conservation strategies such as pre-operative autologous donation, pre-operative erythropoietin therapy, acute normovolaemic haemodilution (ANH) and intra-operative cell salvage. They have shown a reduction in transfusion rate in elective spinal surgery from 74 per cent without blood conservation to 7 per cent with multimodal blood conservation (Karkouti, 2002a). In anaemic total joint arthroplasty patients they showed a reduction from 52 per cent to 12.8 per cent respectively (Karkouti, 2002b).

USA

There were reported to be over 200 programs to improve transfusion practice now operating in the US in 2009 (Thomson, 2009).

Rosengart (Helm, 1998) from the New York Hospital’s Cornell University Medical Center developed a multimodality blood conservation program to reduce allogeneic transfusion in open-heart surgery. Over a three-month period Rosengart and his team successfully carried out 100 consecutive CABG surgeries without using allogeneic blood. They then compared these results (multimodality blood conservation group – MMD) with the records of similar patients whose operations were performed without the multimodality approach and where allogeneic blood transfusions had been used. Results showed that time on the ventilator after surgery was reduced significantly in the MMD group (18 hours versus 22 hours). Although not statistically significant, the average LOS in intensive care was shorter (42 hours versus 44 hours) and postoperative hospital stay was less (7.4 days versus 8.9 days). When compared with another group of patients matched by DRG and operated on before the
multimodality approach, the average costs for the MMD group were 10-24 per cent less and LOS was 16-26 per cent less. This represented a US$387,070 saving in the MMD group or US$3,870 per patient.

Virginia Commonwealth University Hospital established in two phases a multidisciplinary blood conservation program. The first phase involved creating a database and establishing and monitoring transfusion triggers. The second phase, they state, involved ‘pursuing new and innovative methods to avoid transfusion.’ With the implementation of their program in cardiac surgery they reported that their overall blood product transfusion rate decreased from 79 per cent to 39 per cent and red blood cell transfusion rate decreased from 35 per cent to 16 per cent. They also reported improved patient outcomes with the implementation of their program. When they compared patients pre- and post-program, patients had identical overall risk score. But for post-program patients there was a significant reduction in inotropic support (23.3 per cent vs. 43.1 per cent, p=0.05) use of intra-aortic blood pump (6.1 per cent vs. 15.0 per cent, p=0.01), reoperation for bleeding (2.4 per cent vs. 5.9 per cent p<0.05) and acute renal failure (2.8 per cent vs. 5.1 per cent, p<0.01). They estimated that the program resulted in direct cost savings of US$569,862 per annum and US$1.4 to 2.4 million per annum when including indirect costs (DeAnda, 2006; Green, 2004).

Pennsylvania Hospital, established as the first hospital in the United States (1751) and the country’s first medical school (1765) and recently rated as one of the top 10 hospitals in the USA, also instituted a ‘bloodless medicine and surgery’ (BMS) program initially to provide specifically for patients requesting bloodless management. In 2003 the institution extracted data and compared fiscal barometers of final billing and LOS for patients enrolled in the BMS program with the overall patient population. BMS patients were represented in all surgical and medical specialties including obstetrics and haematology/oncology. BMS patients exhibited an average 17 per cent lower final billing amount, representing lower charges, thus lower cost, and a 10 per cent reduced length of hospital stay. From this analysis they estimated a potential US$7 million saving per year for the institution in blood costs alone (not including the associated impact on patient outcomes) if the BMS program was extended hospital wide. A 20 per cent reduction in blood usage would save the hospital US$1.4 million, a 40 per cent reduction US$2.8 million, a 60 per cent reduction US$4.2 million and an 80 per cent reduction US$5.6 million (Data presented at SABM 2003).

The Chief Executive Officer of Pennsylvania Hospital has reported on the hospital-wide expansion of their program resulting in a 10 per cent reduction in blood costs and a 13 per cent reduction in hospital LOS (Morgan, 2005).

Ghiglione has reported that the establishment of a multidisciplinary Blood Management Program across the three campuses of the Swedish Medical Centre in Seattle, Washington had a significant impact on transfusion utilisation, patient outcomes and costs (Ghiglione, 2007). Their program initiated an aggressive ongoing in-house education program in transfusion indications and risks and blood conservation strategies. They also set up an anaemia program offering anaemia consults for surgical patients and in-house anaemic patients. Their blood management program has resulted in significant reductions across their three hospital campuses in red blood cell transfusions, particularly in cardiac (30 per cent) and orthopaedic (20 per cent) surgery, and blood acquisition costs, while also reducing complications. They observed a significant reduction in hospital LOS with their elective orthopaedic surgery patients.

The implementation of a program at the University of Southern California University Hospital in Los Angeles lead to the development of transfusion-free liver transplantation—a procedure traditionally associated with major blood loss and multiple transfusions. The team, headed by the program Medical Director and liver surgeon Dr Nicolas Jabbour, has performed more than 32 (age range 6 months to 66 years) ‘bloodless’ transplants and reported in the literature on 27 of these (Jabbour, 2005a; 2005b). Jabbour and colleagues have compared survival rates between ‘transfusion-free’ and
matched ‘transfusion-eligible’ live donor transplant patients. They report a 100 per cent survival in their transfusion-free live-donor transplant patients (mean follow up of 965 days) compared with a 90 per cent survival in similar transfusion-eligible live-donor transplant patients. Of interest, the authors note that their transfusion-free patients had significantly higher preoperative Hb levels due to preoperative Hb augmentation therapy. This adds further support to the concept of preoperative anaemia identification and treatment (Jabbour, 2004).

In January 2003 the University Hospital of Pennsylvania instituted an anaemia management program for trauma patients in the ICU (Earley, 2006). When compared with a historical control group and after adjusting for confounders the program decreased transfusion from a mean of 23.1 units of red cells per patient to 17.1 units (P=0.057), representing a 22.5 per cent reduction (P=0.097). They also noted a significant reduction in the incidence of ventilator-associated pneumonia (8.1 per cent versus 0.8 per cent; P=0.002). Total red blood cell costs decreased during the study period from $503,000 to $397,000.

Stulberg and Zadzikla from the Cleveland Center for Joint Reconstruction in Cleveland, Ohio report that the introduction of a patient-specific blood management strategy in their area resulted in 20 per cent reduction in their transfusion rate within the first year and a $50,000 saving in direct blood and blood product costs (Stulberg, 2007).

With the institution of an ‘algorithm-based blood conservation program’, Pierson et al. (2004) from St Vincent Center for Joint Replacement, Indianapolis, Indiana, reported that they were able to achieve a 2.1 per cent allogeneic transfusion rate in primary total knee and total hip arthroplasty (1.4 per cent total knee; 2.8 per cent total hip).

With the implementation of a multidisciplinary program, Brevig (2009) from Providence Regional Medical Center Everett, Everett, Washington, reduced their transfusion rate in cardiac surgery over a five-year period from 48 per cent to 18 per cent.

Englewood Hospital and Medical Centre in New Jersey, an affiliate of Mount Sinai School of Medicine, is a major academic tertiary care institution providing the full range of medical/surgical specialties. In 1997 it instituted a formal hospital-wide blood conservation program appointing a medical director, a coordinator and support staff. Englewood designed a transfusion database as a first step towards understanding transfusion decisions and transfusion requirements and progressively introduced a multidisciplinary multimodality approach to blood conservation. The hospital reports the transfusion rate has decreased each year with the institution of its formal program. In the first four years of their program they reduced blood usage by 42 per cent (Perelman, 2001; Shander, 2001; Thomson, 2009).

Englewood’s cardiothoracic surgery blood conservation program, introduced in 2000, demonstrates significantly reduced blood utilisation compared with published transfusion data in US multicentre studies (Figure 14).
FIGURE 14: UNSTRATIFIED CARDIAC SURGERY TRANSFUSION STATISTICS FOR EMHC COMARED WITH PUBLISHED TRANSFUSION STATISTICS IN US MULTI-CENTRE STUDIES


In 2004 they reported their institution’s results with 553 consecutive patients undergoing CABG, VR, and combined CABG and VR procedures. This series included elective, urgent, emergent procedures and re-operations. The overall red blood cell transfusion rate for this spectrum of cardiac surgeries was a low 13 per cent with substantial reductions in plasma, platelet and cryoprecipitate transfusions and a morality rate of 3.5 per cent (Moskowitz, 2004).

In 2010 Moskowitz et al. compared red cell transfusion rates and outcomes in a cohort of 586 patients undergoing isolated CABG surgery operated on in their developed PBM Program, and 586 propensity-score matched patients operated on in institutions without a PBM program. The percentage of patients transfused was 75 per cent lower in the PBM Program cohort compared with the non-PBM Program cohort (10.6 per cent versus 42.5 per cent; P<0.001), mortality was 68 per cent lower in the PBM Program cohort (0.8 per cent versus 2.5 per cent; P=0.02) and there was a 40.6 per cent reduction in serious complications in the PBM Program cohort (11.1 per cent versus 18.7 per cent; P=0.0002).

EUROPE

A landmark Austrian national study by Gombotz H, et al. benchmarked transfusion practice and evaluated blood conservation strategies in 18 hospitals (Gombotz, 2007). This study found wide variations in transfusion practice across participating hospitals and identified predictors of red blood cell transfusion that support the three-pillar concept of blood conservation as a means of reducing transfusions namely:

- correct anaemia prior to surgery;
- minimize perioperative blood loss; and
- adopt a lower transfusion trigger.

The study estimated that adequate preoperative management of anaemia in their patient population may have reduced transfusion by 50 per cent. As blood loss was the main predictor of transfusion, methods to minimise blood loss are highlighted as important blood conservation
strategies. The authors also estimate from their benchmarking that, if the transfusion rates of the one third of the hospitals that reported the lowest blood usage were matched overall, a reduction in transfusion of up to 60 per cent could be achieved. The investigators also identified blood-ordering procedures as another area for potential cost and product savings. Crossmatching was performed routinely in all but one centre. Sixty-one per cent of crossmatched blood was not transfused. A more patient-specific blood ordering system, they suggest, could result in significant savings. Further details of this study are at Appendix 5.

Martinez and colleagues (2007) developed and evaluated a program to change practice and reduce blood transfusions and costs in elective orthopaedic surgery in their institution in Paris, France. Their study included patients scheduled for elective total hip arthroplasty and TKA and was conducted in three phases: 1) initial evaluation, 2) algorithm development and introduction, and 3) post-implementation evaluation. The algorithm was based on patient-specific tolerable blood loss and expected blood loss and plotted on a diagram. Blood-sparing techniques, including preoperative autologous donation (PAD), epoetin, postoperative blood salvage or combinations of these, were listed on the diagram which contained curves indicating where blood loss may exceed patient-specific tolerance, and when and which blood-sparing technique(s) may be required. Once developed, the algorithm was presented to the anaesthetists along with transfusion guidelines.

According to this institution’s stated normal practice patients had an anaesthesia consultation one month prior to surgery where the patient’s red blood cell level was used in conjunction with the algorithm to plan the patient’s blood-sparing strategies. The investigators then performed a post-implementation clinical and economic evaluation. The algorithm resulted in fewer autologous, allogeneic and mixed blood transfusions. The total number of transfused patients was reduced by over 50 per cent. The use of PAD halved after the introduction of the algorithm and the number of wasted autologous units was also halved. Overall, patient mean red blood cell mass was higher on the day before surgery and 5 days after surgery during the post-implementation phase. The authors’ cost assessment revealed a 50 per cent reduction in hospital costs with no increase in overall costs (including out-of-hospital costs).

Slappendel and colleagues (2003) from the Academical Hospital Maastricht, Maastricht, The Netherlands developed a comprehensive perioperative blood conservation program for orthopaedic surgery. Approximately 4,500 orthopaedic surgery procedures are performed each year in their institution. They report that their algorithmic approach resulted in an 80 per cent reduction in red blood cell transfusion and a 40 per cent reduction in deep wound infections.

In Spain the Hospital del Mar, Barcelona, has reported a 67 per cent reduction in allogeneic blood transfusion in elective orthopaedic surgery patients enrolled in their blood conservation program (Lopez Soques, 2002). Muller and colleagues (2004) from the University of Berne and the Winterthur Hospital in Winterthur Switzerland report a reduction in their transfusion rate in hip and knee replacement surgery from 35.0 per cent to 19.8 per cent after the introduction of a blood management algorithm and education program. The General Prefectural Hospital of Aegion instituted a ‘Blood Saving Protocol’ in elective TKA. The protocol included preoperative use of erythropoietin, iron and folate, ANH, and postoperative cell salvage, meticulous haemostasis and patient-specific decreased transfusion triggers. Kourtzis et al. (2004) reported that allogeneic blood utilisation was reduced by 94 per cent (p <0.001).

In the United Kingdom, the UK NHS Circular Better Blood Transfusion Safe and Appropriate Use of Blood (HSC 2007/001) was issued in November 2007, detailing the actions required of NHS Trusts, NHS Blood & Transplant and clinicians to improve transfusion practice. It included an action plan and an ongoing programme for Better Blood Transfusion to be implemented in each Trust by November 2008, when the first national audit of compliance would be undertaken. The Report of the 2008 audit provides an excellent and encouraging example of the outcomes that can be achieved
in national programs to improve transfusion practice and appropriate use in a consistent, effective way. The Executive Summary of the 2008 Audit Report (Murphy, 2008) is set out in Appendix 5.

LESSONS LEARNT FROM APPROPRIATE USE STRATEGIES

This section draws together the key lessons from the experiences of appropriate use strategies in Australia and overseas.

WHO ARE THE KEY DECISION MAKERS?

The success of strategies will depend upon the influence they have over the key decision makers in the transfusion chain of events. This section considers some of the drivers or influences that impact on the appropriate use, as defined, of blood and blood products.

Ultimately it is the clinician who decides how much blood a patient will receive for a given indication. Clinical practice is of course guided by clinical guidelines, but in Australia, the extent of the influence of guidelines is not great. In addition, not all blood and blood products in Australia are covered by active guidelines, and the guidelines that do exist in some instances are very generalised.

As was discussed above, the uptake of guidelines by clinicians is commonly poor. Ways to enhance the uptake of guidelines are addressed below.

Clinicians are influenced by a range of other factors. Stakeholders consulted during the course of the project highlighted the factors below. Based on anecdotal evidence and opinions of stakeholders only, these influences might be arranged in the following descending order of influence:

Patient outcomes

Clinicians are driven by the interests of their patients’ wellbeing. What they believe is good for their patients, however, is influenced in turn by some of the factors appearing below.

Peer practice

Stakeholders, including clinicians themselves and other health care professionals, emphasised that clinicians are influenced very strongly by the practice of their peers. Clinicians view their peers as other clinicians within their area of specialty.

Prescribing ‘culture’

This often pertains to individual institutions. There is much evidence indicating wide variations in prescribing practice from hospital to hospital. Some stakeholders referred to the prescribing culture arising from the practices of senior clinicians within institutions. Because junior clinicians are trained and mentored by these senior clinicians, prescribing norms perpetuate.

Education and training

Clinicians base practice on their formal education, but also vocational training. Many stakeholders expressed the view that formal education of the clinical use of blood could be improved. Appropriate practice needed to be included in vocational training, but that should capture not just registrars, but senior clinicians as well, for the reasons indicated under the discussion of prescribing culture above.
Clinical guidelines

Clinicians consulted during the course of this project agreed that clinical guidelines were an influence on prescribing practice. However, the degree of influence was always qualified. Many clinicians found the current guidelines not to be ‘user friendly’ or readily accessible in a clinical setting. This impeded their effectiveness. A study in NSW in 2007 (Eureka Strategic Report, 2007), for example, found that ‘most doctors assumed that a set of guidelines existed, but very few had specific knowledge of the NHMRC guidelines’.

There was a strong view among clinical stakeholders consulted that training and culture were the factors with greater influence over prescribing practice than the guidelines.

The poor uptake of clinical guidelines is not a factor unique to Australia. This fact, as well as information from research literature on improving the uptake of the guidelines, are taken up further below.

Knowledge and evidence

The NHMRC/ASBT Blood Components guidelines are now 10 years old. The evidence base for use of blood and blood products has not stood still in that time. Stakeholders agreed that the knowledge and evidence base was an influence over clinical practice, with the following qualifications.

Knowledge and evidence had to be accessible, and many clinicians struggle to stay abreast of new knowledge and evidence. The fact that blood and blood products are used by clinicians across many specialties, who are not themselves specialists in blood clinical practice, makes the dissemination of new knowledge and evidence an even greater challenge in the blood sector. Stakeholders felt that the practice of peers was a much stronger influence over behaviour.

Financial incentives

Some stakeholders questioned whether financial incentives were an influence on prescribing behaviour. In particular, stakeholders pointed to the MBS item 13706, which provides for a Medicare Benefit to be paid in respect of the charge a clinician can make for the administration of blood in a private health care setting. For example, some stakeholders relayed anecdotes of ‘prescription splitting’ in some private hospitals. Instead of prescribing a two-unit dosage of red cells, the clinician would split this into two by one unit prescriptions. If this occurred, the clinician would be able to charge a Medicare-claimable fee for each prescription.

- The project team has no evidence as to whether this practice occurs. It is also unclear whether the practice would influence the demand for blood and blood products.
- The remuneration arrangement (perhaps ironically) could encourage compliance with one aspect of the NHMRC/ASBT Blood Components guidelines, namely, to prescribe blood one unit at a time to enable progressive assessment of the patient. As will be indicated later in this report, common practice in Australia is to prescribe multiple units at a time.
- On the other hand, Medicare item 13706 could encourage clinicians to over-prescribe blood.

A New Paradigm—Patient Blood Management

The 2007 paper by Isbister (2007) questions the current paradigm, in which there is excessive focus on the supply side of the blood transfusion chain rather than the clinical problem facing patients and clinicians. Blood transfusion should no longer be the default therapeutic decision when evidence for efficacy is lacking and there is clinical uncertainty. The appropriateness of transfusion practices will only improve, not by expecting clinicians to be gatekeepers of the blood supply, but with better patient blood management based on a sound understanding of pathophysiology and better evidence
for transfusion efficacy. Evidence-based transfusion medicine should view a patient’s own blood as a valuable and unique natural resource that should be conserved and managed appropriately. Allogeneic blood transfusion should only be used as therapy when there is evidence for potential benefit, there are no alternatives, a quality product is available and the risks are appropriately considered and balanced against the benefits.

There is now a compelling and growing body of evidence, which indicates that the level of inappropriate use of allogeneic blood components provides a strong argument for transfusion to be much more focussed on patient outcomes, and therefore more on appropriate use based on evidence. Much of the evidence in this regard relates to red cells with less evidence available on platelets and FFP.

The need for more appropriate use of blood products is increasingly being linked with data and information about costs and trends in order to achieve both improved patient outcomes and cost savings for health systems.

According to an editorial in the British Medical Journal, changing transfusion practice requires ‘a cultural shift among clinicians, managers and policy makers.’ (Mortimer, 2002) There is therefore a growing need to develop new and innovative ways of thinking about and practicing patient blood management and transfusion medicine (Goodnough, 2003b; Seeber, 2008; Shander, 2003; Spahn, 2000). Cost-effective blood-conservation techniques should be utilised and further developed and more appropriate evidence-based transfusion practice investigated and applied.

Most evidence suggests that a ‘complex’ intervention is needed, combining clinical criteria for appropriate use, integration of quality improvement measures (including informed consent for patients) into practice and ongoing monitoring and review (National Health and Medical Research Council, 2001).

The concept of comprehensive patient blood management constitutes a significant improvement in transfusion philosophy. Patient blood management seeks to realign the transfusion paradigm to centre on patients, rather than the products. The primary focus is on conservation and appropriate management of the patient’s own blood by means of effective coordinated, multidisciplinary, multimodal clinical medicine. Within the patient-blood-management model transfusion decisions are based on correct diagnosis and patient-specific clinical and physiological factors, with clinicians considering patient values and choices (Haynes, 2002; Sazama, 2007). Authorities have suggested informed and empowered patients can be important drivers for change in transfusion practice (National Health and Medical Research Council, 2001). Another force for change in recent years has been the international evolution of comprehensive patient blood management programs (Farmer, 2000; Goodnough, 2007; Martyn, 2002; Spiess, 2006). The structure of most of these programs incorporates the principles of the John Kotter model for successful change management (Kotter, 1979; 2002) and utilises an established and proven model including:

- leadership for successful implementation;
- accurate data collection and monitoring as a basis for evaluation, feedback, continuous practice improvement and risk management;
- multiple ongoing education and communication strategies for all stakeholders to bring about a sustained realignment of the organisation’s culture;
- empowerment of a broad base of people to take action and introduce new evidence-based approaches and practices;
• adoption of a coordinated, integrated, perioperative/peri-event, multidisciplinary and multimodality team approach to patient blood management.

Data from these programs show they are effecting significant reductions in blood usage, reporting between 10-95 per cent reductions depending on baseline blood usage and extent of program implementation (Wong, 2007; Ghiglione, 2007; Helm, 1998; Moskowitz, 2004; Brevig, 2009; Slappendel, 2003; Pierson, 2004; Bui, 2002; DeAnda, 2006; Ferraris, 2007; Freedman, 2005; 2007; Green, 2004; Reddy, 2009; Van Der Linden, 2001; Kourtiz, 2004; Martinez, 2007). At the same time they are achieving improved patient outcomes while reducing costs (Helm, 1998; DeAnda, 2006; Freedman, 2007; Green, 2004; Morgan, 2004; 2005).

These coordinated programs adopt aggressive education strategies enabling all stakeholders - including patients and all clinical and non-clinical hospital staff - to be fully informed of current evidence on the risks and benefits of transfusion along with measures to minimise transfusion and utilise appropriate alternatives. They implement an integrated multidisciplinary, multimodal medical/surgical approach that has as its focus individualised advanced patient blood management with the view of improving patient care and outcomes (Goodnough, 2003a). The accumulating evidence demonstrates that these programs can dramatically reduce blood usage, at the same time reducing morbidity, mortality and length of hospital stay, as well as minimising costs. Following are results and data from some of these programs.

Table 7 summarises the relative red cell unit savings of the above PBM modalities, highlighting that a significant percentage of transfusions could be eliminated if these strategies were employed as part of a coordinated multidisciplinary multimodal PBM Program.
TABLE 7: SUMMARY TABLE OF RELATIVE RBC UNIT SAVINGS OF VARIOUS PBM MODALITIES

<table>
<thead>
<tr>
<th>Approximate contributions of selected PBM modalities in the surgical patient</th>
<th>Number of</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Perioperative</strong></td>
<td></td>
</tr>
<tr>
<td>Harnessing patient’s tolerance of anaemia (restrictive transfusion trigger)</td>
<td>1-2</td>
</tr>
<tr>
<td>(Hebert, 1999)</td>
<td></td>
</tr>
<tr>
<td>Restricted phlebotomy</td>
<td>1</td>
</tr>
<tr>
<td>(Smoller, 1986)</td>
<td></td>
</tr>
<tr>
<td><strong>Pre-operative</strong></td>
<td></td>
</tr>
<tr>
<td>Optimisation of RBC mass (perioperative anaemia management)</td>
<td>2</td>
</tr>
<tr>
<td>(Goodnough, 1992; 2000)</td>
<td></td>
</tr>
<tr>
<td><strong>Intra-operative</strong></td>
<td></td>
</tr>
<tr>
<td>Meticulous haemostasis &amp; surgical technique</td>
<td>1 or more</td>
</tr>
<tr>
<td>(Spence, 1993)</td>
<td></td>
</tr>
<tr>
<td>Acute normovolaemic haemodilution (ANH)</td>
<td>1 or more</td>
</tr>
<tr>
<td>(Monk, 1995; Goodnough, 1998)</td>
<td></td>
</tr>
<tr>
<td>Autologous cell salvage</td>
<td>1 or more</td>
</tr>
<tr>
<td>(Goodnough, 1996)</td>
<td></td>
</tr>
<tr>
<td><strong>Post-operative</strong></td>
<td></td>
</tr>
<tr>
<td>Autologous blood salvage</td>
<td>1</td>
</tr>
<tr>
<td>(Goodnough, 1999)</td>
<td></td>
</tr>
</tbody>
</table>

Many of the approaches inherent in the structure of PBM have been highlighted for many years as required in the blood sector in Australia. For example, in 2003, the report of the Blood Transfusion Improvement Collaboration in NSW (p76) recommended that to sustain and spread the good work of the collaborative in reducing inappropriate red cell transfusion, performance measurement and governance of transfusion practice in the clinical setting was required. The report recommended:

- strengthening local commitment to ensuring appropriate transfusion practice in the hospitals;
- establishing measurement systems that can provide data on management and use of blood;
- introduction of vetting of transfusion requests including dose;
- hospitals to be accountable for their use of blood and blood components, issued from the Blood Service;
- development of standardised transfusion ordering/practice;
- improved education of clinical staff who prescribe and administer blood products;
• increased patient/consumer education and involvement;

• review of the current NHMRC/ASBT Blood Components guidelines in relation to patients with chronic anaemia; and

• promotion of spread and sustainability of improvement, including to other blood products using ‘top down’ policy development by NSW Health. (Harrison, 2003)

In 2005, Boyce and Brook (2005), in their report for the Australian Council for Safety and Quality in Health Care, recommended the basic foundations of a patient blood management system for Australia – the Better, Safer Transfusion (BeST) Program:

• Future investment in enhancing the safety of transfusion must address clinical transfusion practice improvement, not just blood product quality. In 2005 the major risks from transfusion are associated with unsafe clinical transfusion practices and inappropriate blood product transfusion.

• Healthcare professionals involved in everyday transfusion practice must receive more adequate education and training to support safe and appropriate transfusion.

• Australia should adopt a national clinical governance model for the safety and quality of blood and blood product transfusion. This would see organisations that currently contribute to aspects of the safety and quality of transfusion practice integrated within a single governance framework that addresses all aspects of the transfusion ‘safety chain’.

• A national BeST program should be established to promulgate transfusion practice standards, oversee monitoring of transfusion performance and lead a parsimonious core of transfusion practice improvement activities. A national BeST Advisory Committee should develop this program. This Committee should report, via the JBC, to Australian Health Ministers.

• This national BeST program should operate through the normal accountability and responsibility channels of acute healthcare. Program implementation should be through jurisdictions. Jurisdictional BeST Committees with clear linkages to Hospital Transfusion Committees should work together on identified national transfusion safety and quality priorities.

• Haemovigilance activities should be part of this national BeST program.

• Hospital Transfusion Committees and Hospital Transfusion Teams will only deliver enhanced transfusion safety and appropriateness if adequately resourced. This resourcing must include access to appropriately trained Medical staff and where relevant a trained Transfusion Nurse (or equivalent).

• The safety and appropriateness of hospital transfusion practice should be an explicit responsibility of Executive Managers of Health Services.

The key components of the BeST Program were:

• a strong focus on changing, then improving, clinical transfusion practice rather than concentrating on blood product safety, with adequate training and education for clinicians to support appropriate transfusion practice;

• a national program with an appropriate policy, governance, and performance management and monitoring and reporting (of transfusion) framework under which to develop and implement a funded transfusion practice improvement program to ‘promulgate transfusion practice
standards, oversee monitoring of transfusion performance and lead a parsimonious core of transfusion practice improvement activities’;

- a national clinical governance model with appropriate governance arrangements all the way along the transfusion ‘safety chain’ from the national governance framework to hospitals with Blood Transfusion Committees, Hospital Transfusion Teams (including Transfusion Nurses); and

- Executive Managers of health services/hospitals to have explicit responsibility for the safety and appropriateness of hospital transfusion practice.

Just over three years later, when launching the WAPBM Program at the seminal November 2008 NBA Conference, Dr Simon Towler (Western Australian Department of Health, 2008) described the main components of the WA PBM Program as:

- a state-wide approach to patient blood management;
- working from change management principles (the Kotter Principles (1995));
- using international expertise to lead the project;
- building a local team for long term success;
- using data as the driver for change; and
- using a system approach within a quality framework.

The similarities, between the WAPBM Program and the Boyce and Brook recommended program, are noteworthy.

Over the last decade those associated with blood transfusion practice have come to understand the patient blood management approach. PBM views a patient’s own blood as a valuable and unique natural resource that should be conserved and managed appropriately. This concept is depicted graphically below (Figure 15).

**FIGURE 15: PATIENT BLOOD MANAGEMENT CONCEPTS**

![Patient Blood Management Diagram](source: SABM website: www.sabm.org)

PBM is a multidisciplinary, multimodal and patient centred approach to optimising, conserving and managing the patient’s own blood. It aims to identify patients at high risk of transfusion and provide
a management plan aimed at reducing the need for blood transfusion and improving patient outcomes. Patient blood management is built around three pillars:

- anaemia management to optimise the red cell mass;
- minimise blood loss; and
- tolerance of anaemia (appropriate transfusion decision and optimising the patient’s physiological tolerance of anaemia).

These three pillars are applied in three integrated phases (Figure 16). Although set out for surgical patients, similar principles apply to medical/haematological patients with pre-, intra- and post-event phases.
FIGURE 16: THREE PILLARS OF MULTIDISCIPLINARY MULTIMODAL PATENT BLOOD MANAGEMENT

Source: Figure courtesy of the Western Australian Patient Management Program from a presentation given by Dr Simon Towler, Chief Medical Officer, WA Department of Health
The effectiveness and experience of the Australian (Boyce, 2005) recommendations, the WAPBM Program (Western Australian Department of Health, 2008) and the NBA NPBMP (National Blood Authority, 2010b) and international programs described above are testament to the effectiveness or impact of multidisciplinary multimodal PBM programs, with suggesting that one of the most effective ways to bring about change in transfusion practice involves establishing formal, comprehensive, hospital-wide Blood Conservation/Management Programs (Ferraris, 2007; Goodnough, 2007; Seeber, 2008) within a national or regional framework.

Most recently, in an Editorial (Vamvakas, 2011) and Article (Isbister, 2011) in Transfusion Medicine Reviews, and the NBA Perioperative PBM Guidelines (National Blood Authority, 2011) up-to-date views have been expressed in relation to both the need for patient blood management and PBM programs.

The lessons from the Australian and overseas experiences described above point to the desirability of a nationally consistent approach to patient blood management with the following features:

- strong focus on changing clinical transfusion practice, with adequate training and education for clinicians to support appropriate transfusion practice;
- an approach based on proven change management approach, for example the Kotter Change Model: (Kotter, 1995);
  
  : Establish a Sense of Urgency
  : Form a Guiding Coalition
  : Develop a Vision and Strategy
  : Communicate the Vision
  : Enable Action and Removal of Obstacles
  : Generate Short-term Wins
  : Hold the Gains and Build on Change
  : Anchor Changes in the Culture
- implementation of tailored PBM programs at the individual hospital level;
- transfusion practice standards and a new way of looking at evidence in line with the approaches espoused by Isbister (2011) and those in the NBA Perioperative PBM Guidelines (National Blood Authority, 2011);
- an appropriate policy, governance, and performance management framework similar to the NBA NPBMP (National Blood Authority, 2010b) which is already in place;
- use of data and information about best clinical transfusion practice and evidence, the true costs of transfusion (product costs, in-hospital pre- and post-transfusion costs and wider health care system and societal costs) as the main driver for change, and which
draws on international expertise to lead or support the program during its development and implementation;

- a clinical governance model with appropriate governance arrangements all the way along the transfusion ‘safety chain’ from the national governance framework to hospitals with Blood Transfusion Committees, Hospital Transfusion Teams (including Transfusion Nurses). This would draw on successful arrangements already in place and being tested in Australia;

- executive managers of health services/hospitals have explicit responsibility for the safety and appropriateness of hospital transfusion practice;

- sustainability of change, built through cultural changes towards changed transfusion practice and improved appropriate use of blood and blood products.

**IMPROVING THE UPTAKE OF CLINICAL GUIDELINES**

In Australia, studies suggest that patient care and outcomes could be significantly improved if the knowledge gained from health research was better translated into practice. This situation is not unique to Australia and many overseas studies highlight the similar issue.

Studies reported in an article by Buchan (2004) suggest that 30 per cent–40 per cent of patients do not receive treatments of proven effectiveness and that 20 per cent–25 per cent have treatments that are unnecessary or potentially harmful (Grol, 2001b; McGlynn, 2003).

Dr Buchan works at the National Institute of Clinical Studies (NICS) (National Health and Medical Research Council, 2011) which the Australian Government established in late 2000 to improve healthcare by helping to close important gaps between the best available evidence and current clinical practice. The NICS aims to do this by working with clinicians to support evidence uptake, helping to increase knowledge about the science of evidence uptake in clinical care, building national capacity for evidence uptake, and advocating for systemic change that will improve the use of evidence in clinical practice.

The NICS has also been identifying which measures are known to improve evidence uptake and which are seemingly ineffective, and is seeking advice on ways this knowledge might be best applied in Australia. In November 2003, the Institute held a meeting in Hobart at which a wide range of healthcare professionals, social scientists, policymakers and consumers met to discuss possible approaches to improving evidence uptake across the Australian healthcare system – a Supplement which presents a report of this meeting was later published (Sweet, 2004).

Irving, et al. (2006) studied iron management processes at six Australian dialysis units varying in size and locality. The study evaluated the outcomes of and barriers to implementing standard guidelines (Caring for Australasians with renal impairment [CARI]), using iron management in patients having dialysis. Irving found that there was considerable variability among the units in achievement of Hb and iron targets. Implementation barriers included lack of knowledge, lack of awareness of or trust in the CARI guideline, inability to implement the guideline, and inability to agree on a uniform unit protocol. Factors associated with achieving the CARI guideline targets included nurse-driven iron management protocols, use of an iron management decision aid, fewer nephrologists per dialysis unit, and a ‘proactive’ (actively keeping iron levels within target range) rather than ‘reactive’ (only reacting if iron levels are out of the range) protocol.

The Irving et al. study evaluated the outcomes of a standard implementation strategy (passive dissemination of guidelines in hardcopy form and on the Internet) of the CARI
guidelines. In assessing this strategy, they sought to identify barriers to guideline implementation (Grol, 2001b; 2003; Gros, 2001) using a ‘process of care’ approach, with a view to developing strategies to increase uptake of evidence into practice. The study found that passive dissemination of the CARI guidelines in March 2000 resulted in awareness of the iron guideline, but also found significant variation in implementation of the guideline across the six dialysis units examined. All units had an iron management process in place, however, the variability of the levels achieved for the iron indices is a measure of the effectiveness of the process. An effective process seemed to depend on the strength of a unit’s local protocol and the staff available to drive the protocol processes. More details of the Irving study are at Appendix 5.

As was mentioned above, poor uptake of clinical guidelines occurs in other countries as well. Details on several relevant studies, from the United States, the Netherlands and Norway are at Appendix 5.

In a 2006 article in the Medical Journal of Australia, Grol and Buchan (2006) say that, in the past decade, evidence-based clinical guidelines have become a major feature of health care. Researchers and clinicians in many countries have established programs to summarise the evidence for managing specific health problems and to disseminate practice guidelines. However, clinical use of guideline recommendations does not necessarily follow. Numerous studies show that recommendations are frequently not applied in practice and that many patients do not profit from evidence-based insights (McGlynn, 2003). Large variations in performance between clinicians, practices and institutions are commonly observed.

Two reports in the Medical Journal of Australia illustrate this well (Bryant, 2006; Irving, 2006). In the first, an audit in a hospital outpatient clinic showed that large numbers of patients with diabetes do not achieve recommended treatment targets for control of glycaemia, blood pressure and lipid levels, despite evidence that control of these risk factors produces better outcomes (Bryant, 2006). The second, a study of six Australian dialysis units, showed that, despite high levels of awareness of iron guideline recommendations in participating units, there is considerable variation in achievement of targets and widely differing practices in unit processes for iron management (Irving, 2006).

The reasons why evidence is not translated well into practice are varied. There may be barriers to evidence uptake at the patient, clinician, team, organisation or system level. There is no single strategy that will work in all situations to improve evidence uptake. Strategies aimed at improving knowledge or skills of individual clinicians will not be helpful if the core problem relates to the way in which work flows and processes operate within an organisation, a situation that largely applies to how transfusion practice occurs in many Australian public and private hospitals. Ways to improve uptake of research evidence are most successful if the barriers to implementation in specific areas are understood, and interventions tailored to overcome these barriers are applied. Indeed, the NICS publication cited above includes a specific volume on such barriers (National Health and Medical Research Council, 2006), although it does not include any coverage of barriers to implementation in translating clinical practice guidelines for transfusion into improved transfusion practice.

Possible barriers to successful implementation of the iron guideline referred to earlier were identified by Irving from various perspectives as follows:

- Nephrologist
  - Lack of awareness or knowledge of a guideline
Lack of knowledge regarding iron requirements
Lack of ‘trust’ in the guideline
Lack of ability to implement the guideline in own practice

• Renal nurse
  Lack of awareness or knowledge of guideline
  Lack of knowledge regarding iron requirements
  Has to follow/wait for instruction from nephrologist regarding iron management
  Possible increased workload
  Following up home dialysis patients

• Patient
  Not accepting iron as important
  Side effects from prescribed treatments
  Comorbid conditions may take precedence
  May be a home dialysis patient
  Unit level issues
  Large numbers of nephrologists working within the one dialysis unit
  Lack of agreement on iron targets among nephrologists
  Lack of effective iron protocol available for staff to follow
  Lack of care plan available for staff to follow for iron management

• Management issues
  May not realise that iron management is an issue
  Unaware of the reduction in relative cost of anaemia management with epoetin, by provision of adequate iron

• Infrastructure issues
  Increased nursing time to check laboratory results of iron studies
  Lack of computerised results
Laboratories do not automatically send blood test results to dialysis units; nurses are required to access results for their patients.

Iron measurements come from a range of laboratories with different ordering processes and accessibility of results.

Guideline:

Lack of evidence for dosage requirements for iron management.

Some of these barriers and gaps were echoed in relation to the NHMRC/ASBT Blood Components guidelines in a report commissioned by the CEC and the NBA on ‘understanding and influencing blood prescription’ (Eureka Strategic Report, 2007). For example, the report indicated that:

- there was a broad assumption that guidelines exist, but little knowledge of details such as by whom they were written or distributed, what format they come in, or where they might have come across them;
- further, there was a common perception among clinicians that their own practice was already consistent with guidelines and, as such, that the guidelines merely reinforced their own prescribing habits and did not contain any new information;
- some went further, believing the guidelines to be unhelpful and insufficiently specific for their specialty;
- there was a general perception that the guidelines would be of the most utility for those in the early stages of their career, or during university studies again, highlighting that it is felt to be others, especially juniors, who are not complying with best practice;
- guidelines related to other blood products were often seen as more useful than those relating to red cells, as red cell transfusions are typically seen as a more routine and less complicated procedure than some other types of blood product transfusions. Materials to guide red blood transfusion decisions were rarely, if ever, used by any of the research participants;
- there was a common perception that doctors’ own practices fell within the guidelines, even when they had described practices earlier in the interviews, which would not comply. The guidelines were felt to be of limited utility, although many thought that they could be useful early in doctors’ careers. Some felt them to be useful for reinforcing their own practices, although some also felt that they were not tailored specifically to their specialisation. Guidelines were not seen to constrain clinical judgment, although clinicians rarely, if ever, used materials to guide their transfusion decisions.

There is a growing body of research on how evidence is taken up into clinical practice. The most common strategies in use — continuing medical education and passive dissemination of guidelines — have consistently been shown to have very little impact on practice patterns or improving patient outcomes (Bero, 1998; Eccles, 2004; Grimshaw, 2001; Grol, 2001b; NHS Centre for Reviews and Dissemination, 1999). For successful implementation of guidelines, it is necessary to devise a strategy or plan for the project. The first task is to understand the local setting for implementation and the target group, as well as (Grol, 2004) the current process or clinical pathway that needs to be altered. Understanding each step in the clinical
pathway and how individual units move through these stages will reveal the barriers to change for those units, and a multifaceted implementation plan can be devised to overcome these barriers (Locatelli, 2000).

In the Irving, et al. study, identification of barriers was made at seven different levels of the organisations using the National Institute for Clinical Studies barrier tool (National Health and Medical Research Council, 2005). The ‘NICS Barrier Tool’ was developed by the NICS to help health professionals identify the barriers to applying evidence and changing practice within Australian health care settings. The tool can be adapted for the particular situation. As an illustration, the ‘NICS Barrier Tool’ includes an example of the barrier tool being used to identify barriers to influenza vaccination in ‘at risk’ groups.

Research into effective methods for implementing clinical practice guidelines lags behind the research methods involved in producing guidelines. The Irving (2006) highlights the possible barriers to implementing the CARI guideline for iron, and shows that, in order to truly gain an understanding of which guideline implementation methods are most successful, controlled-intervention observational studies and completion of the quality cycle, with critical review of the achievement of targets, should be undertaken in renal medicine.

Passive dissemination of the CARI iron guideline raised awareness of the guideline, but Irving, et al. said that improving iron management and patient outcomes would take commitment to change within the renal care team, an agreed iron protocol with a decision support aid, a working process for iron management, and skills improvement for renal nursing staff. Factors affecting iron management and barriers to change are numerous. For successful guideline implementation, a strategy to overcome these barriers in individual units should be planned and executed.

This example could be adapted to other clinical settings across a range of medical disciplines, including blood transfusion. Successful implementation of clinical practice guidelines is not achieved by forcing physicians to obey ‘rules’, but rather by creating an environment in which they are given the skills, knowledge, attitudes and support systems to help them provide their patients with the best possible care, based on the best possible evidence.

Policymakers who seek to change health care practices need to understand that some current expectations about the impact of clinical guidelines are unrealistic. A belief that developing and disseminating systematic reviews and guidelines will improve patient care ignores the complexity of change in health care. Guidelines do not implement themselves — most need well developed, well executed and sustained implementation programs (Grol, 2004b), and even such programs usually have only a moderate effect on performance in terms of care improvement (around 8–10 per cent) (Grimshaw, 2004).

The NBA-NSW CEC marketing study (Eureka Strategic Research, 2007) also provided some insight into practical communication tools suitable in terms of the blood sector. For example, the report indicated that:

- seminars or in-service were the best options, but generally enthusiasm for an interest in the topic were low;

- there was a moderate amount of interest in reading transfusion articles in journals, but most doctors said they will only read articles or journals that are relevant to their specialty, and certainly will not seek out such articles (‘I have too many journal articles that I should read that pertain to orthopaedics that I don’t have time to read. (Ortho Registrar)’);
• some reported that they do not have time to seek out information and claimed that they would prefer direct mail or email so that it was presented to them and they would not miss it. There were, however, some doubts as to whether direct forms of communication would make it past ‘filters’ such as auxiliary staff or even junk mail email filters, and whether it would be read even if it did reach doctors;

• ward walls were widely seen as already too cluttered to viably support any message on blood transfusion. Material on walls is liable to be overlooked or go unnoticed regardless of placement or prominence. When asked specifically about whether messages in bathrooms or on toilet doors would be read, some doctors were hesitant about this idea.

Guidelines are expensive. The cost of producing a single guideline may range from $US50 to $US500,000 not to mention the substantial donated time from many contributors (Burgers, 2002).

Guideline developers, research funders, health care managers and policymakers may need to consider a few key strategies:

• the need for greater focus on producing guidelines in formats that promote their use;

• the requirement for planned (and funded) implementation programs that take into account the complexity of change in health care; and

• the need to improve knowledge about cost-effective methods of achieving sustained practice changes.

Many current programs for guideline development seem to be ‘science-driven’, rather than scientifically based but ‘customer-driven’. Guideline developers would do a far better job if they focused on the needs of the end user and provided clear statements, decision aids, patient education materials and practical tools to manage difficult problems in practice. More guidelines need to identify specific evidence-based indicators and criteria for clinical performance (as the guidelines discussed in this issue of the journal do). These provide the capacity to monitor performance and give feedback to clinicians. Public reporting of significant aspects of care quality would help meet the urgent need in society for more transparency about important aspects of health care provision, and would provide a clear imperative to improve implementation and ensure guideline recommendations are feasible and do not become out-dated.

There is also a need to seek a better balance between the resources devoted to summarising evidence and developing guidelines and those spent on finding the most effective ways to improve patient care. Evidence-based guideline development reflects just one specific approach to improving care — it assumes that professionals are rational decision makers who will act on convincing information about the pros and cons of specific routines.

Many factors play crucial roles in blocking or stimulating relevant changes in performance. These are not only related to professional decision making, but also to patient behaviour, interaction with colleagues, team functioning, organisational conditions for change, resources, and economic or legal conditions (Cabana, 1999; Grol, 2001a; Soldberg, 2000).

Individual professionals need to be informed, motivated and perhaps trained to incorporate the latest evidence into their daily work. For instance, Cabana et al. (1999) used a ‘professional perception model’. Based on a review of 76 studies on barriers to guideline adherence, they identified salient factors as lack of awareness, lack of familiarity, lack of
agreement, lack of self-efficacy (that is, the belief in one’s ability to perform a behaviour), low expectancy of favourable outcomes, inertia/lack of motivation, and perceived external barriers beyond the control of individuals. Empirical data showed that lack of awareness and motivation, as well as perceived external factors, were particularly important barriers to adopting guidelines.

Based on analyses of the literature and research conducted by Grol and Wensing, they proposed that barriers and incentives be examined at six different levels: the innovation itself, the individual professional, the patient, the social context, the organisational context, and the economic and political context (Table 8). Relatively little attention has been given so far to research on characteristics of the innovation itself that affect its likelihood of being implemented (Grol, 2003).

**TABLE 8: BARRIERS TO AND INCENTIVES FOR CHANGE AT DIFFERENT LEVELS OF HEALTHCARE**

<table>
<thead>
<tr>
<th>Level</th>
<th>Barriers and Incentives</th>
</tr>
</thead>
<tbody>
<tr>
<td>Innovation</td>
<td>Advantages in practice, feasibility, credibility, accessibility, attractiveness</td>
</tr>
<tr>
<td>Individual professional</td>
<td>Awareness, knowledge, attitude, motivation to change, behavioural routines</td>
</tr>
<tr>
<td>Patient</td>
<td>Knowledge, skills, attitude, compliance</td>
</tr>
<tr>
<td>Social context</td>
<td>Opinion of colleagues, culture of the network, collaboration, leadership</td>
</tr>
<tr>
<td>Organisational context</td>
<td>Organisation of care processes, staff, capacities, resources, structures</td>
</tr>
<tr>
<td>Economic and political context</td>
<td>Financial arrangements, regulations, policies</td>
</tr>
</tbody>
</table>


In Australia, in early 2008, the NICS Stroke CRG was formed to develop an acute stroke care resource for use in emergency departments (EDs) in Australian hospitals – the account of the development and initial implementation of this tool was published by Weeraratne, JI et al. in October 2010 (Weeraratne, 2010). The NICS reference group used a care bundle approach to develop a guideline implementation tool based on specific recommendations from the 2007 National Stroke Foundation (NSF) *Clinical guidelines for acute stroke management* relevant for ED care (National Stroke Foundation, 2010). Although these guidelines were already available, there are well known barriers to guideline implementation in the ED. These include increasing demand and acuity, and the broad diversity of clinical presentations.

A care bundle is made up of a small number of best-practice recommendation components, is not as comprehensive as a guideline, and aims to identify critical recommendations relating to areas in which there is a significant practice gap or to act as a trigger to other best practice (Haraden, 2006). The NICS care bundle was designed to bring together several components to help clinicians provide quality care to adult patients who present to the ED with suspected stroke or transient ischaemic attack (TIA) by reducing morbidity and mortality and optimising patient outcomes.

The Stroke CRG believes that an emphasis on the first component of the bundle — a rapid initial stroke screen — could lead to earlier referral to stroke specialists and rapid access to computed tomography or magnetic resonance imaging to confirm the diagnosis and develop
a management plan that would consider thrombolysis if clinically appropriate (Nor, 2005). This illustrates how the components of the care bundle may trigger additional best practice recommendations as a natural consequence and establish joint clinical decision making with other disciplines to improve patient care. More details of this study are at Appendix 5.

With a change of focus in current guideline development and more realistic expectations of the role of guidelines in improving patient care, with better knowledge about costs and effects of change strategies, and with clinical guidelines embedded in comprehensive programs for change, evidence-based guidelines for clinical practice may become more relevant in the future.
Price Signalling

This section examines one particular strategy for promoting appropriate use of blood and blood products, namely the use of price signals in the system. Specifically, it looks at:

- the role of price signals in the context of blood and blood products;
- ‘upstream’ and ‘downstream’ price signals, given the nature of the Australia blood and blood product supply chain;
- the experience with applying (mainly ‘downstream’) price signals internationally and in Australia, including through the devolution of blood budgets to health providers;
- options for the possible extension of price signals in the blood sector in Australia.

THE ROLE OF PRICE SIGNALS

Reducing inappropriate blood and blood product use helps secure sufficient blood to meet current and future needs and helps manage the growing cost of treatment.

Economic techniques such as price signals, aligned to the cost of blood, can provide the right incentives for more efficient demand and supply outcomes throughout the blood supply chain.

A price is like an economic signal to suppliers and consumers to help guide supply and demand responses. Prices reflect the value that suppliers and consumers place on a product.

Prices help consumers compare products or activities and choose those with the greatest value, when faced with a limited budget. When consumers are willing to pay a price that recovers a supplier’s costs, the supplier also has incentive to produce the product.

In a blood and blood products context, price signals generally refer to the extent to which different consumers in the blood supply chain face prices and bear the budget consequences as part of their consumption choices. The principal focus is closest to the final consumer – within hospitals or other health providers – as this drives demand (and associated signals) upwards through the supply chain.

Where there is no price signal faced, use of blood and blood products is potentially viewed as ‘costless’. If a consumer (for example, a clinician, or a hospital generally) does not bear the budget consequence, there is likely to be over-demand. This over-demand does have a cost – but it is borne by others.

Conceptually, effective price signals encourage optimal blood product use by ensuring that consumers consider the costs of utilising blood products relative to alternative actions, over

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13 The prices for blood products in Australia – for example, at a bulk level purchased by the NBA – are generally administered prices, determined on an annual basis in line with the institutional framework for blood product supply planning. They are not market-based or ‘free’. This does not change the fundamental concept of price signals as providing a general indicator of value and opportunity cost.
time. Price has most substantial influence over blood product use when it is felt not only in the middle of the supply chain, but closer to the final consumer.

**Consumption Roles**

Consumers can be considered from three perspectives:

- the user – the person or entity who derives the benefit from the product’s consumption;
- the buyer – the person or entity who makes the consumption decision; and
- the payer – the person or entity who bears the cost of the consumption decision.

In some circumstances, one party undertakes each of these three roles, in others, the roles might be divided among different parties.

For example – using the example of final consumption in health providers, the user could be the patient, the buyer could be the prescribing clinician, and the payer could be states/territories and the Australian Government through the National Blood Authority.

The best and most efficient consumption outcomes are achieved when incentives of each of these roles are aligned, within and across the supply chain. Transparency of price signals can be a positive tool for aligning incentives.

The Australian blood product supply chain in terms of these three consumption roles is examined below.

**Price Responsiveness and Substitutes**

The impact of price on blood use depends on how responsive demand is to the level of or changes in price. In economic terms, this is called the ‘price elasticity of demand’ – or in simpler language, price responsiveness.

When facing a price signal, factors affecting the level of price responsiveness include:

- the availability of substitutes for blood and blood products or alternative clinical approaches;
- the proportion of available budgets spent on individual usages;
- the timeframe for making the usage decision; and
- the relative importance of cost considerations in influencing clinical decision-making.

Use of blood products, like most in-patient hospital services, is generally recognised as highly price inelastic – that is, price does not have a substantial impact on the level of demand. While quantitative studies specific to blood products are lacking, a well-cited study (Newhouse, 1993) based on American data suggests a price elasticity of demand of -0.16 at a category of 0-25 per cent levels of insurance co-payment for inpatient acute medical services, or a 1.6 per cent decrease in demand for a 10 per cent increase in price. By comparison, an analysis (Siminski, 2008) of pharmaceutical use amongst high-income Australian older people – conceptually similar (but not the same) to blood products in the Australian environment – finds ‘no evidence that elasticity is significantly different from zero’, giving a headline point estimate of -0.1 and a ‘range of plausible estimates’ approximately -0.3 to 0.
However, with technology change developing substitutes for blood use and greater clinical acceptance of these substitutes, blood use may be becoming slightly more price responsive over time (Hannon, 2006, p.20). This is because consumers are able to switch to alternatives that achieve the same or better outcomes at the same or lower price. An example of a substitute might be saline instead of albumin, which some evidence suggests has similar clinical outcomes (p65).

‘DOWNSTREAM’ AND ‘UPSTREAM’ PRICE SIGNALS IN AUSTRALIA’S BLOOD SUPPLY CHAIN

INSTITUTIONAL CONTEXT

There is a long institutional history of blood products being ‘free of charge’ to health providers and patients in Australia.

Although the NBA pays the parties that supply it with blood14, the NBA is funded from government rather than from users of blood products or services. The NBA is 63 per cent funded by the Australian Government, 37 per cent funded by State and Territory governments.

A special sensitivity is the secondary objective of the National Blood Agreement which is ‘to provide products to patients free of charge and based on clinical need and appropriate clinical practice’ (our emphasis). This constrains the ability for the supply chain to fully pass on the cost of blood products to patients. State-based human tissue legislation also limits the extent to which blood (as a human tissue) can be used and traded.

However, a further secondary objective is ‘to make best use of available resources, and to give financial and performance accountability for the use of resources by all entities involved in the Australian blood sector’ (our emphasis). The application of a price signal to a broader range of entities in the supply chain can be one tool to achieve this, and a devolved price signal faced by the payer and buyer at the point of final consumption is not necessarily inconsistent with providing products to patients – the user at the point of final consumption – free of charge.

PRICE SIGNALS IN THE AUSTRALIAN SUPPLY CHAIN

The blood and blood products supply chain is a useful tool to consider who in the Australian blood system faces price signals. ‘Upstream’ parts of the supply chain relate to blood collection, processing and distribution. ‘Downstream’ parts of the supply chain relate to blood utilisation within hospitals and in clinical situations.

Upstream

Price signals are generally applied across the ‘upstream’ supply chain with the exception of remunerating blood donations. The Blood Service and other suppliers provide blood products to the bulk purchaser NBA at negotiated prices for collection, processing and distribution, and those prices are borne by the Australian Government and the states as funders of the bulk purchaser and as proxies for health providers.

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14 The NBA purchases blood from the Blood Service. In turn, the Blood Service sources its blood from donations. The NBA also pays CSL for fractioning plasma sourced from the Blood Service to derive other products, and purchases blood-related products from CSL and other pharmaceutical companies.
There may be opportunities, however, to allow the price signal to work to better to more accurately reflect consumer and supplier preferences and utilise market forces to make the system more efficient. This is considered further below.

**Downstream**

The key price signal gap is that, in most locations, blood products are provided ‘downstream’ at no charge to hospitals by states and territories15. There are a lack of price signals applicable to many key decision makers affecting the volume of blood and blood products consumed, including laboratory managers and prescribing clinicians.

For each main stage of the Australian blood and blood product supply chain, the supplier, user, payer and buyer are summarised in Table 9. This shows a complex set of consumption decisions: the user, payer and buyer are rarely the same entity.

**TABLE 9: CONSUMPTION RELATIONSHIPS IN THE AUSTRALIAN BLOOD SECTOR**

<table>
<thead>
<tr>
<th>Product</th>
<th>Processed products</th>
<th>bulk blood products to hospital</th>
<th>Individual blood products for procedures</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Supplier</strong></td>
<td>Blood Service / CSL / other supplier</td>
<td>Blood Service</td>
<td>Blood Service / central blood banks</td>
</tr>
<tr>
<td><strong>User</strong></td>
<td>States and territories</td>
<td>Hospital</td>
<td>Patient</td>
</tr>
<tr>
<td><strong>Payer</strong></td>
<td>States and territories / Australian Government</td>
<td>Centralised (state) or devolved (hospital) blood budget holder</td>
<td>Centralised (state) or devolved (hospital) blood budget holder</td>
</tr>
<tr>
<td><strong>Buyer</strong></td>
<td>NBA</td>
<td>Hospital</td>
<td>Clinician</td>
</tr>
</tbody>
</table>

Source: Sapere Research Group Limited analysis

A stylised, simplified representation is shown in Figure 17 below, where price signals stop well before the end-buyer and end-user.

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15 NSW and Tasmania are exceptions, where through budget devolution the price signal has been extended to the health provider administrative unit, but not necessarily at this stage to be transparent or accountable *within* the health provider.
FIGURE 17: STYLISED REPRESENTATION OF CURRENT SUPPLY CHAIN OF PRICE AND PRODUCT

Source: Sapere Research Group Limited analysis

A ‘downstream’ price signal could take a number of forms. Given the current institutional arrangements for blood funding in Australia, one form often suggested has been the devolution of blood budgets beyond the centralised budget holder – for example, to health providers or administrative units of health providers.

IMPACTS OF CURRENT SITUATION

Lack of a ‘downstream’ price signal creates unaligned incentives because of a lack of transparency of costs to clinician and (in some cases) hospital buyers, and lack of moderating influence by government or insurance payers on consumption behaviour.

Lack of price signal would likely be a principal driver of hospital-level impacts including potential for:

- increased incentive for excessive use;
• reduced incentive to act against wastage;
• distortion in comparison and use of substitutable products or practices;
• reduced incentive for introducing measures to reduce the amount of blood use, for example through application of cell salvage technology, treatment of iron deficiency pre and post operatively by alternative means;
• reduced incentive to collect usage data, and monitor usage rates and use against guidelines; and
• reduced incentive for tight inventory control.

For example, in the absence of a price signal for blood, and where there is a price signal for substitutes, there is a structural disincentive to adopting alternatives. There is a particular disincentive for large-scale, high-impact measures which can affect blood use over time such as auditing and education or capital investments such as information systems, when hospitals bear the cost for these measures but do not benefit from the consequent cost-reduction in blood use.


OVERSEAS AND AUSTRALIAN EXPERIENCES OF PRICE SIGNALS FOR BLOOD AND BLOOD PRODUCTS

Overall, cost structures and pricing policies of blood services remain obscure. This is also reflected by the fact that pricing information on blood and blood products in many countries is not public, although long ago all aspects of blood services have become matters of immediate public interest (Cumming, 1974). This context helps to understand that price signalling for blood and blood products can be unpopular in some quarters.

‘Downstream’ price signals have been adopted as part of broader approach to appropriate use in England and Wales, and the United States has a greater focus on pricing throughout the supply chain. ‘Downstream’ price signals have also been introduced in recent years within public hospitals in NSW and Tasmania.

ENGLAND AND WALES

For a number of years, consistent with the UK’s guidelines for safe and appropriate use of blood, in many areas of England and Wales blood budgets have been devolved to ‘end-buyers’ at the point of or near to the point of final consumption (as opposed to patient ‘end-users’).

The National Blood Service (NBS) for England and North Wales charges hospitals monthly for the purchase of blood products, which are provided at fixed national prices. Hospitals have a set budget to spend on buying blood components, known as a blood budget (Katsaliaki, 2008).

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16 Part of English NHS Blood and Transplant (NHSBT), a special health authority of the NHS.
Many hospitals have further devolved blood budgets to individual clinical directorates or disciplines or to other parts of hospitals. This is an attempt to extend decisions and (cost) consequences of the use of blood and blood products further into the organisation, and as a result bring the price signal closer to end-users.

A survey in 2008 showed that most England and Wales public hospital blood budgets are held in pathology departments (36 per cent) or transfusion laboratories (26 per cent), and 20 per cent of public hospitals had devolved blood budgets to clinical specialties. This is shown in Figure 18 below.

**FIGURE 18: HOLDER OF BLOOD BUDGETS WITHIN NHS TRUSTS AND INDEPENDENT HOSPITALS, ENGLAND AND WALES, 2008**

![Graph showing distribution of blood budgets](image)

*Source: Derived from data in NHS National Blood Transfusion Committee 2008*

The NHS considered that ‘placing clinical directorates in control of their own blood budget may encourage them to be more receptive to the various better blood transfusion initiatives such as minimising waste resulting from inappropriate handling and storage of blood components’ (Qureshi, 2005).

The NHS also identified professional self-interest as a potential motive to generate more appropriate use: ‘the incentive that individual directorates may be able to re-channel any savings thus realised to other areas of service improvements within the directorates’ (Ibid.).
The case study below demonstrates a practical example of this in action.

**Case Study: Devolved Blood Budget as enabler of greater Appropriate Use in Bournemouth**

Devolution of the blood and blood product budget for the Royal Bournemouth and Christchurch Hospitals to the Transfusion Laboratory and establishment of a Hospital Transfusion Committee created an incentive to pursue innovative, self-funding and multifaceted ways to reduce inappropriate use.

The laboratory constructed ‘league tables’ of red cell use by individual consultants and their medical specialty (simply generated from the laboratory information system). These were distributed by global e-mail quarterly, and the transparency and natural competition contributed to an immediate reduction in red cell use.

With these cost savings, the laboratory funded a part-time Transfusion Auditor to audit blood use by clinician, anaesthetist, infusion location and diagnosis. With ongoing results examined by the Hospital Transfusion Committee, recommendations for change in practice are made to the clinicians involved.

The process has saved over £500,000 since its introduction, facilitated improved clinical transfusion medicine, reduced clinical risk, and funded technology solutions to support more efficient blood product use. Even with an 11.5 per cent increase in clinical activity, red cell use reduced by 30 per cent from 13,605 units per annum in 1999 to 9,551 in 2005. Wastage of red cells and platelets reduced in cost from £30,000 per annum in 1999 to £14,630 in 2005.

*Source: Johnson J et al 2006*

NHS Blood and Transplant in England and Wales has not yet consolidated lessons from their experience of local management of blood budgets. However, in late 2011, NHS Blood and Transplant aims to undertake a bespoke survey of the management of blood budgets to better understand how the different approaches support appropriate use.²⁷

**United States**

In the United States, there is wider adoption of price signals throughout the hospital system, given the generally more private orientation.

Individual public, not-for-profit and private hospitals purchase blood products from blood product suppliers.¹⁸ Hospitals’ blood costs are typically passed through to patients and their (public and private) insurers – a substantial difference from the Australian supply chain.

The Lewin Group study in 2002 noted that, of high blood-use discharges from hospital in the US, patient payment types are around 56 per cent public insurance, 36 per cent private insurance, with the remainder uninsured, self-pay or other (Goodman, 2003).

Medicare, Medicaid and increasingly private insurance payments to hospitals are not based on the individual cost of blood products but for fixed amounts for each patient in a Diagnosis

¹⁷ Personal communication with Catherine Howell, Chief Nurse Patient Services, NHS Blood and Transplant, 26 November 2010

¹⁸ Blood product suppliers in the US are mostly not-for-profit, principally the American Red Cross.
Related Group (DRG) or case mix approach, in Medicare called prospective payment reimbursement.

Sometimes, operational factors limit the extent to which blood costs are passed on to patients and their insurers. The Lewin Group identified systematic under-coding and inaccurate charging. This points to the importance of effective accounting practices and data capture.

**Austria**

In order to optimize the utilisation of blood and blood products, the third largest public hospital in Austria (General Hospital Linz, AKH Linz) has recently introduced electronic price signalling to clinicians as part of a hospital wide PBMP. At General Hospital Linz, AKH Linz, clinicians of all departments can only order blood products through the hospital’s electronic ordering system (Lauris). Actual prices of all blood products or components are displayed on the screen as soon as the products are selected. Prices or cost for special product treatments like radiation or washing of red cells and also all transfusion related laboratory test procedures such as cross matching, antibody screening, direct Coombs test etc. are also displayed and priced. Before the actual order is sent to the blood bank, the total amount payable is shown on the screen. The clinician then makes a final ordering decision on the number of products and laboratory tests.

It is noteworthy that the transfusion and blood utilisation rate in the General Hospital Linz is one of the lowest in the Federal Republic of Austria.

**New South Wales and Tasmania**

This section highlights devolved blood budgets for public hospitals in NSW and Tasmania, and the proposed removal of funding for blood products to NSW private hospitals.

New South Wales and Tasmania - devolution of blood budgets to public hospitals

In Australia, devolved blood budgets for public hospitals have been established in NSW and Tasmania, as part of broader approaches to appropriate use. Queensland has taken the policy decision to devolve its State blood budget from July 2011.

NSW has had the longest experience with blood budget devolution, since 2005. The aim of the move was to drive practice change in blood use. Annual supply planning and budgeting is still determined centrally, and individual Area Health Services are responsible for the management of the allocated blood budget.

NSW Health is not prescriptive about how individual Area Health Services should manage their blood budget, given the wide variation in contexts (for example types of procedures, geographic scale, clinical structures), and anecdotally different Area Health Services have implemented different processes.

Reconciled on an annual basis, Area Health Services are able to benefit from savings or bear the cost of risk of additional use, relative to the budget. This only relates to NSW’s proportion of funding for blood and blood products used in the state, not the Australian Government component of blood product funding.19

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19 Personal communication with Bill Heiler, NSW Health, 6 December 2010
While only early into the devolved blood budget experience, a survey of senior NSW surgeons and physicians in 2007 found that, at a clinical level, price signals were not yet a major influence on use of blood and blood products:

_When asked about the cost of blood, most doctors admitted that they were unsure of the per-unit price, but were aware that blood is not free._

_However, the price of blood is unlikely to factor into doctors’ prescribing decisions, as the decision is made for clinical, rather than financial, reasons. Indeed, most doctors admit that the health and wellbeing of their patient is their priority, and the cost of blood has little bearing on their decision to prescribe it (Eureka Strategic Report, 2007)._  

Blood Watch, NSW’s statewide transfusion medicine improvement program, was introduced subsequent to blood budget devolution. While there are a range of factors that might influence outcomes, anecdotally a number of NSW Area Health Services only experienced use reductions after Blood Watch’s introduction, not with the introduction of devolved blood budgets alone.

Indicatively, this suggests a continued need for complementary activities to support appropriate blood use, and it is reasonable to suggest that price signals can provide the incentive to take-up patient blood management activities at a hospital level.

Advice from health authorities in NSW was that, on the basis of current data and understanding, it was not possible to clearly differentiate the impact of devolved blood budgets from other appropriate use initiatives. However, the experience of NSW provides some formative insights into the positive general experience of both price signals and complementary activities.

For example, the North Sydney Central Coast Area Health Service (NSCCAHS) instituted a Blood Management Programme in January 2007, recognising the high and rising cost of transfusions and other quality and safety drivers. In the two years to January 2009, alongside various actions NSCCAHS established a governance system for approving transfusions, reduced utilisation of red cells (18 per cent), platelets (32 per cent) and cryoprecipitate (31 per cent) and improved compliance with NHMRC/ASBT Blood Components guidelines, and improved clinical and laboratory inventory control by reducing wastage of platelets (48 per cent) and FFP (15 per cent). This resulted in financial savings, for example $800,000 in the 2007-08 financial year for fresh blood products issued to NSCCAHS. (New South Wales Health Awards and Expo, 2009). Further observations were made earlier from the data available to this project about the rates of transfusion of various blood components and products in NSW (Appropriate Use Strategies-New South Wales (NSW), p76).

**New South Wales – removal of funding for blood products to private hospitals**  

In 2008, the NSW Government announced an intention to end ‘subsidies from NSW Health to private hospitals for the cost of providing blood and blood products’ (Department of Premier and Cabinet, 2008). The proposal was for the NSW Government to continue to plan for and order bulk purchase of blood products for private hospitals through the NBA, but for private hospitals to bear that proportion of costs traditionally funded by the NSW Government for private hospital blood products use (37 per cent).
Unlike extending the price signal further down the public hospital supply chain (but not increasing the net cost of blood products for the public sector); this proposal would increase the net cost payable by the private sector.

Arguably, this proposal did not directly contravene the National Blood Agreement objective to ‘provide products to patients free of charge’, as patients were not directly involved in the proposed change of arrangements between the NSW Government and private hospitals.

However, it would have resulted in an additional cost to private hospitals. In the absence of (inefficient) cross-subsidy, the natural and reasonable implication is that this cost would be passed through in some form to patients and private health insurers (and potentially the Australian Government through Medicare and the private health insurance rebate).

**KEY LESSONS FROM JURISDICTIONAL EXPERIENCES**

Financial and performance accountability for the use of resources by all entities can be supported by greater transparency, information and (in some cases) consequence of blood product use decisions being experienced throughout the blood product supply chain.

As demonstrated by these jurisdictional examples, price signals if appropriately cited within the institutional context can help to achieve this. Price signals are not an end in themselves – they are a ‘necessary but not sufficient’ enabler, helping to incentivise actions towards appropriate use but not, in and of themselves, supporting appropriate use. They might therefore be seen as tools for supporting accountability of various parts of the blood system for blood product demand, in a context of appropriate use.

Where price signals have been devolved to health providers, they have not always been fully devolved to clinical departments, which may limit their effectiveness in transmitting information on costs and alternatives throughout the health provider.

The effectiveness of price signals is also limited in there is insufficient (and inconsistent) data capture and management information on use and costs.

**OPTIONS AND IMPACTS FOR THE EXTENSION OF PRICE SIGNALS IN THE BLOOD SECTOR**

**Options for ‘Downstream’ Price Signals**

There is potential for further price signals to be nationally adopted in the ‘downstream’ elements of the supply chain – between state and territory governments and health providers, and then within health providers – in the broader context of various activities towards supporting appropriate use.

A set of design principles can help frame a national model for effective ‘downstream’ price signals. Agreed national principles can guide the establishment and implementation of appropriate and consistent price signals by clarifying objectives and institutional context.

The following figure suggests some principles for an effective ‘downstream’ price signal that could be adopted nationally.
FIGURE 19: PRINCIPLES FOR AN EFFECTIVE ‘DOWNSTREAM’ PRICE SIGNAL FOR BLOOD AND BLOOD PRODUCTS

Principles for an effective ‘downstream’ price signal for blood and blood products

Effective ‘downstream’ price signals for blood and blood products would meet the following principles:

- reflect the costs borne by governments for the provision of blood products;
- help to promulgate information on costs throughout the system, to support best use of available resources and financial and performance accountability for the use of resources;
- be devolved to the level of responsibility closest to the end use of the blood and blood product (in most cases, clinical directorates);
- be complementary to other actions to support appropriate use of blood products and better information on the use of blood products;
- have a level of administrative and compliance burden appropriate to the potential gain from its application;
- be able to be implemented in the short-to-medium term, and allow for adaptation to any special characteristics of individual jurisdictions;
- support other health reform and better practice for health administration;
- accord with the Commonwealth-State relativities of blood product funding;
- accord with National Blood Agreement provisions;
- support hospital administrators gaining some level of benefit or carry some level of risk from a reduction or increase in blood product use relative to a situation where there is no price signal.

Source: Sapere Research Group analysis

From these principles, there are a number of options that could be considered to support more effective ‘downstream’ price signals, relative to the current situation. A stylised representation of a possible future situation is provided in Figure 20.
Options for ‘downstream’ price signals are discussed in *Part 3: Key Findings and The Way Forward* which accompanies this report. In brief, the options are to:

- incorporate the cost of blood and blood products into casemix funding;
- devolve the national blood budget to public hospitals and charge private hospitals for the costs of blood and blood product;
- introduce ‘soft’ price signals, that is, price visibility, to a range of decision makers in the system, including laboratory staff, clinicians and other clinical staff responsible for handling blood and blood products.
**Impacts of Further ‘Downstream’ Price Signals**

Each option addresses health providers’ structural disincentive by allowing health providers to benefit from blood product usage savings. The options are agnostic to the nature of blood product use within hospitals, but would provide an incentive at a hospital level towards treating blood products as any other resource.

If managed effectively, each option would provide no-net-funding-loss to health providers, and could advantage health providers (without disadvantaging Australian Government and State and Territory funders) if greater appropriate use led to relatively less demand for blood products at similar procedure levels.

The information that would likely arise from the application of ‘downstream’ price signals would also be very helpful to support future blood sector planning.

To support national consistency, it may be positive to codify national principles for the development of ‘downstream’ price signals for blood products. The principles could be formally adopted as part of the National Blood Agreement. However, the National Blood Agreement does not necessarily need to specify arrangements within jurisdictions.

**Complementary Actions to Address Potential Risks**

There are some potential operational risks in a hospital context associated with greater devolution of price signals through ‘downstream’ parts of the supply chain.

The Blood Service (Williams, 2010) identifies potential for:

- incentives for hospitals to hold inappropriately low levels of inventory because of cost concerns over potential waste, and a skewing of blood groups in the inventory;

- sub-optimal transfusion decisions if there is pressure to prescribe less expensive products; and

- a shift of workload and cost from the private sector to the public sector if private institutions reduce their transfusion-dependent case-mix.

Sub-optimal transfusion decisions might result from decisions principally based on the cost of procedures rather than the clinical efficacy. However, clinicians face similar incentives with every other product or procedure that involves a cost, and previous discussion has shown that price alone will not be primary driver of transfusion decisions.

A further disadvantage may be potential reductions in voluntary blood donation, given potential donor discomfort that their blood donation becomes part of a commercial, price-based transaction. There is a lack of data to indicate whether there would be a material effect on donation. However, with public attention to the NSW Government’s proposal to charge private hospitals for blood products in 2008, the Blood Service stated that a ‘large number’ of donors had contacted the Red Cross call centre to express their ‘intention to discontinue giving blood’ (Metherell, 2008).

To reduce risk of donation impact, one potential action might be communication campaigns to inform the donation community that the concept is not paying for the blood they donate, but for the necessary ancillary collection, processing and distribution of that blood and resultant products, and the potential benefits of price signals. Over time, community opposition to price signals would likely dissipate.
Finally, there may be concern that ‘high cost blood products could negatively impact access to best therapy in selected patient populations (such as haemostatic factors) dependent on access to such expensive, low-volume blood products (and alternatives)’ (Boyce, 2005). A funding approach dependent on levels of activity, rather than a fixed budget not dependent on levels of activity, would mitigate risks of this nature.

**Options and Impacts for ‘Upstream’ Price Signals**

As noted earlier (Price Signals in The Australian Supply Chain--Upstream, p119) there may be opportunities to allow ‘upstream’ price signals to work better to more accurately reflect consumer and supplier preferences and utilise market forces to make the system more efficient.

There may be strong efficiencies and price benefits for consumers from greater contestability around the various elements of collecting, manufacturing, testing, and storage and distribution. However, suppliers may also have economies of scale or scope associated with continued integrated provision or with providing the full Australian market, which would reduce in a more competitive environment. Greater information and more specific analysis is probably required to identify potential benefits of more effective price signals in specific areas of the ‘upstream’ supply chain.

However, there are also ways to progressively make improvements in the ‘upstream’ supply chain – for example current work towards purchase recording being based on demand-based hospital ordering and receipt of blood product units, rather than supply-based delivery of units.
Modelling Future Demand

The terms of reference for this project seek modelling of the potential impacts of a range of price signalling options. Prior to discussing price signal impacts, the report outlines the basis for the modelling of future demand that was developed for the report *Analysis of Cost Drivers and Trends in the Blood Sector*.

**DEVELOPING A BLOOD DEMAND FORECAST MODEL**

The Blood Demand Forecast Model (the model) is derived from consideration of the factors which influence future demand for blood and blood products.

**INFLUENCES ON FUTURE DEMAND FOR BLOOD AND BLOOD PRODUCTS**

There are several factors which have influenced demand in the past, and are expected to do so into the future. While the future demand model should accommodate the influence of all of these factors, lack of available data has prevented the inclusion of most of them. However, the likely future trends in each of these areas are discussed below to establish context for the statistical projections in the model.

**Demographic Change**

Australia’s population is ageing. This is an important factor for blood demand as available data tends to indicate that blood consumption is positively correlated with age.

For example, in regard to fresh blood products, a study of WA data from 2001-02 found that the older age groups used greater quantities of blood products on a per population basis (Cobain, 2007) (Figure 21).
The pattern was particularly pronounced for red cells.

This general pattern of use for red cells was supported also in a study using data from a nine-month period during 2007-08 in Victoria (Shortt, 2009). People in the older age groups, particularly over 60 years of age, received a higher number of transfusions than those in the younger age groups.

Unpublished data provided by SA for the period 2006-07 to 2008-09 also show, for red cells, the use is positively correlated with age (Figure 22).
FIGURE 22: TOTAL AMOUNT OF RED CELLS UNITS TRANSFUSED, BY AGE GROUP OF RECIPIENT, SA 2006, PUBLIC HOSPITALS

Source: SA Department Of Health

In general, older age groups use a greater amount of red cells, although some younger age groups are the major recipients of certain procedures, for example, liver transplants.

The similar demographic pattern associated with transfusion is also evident in hospital separations data. Separations for procedures involving transfusion show that the pattern is mirrored in the private sector as well (Figure 23).

FIGURE 23: PERCENTAGE OF SEPARATIONS ASSOCIATED WITH TRANSFUSION, BY AGE OF PATIENT, 2008-09

Source: National Admitted Patient Care Collection, Department of Health and Ageing

Information on population projections was readily available from the ABS. This enabled demographic assumptions to be built into the model for forecasting blood demand.
Rates And Incidence Of Disease

Blood and blood products have different indicated uses. Some of the blood products in focus in this report have very limited and well defined clinical uses, for example, anti-D preparations which are used to prevent maternal sensitisation and HDNB and the various clotting factors and recombinant products which are used in the treatment of haemophilia and other bleeding disorders. Initiatives such as the Australian Bleeding Disorders Register, which is held by NBA, assist with the prediction of demand for blood products indicated for haemophilia and other bleeding disorders.

Other products, however, by the nature of the breadth of their clinical indications, particularly the fresh blood products, IV Ig and albumin, are used in many clinical procedures. This is true also for Prothrombinex-VF, which, while narrowly defined in its primary use in one sense (for warfarin reversal), crosses use in a range of procedures as it depends on the incidence of warfarin use.

For these types of broadly used products, demand is influenced by the medical conditions, which generate the indicated uses. As a rule, data on the end use of blood and blood products is not routinely collated and reported in the sector. A limited amount of data was available to the project to analyse the main uses of particular blood products. This is summarised in the boxed text below. However, in the time available for the project, information that would allow credible predictions of future trends for the underlying medical conditions could not be sourced. This has prevented incorporation of this aspect into the model.
MAIN CLINICAL USES FOR SELECTED BLOOD PRODUCTS: SUMMARY OF AVAILABLE DATA

Red cells

A synthesis of information from published and unpublished sources indicates that the main uses of red cells are as follows:

- haematology/oncology;
- surgical procedures;
- cardiothoracic surgery;
- orthopaedic procedures, particularly knee and hip replacements;
- organ transplants.

These two broad areas could account for around 50-60 per cent of total red cell use.

Other main clinical uses include

- gastroenterology and gastrointestinal bleeding;
- trauma cases;
- obstetrics and gynaecology.

Platelets and Fresh Frozen Plasma

A published study of WA data from 2001-02 (Cobain, 2007) indicated the following main uses of platelets and FFP:

<table>
<thead>
<tr>
<th>Treatment area for platelets</th>
<th>Proportion of total platelet use (per cent)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haematology</td>
<td>34</td>
</tr>
<tr>
<td>Cardiovascular surgery</td>
<td>22</td>
</tr>
<tr>
<td>Trauma</td>
<td>13</td>
</tr>
<tr>
<td>Bone marrow transplantation</td>
<td>7</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Treatment area for FFP</th>
<th>Proportion of FFP use (per cent)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trauma</td>
<td>27</td>
</tr>
<tr>
<td>Cardiovascular surgery</td>
<td>23</td>
</tr>
<tr>
<td>GI surgery</td>
<td>11</td>
</tr>
<tr>
<td>Other orthopaedic surgery</td>
<td>6</td>
</tr>
<tr>
<td>Haematology</td>
<td>5</td>
</tr>
<tr>
<td>Hepatic/Biliary</td>
<td>5</td>
</tr>
</tbody>
</table>

Intravenous immunoglobulin

The top five clinical areas of use for IVIg, accounting for 70 per cent of total use in 2009-10, were as follows:

<table>
<thead>
<tr>
<th>Condition</th>
<th>Proportion of IVIg use (per cent)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acquired hypogammaglobulinemia secondary to haematological malignancy</td>
<td>21</td>
</tr>
<tr>
<td>Chronic inflammatory demyelinating polyneuropathy (CIDP)</td>
<td>22</td>
</tr>
<tr>
<td>Primary immune deficiency</td>
<td>16</td>
</tr>
<tr>
<td>Myasthenia Gravis (MG)</td>
<td>6</td>
</tr>
<tr>
<td>Multifocal motor neuropathy (MMN)</td>
<td>6</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>71</strong></td>
</tr>
</tbody>
</table>

*Source: Australian Red Cross Blood Service Intravenous Immunoglobulin Use in Australia, August 2010*

Clinical guidelines and changes to indicated uses for products

As discussed earlier, a review of the 2001 NHMRC/ASBT Blood Components guidelines is being undertaken with funding and project management provided by NBA on behalf of all Australian governments (Appropriate Use Strategies-p67).

The blood product use impacts of changed guidelines are not known and have therefore not been incorporated into the model.

**INTRAVENOUS IMMUNOGLOBULIN**

In its Trend and Analysis Report 2008-09 (Australian Red Cross Blood Service, 2009) the Blood Service noted that it ‘estimates that the demand for IVIg will continue to significantly increase over the next 3 years, in the order of approximately 10 per cent per annum. Clinical demand for IVIg will continue to be strongly influenced by the Criteria for the Clinical Use of Intravenous Immunoglobulin in Australia and its planned revision by mid-2011.

The availability of IVIg in Australia relative to clinical need and demand has been reviewed repeatedly since at least the early 1990s. Three approaches have been used to ensure that IVIg is available for the patients who need it most:

- aligning the use of IVIg with conditions for which there is evidence of benefit;
- increasing the manufacture of IVIg in Australia; and
- importing IVIg from overseas suppliers.

The possible approval of IVIg as a therapy for new and emerging indications would put pressure on demand for this product. For example, the results of a current Phase III clinical trial looking at IVIg therapy in AD by Baxter Healthcare Corporation would have a very
significant impact on the demand for IVlg if the results show efficacy and if AD is indicated for use in the Criteria (Jurisdictional Blood Committee, 2007).

TABLE 9: CONDITIONS FOR WHICH TREATMENT BY IVIG IS UNDER ACTIVE INVESTIGATION

<table>
<thead>
<tr>
<th>Disease</th>
<th>Criteria Chapter</th>
<th>Trial details</th>
<th>IVIG Dosage under Investigation</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alzheimer's Disease</td>
<td>-</td>
<td>Baxter Phase 3 trial completion expected July 2011. (NCT00818662) Octapharma Phase 2 trial also in progress. (NCT00812565)</td>
<td>0.2 – 0.4 g/kg every 2 weeks for 70 weeks.</td>
<td>0.76 per 100 people in 2009 (AUS)</td>
</tr>
<tr>
<td>Complex Regional Pain Syndrome (CRPS)</td>
<td>-</td>
<td>Phase 3 trial completion expected January 2011. (NCT00949065)</td>
<td>0.36 – 0.44 g/kg every 4 weeks</td>
<td>20.57 cases per 1,000,000</td>
</tr>
<tr>
<td>Myocardial Infarction (MI)</td>
<td>-</td>
<td>Phase 3 trial completion expected July 2010. (NCT00430865)</td>
<td>0.4 g/kg as induction therapy for 5 days, followed by monthly infusions</td>
<td>1 in 32 people in AUS (2005)</td>
</tr>
<tr>
<td>Idiopathic Cardiomyopathy (ICM)</td>
<td>-</td>
<td>Phase 3 trial completion expected August 2013. (NCT00892112)</td>
<td>2 g/kg administered over 4 consecutive days</td>
<td>1 in 5440 people in AUS for general cardiomyopathy</td>
</tr>
<tr>
<td>Neonatal Sepsis</td>
<td>7</td>
<td>Phase 4 trial completion expected December 2010. (NCT01054999)</td>
<td>0.25 g/kg over 4 hours for 3 days, in conjunction with standard treatment.</td>
<td>Incidence of 1 to 8 per 1000 live births in AUS</td>
</tr>
<tr>
<td>Secondary Recurrent Miscarriage (SRM)</td>
<td>8</td>
<td>Phase 3 trial completion expected November 2011. (NCT00722475)</td>
<td>24 g to 36 g administered b/w 4th and 15th week of gestation.</td>
<td>Between 0.5 % to 3 % of women have recurrent miscarriages</td>
</tr>
</tbody>
</table>

Source: Australian Red Cross Blood Service Trend and Analysis Report 2008-09. (COMMERCIAL-IN-CONFIDENCE)

Clinician prescribing practices

The factors influencing clinician-prescribing practices were discussed earlier (Lessons Learnt from Appropriate Use - Who are the key decision makers? p99). Clinician prescribing practices should continue to be influenced into the future by patient blood management initiatives.

Treatment technologies and techniques

Upward pressure on fresh blood use, particularly red cells and platelets is likely to occur due to increases in haematology oncology activity, including:

- the expansion of regional haematology oncology day units;
• expansion of haematology day clinical programs to seven days a week, in response to clinical need;

• increases in the number of haematologists in some jurisdictions, for example, Queensland;

• changes in haematology treatment regimes;

• tending to be more aggressive earlier in the treatment course, resulting in longer survival but patients remaining transfusion dependent for longer periods (National Blood Authority, undated – b).

Effective alternative therapies to IVIg (Australian Red Cross Blood Service, 2009) are becoming available for some conditions such as specific monoclonal antibodies (for example, rituximab) and thrombopoietin receptor agonists (for example, romiplostin and eltrombopag) for the management of chronic Idiopathic Thrombocytopenic Purpura (ITP). The availability and widespread use of such alternatives may reduce the future clinical demand for IVIg.

**Policy decisions and policy initiatives**

The primary policy decision affecting demand for blood and blood products is the size of the overall budget that governments allocate to this area of expenditure. It can be expected that if the budget available for purchasing blood and blood products is expanded, then more product will be demanded.

Some examples of future areas of policy initiative affecting overall demand for blood and blood products could include:

• possible devolution by further jurisdictions to devolve blood budgets to area health services and hospitals (this decision has already been taken in Queensland, to be implemented from July 2011);

• continued or expanded patient blood management initiatives;

• further initiatives such as was taken in 2007-08 with the injection by the Australian Government of up to $600 million over four years from 2007-08 to the states and territories for the Elective Surgery Waiting List Reduction Plan.

The model has been designed in such a way as to be able to estimate the outcomes on blood product use from specific policy proposals.

**THE BLOOD DEMAND FORECAST MODEL**

A major element of this project was the construction of a data-based model capable of forecasting future demand and the future product cost of supply for blood and blood products in Australia (excepting diagnostic products).
Essentially, the model indicates that the cost of any single blood product is a function of its price and volume. The model is based on projected national prices and jurisdictional volumes for all blood and blood products as supplied by NBA\textsuperscript{20}.

Price has been constructed on the basis of a baseline price, which is then indexed by an assumed price index. In each of the future scenarios provided below, the price indices used for the various products are those advised by the NBA as built into the forward estimates as at end January 2011. For the years beyond 2012-13 to the end of the forecasting period, the price indices are held at the 2012-13 levels. Details on the price indices used per product are at Appendix 7.

The volume function is essentially the same as for price. It takes a baseline volume in a given year and inflates it by a volume index. The volume index has been constructed with the capability of incorporating a range of factors affecting demand for blood and blood products into the future, including, for example:

- population size and composition (particularly ageing);
- changes in clinical practice;
- impact of Patient Blood Management strategies;
- changes in clinical guidelines, including indicated uses for products;
- changes in technology and/or surgical techniques;
- changes in patterns of medical conditions associated with transfusion.

A diagrammatic representation of the logic underpinning the model is provided in Figure 24 below.

Very little reliable information was available to be able to construct credible future demand scenarios, at this point in time, other than for population size, and the effects of ageing on red cell consumption. It will be possible to enhance the volume index as greater levels of data come to hand.

This report presents three future forecast scenarios, using the model. In summary, these are:

- baseline scenario—demographic change;
- a scenario based on Patient blood management (PBM) programs focussed on red cell use;
- a scenario based on Patient blood management (PBM) programs covering all major blood and blood products.

\textsuperscript{20} Prices and volumes are based on the 2010-11 NBA National Supply Plan and Budget as at 27 January 2011, and prices for 2011-12 to 2014-15 as supplied to CTEPC for approval in 2011. These prices are for planning purposes only and may not reflect prices negotiated in individual supplier contracts.
FIGURE 24: BLOOD DEMAND MODEL

Source: Sapere Research Group
BASELINE SCENARIO—DEMOGRAPHIC CHANGE

The baseline scenario projects volumes and the product cost of supply of blood and blood products, except diagnostic products, taking into account available information on current rates of use and forward projections of population size and ageing. For the purposes of the baseline scenario forecast of demand and costs, the volume index comprises a demographic index. This is product specific.

- In the case of red cells, it has been constructed on the basis of information about the relative volumes of use for the three age brackets—less than 40 years old (< 40 years), 41 to 69 years of age and over 70 years old (> 70 years). These relativities were drawn from the Cobain (2007) study. Though a little dated, this was the only published information made available to the project team.

- For all other blood products, the baseline scenario assumes a uniform consumption pattern across age groups:

  This is because no data was available to inform demographic-based usage rates.

Under this scenario, prices are indexed according to the values at Appendix 7.

The baseline scenario draws on:

- volume and price data provided by the NBA for all blood and blood products (except diagnostic products), and all Australian jurisdictions;

- population projections data obtained from ABS (Australian Bureau of Statistics, 2008).

Baseline scenario cost results

Results are presented below for the future product cost implications for the supply of blood and blood products over the next 25 years. The cost implications are identified at the national level (that is, the cost to all Australian governments), and at the jurisdictional level (that is, the total cost of supply of blood and blood products to each individual jurisdiction).

NATIONAL RESULTS

The product cost of supply of blood and blood products across all product groups is estimated to be approximately $937 million in 2010-11. Under the Scenario 2 assumptions, this amount was forecast to rise to $1.6 billion in 2020-21, to reach $2.8 billion in 2030-31, and $3.6 billion in 2035-36 (the end of the forecast period) (Table 10). This represents an increase in total costs of over 70 per cent over the next ten years. Assuming current contribution rates, the Australian Government share of this expenditure would be 63 per cent, and the combined contribution of the jurisdictions 37 per cent.

The product cost of the blood supply is forecast to grow in real terms, at an average of approximately 3 per cent per annum. Under the assumptions of the model, the real cost to Australian governments for the supply of blood and blood products is expected to nearly double in 25 years.
TABLE 10: BASELINE SCENARIO - PROJECTED TOTAL PRODUCT COST OF SUPPLY OF BLOOD AND BLOOD PRODUCTS

<table>
<thead>
<tr>
<th></th>
<th>2010-11</th>
<th>2015-16</th>
<th>2020-21</th>
<th>2025-26</th>
<th>2030-31</th>
<th>2035-36</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nominal Costs</td>
<td>$937</td>
<td>$1,207</td>
<td>$1,606</td>
<td>$2,124</td>
<td>$2,790</td>
<td>$3,630</td>
</tr>
<tr>
<td>Real Costs</td>
<td>$937</td>
<td>$1,067</td>
<td>$1,255</td>
<td>$1,466</td>
<td>$1,703</td>
<td>$1,958</td>
</tr>
</tbody>
</table>

Source: Results Sapere Research Group Limited model, adjusted for inflation on basis of 2.5 per cent annual inflation as contained in the 2010 Intergenerational Report (Department of the Treasury, 2010)

The main driver of the increase in costs in this scenario comes from the increase in the cost of red cells. To the extent that usage rates of other blood products are positively correlated with age of recipient, this model understates the impact of demographic change on the total blood budget.

Table 11 shows the significant rise in the per capita cost of blood and blood products, including, again, in real terms.

TABLE 11: BASELINE SCENARIO - PROJECTED PRODUCT COST OF BLOOD SUPPLY PER CAPITA

<table>
<thead>
<tr>
<th></th>
<th>2010-11</th>
<th>2015-16</th>
<th>2020-21</th>
<th>2025-26</th>
<th>2030-31</th>
<th>2035-36</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nominal Cost Per Capita</td>
<td>$41.96</td>
<td>$50.36</td>
<td>$65.49</td>
<td>$77.98</td>
<td>$96.93</td>
<td>$120.04</td>
</tr>
<tr>
<td>Real Cost Per Capita</td>
<td>$41.96</td>
<td>$44.57</td>
<td>$48.98</td>
<td>$53.84</td>
<td>$59.15</td>
<td>$64.75</td>
</tr>
</tbody>
</table>

Source: Results of Sapere Research Group Limited model, adjusted for inflation on basis of 2.5 per cent annual inflation as per the Intergenerational Report 2010 (Ibid.)

STATE AND TERRITORY COST RESULTS

The general result is that the cost of the blood supply for those states with relatively younger age profiles will rise more steeply than those with relatively older profiles. The differences between the jurisdictions in the rates of growth rates are very small. However, this is sufficient to create significant divergences in the proportional shares of national blood costs. The relative position of Queensland and Victoria is an example. Their relative shares are on par at the beginning of the period, but significantly diverged by the end of the forecast period (Figure 26).
FIGURE 25: BASELINE SCENARIO—PROJECTED GROWTH IN PRODUCT COST OF BLOOD SUPPLY, BY STATE AND TERRITORY (NOMINAL TERMS)

![Bar chart showing projected growth in product cost of blood supply by state and territory.]

Source: Sapere Research Group Limited model

BASELINE SCENARIO PRODUCT VOLUME RESULTS

The results for forecasts of growth in national demand for red cells, platelets and IVlg under the baseline scenario are presented below.

Red cells

FIGURE 26: BASELINE SCENARIO—PROJECTED DEMAND FOR RED CELLS

![Line graph showing projected demand for red cells by state and territory.]

Source: Sapere Research Group Limited model
The baseline scenario assumptions produce growth in volumes on a per population basis as well (Figure 27 and Table 12). Under the assumptions of the model, the average usage rate for red cells will increase, nationally, from 37 units per 1000 in 2010-11, to 47 units by 2035-36.

**FIGURE 27: BASELINE SCENARIO—PROJECTED RED CELL DEMAND PER 1000 POPULATION**

![Graph showing projected red cell demand per 1000 population from 2010-11 to 2035-36](image)

*Source: Sapere Research Group Limited model*

**TABLE 12: BASELINE SCENARIO—PROJECTED RED CELL DEMAND PER 1000 POPULATION, BY STATE AND TERRITORY**

<table>
<thead>
<tr>
<th>Year</th>
<th>ACT</th>
<th>NSW</th>
<th>NT</th>
<th>QLD</th>
<th>SA</th>
<th>TAS</th>
<th>VIC</th>
<th>WA</th>
<th>National</th>
</tr>
</thead>
<tbody>
<tr>
<td>2010-11</td>
<td>36</td>
<td>35</td>
<td>28</td>
<td>38</td>
<td>43</td>
<td>31</td>
<td>38</td>
<td>33</td>
<td>37</td>
</tr>
<tr>
<td>2015-16</td>
<td>38</td>
<td>37</td>
<td>29</td>
<td>40</td>
<td>45</td>
<td>33</td>
<td>40</td>
<td>34</td>
<td>38</td>
</tr>
<tr>
<td>2020-21</td>
<td>41</td>
<td>39</td>
<td>31</td>
<td>43</td>
<td>47</td>
<td>36</td>
<td>42</td>
<td>36</td>
<td>41</td>
</tr>
<tr>
<td>2025-26</td>
<td>44</td>
<td>41</td>
<td>33</td>
<td>45</td>
<td>50</td>
<td>38</td>
<td>45</td>
<td>39</td>
<td>43</td>
</tr>
<tr>
<td>2030-31</td>
<td>47</td>
<td>43</td>
<td>34</td>
<td>47</td>
<td>53</td>
<td>41</td>
<td>47</td>
<td>40</td>
<td>45</td>
</tr>
<tr>
<td>2035-36</td>
<td>48</td>
<td>45</td>
<td>35</td>
<td>49</td>
<td>55</td>
<td>42</td>
<td>49</td>
<td>42</td>
<td>47</td>
</tr>
</tbody>
</table>

*Source: Sapere Research Group Limited model*
Platelets

Figure 28 and Table 13 show the forecast rise in platelet demand under the baseline scenario, by jurisdiction. As indicated earlier, to the extent that platelet demand is correlated with an ageing population, these growth trajectories will understate future demand.

FIGURE 28: BASELINE SCENARIO—PROJECTED DEMAND FOR PLATELETS, BY STATE AND TERRITORY

Source: Sapere Research Group Limited model

TABLE 13: BASELINE SCENARIO—PROJECTED DEMAND FOR PLATELETS, BY STATE AND TERRITORY

<table>
<thead>
<tr>
<th></th>
<th>ACT</th>
<th>NSW</th>
<th>NT</th>
<th>QLD</th>
<th>SA</th>
<th>TAS</th>
<th>VIC</th>
<th>WA</th>
<th>National</th>
</tr>
</thead>
<tbody>
<tr>
<td>2010-11</td>
<td>2,250</td>
<td>35,095</td>
<td>920</td>
<td>40,729</td>
<td>9,155</td>
<td>2,290</td>
<td>33,000</td>
<td>9,100</td>
<td>132,539</td>
</tr>
<tr>
<td>2015-16</td>
<td>2,381</td>
<td>37,055</td>
<td>991</td>
<td>45,106</td>
<td>9,601</td>
<td>2,364</td>
<td>35,303</td>
<td>10,033</td>
<td>142,834</td>
</tr>
<tr>
<td>2020-21</td>
<td>2,509</td>
<td>39,009</td>
<td>1,063</td>
<td>49,516</td>
<td>10,041</td>
<td>2,431</td>
<td>37,604</td>
<td>10,976</td>
<td>153,149</td>
</tr>
<tr>
<td>2025-26</td>
<td>2,631</td>
<td>40,911</td>
<td>1,136</td>
<td>53,904</td>
<td>10,459</td>
<td>2,486</td>
<td>39,858</td>
<td>11,913</td>
<td>163,299</td>
</tr>
<tr>
<td>2030-31</td>
<td>2,744</td>
<td>42,693</td>
<td>1,210</td>
<td>58,200</td>
<td>10,841</td>
<td>2,527</td>
<td>42,004</td>
<td>12,827</td>
<td>173,045</td>
</tr>
<tr>
<td>2035-36</td>
<td>2,848</td>
<td>44,309</td>
<td>1,284</td>
<td>62,346</td>
<td>11,175</td>
<td>2,552</td>
<td>43,998</td>
<td>13,709</td>
<td>182,219</td>
</tr>
</tbody>
</table>

Source: Sapere Research Group Limited model
Intravenous Immunoglobulin

Figure 29 and Table 14 show the forecast rise in IVIg demand for the baseline scenario. Information from the Blood Service indicates that IVIg demand correlates positively with ageing as well (ARCBS, 2010). However, as mentioned above, no data were available to the project to measure the impact. The figures below therefore underestimate future IVIg demand, based on current trends.

**FIGURE 29: BASELINE SCENARIO—PROJECTED DEMAND FOR INTRAVENOUS IMMUNOGLOBULIN, BY STATE AND TERRITORY**

*Source: Sapere Research Group Limited model*
TABLE 14: BASELINE SCENARIO—PROJECTED INTRAVENOUS IMMUNOGLOBULIN DEMAND, BY STATE AND TERRITORY

<table>
<thead>
<tr>
<th>Year</th>
<th>ACT</th>
<th>NSW</th>
<th>NT</th>
<th>QLD</th>
<th>SA</th>
<th>TAS</th>
<th>VIC</th>
<th>WA</th>
<th>National</th>
</tr>
</thead>
<tbody>
<tr>
<td>2010-11</td>
<td>44</td>
<td>1040</td>
<td>10.9</td>
<td>725</td>
<td>203</td>
<td>87</td>
<td>605</td>
<td>210</td>
<td>2924.9</td>
</tr>
<tr>
<td>2015-16</td>
<td>47</td>
<td>1,098</td>
<td>12</td>
<td>803</td>
<td>213</td>
<td>90</td>
<td>647</td>
<td>232</td>
<td>3,141</td>
</tr>
<tr>
<td>2020-21</td>
<td>49</td>
<td>1,156</td>
<td>13</td>
<td>881</td>
<td>223</td>
<td>92</td>
<td>689</td>
<td>253</td>
<td>3,357</td>
</tr>
<tr>
<td>2025-26</td>
<td>51</td>
<td>1,212</td>
<td>13</td>
<td>960</td>
<td>232</td>
<td>94</td>
<td>731</td>
<td>275</td>
<td>3,569</td>
</tr>
<tr>
<td>2030-31</td>
<td>54</td>
<td>1,265</td>
<td>14</td>
<td>1,036</td>
<td>240</td>
<td>96</td>
<td>770</td>
<td>296</td>
<td>3,772</td>
</tr>
<tr>
<td>2035-36</td>
<td>56</td>
<td>1,313</td>
<td>15</td>
<td>1,110</td>
<td>248</td>
<td>97</td>
<td>807</td>
<td>316</td>
<td>3,961</td>
</tr>
</tbody>
</table>

Source: Sapere Research Group Limited model

MODELLING THE IMPACTS OF PRICE SIGNALLING OPTIONS

The terms of reference for this report sought modelling of the impacts of price signalling options. However, these impacts cannot be modelled in isolation. This is due to technical reasons as well as policy reasons.

The technical reasons pertain mainly to lack of data. There is no history of response to the price signals already in the supply chain that can be used to extrapolate information on the price elasticity of demand (or demand responsiveness to price changes). This is because governments have met any price increases in the sector with expanded budgets—that is, there has been no price response.

The earlier section on Price Signalling discussed some measurements of price elasticities of demand for pharmaceutical co-payments (p118). Price elasticities of demand can be used to measure the impact on demand of marginal changes in price. However, the options that have been discussed elsewhere in this report do not involve marginal changes to price, but the introduction of price to players in the system who have not to date seen any price at all. In mathematical terms, the marginal price change in this instance is infinite. It would be possible to assume a level of response for the introduction of a price signal where the signal was previously zero, if there were information to do this. No such information was found in the literature. Further, officials in NSW, the State that has the longest history of devolved blood budgets in Australia, advised that they were unable to separate the impact on demand from the price signal, from other blood management measures.
This leads to the policy reasons why price signalling options cannot be modelled in isolation. The discussion of price signals earlier in this report indicated that the impact of price on demand depends on a range of other factors, including who bears the price (who pays), the availability of substitutes and levels of discretionary demand. In the case of blood and blood products, the clinician is this decision maker, acting on behalf of the end user (the patient).

The strength of the price signal on the clinician differs under the different options. However, under all options, the price signal introduces an incentive for containing the use of blood and blood products to appropriate levels of use. The leap between the introduction of the incentive and effecting a change in demand is not, however, a one-step process.

For example, NSW officials interviewed during the project indicated that no changes on the patterns of blood use occurred following the devolution of blood budgets between 2004-2007. However, they did remark that budget devolution had been a positive force in gaining support among hospital senior management for the implementation of appropriate use initiatives. This experience appears to demonstrate that improving blood usage involves multi-modal intervention strategies.

For clinicians to change prescribing behaviour on the basis of the incentive provided by a price signal, a range of other conditions need to be met or measures take place. These include, for example:

- willingness to change prescribing behaviour;
- knowledge of what is appropriate use for individual blood products and in clinical situations;
- knowledge of the clinician’s own practice against appropriate use levels;
- knowledge of substitute therapies, products or treatments;
- acceptance that substitute therapies, products or treatments uphold patient outcomes;
- access to substitute therapies, products or treatments.

In essence, introduction of price signals further down the supply chain in the blood sector will have little discernible impact in the absence of a range of complementary measures that can address the list of factors above. Indeed, the devolution of blood budgets in NSW and Tasmania has been introduced in concert with complementary measures incorporating some or all of the elements above.

**Modelling Scenarios**

Given that the impact of price signals cannot be modelled in isolation, this report, as indicated above, presents instead a number of future scenarios for consideration and analysis.

Each of the scenarios is built upon the ‘baseline model’, that is the demographic change model above. Under each of the PBM scenarios, prices are adjusted as per the baseline scenario.

Under each of the scenarios, the Australian Government would bear 63 per cent of the forecast nominal costs.

**Patient Blood Management—Red Cells**

This scenario (PBM—Red Cells’ Scenario) assumed that Patient Blood Management programs would be extended to public and private hospitals in Australia, resulting in a reduction in red cell usage, nationally, of 5 per cent per annum, over the period 2014-15 to 2018-19. The 5 per cent reduction
applied to the baseline scenario growth, that is, it was a reduction on growth in red cell use due to population size and ageing. In effect, the implementation of PBM Programs was assumed to temper the rate of growth due to demographic change.

The rate of reduction in red cells was a judgement made by Sapere, informed in part by results from NSW CEC of transfusions of red cells possibly avoided over the period 2008-09 in NSW hospitals targeted by the Blood Watch program (see Appropriate Use Strategies, New South Wales (NSW), p76). The assumed rate of reduction in red cell use under this scenario is indicative only.

The impact of the Patient Blood Management initiatives is assumed to level off after a five year period. That is, the initiatives would take around five years to establish usage patterns at an appropriate level—a level commensurate with patient needs and compliance with clinical guidelines. This would establish, in effect, a new baseline usage rate. From this point, the impact of ageing in the population would take over, producing a new growth curve for red cells.

**Modelling Results**

Under the PBM—red cells scenario, the product cost of the national blood supply would rise, in nominal terms, from approximately $937 million in 2010-11 to $1.5 billion in 2020-21 (compared with the baseline scenario projection of $1.6 billion) and to around $3.3 billion by 2035-36 (compared with the baseline scenario projection of $3.6 billion). In real terms, the product cost of the national blood supply would rise by 24 per cent in 10 years.

**Table 15: PBM-Red Cells Scenario, Projected Product Cost Supply of Blood and Blood Products**

<table>
<thead>
<tr>
<th></th>
<th>2010-11</th>
<th>2015-16</th>
<th>2020-21</th>
<th>2025-26</th>
<th>2030-31</th>
<th>2035-36</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nominal Costs</td>
<td>$937</td>
<td>$1,170</td>
<td>$1,487</td>
<td>$1,961</td>
<td>$2,568</td>
<td>$3,334</td>
</tr>
<tr>
<td>Real Costs</td>
<td>$937</td>
<td>$1,034</td>
<td>$1,162</td>
<td>$1,354</td>
<td>$1,567</td>
<td>$1,798</td>
</tr>
</tbody>
</table>

*Source: Results Sapere Research Group Limited Model, Adjusted For Inflation On Basis Of 2.5 Per Cent Annual Inflation As Contained In The 2010 Intergenerational Report (Department of the Treasury, 2010)*

The real cost per capita for the national blood supply would be $45.36 in 10 years, compared with $48.98 under the baseline scenario.

**Table 16: PBM-Red Cells Scenario, Projected Impact on Product Cost of the Blood Supply Per Capita Costs**

<table>
<thead>
<tr>
<th></th>
<th>2010-11</th>
<th>2015-16</th>
<th>2020-21</th>
<th>2025-26</th>
<th>2030-31</th>
<th>2035-36</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nominal Cost Per Capita</td>
<td>$41.96</td>
<td>$48.83</td>
<td>$58.06</td>
<td>$71.99</td>
<td>$89.22</td>
<td>$110.26</td>
</tr>
<tr>
<td>Real Cost Per Capita</td>
<td>$41.96</td>
<td>$43.16</td>
<td>$45.36</td>
<td>$49.70</td>
<td>$54.45</td>
<td>$59.47</td>
</tr>
</tbody>
</table>

*Source: Sapere Research Group Limited Model*

**State and Territory Cost Results**

The state and territory cost results for all products is summarised in Table 17 and Figure 30.
TABLE 17: PBM-RED CELLS SCENARIO, PROJECTED PRODUCT COST OF BLOOD SUPPLY, BY STATE AND TERRITORY

($ Million, Nominal)

<table>
<thead>
<tr>
<th></th>
<th>ACT</th>
<th>NSW</th>
<th>NT</th>
<th>QLD</th>
<th>SA</th>
<th>TAS</th>
<th>VIC</th>
<th>WA</th>
<th>National</th>
</tr>
</thead>
<tbody>
<tr>
<td>2010-11</td>
<td>13.8</td>
<td>319.5</td>
<td>5.2</td>
<td>212.0</td>
<td>73.6</td>
<td>20.9</td>
<td>208.3</td>
<td>83.3</td>
<td>936.6</td>
</tr>
<tr>
<td>2015-16</td>
<td>17.0</td>
<td>394.5</td>
<td>6.4</td>
<td>275.3</td>
<td>89.7</td>
<td>25.1</td>
<td>256.5</td>
<td>105.8</td>
<td>1,170.2</td>
</tr>
<tr>
<td>2020-21</td>
<td>21.4</td>
<td>495.0</td>
<td>8.0</td>
<td>360.3</td>
<td>111.0</td>
<td>31.1</td>
<td>323.6</td>
<td>136.9</td>
<td>1,487.4</td>
</tr>
<tr>
<td>2025-26</td>
<td>27.9</td>
<td>642.7</td>
<td>10.6</td>
<td>486.1</td>
<td>143.3</td>
<td>39.7</td>
<td>426.6</td>
<td>183.7</td>
<td>1,960.6</td>
</tr>
<tr>
<td>2030-31</td>
<td>36.1</td>
<td>830.5</td>
<td>14.0</td>
<td>650.2</td>
<td>184.0</td>
<td>50.4</td>
<td>559.0</td>
<td>244.1</td>
<td>2,568.4</td>
</tr>
<tr>
<td>2035-36</td>
<td>46.3</td>
<td>1,064.5</td>
<td>18.3</td>
<td>860.9</td>
<td>234.0</td>
<td>63.1</td>
<td>725.8</td>
<td>321.2</td>
<td>3,334.2</td>
</tr>
</tbody>
</table>

Source: Sapere Research Group Limited Model

FIGURE 30: PBM-RED CELLS SCENARIO, PROJECTED PRODUCT COST OF BLOOD SUPPLY, BY STATE AND TERRITORY

($ Million, Nominal)

Source: Sapere Research Group Limited Model

Under the assumptions of PBM-red cells scenario, the total product cost of the national blood supply would rise by the greatest factor in Queensland, by 70 per cent to 2020-21, compared with the national average of 59 per cent (Figure 31).
FIGURE 31: PBM-RED CELLS SCENARIO, PROJECTED GROWTH IN PRODUCT COST OF BLOOD SUPPLY, BY STATE AND TERRITORY

Source: Sapere Research Group Limited Model

The cost impacts under this scenario for individual products are examined below.

PRODUCT COST RESULTS

The impact of the PBM-red cells scenario assumptions on the costs of selected products is summarised in Table 18 and the state and territory total cost patterns in the figures which follow.

TABLE 18: PBM-RED CELLS SCENARIO, PROJECTED PRODUCT COST OF SUPPLY OF SELECTED PRODUCTS

<table>
<thead>
<tr>
<th></th>
<th>Red Cells</th>
<th>Albumin</th>
<th>IVIg</th>
</tr>
</thead>
<tbody>
<tr>
<td>2010-11</td>
<td>290.8</td>
<td>29.3</td>
<td>190.5</td>
</tr>
<tr>
<td>2015-16</td>
<td>340.8</td>
<td>38.2</td>
<td>220.9</td>
</tr>
<tr>
<td>2020-21</td>
<td>406.6</td>
<td>49.5</td>
<td>290.5</td>
</tr>
<tr>
<td>2025-26</td>
<td>558.5</td>
<td>63.7</td>
<td>380.2</td>
</tr>
<tr>
<td>2030-31</td>
<td>758.9</td>
<td>81.5</td>
<td>494.9</td>
</tr>
<tr>
<td>2035-36</td>
<td>1,011.4</td>
<td>29.3</td>
<td>640.6</td>
</tr>
</tbody>
</table>

Source: Sapere Research Group Limited Model
FIGURE 32: PBM-RED CELLS SCENARIO, PROJECTED PRODUCT COST OF SUPPLY OF RED CELLS, BY STATE AND TERRITORY

($ Million, Nominal)

Source: Sapere Research Group Limited Model

FIGURE 33: PBM-RED CELLS SCENARIO, PROJECTED PRODUCT COST OF SUPPLY OF IVIG, BY STATE AND TERRITORY

($ Million, Nominal)

Source: Sapere Research Group Limited Model
FIGURE 34: PBM-RED CELLS SCENARIO, PROJECTED PRODUCT COST OF SUPPLY OF ALBUMIN, BY STATE AND TERRITORY

($ Million, Nominal)

Source: Sapere Research Group Limited Model

Under the PBM-red cells scenario, red cell use per 1000 population would decline over the 10 years to 2020-21 (Table 19).

TABLE 19: PBM-RED CELLS SCENARIO, PROJECTED RED CELL DEMAND PER 1000 POPULATION

<table>
<thead>
<tr>
<th>Year</th>
<th>Standard Units</th>
</tr>
</thead>
<tbody>
<tr>
<td>2010-11</td>
<td>36.6</td>
</tr>
<tr>
<td>2015-16</td>
<td>34.5</td>
</tr>
<tr>
<td>2020-21</td>
<td>31.5</td>
</tr>
<tr>
<td>2025-26</td>
<td>33.3</td>
</tr>
<tr>
<td>2030-31</td>
<td>35.0</td>
</tr>
<tr>
<td>2035-36</td>
<td>36.3</td>
</tr>
</tbody>
</table>

Source: Sapere Research Group Limited Model
FIGURE 35: PBM-RED CELLS SCENARIO, PROJECTED DEMAND FOR RED CELLS BY STATE AND TERRITORY

Source: Sapere Research Group Limited Model

Patient Blood Management—All Products

This scenario (‘PBM-all products’ scenario) assumed that the scope of PBM programs would take in products other than red cells. It was assumed that the impact would be a 2 per cent reduction in use of all blood components and products over the 10 year period 2014-15 to 2023-24. As for the PBM-red cells scenario, the reduction was assumed to come off the baseline scenario projections.

The 2 per cent factor and the time period for this scenario represent judgements made by Sapere, based on the analysis of PBM programs and impacts as part of this project.

Under the PBM-all products scenario, the product cost of the national blood supply would rise, in nominal terms, from approximately $937 million in 2010-11 to $1.3 billion in 2020-21 (compared with the baseline scenario projection of $1.6 billion) and to around $2.2 billion by 2035-36 (compared with the baseline scenario projection of $3.6 billion). In real terms, the product cost of the national blood supply would rise by 24 per cent in 10 years.
TABLE 20: PBM-ALL PRODUCTS SCENARIO—PROJECTED PRODUCT COST OF SUPPLY OF BLOOD AND BLOOD PRODUCTS

($ Million)

<table>
<thead>
<tr>
<th>Year</th>
<th>2010-11</th>
<th>2015-16</th>
<th>2020-21</th>
<th>2025-26</th>
<th>2030-31</th>
<th>2035-36</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nominal Costs</td>
<td>$ 937</td>
<td>$ 1,091</td>
<td>$ 1,312</td>
<td>$ 1,569</td>
<td>$ 1,863</td>
<td>$ 2,191</td>
</tr>
<tr>
<td>Real Costs</td>
<td>$ 937</td>
<td>$ 964</td>
<td>$ 1,025</td>
<td>$ 1,083</td>
<td>$ 1,137</td>
<td>$ 1,182</td>
</tr>
</tbody>
</table>

Source: Results Sapere Research Group Limited Model, adjusted for inflation on basis of 2.5 per cent annual inflation as contained in The 2010 Intergenerational Report (Department of the Treasury, 2010)

The real per capita cost of the national blood supply would be $51.23 in 10 years, compared with $48.98 under the baseline scenario.

TABLE 21: PBM-ALL PRODUCTS SCENARIO—PROJECTED IMPACT ON PRODUCT COST OF BLOOD SUPPLY PER CAPITA

<table>
<thead>
<tr>
<th>Year</th>
<th>2010-11</th>
<th>2015-16</th>
<th>2020-21</th>
<th>2025-26</th>
<th>2030-31</th>
<th>2035-36</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nominal Cost Per Capita</td>
<td>$ 41.96</td>
<td>$ 45.52</td>
<td>$ 51.23</td>
<td>$ 57.59</td>
<td>$ 64.71</td>
<td>$ 72.44</td>
</tr>
<tr>
<td>Real Cost Per Capita</td>
<td>$ 41.96</td>
<td>$ 40.24</td>
<td>$ 40.02</td>
<td>$ 39.77</td>
<td>$ 39.49</td>
<td>$ 39.07</td>
</tr>
</tbody>
</table>

Source: Sapere Research Group Limited Model

STATE AND TERRITORY COST RESULTS

The state and territory cost results for all products are summarised in Table 22 and Figure 36.

TABLE 22: PBM-ALL PRODUCTS SCENARIO—PROJECTED PRODUCT COST OF BLOOD SUPPLY, BY STATE AND TERRITORY

($ Million, Nominal)

<table>
<thead>
<tr>
<th>Year</th>
<th>ACT</th>
<th>NSW</th>
<th>NT</th>
<th>QLD</th>
<th>SA</th>
<th>TAS</th>
<th>VIC</th>
<th>WA</th>
<th>National</th>
</tr>
</thead>
<tbody>
<tr>
<td>2010-11</td>
<td>13.8</td>
<td>319.5</td>
<td>5.2</td>
<td>212.0</td>
<td>73.6</td>
<td>20.9</td>
<td>208.3</td>
<td>83.3</td>
<td>936.6</td>
</tr>
<tr>
<td>2015-16</td>
<td>15.9</td>
<td>366.7</td>
<td>6.0</td>
<td>256.2</td>
<td>83.9</td>
<td>23.3</td>
<td>240.3</td>
<td>98.8</td>
<td>1,091.1</td>
</tr>
<tr>
<td>2020-21</td>
<td>19.0</td>
<td>433.4</td>
<td>7.3</td>
<td>316.5</td>
<td>98.7</td>
<td>27.2</td>
<td>289.0</td>
<td>121.3</td>
<td>1,312.4</td>
</tr>
<tr>
<td>2025-26</td>
<td>22.5</td>
<td>510.1</td>
<td>8.8</td>
<td>387.1</td>
<td>115.6</td>
<td>31.5</td>
<td>345.4</td>
<td>147.6</td>
<td>1,568.7</td>
</tr>
<tr>
<td>2030-31</td>
<td>26.4</td>
<td>597.5</td>
<td>10.5</td>
<td>469.3</td>
<td>134.6</td>
<td>36.2</td>
<td>410.4</td>
<td>177.9</td>
<td>1,862.8</td>
</tr>
<tr>
<td>2035-36</td>
<td>30.7</td>
<td>693.6</td>
<td>12.4</td>
<td>562.8</td>
<td>155.1</td>
<td>41.1</td>
<td>482.7</td>
<td>212.1</td>
<td>2,190.5</td>
</tr>
</tbody>
</table>

Source: Sapere Research Group Limited Model
FIGURE 36: PBM-ALL PRODUCTS SCENARIO—PROJECTED PRODUCT COST OF BLOOD SUPPLY, BY STATE AND TERRITORY

($ Million, Nominal)

Source: Sapere Research Group Limited Model

Under the assumptions of PBM-all products scenario, the total product cost of the national blood supply would rise by the greatest factor in Queensland, by 49 per cent to 2020-21, compared with the national average of 40 per cent (Figure 37).

FIGURE 37: PBM-ALL PRODUCTS SCENARIO—PROJECTED GROWTH IN PRODUCT COST OF BLOOD SUPPLY, BY STATE AND TERRITORY

Source: Sapere Research Group Limited Model
The cost impacts under this scenario for individual products are examined below.

**PRODUCT COST RESULTS**

The impact of the PBM-all products scenario assumptions on the costs of selected products is summarised in Table 23 and the state and territory total cost patterns in the figures which follow.

**TABLE 23: PBM-ALL PRODUCTS SCENARIO—PROJECTED PRODUCT COSTS OF SUPPLY FOR SELECTED PRODUCTS**

<table>
<thead>
<tr>
<th></th>
<th>Red Cells</th>
<th>Albumin</th>
<th>IVig</th>
</tr>
</thead>
<tbody>
<tr>
<td>2010-11</td>
<td>290.8</td>
<td>22.6</td>
<td>190.5</td>
</tr>
<tr>
<td>2015-16</td>
<td>341.3</td>
<td>26.5</td>
<td>199.6</td>
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<tr>
<td>2020-21</td>
<td>429.3</td>
<td>31.2</td>
<td>237.3</td>
</tr>
<tr>
<td>2025-26</td>
<td>533.1</td>
<td>36.6</td>
<td>280.8</td>
</tr>
<tr>
<td>2030-31</td>
<td>654.7</td>
<td>42.5</td>
<td>330.4</td>
</tr>
<tr>
<td>2035-36</td>
<td>788.8</td>
<td>49.2</td>
<td>386.6</td>
</tr>
</tbody>
</table>

*Source: Sapere Research Group Limited Model*
FIGURE 38: PBM-ALL PRODUCTS SCENARIO—PROJECTED PRODUCT COST OF SUPPLY FOR RED CELLS, BY STATE AND TERRITORY

($ Million, Nominal)

Source: Sapere Research Group Limited Model
FIGURE 39: PBM-ALL PRODUCTS SCENARIO—PROJECTED PRODUCT COST OF SUPPLY FOR IVIG, BY STATE AND TERRITORY

($ Million, Nominal)

Source: Sapere Research Group Limited Model
FIGURE 40: PBM-ALL PRODUCTS SCENARIO—PROJECTED PRODUCT COST OF SUPPLY FOR ALBUMIN, BY STATE AND TERRITORY

($ Million, Nominal)

Source: Sapere Research Group Limited Model

Under the PBM-all products scenario, both red cell and IVlg use per 1000 population would see significant declines over the 10 years to 2020-21 and to the end of the forecasting period (Table 24).

TABLE 24: PBM-ALL PRODUCTS SCENARIO—PROJECTED DEMAND PER 1000 POPULATION, RED CELLS AND INTRAVENOUS IMMUNOGLOBULIN

<table>
<thead>
<tr>
<th>Year</th>
<th>Red Cells (Standard Units)</th>
<th>IVlg (Grams)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2010-11</td>
<td>36.6</td>
<td>131.0</td>
</tr>
<tr>
<td>2015-16</td>
<td>34.6</td>
<td>118.5</td>
</tr>
<tr>
<td>2020-21</td>
<td>33.3</td>
<td>107.1</td>
</tr>
<tr>
<td>2025-26</td>
<td>31.8</td>
<td>96.8</td>
</tr>
<tr>
<td>2030-31</td>
<td>30.2</td>
<td>87.5</td>
</tr>
<tr>
<td>2035-36</td>
<td>28.3</td>
<td>79.1</td>
</tr>
</tbody>
</table>

Source: Sapere Research Group Limited Model
FIGURE 41: PBM-ALL PRODUCTS SCENARIO—PROJECTED DEMAND FOR RED CELLS BY STATE AND TERRITORY

Source: Sapere Research Group Limited Model
FIGURE 42: PBM-ALL PRODUCTS SCENARIO—PROJECTED DEMAND FOR INTRAVENOUS IMMUNOGLOBULIN BY STATE AND TERRITORY

Source: Sapere Research Group Limited Model

A summary of the nominal cost outcomes of the three scenarios is provided in Table 25.
TABLE 25: SUMMARY OF SCENARIO OUTCOMES FOR PRODUCT COST OF BLOOD SUPPLY

($ Million, Nominal)

<table>
<thead>
<tr>
<th></th>
<th>2010-11</th>
<th>2015-16</th>
<th>2020-21</th>
<th>2025-26</th>
<th>2030-31</th>
<th>2035-36</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BASELINE SCENARIO</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nominal Costs</td>
<td>$937</td>
<td>$1,207</td>
<td>$1,606</td>
<td>$2,124</td>
<td>$2,790</td>
<td>$3,630</td>
</tr>
<tr>
<td>Real Costs</td>
<td>$ 937</td>
<td>$1,067</td>
<td>$1,255</td>
<td>$1,466</td>
<td>$1,703</td>
<td>$1,958</td>
</tr>
<tr>
<td><strong>PBM-RED CELLS SCENARIO</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nominal Costs</td>
<td>$937</td>
<td>$1,170</td>
<td>$1,487</td>
<td>$1,961</td>
<td>$2,568</td>
<td>$3,334</td>
</tr>
<tr>
<td>Real Costs</td>
<td>$ 937</td>
<td>$1,034</td>
<td>$1,162</td>
<td>$1,354</td>
<td>$1,567</td>
<td>$1,798</td>
</tr>
<tr>
<td><strong>PBM-ALL PRODUCT SCENARIO</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nominal Costs</td>
<td>$937</td>
<td>$1,091</td>
<td>$1,312</td>
<td>$1,569</td>
<td>$1,863</td>
<td>$2,191</td>
</tr>
<tr>
<td>Real Costs</td>
<td>$ 937</td>
<td>$ 964</td>
<td>$1,025</td>
<td>$1,083</td>
<td>$1,137</td>
<td>$1,182</td>
</tr>
</tbody>
</table>

Source: Sapere Research Group Limited Model
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# Acronyms and Abbreviations

<table>
<thead>
<tr>
<th>Acronym</th>
<th>Full Form</th>
</tr>
</thead>
<tbody>
<tr>
<td>AACB</td>
<td>Australasian Association of Clinical Biochemists</td>
</tr>
<tr>
<td>AAPP</td>
<td>Australian Association of Pathology Practices</td>
</tr>
<tr>
<td>ABA</td>
<td>American Burn Association</td>
</tr>
<tr>
<td>ABD</td>
<td>autologous blood donation</td>
</tr>
<tr>
<td>ABDR</td>
<td>Australian Bleeding Disorders Registry</td>
</tr>
<tr>
<td>ABS</td>
<td>Australian Bureau of Statistics</td>
</tr>
<tr>
<td>ABLE</td>
<td>The Age of Blood Evaluation</td>
</tr>
<tr>
<td>ABT</td>
<td>allogeneic blood transfusion</td>
</tr>
<tr>
<td>ACSQHC</td>
<td>Australian Commission on Safety and Quality in Health Care</td>
</tr>
<tr>
<td>AD</td>
<td>Alzheimer’s Disease</td>
</tr>
<tr>
<td>AG</td>
<td>Australian Government</td>
</tr>
<tr>
<td>AGD</td>
<td>Attorney-General’s Department</td>
</tr>
<tr>
<td>AGREE</td>
<td>Appraisal of Guidelines Research &amp; Evaluation</td>
</tr>
<tr>
<td>AHICDO</td>
<td>Australian Haemophilia Centre Directors Organisation</td>
</tr>
<tr>
<td>AHMAC</td>
<td>Australian Health Ministers’ Advisory Council</td>
</tr>
<tr>
<td>AHMC</td>
<td>Australian Health Minister’s Council</td>
</tr>
<tr>
<td>AHP</td>
<td>Approved Health Providers</td>
</tr>
<tr>
<td>AHS</td>
<td>Area Health Services</td>
</tr>
<tr>
<td>AIDS</td>
<td>Acquired Immunodeficiency Syndrome</td>
</tr>
<tr>
<td>AIMS</td>
<td>Australian Institute of Medical Scientists</td>
</tr>
<tr>
<td>ALI</td>
<td>acute lung injury</td>
</tr>
<tr>
<td>ALS</td>
<td>Australian Laboratory Services</td>
</tr>
<tr>
<td>ANH</td>
<td>acute normovolaemic haemodilution</td>
</tr>
<tr>
<td>ANZICS</td>
<td>Australian and New Zealand Intensive Care Society</td>
</tr>
<tr>
<td>ANZSBT</td>
<td>Australian and New Zealand Society of Blood Transfusion</td>
</tr>
<tr>
<td>AO</td>
<td>Officer of the Order of Australia</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Description</td>
</tr>
<tr>
<td>--------------</td>
<td>-------------</td>
</tr>
<tr>
<td>AR</td>
<td>Approved Recipient</td>
</tr>
<tr>
<td>ARCBS</td>
<td>Australian Red Cross Blood Service</td>
</tr>
<tr>
<td>ARDS</td>
<td>acute respiratory distress syndrome</td>
</tr>
<tr>
<td>ASBT</td>
<td>Australasian Society of Blood Transfusion Incorporated</td>
</tr>
<tr>
<td>ASC</td>
<td>Australian Society of Cytology</td>
</tr>
<tr>
<td>ASCEPT</td>
<td>Australasian Society of Clinical and Experimental Pharmacologists and Toxicologists</td>
</tr>
<tr>
<td>ASCIA</td>
<td>Australasian Society of Clinical Immunology and Allergy</td>
</tr>
<tr>
<td>ASH</td>
<td>American Society of Hematology</td>
</tr>
<tr>
<td>ASM</td>
<td>Australian Society for Microbiology</td>
</tr>
<tr>
<td>ASTH</td>
<td>Australasian Society of Thrombosis and Haemostasis</td>
</tr>
<tr>
<td>AUBRG</td>
<td>Appropriate Use of Blood Reference Group</td>
</tr>
<tr>
<td>BCA</td>
<td>blood conservation algorithm</td>
</tr>
<tr>
<td>BCSAC</td>
<td>Blood Clinical and Scientific Advisory Committee</td>
</tr>
<tr>
<td>BeST</td>
<td>Better Safer Transfusion</td>
</tr>
<tr>
<td>BMS</td>
<td>bloodless medicine and surgery</td>
</tr>
<tr>
<td>BTIC</td>
<td>Blood Transfusion Improvement Collaborative</td>
</tr>
<tr>
<td>CABG</td>
<td>coronary artery bypass graft</td>
</tr>
<tr>
<td>CARI</td>
<td>Caring for Australasians with renal impairment</td>
</tr>
<tr>
<td>CCCTG</td>
<td>Canadian Critical Care Trials Group</td>
</tr>
<tr>
<td>CEC</td>
<td>Clinical Excellence Commission</td>
</tr>
<tr>
<td>CIDP</td>
<td>chronic inflammatory demyelinating polyneuropathy</td>
</tr>
<tr>
<td>CIG</td>
<td>Cochrane Injuries Group</td>
</tr>
<tr>
<td>CRD</td>
<td>Centre for Reviews and Dissemination</td>
</tr>
<tr>
<td>CRG</td>
<td>Clinical Reference Group</td>
</tr>
<tr>
<td>CSL</td>
<td>CSL Limited</td>
</tr>
<tr>
<td>CTEPC</td>
<td>Clinical, Technical and Ethical Principal Committee</td>
</tr>
<tr>
<td>DHS</td>
<td>Victorian Government Department of Human Services</td>
</tr>
<tr>
<td>DIC</td>
<td>disseminated intravascular coagulation</td>
</tr>
<tr>
<td>DNR</td>
<td>do-not-resuscitate</td>
</tr>
<tr>
<td>DOHA</td>
<td>Department of Health and Ageing</td>
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<td>Description</td>
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<td>--------------</td>
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</tr>
<tr>
<td>DPC</td>
<td>Department of Premier and Cabinet</td>
</tr>
<tr>
<td>DRG</td>
<td>Diagnostic Related Group</td>
</tr>
<tr>
<td>EC</td>
<td>European Community</td>
</tr>
<tr>
<td>EIMS</td>
<td>Emergency and Incident Management Services</td>
</tr>
<tr>
<td>EQuIP</td>
<td>Evaluation and Quality Improvement Program</td>
</tr>
<tr>
<td>ESA</td>
<td>Endocrine Society of Australia</td>
</tr>
<tr>
<td>FEIBA</td>
<td>factor eight (VIII) inhibitor bypass agent</td>
</tr>
<tr>
<td>FFP</td>
<td>fresh frozen plasma</td>
</tr>
<tr>
<td>GCS</td>
<td>Glasgow Coma Scale</td>
</tr>
<tr>
<td>HAC</td>
<td>Haemovigilance Advisory Committee</td>
</tr>
<tr>
<td>Hb</td>
<td>haemoglobin</td>
</tr>
<tr>
<td>HBV</td>
<td>hepatitis B virus</td>
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<td>Hct</td>
<td>haematocrit</td>
</tr>
<tr>
<td>HCV</td>
<td>hepatitis C virus</td>
</tr>
<tr>
<td>HDNB</td>
<td>Hemorrhagic Disease of the Newborn</td>
</tr>
<tr>
<td>HFA</td>
<td>Haemophilia Foundation Australia</td>
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<tr>
<td>HGSA</td>
<td>Human Genetics Society of Australasia</td>
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<td>HHDI</td>
<td>High Human Development Index</td>
</tr>
<tr>
<td>HISA</td>
<td>Health Informatics Society of Australia Limited</td>
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<tr>
<td>HIV</td>
<td>human immunodeficiency virus</td>
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<tr>
<td>HSANZ</td>
<td>Haematology Society of Australia and New Zealand</td>
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<tr>
<td>HTC</td>
<td>Haemophilia Treatment Centres</td>
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<tr>
<td>ICCTO</td>
<td>International Consensus Conference on Transfusion Outcomes</td>
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<tr>
<td>ICD</td>
<td>International Statistical Classification of Diseases and Related Health Problems</td>
</tr>
<tr>
<td>ICU</td>
<td>intensive care unit</td>
</tr>
<tr>
<td>IDA</td>
<td>iron deficiency anaemia</td>
</tr>
<tr>
<td>IDFA</td>
<td>Immune Deficiency Foundation of Australia</td>
</tr>
<tr>
<td>IDMS</td>
<td>Integrated Data Management System</td>
</tr>
<tr>
<td>IHI</td>
<td>Institute of Healthcare Improvement</td>
</tr>
<tr>
<td>IIMS</td>
<td>Incident Information Management System</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Description</td>
</tr>
<tr>
<td>--------------</td>
<td>-------------</td>
</tr>
<tr>
<td>INR</td>
<td>international normalised ratio</td>
</tr>
<tr>
<td>IREF</td>
<td>Ischemia Research and Education Foundation</td>
</tr>
<tr>
<td>ISS</td>
<td>Injury Severity Score</td>
</tr>
<tr>
<td>ITP</td>
<td>idiopathic thrombocytopenic purpura</td>
</tr>
<tr>
<td>IVIg</td>
<td>intravenous immunoglobulin</td>
</tr>
<tr>
<td>JACC</td>
<td>Japan Collaborative Cohort Study</td>
</tr>
<tr>
<td>JBC</td>
<td>Jurisdictional Blood Committee</td>
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<tr>
<td>LOS</td>
<td>length of stay</td>
</tr>
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<td>MBS</td>
<td>Medicare Benefits Scheme</td>
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<tr>
<td>MCA</td>
<td>Multi-Criteria Analysis</td>
</tr>
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<td>McSPI</td>
<td>Multicenter Study of Perioperative Ischemia Research Group</td>
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<tr>
<td>MCTG</td>
<td>Multicenter Trials Group</td>
</tr>
<tr>
<td>MMD</td>
<td>multimodality blood conservation group</td>
</tr>
<tr>
<td>MOU</td>
<td>Memorandum of Understanding</td>
</tr>
<tr>
<td>NAT</td>
<td>Nucleic Acid Testing</td>
</tr>
<tr>
<td>NATA</td>
<td>National Association of Testing Authorities</td>
</tr>
<tr>
<td>NBA</td>
<td>National Blood Authority</td>
</tr>
<tr>
<td>NBS</td>
<td>National Blood Service</td>
</tr>
<tr>
<td>NBTC</td>
<td>National Blood Transfusion Committee</td>
</tr>
<tr>
<td>NCOPP</td>
<td>National Coalition of Public Pathology</td>
</tr>
<tr>
<td>NHLBI</td>
<td>National Heart, Lung, and Blood Institute</td>
</tr>
<tr>
<td>NHMRC</td>
<td>National Health and Medical Research Council</td>
</tr>
<tr>
<td>NHS</td>
<td>National Health Service</td>
</tr>
<tr>
<td>NHSBT</td>
<td>National Health Service Blood and Transplant</td>
</tr>
<tr>
<td>NI</td>
<td>nosocomial infection</td>
</tr>
<tr>
<td>NICS</td>
<td>National Institute of Clinical Studies</td>
</tr>
<tr>
<td>NPAAC</td>
<td>National Pathology Accreditation Advisory Council</td>
</tr>
<tr>
<td>NPBMP</td>
<td>National Patient Blood Management Program</td>
</tr>
<tr>
<td>NPSL</td>
<td>National Product and Services List</td>
</tr>
<tr>
<td>NSCCAHS</td>
<td>North Sydney Central Coast Area Health Service</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Description</td>
</tr>
<tr>
<td>--------------</td>
<td>-------------</td>
</tr>
<tr>
<td>NSF</td>
<td>National Stroke Foundation</td>
</tr>
<tr>
<td>O&amp;PMs</td>
<td>Outcome and Performance Measures</td>
</tr>
<tr>
<td>OECD</td>
<td>Organisation for Economic Cooperation and Development</td>
</tr>
<tr>
<td>ORBS</td>
<td>Ordering Receipting Blood System</td>
</tr>
<tr>
<td>PAC</td>
<td>Pathology Associations Council</td>
</tr>
<tr>
<td>PBM</td>
<td>Patient Blood Management</td>
</tr>
<tr>
<td>PBS</td>
<td>Pharmaceutical Benefits Scheme</td>
</tr>
<tr>
<td>PBMP</td>
<td>Patient Blood Management Program</td>
</tr>
<tr>
<td>PCC</td>
<td>prothrombin complex concentrate</td>
</tr>
<tr>
<td>PI</td>
<td>postoperative infection</td>
</tr>
<tr>
<td>PICU</td>
<td>paediatric intensive care unit</td>
</tr>
<tr>
<td>PRBC</td>
<td>packed red blood cells</td>
</tr>
<tr>
<td>QBMP</td>
<td>Queensland Blood Management Program</td>
</tr>
<tr>
<td>RACP</td>
<td>Royal College of Physicians of Australasia</td>
</tr>
<tr>
<td>RAND</td>
<td>Research And Development</td>
</tr>
<tr>
<td>RBC</td>
<td>red blood cell</td>
</tr>
<tr>
<td>RCPA</td>
<td>Royal College of Pathologists of Australasia</td>
</tr>
<tr>
<td>RCT</td>
<td>randomised controlled trial</td>
</tr>
<tr>
<td>REDS</td>
<td>Retrovirus Epidemiology Donor Study</td>
</tr>
<tr>
<td>rFVIIa</td>
<td>recombinant activated factor VII</td>
</tr>
<tr>
<td>rHuEPO</td>
<td>recombinant human erythropoietin</td>
</tr>
<tr>
<td>SAA</td>
<td>Standards Association of Australia</td>
</tr>
<tr>
<td>SABM</td>
<td>Society for the Advancement of Blood Management</td>
</tr>
<tr>
<td>SABSAC</td>
<td>South Australian Department of Health’s Blood Sector Advisory Committee</td>
</tr>
<tr>
<td>SAFE</td>
<td>Saline versus Albumin Fluid Evaluation</td>
</tr>
<tr>
<td>SANGUIS</td>
<td>Safe and Good Use of Blood in Surgery</td>
</tr>
<tr>
<td>SCA</td>
<td>The Society of Cardiovascular Anesthesiologists</td>
</tr>
<tr>
<td>SJOG</td>
<td>St John of God</td>
</tr>
<tr>
<td>SHOT</td>
<td>Serious Hazards of Transfusion</td>
</tr>
<tr>
<td>SIRS</td>
<td>systematic inflammatory response syndrome</td>
</tr>
<tr>
<td>Acronym</td>
<td>Description</td>
</tr>
<tr>
<td>---------</td>
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</tr>
<tr>
<td>SRG</td>
<td>Sapere Research Group</td>
</tr>
<tr>
<td>SSI</td>
<td>surgical site infections</td>
</tr>
<tr>
<td>STIR</td>
<td>Serious Transfusion Incident Reporting</td>
</tr>
<tr>
<td>TACO</td>
<td>transfusion associated circulatory overload</td>
</tr>
<tr>
<td>TBI</td>
<td>traumatic brain injury</td>
</tr>
<tr>
<td>TCH</td>
<td>Canberra Hospital</td>
</tr>
<tr>
<td>TGA</td>
<td>Therapeutic Goods Administration</td>
</tr>
<tr>
<td>THJA</td>
<td>total hip joint anthropoplasty</td>
</tr>
<tr>
<td>TIA</td>
<td>transient ischaemic attack</td>
</tr>
<tr>
<td>TKA</td>
<td>total knee anthropoplasty</td>
</tr>
<tr>
<td>TMAC</td>
<td>Transfusion Medicine Advisory Committee</td>
</tr>
<tr>
<td>TMT</td>
<td>Transfusion Medicine Team</td>
</tr>
<tr>
<td>TNC</td>
<td>Transfusion Nurse Consultant</td>
</tr>
<tr>
<td>TRACS</td>
<td>transfusion requirements after cardiac surgery</td>
</tr>
<tr>
<td>TRALI</td>
<td>transfusion-related acute lung injury</td>
</tr>
<tr>
<td>TRIPICU</td>
<td>Transfusion Requirements in Pediatric Intensive Care Unit</td>
</tr>
<tr>
<td>TTDR</td>
<td>Total Transfusion Dependency Ratio</td>
</tr>
<tr>
<td>TTP</td>
<td>Thrombotic Thrombocytopenic Purpura</td>
</tr>
<tr>
<td>Tx</td>
<td>transfusion</td>
</tr>
<tr>
<td>UC</td>
<td>usual care</td>
</tr>
<tr>
<td>UCLA</td>
<td>University of California, Los Angeles</td>
</tr>
<tr>
<td>UR</td>
<td>Unit Record</td>
</tr>
<tr>
<td>VNI</td>
<td>Victorian Neurotrauma Initiative</td>
</tr>
<tr>
<td>WAPBMP</td>
<td>Western Australian Patient Blood Management Program</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organization</td>
</tr>
</tbody>
</table>
OPTIONS TO MANAGE APPROPRIATE USE OF BLOOD AND BLOOD PRODUCTS

The Consultant will evaluate the strategies to ensure the appropriate use of blood and their impact on patient outcomes. Within this context, services will cover:

- the evidence base and strategies supporting appropriate use of blood;
- use of a range of strategies including, but not exclusively, clinical detailing, improved use of clinical data to support better practice, strategies to increase compliance with clinical guidelines, and the introduction of price signals in the supply chain.

The analysis of price signalling should include:

- an investigation of the outcomes of any signalling mechanisms, e.g. from international programs and in New South Wales;
- assessment of potential options for mechanisms to introduce price signalling;
- modelling the potential impacts of a range of price signalling options; and
- consultation with clinical and consumer groups to determine the potential clinical impact of price signalling.

The consideration of price signalling and any recommendations to introduce price signalling (independently or in combination with other strategies to drive the appropriate use of blood) should include a national model for price signalling and appropriate positioning in the supply chain (but excluding direct charging to patients - National Blood Agreement, 2003);

The Consultant is required to work with a Reference Group comprising a member of the Commonwealth, a representative from the National Blood Authority, a representative from the Australian Red Cross Blood Service, one small state representative and one large state representative from the Jurisdictional Blood Committee to be specified by the Department.

The Consultant is required to undertake consultation with key stakeholders, including but not limited to:

- the National Blood Authority;
- the Australian Red Cross Blood Service;
- Department of Health and Ageing;
- Jurisdictional Blood Committee;
- clinical and consumer groups including the Pathology Associations Council, the Australian and New Zealand Society of Blood Transfusion and the Haemophilia Foundation of Australia;
• National Health and Medical Research Council; and

• other stakeholders as mutually agreed by the Department of Health and Ageing, as required and at the contractor’s discretion.
Reference Group Participants

Donna Burton, Assistant Secretary, Blood, Organ and Regulatory Policy Branch, Department of Health and Ageing

Dr Alison Turner, Chief Executive Officer, National Blood Authority

Jennifer Williams, Chief Executive, Australian Red Cross Blood Service

Rachel Allden, Principal Consultant, Blood Organ and Tissues Program, SA Health

Karen Botting, Senior Program Adviser, Blood and Pharmaceutical Programs, Department of Health, Victoria

Geoff Simon, Scientific Advisor, Queensland Blood Management Program, Queensland Health

Dr Gina Clare, Queensland Blood Management Program, Queensland Health

Prof Henry Ekert, Clinical Haemotologist, Royal Children’s Hospital, Parkville, Victoria

Dr Chris Hogan, Consultant Haematologist and Transfusion Specialist, Royal Melbourne Hospital (Principal Medical Adviser, National Blood Authority)
Data Sources

There were several large datasets used in the analysis for this project. These are detailed in the table below.

Additional specific elements of data were obtained from the literature, and as a result of specific requests, mainly to state health authorities, the Australian Red Cross Blood Service and the Department of Health and Ageing. Relevant sources are noted throughout the text of the report.

<table>
<thead>
<tr>
<th>DATA SET</th>
<th>SOURCE</th>
<th>MAIN USE</th>
</tr>
</thead>
<tbody>
<tr>
<td>National Supply Plan and Budget data</td>
<td>National Blood Authority</td>
<td>Historical volume and cost information for blood and blood products</td>
</tr>
<tr>
<td>2003-04 to 2009-10—product prices and actual volumes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>National Supply Plan and Budget data</td>
<td>National Blood Authority</td>
<td>Basis of projections for future demand and cost scenarios</td>
</tr>
<tr>
<td>2010-11—planned product prices and volumes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2011-12 to 2014-15—product prices for planning purposes only</td>
<td></td>
<td></td>
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<tr>
<td>National Admitted Patient Care Collection,</td>
<td>Department of Health and Ageing</td>
<td>Hospital separations data, showing trends in separations involving transfusion</td>
</tr>
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<td>2003-04 to 2008-09</td>
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<td></td>
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<tr>
<td>Australian Demographic Statistics</td>
<td>Australian Bureau of Statistics</td>
<td>Historical per population and per capita figures</td>
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<tr>
<td>ABS catalogue 3101.0</td>
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<tr>
<td>Population Projections, Australia, 2006 to</td>
<td>Australian Bureau of Statistics</td>
<td>Basis of projections for future demand and cost scenarios</td>
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<tr>
<td>ABS catalogue 3222.0</td>
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<tr>
<td>Medicare Group Reports</td>
<td>Medicare Australia</td>
<td>Trends in MBS items relating to administration of blood and blood products</td>
</tr>
<tr>
<td>Red cell utilisation data 2006</td>
<td>SA Health</td>
<td>Clinical uses (according to Diagnostic Related Groups) and age profile of red cell use in SA public hospitals in 2006</td>
</tr>
</tbody>
</table>
Persons and Organisations Consulted

Rachel Allden, Department of Health, South Australia
Professor Warwick Anderson AM, National Health & Medical Research Council
Dr Tony Badrick, Pathology Associations Council
Dr Raymond Banh, Mater Childrens' Hospital, Brisbane
Dr Peter Bardy, Adelaide Health Service
Mr Ken Barker, National Blood Authority Board
Julie-Anne Bates, Australian Red Cross Blood Service
Mr Stephen Begg, Queensland Health
Professor Jim Bishop AO, Department of Health and Ageing
Karen Botting, Department of Health, Victoria
Professor Chris Brook, Department of Health, Victoria
Dr Heather Buchan, National Institute of Clinical Studies, National Health & Medical Research Council
Professor Leslie Burnett, Australasian Association of Clinical Biochemists
Donna Burton, Department of Health and Ageing
Dr Elizabeth Campbell, CSL Limited
Sharon Caris, Haemophilia Foundation Australia
Dr Kevin Carpenter, Human Genetics Society of Australasia
Dr Jill Carstairs, NSW Health
Ray Carty, Department of Health and Ageing
Dr Kerry Chant, NSW Health
Professor John Christadoulou, Human Genetics Society of Australasia
Michaela Coleborne, Department of Health and Ageing
Professor Jamie Cooper, Alfred Hospital, Melbourne
Mr Paul Coulter, CSL Limited
Julie Crowe, Department of Health & Human Services, Tasmania

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Ms Erin Finn, Queensland Health
Dr Jan Fizzell, NSW Health
Dr Peter Flanagan, New Zealand Blood Service
Ms Rosie Forster, National Institute of Clinical Studies, National Health & Medical Research Council
Dr Craig French, Australia and New Zealand Intensive Care Society
Professor Michael Good AO, National Health & Medical Research Council
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Peter Graves, Department of Health and Ageing
Ms Stephanie Gunn, National Blood Authority
Ms Bernie Harrison, Bloodwatch, Clinical Excellence Commission, NSW
Dr Michael Harrison, Australian Association of Pathology Practices
Dr Anne Haughton, Sullivan Nicolaides Pathology, Queensland
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Medicare Benefits Division, Department of Health and Ageing
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Jo Murray, Department of Health and Ageing
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Dr Paddy Phillips, Department of Health, South Australia
Dr Sue Phillips, National Institute of Clinical Studies, National Health & Medical Research Council
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Dr Helen Savoia, Royal Children’s Hospital, Victoria
Dr Ben Saxon, Women’s and Children’s Hospital, South Australia
Mr Geoff Simon, Queensland Health
Dr Romi Sinha, Department of Health, South Australia
Dr Andrew Spence, Haematology Society of Australia and New Zealand

Tracey Spiegel, Australian Red Cross Blood Service

Jane Spittle, Department of Health and Ageing

Dr Greg Stewart, NSW Health

Mr Michael Stone, National Blood Authority

Dr Simon Towler, Department of Health, Western Australia

Dr Alison Turner, National Blood Authority

Dr Santosh Verghese, Flinders Medical Centre, South Australia

Therese Verma, Department of Health and Ageing

Dr Craig White, Department of Health and Human Services, Tasmania

Dr Bronwyn Williams, Queensland Health

Ms Jennifer Williams, Australian Red Cross Blood Service

Paul Williams, Endocrine Society of Australia

Associate Professor Vin Williams, Australian Society of Cytology

Associate Professor Roger Wilson, National Coalition of Public Pathology

Dr Erica Wood, Australia and New Zealand Society of Blood Transfusion and Australian Red Cross Blood Service

Associate Professor Tony Woods, Pathology Associations Council
Research References

APPROPRIATE USE OF BLOOD AND BLOOD PRODUCTS

Reference


Key Findings

Isbister, J.P., et al. point out that because of the already recognised serious hazards of allogeneic transfusion, the Precautionary Principle and ongoing evidence of inappropriate blood transfusion, causation, and not the demand for RCTs should be what drives clinicians and researchers, including those that develop clinical practice guidelines for transfusion. Moreover, there is a challenge in establishing causation between transfusion and adverse outcomes in the absence of, or while awaiting, evidence from large well-designed and conducted RCTs.

Isbister, J.P., et al. point out that, whilst there is an extensive literature on transfusion alternatives for minimizing allogeneic RBC transfusion, caution is advisable in the use of the term “transfusion alternatives,” as only some are indeed truly alternatives. Patient blood management is regarded by some as an “intervention” and alternative to allogeneic blood transfusion when the real focus in patient blood management is on optimal medical management and standard of care. Timely diagnosis and management of reversible anemia, meticulous surgical haemostasis, limiting test sampling blood loss, and tolerance of anaemia in haemodynamic stable patients are not “alternatives” to RBC transfusions. On the other hand, the use of autologous transfusion techniques, erythroid stimulating agents, and antifibrinolytics are transfusion alternative interventions that have benefits, but may bring with them hazards that need balancing in the same manner as the decision to transfuse.

Details

In relation to Evidence-Based Medicine (EBM), the RCT is considered the criterion standard, applying statistical probabilities to arrive at “the truth.” This current view of EBM often fails to acknowledge that most important advances in medicine usually start with clinical observations, and the RCT is but one tool for acquiring knowledge about causation. The EBM classifications of levels of evidence, which invariably give the highest quality ranking to evidence derived from RCTs, are based on probabilistic causation.

As a result, Isbister, J.P., et al. say, it offers only a limited perspective of evidence of causation and efficacy for many of modern medicine's understanding of disease and therapeutic interventions. Observational registry data on tuberculosis and occupational lung disease in Welsh mining villages was collected by Cochrane in the 1950s, who established his reputation as the father of medical registries. advocated observation before making decisions about underlying causes and possible interventions.

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Austin Bradford Hill, often called the father of medical RCTs, established cigarette smoking as a causative factor for development of lung cancer in a situation where RCTs could never be done. Many similarities exist between cigarette smoking being causative for disease and RBC transfusions contributing to adverse or suboptimal clinical outcomes. Hill recognized the problems and limitations of RCTs and proposed nine criteria whose purpose was to address the problem of supporting causation when there is an association, but it is impractical or unethical to conduct RCTs. Such an approach was used in the smoking and lung cancer debate and, more recently, in establishing the causal relationship between asbestos-related lung disease and mesothelioma. Hill’s nine criteria are:

- availability of experimental evidence;
- strength of association;
- temporality;
- biological gradient;
- biologic plausibility;
- coherence;
- consistency;
- analogy; and
- specificity.

Hill emphasised that these criteria are to be considered in deciding if the most likely interpretation of an observed association is a causation; they are not intended to provide indisputable evidence for or against causation, and causation may still exist in absence of one or more of these criteria (except for temporality). Several attempts at modifying Bradford Hill’s criteria have been made to clarify and simplify their application. Howick et al. recently proposed organizing Bradford Hill’s criteria into three categories of evidence: direct, mechanistic, and parallel. Table 26 summarises how Bradford Hill’s criteria fit within these three categories and illustrates their application to transfusion outcomes. The one exception is Bradford Hill’s criteria of specificity, which has been eliminated given that diseases usually have multiple causes and effects and most interventions also have multiple effects. This exclusion of specificity has been proposed by Howick et al. in their simplified approach to applying Hill’s approach to increasing the probability of causation from observational evidence. This is certainly the case in the clinical circumstance of RBC transfusion and adverse transfusion outcomes.

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TABLE 26: BRADFORD HILL CRITERIA MODIFIED INTO GUIDELINES\textsuperscript{32} THAT SUPPORT CAUSATION WHEN AN ASSOCIATION IS PRESENT

<table>
<thead>
<tr>
<th>Type of evidence</th>
<th>Proposed structured guidelines</th>
<th>Modified Bradford hill criteria</th>
<th>Application to transfusion outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Direct evidence based on probabilistic association between intervention and outcome is causal and not spurious.</td>
<td>Size of effect not attributable to plausible confounding.</td>
<td>Experimental evidence</td>
<td>Experimental interventions including RCTs, observational studies, and case control studies have shown that avoiding or minimizing transfusion and prestorage leukoreduction can reduce adverse outcomes in animal and human studies. There is increasing evidence of a strong association between allogeneic transfusion and poor clinical outcomes.</td>
</tr>
<tr>
<td>Strength</td>
<td>Strength</td>
<td></td>
<td>Transfusion proceeds the occurrence of adverse outcomes from days to months and even years.</td>
</tr>
<tr>
<td>Appropriate temporality and/or spatial proximity</td>
<td>Biological gradient</td>
<td>Temporality</td>
<td>There is evidence for a dose-response relationship between allogeneic transfusion and adverse outcomes. In addition, there is evidence that the older age of storage of red cell concentrates is associated with poorer outcomes.</td>
</tr>
<tr>
<td>Mechanistic evidence for alleged causal intervention that connects with the clinical outcome</td>
<td>There are dose-responsiveness and reversibility</td>
<td>Biological plausibility</td>
<td>Mechanisms for most transfusion-related adverse outcomes have been established or proposed.</td>
</tr>
<tr>
<td>Pathophysiological explanation and mechanism of action</td>
<td>Coherence</td>
<td>Coherence</td>
<td>A coherent case not contradicted by current knowledge can be made, supporting the proposition that association of allogeneic blood transfusions and poorer clinical outcomes is causal. The association is generally consistent across a wide range of studies (cardiac surgery, orthopedics, trauma, burns etc).</td>
</tr>
<tr>
<td>Parallel evidence that supports the suggested causal hypothesis, with related studies that have similar results</td>
<td>Coherence</td>
<td>Coherence</td>
<td></td>
</tr>
<tr>
<td>Replicability</td>
<td>Consistency</td>
<td></td>
<td>The association is generally consistent across a wide range of studies (cardiac surgery, orthopedics, trauma, burns etc).</td>
</tr>
<tr>
<td>Similarity</td>
<td>Analogy</td>
<td></td>
<td>Transplantation of any tissue, including blood, modulates the immune response.</td>
</tr>
</tbody>
</table>

It is not questioned that allogeneic blood transfusions have risks and can cause serious adverse events. However, notwithstanding the cases of profound anaemia and haemorrhage with impaired oxygen delivery to tissues, Isbister, J.P., et al. argue that in most patients who are currently considered to be transfusion candidates, blood transfusions do not improve the outcomes and, conversely, cause worse clinical outcomes. The evidence comes from a multitude of mostly observational studies comparing the outcomes of transfused and not transfused patients in various common clinical settings. Subjecting observational data to Bradford Hill criteria can help strengthen the case for a causal relationship.

From the patient’s perspective, the primary responsibility of clinicians is to manage the patient’s own blood as a precious and unique resource that should not be wasted and to only consider allogeneic blood component therapy when there is no other option – the so-called new paradigm in transfusion practice – Patient Blood Management (see further discussion below). The Isbister, J.P., et al. review, addressing issues surrounding the safety and efficacy of RBC transfusions for treating anaemia, challenges the dogmas long embedded in clinical practice regarded as standard of care. Central to problem-based transfusion medicine, in relationship to RBC transfusions, are the diagnosis and management of anaemia. Anaemia is common and generally poorly managed despite good scientific understanding of mechanisms and sophisticated diagnostic methods (see further discussion elsewhere in this Report on this topic in relation to inappropriate transfusion practice). In most circumstances, anaemia is mild, and its significance per se in terms of impacting adversely on clinical outcomes in the absence of confounding co morbidities is questionable. Although there is literature associating anaemia with poorer outcomes in some circumstances, there is no good evidence that RBC transfusions improve the outcomes.

Isbister, J.P., et al. point out that, whilst there is an extensive literature on transfusion alternatives for minimizing allogeneic RBC transfusion, caution is advisable in the use of the term “transfusion alternatives,” as only some are indeed truly alternatives. Patient blood management is regarded by some as an “intervention” and alternative to allogeneic blood transfusion when the real focus in patient blood management is on optimal medical management and standard of care. Timely diagnosis and management of reversible anemia, meticulous surgical haemostasis, limiting test sampling blood loss, and tolerance of anaemia in haemodynamic stable patients are not “alternatives” to RBC transfusions. On the other hand, the use of autologous transfusion techniques, erythroid stimulating agents, and antifibrinolytics are transfusion alternative interventions that have benefits, but may bring with them hazards that need balancing in the same manner as the decision to transfuse. The hazards of autologous transfusion are also set out in the NSW CEC Blood Program Myth Buster Poster 4\(^3\): *Autologous blood (pre-donated) is risk-free,* which says that, “... Pre-donated autologous transfusion is not risk-free and there are a variety of adverse events associated with this practice.”

Although their review focuses on the risks and benefits of RBC transfusions in anaemic haemodynamically stable patients without co morbidities, Isbister, J.P., et al. acknowledge that the use of transfusion alternatives demands similar attention to the benefits and safety. However, it is important that, when balancing all the options, it should be done on a “level playing field” and RBC transfusion should no longer be regarded as the default and “safe” option when there is clinical uncertainty.

Isbister, J.P., et al. postulate that a compelling case for applying the precautionary principle to transfusion medicine existed long before RBC transfusions were implicated as a general risk factor for adverse clinical outcomes. The “tissue transplant” of blood transfusion has always been a potentially hazardous therapeutic intervention, with numerous clearly understood complications, some avoidable, but many not. As advocated by Beale, “Blood transfusion is like marriage: it should not be entered upon lightly, unadvisedly or wantonly, or more often than is absolutely necessary.” The recognized hazards of allogeneic blood transfusion aside, the case for a precautionary approach is strengthened further with the possible, and now probable, recognition that transfusions are a risk factor for adverse clinical outcomes.

A general change in transfusion medicine practice is urgently needed say Isbister, J.P., et al. Neither the quality and safety issues nor the economic implications can continue to be ignored awaiting the results of RCTs currently in progress, or may never be possible. Waiting for levels of evidence demanded by Frequentist outcome-focused epidemiology is no longer advisable and may be exposing patients to harm. Bradford Hill himself noted; “All scientific work is incomplete whether it be observational or experimental. All scientific work is liable to be upset or modified by advancing knowledge. This does not confer upon us a freedom to ignore the knowledge we already have, or to postpone the action that it appears to demand at a given time.”

Political, financial, and ethical considerations inevitably play a part in decision making in the blood sector; however, there are undeniable reasons why there should be greater focus on the precautionary principle on the demand side of transfusion medicine. It is difficult to understand why this change has met resistance from some clinicians and players in the blood sector. Delaying actions until harm is proven in the context of questionable efficacy would not be acceptable in other areas of medical practice, and we believe that blood transfusion should be treated similarly. Support for adopting a precautionary approach to the transfusion of labile blood components includes the following:

- The evidence for efficacy of many blood components in a range of clinical settings, especially in relationship to haemodynamically stable perioperative patients (a large group of blood recipients), is questionable or non-existent. Randomized controlled trials of a restrictive RBC transfusion policy have confirmed that restrictive transfusion policies are safe and reduce adverse outcomes;
- Inappropriate RBC transfusion practices, contrary to guidelines, persist, and as demonstrated extensively elsewhere in this Report;

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• Benchmarking studies have identified a wide variation in RBC transfusion practices between countries, hospitals, and individual clinicians\textsuperscript{42}, and as demonstrated extensively elsewhere in this Report;
• More appropriate and alternative therapies and interventions are available to avoid or minimize the use of allogeneic blood components\textsuperscript{43} \textsuperscript{44};
• Implementation of patient blood management is a quality and safety measure that could lead to substantial cost savings\textsuperscript{45} \textsuperscript{46} \textsuperscript{47}, and as demonstrated elsewhere in this Report.

Apart from recommending the implementation of patient blood management approaches, Isbister, J.P., et al. concluded that, “... it is no longer acceptable to maintain a laissez faire approach and assume the benefits and accept the risks of allogeneic blood transfusion. Evidence has accumulated questioning RBC transfusion efficacy and establishing transfusion as a contributing risk factor for adverse clinical outcomes in many clinical settings. Acknowledging that most available data are observational and that rigorous evidence to establish risks and benefits is needed, we should no longer accept transfusions as the default decision when there is clinical uncertainty.”

Reference


Key Findings

The study concluded that IVIg shortages were followed by a decrease in the number of single-use recipients, who probably represented empirical use of IVIg, but that this had little effect on the total amount of IVIg distributed annually. Stricter adherence to currently available published recommendations may not be the optimal means of controlling IVIg use within an academic hospital setting. Rather, emphasis may be better placed on improving the evidence base upon which these recommendations are made, for example by conducting controlled prospective clinical trials.

Details

This study noted that Canadian consumption of intravenous immunoglobulin (IVIg) had increased dramatically since it was first marketed in the early 1980s, and Canada had become the world’s largest per capita consumer. During the late 1990s, worldwide product shortages of IVIg occurred and this study was designed to identify the disease conditions for which IVIg was being prescribed in academic hospitals during this period, and to explore the effects that IVIg shortages had on prescribing patterns.

Blood bank and pharmacy records of IVIg distribution were collected retrospectively from four Toronto teaching hospitals for the period 1995–2000. These records were then cross-referenced with patient medical records to determine the indication for IVIg administration. The results were derived from a total of 100,208g of IVIg prescribed to 429 patients over a 6-year period. Most of the IVIg consumption was in patients with haematological (22%) or neurological (20%) conditions, in recipients of bone marrow transplants (19%) and in patients with infectious disease-related conditions (including congenital and acquired hypogammaglobulinaemia, 18%). Dermatological conditions (7%) were the most rapidly growing indication for IVIg usage during the 6-year period of review, increasing from 0% of annual IVIg usage in 1995 to 16% in 2000. Over 80% of the diseases treated were supported by published recommendations. After 1997 there was an abrupt decline in the annual number of patients treated, primarily owing to a decline in single-use recipients. Annual consumption of IVIg, however, remained stable.

The authors concluded that IVIG shortages were followed by a decrease in the number of single-use recipients, who probably represented empirical use of IVIg, but that this had little effect on the total amount of IVIg distributed annually. Stricter adherence to currently available published recommendations may not be the optimal means of controlling IVIg use within an academic hospital setting. Rather, emphasis may be better placed on improving the evidence base upon which these recommendations are made, for example by conducting controlled prospective clinical trials.

Reference


Key Findings

In an unprecedented move the Senior Vice President, Health Affairs and President, UF Shands Health System, in “On the Same Page: Saving blood, saving money, saving lives”, 1 October 2010 wrote to all his staff about the risks, costs, adverse events and benefits associated with transfusion. The article is compelling in relation to the need to change transfusion practice for the benefit of patients and health institutions. It is reproduced in full below.

Details

“You’ve heard it before, but it bears repeating: Quality patient care is our first and most essential focus. Now imagine a procedure performed about 15 million times per year in U.S. hospitals that increases the likelihood of death by 70% and the risk of infection by about 80%, and is associated with other complications such as acute respiratory distress syndrome.

This procedure, performed at an annual cost of $10 billion to $15 billion, is blood transfusion. It is the single most commonly coded procedure for hospital discharges in the United States, according to the Agency for Healthcare Research and Quality.

Interviews with several of our own faculty suggest that improving the quality of care for our patients by developing literature-based protocols for blood transfusion and reducing adverse events is good medicine. And it also saves money.

So we’ve gathered a team of physicians, nurses and laboratory staff to develop common protocols to ensure an evidence-based approach to blood product transfusion. In Gainesville, this team will be led by Marc Zumberg, M.D., an associate professor of medicine, and Philip Efron, M.D., an assistant professor of surgery and anaesthesiology. In Jacksonville,
the team leaders will be David Wolfson, M.D., an assistant professor of pathology and laboratory medicine, and Agnes Aysola, M.D., an assistant professor of pathology and laboratory medicine.

Each year, approximately 28,000 units of red blood cells are transfused at Shands at UF, and about 11,000 units at Shands Jacksonville. Although the direct cost of each unit of blood is about $175, the total cost is much greater.

After precisely mapping all diagnostic, therapeutic, technical, laboratory, logistic, administrative and informational activities involved in the transfusion of blood in real-world surgical settings, researchers constructed an activity-based cost model capturing all the actual direct and indirect costs of acquiring, delivering, administering and monitoring red blood cell transfusions from the hospital perspective. (Transfusion 2010; 50:753-65) This yielded an estimate of $520 to $1,180 for the total cost per unit of blood that reflects the complexities of real-world blood utilization, depending on the circumstances surrounding the transfusion.

Even if the average were at the low end (e.g., $600 per unit), a reduction of only 10% across Shands at UF and Shands Jacksonville (i.e., about 4,000 units) would save $2.4 million per year.

Achieving such a reduction is a realistic goal. According to data from the University Health System Consortium, which consists of 93 peer institutions, use of red blood cell units by Shands at UF per annual inpatient discharges is 0.87. When UHC hospitals are sorted by numbers of inpatient discharges, all hospitals of our size or larger have lower rates of red blood cell use. For example, the rates for Barnes-Jewish (Washington University), Vanderbilt University and University of Arizona are 0.68, 0.64 and 0.56, respectively.

In addition, data reported to UHC indicate an annual use of 13,500 units of plasma by Shands at UF and 8,200 units by Shands Jacksonville. Plasma is the liquid part of the blood in which the blood cells are suspended. Plasma for transfusion is usually termed fresh-frozen plasma, or FFP. FFP is commonly used for a wide variety of indications, but review of the literature would suggest that the evidence favours plasma transfusion in only a very limited number of clinical situations.

Specifically, a recent report from a blue-ribbon multidisciplinary guidelines panel (Transfusion 2010;50:1227-1239), which conducted a systematic review and meta-analysis of randomized and observational studies, concluded that FFP was indicated in patients with blood loss requiring massive transfusion and in patients with warfarin therapy in association with intracranial haemorrhage. The panel did not favour plasma transfusion for other selected groups of patients.

Other opportunities become apparent after reviewing the contemporary medical literature and listening to our haematology faculty’s expert judgments. For example, it is still common practice to attempt to correct “abnormal” laboratory values of haemostasis prophylactically in patients with liver disease by administering blood products. But a recent review of the literature suggests that such a practice is not supported by the evidence. Thanks to tremendous progress in the understanding of haemostatic function in patients with liver disease, the long-standing dogma that patients with liver disease have a bleeding tendency that can be corrected by transfusion no longer appears to be supported by data from both clinical and laboratory studies (Blood 2010;116:878-885). Rather, it appears that attempts at preoperative transfusion in patients with liver disease does not reduce, and may in fact promote, bleeding.
A recent review in *Critical Care Medicine* classified 45 studies including 272,596 patients as 1) risks outweigh benefits, 2) neutral risk and 3) benefits outweigh risks. In 42 of 45 studies, the risks of red blood cell transfusion outweighed the benefits, the risk was neutral in two studies, and the benefits outweighed the risks in a single subgroup of a single study (elderly patients with an acute heart attack and a hematocrit less than 30%.

Still, blood transfusion can be a life-saving procedure for many patients in specific situations involving haemorrhage from trauma or surgery, or in many cases of severe anemia in patients who are critically ill. The data are quite sobering, however. As suggested in an editorial by Drs Howard Corwin and Jeffrey Carson (NEJM 2007;356:1667-8): "Red-cell transfusion should no longer be regarded as “may help, will not hurt” but, rather, should be approached as “first, do no harm.”"

Yet over the past several decades, with the exception of concern about transfusion-related infection that has been largely eliminated thanks to effective testing for hepatitis and HIV, the practice of transfusion has grown dramatically under the "may help, can't hurt" mindset.

In 1999, the results of an important clinical trial, Transfusion Requirements in Critical Care, were reported (NEJM 1999;340:409-17). In this randomized, controlled study involving critically ill adults, a liberal strategy (transfuse if the hemoglobin level drops below 10.0 g/dL) was compared with a restrictive strategy (transfuse if hemoglobin drops below 7.0 g/dL). Patients randomly assigned to restrictive management received 54% fewer red-cell units than did the liberal management group, and the restrictive strategy was found to be at least as effective as the liberal strategy with respect to mortality. In patients who were less acutely ill or under 55 years of age, the restrictive strategy was actually superior, in that compared with the liberal strategy it was associated with lower mortality.

A study of children in a Pediatric Intensive Care Unit (NEJM 2007;365:1609-19) reached similar conclusions. Using multiple organ dysfunctions as an endpoint, a restrictive transfusion strategy was at least equivalent to the liberal strategy in this outcome, and was associated with a 44% reduction in the number of red-cell transfusions.

These findings come at a time when a quarter of a century of research demonstrates that transfused patients, in general, have much poorer outcomes than similar untransfused patients, and that patients who receive more transfusions do progressively worse in a dose-dependent fashion (Transfusion 2005 45[Supplement]: 33S-40S).


The history of blood transfusion is intertwined with the history of medicine generally, and is one of the great examples of true translational science. The first successful transfusion of human blood was performed by Dr James Blundell, a British obstetrician, who treated a woman who developed postpartum haemorrhage using her husband's blood. Through the 1800s, transfusions were only infrequently performed (e.g., to treat conditions such as haemophilia), as many recipients died due to what we now know were haemolytic reactions from blood group incompatibility.

The ABO blood group system was discovered by the Austrian Karl Landsteiner, M.D., in 1901 (for which he won the Nobel Prize in Medicine or Physiology in 1930), providing the scientific basis for improving the safety of blood transfusion. In 1939, Drs Landsteiner, Levine and
Weiner discovered the Rh blood group system. In 1961, Rh immune globulin was commercially introduced to prevent Rh disease in newborns of Rh-negative women.

Since then, advances have occurred in the systems of infection screening, storage, distribution and processing of blood products. Currently accepted blood transfusion practices evolved prior to the concepts of randomized trials and clinical outcomes studies, however, and developed all the sanctity expected of time-honoured therapies.

In summary, interviews with faculty involved in blood transfusion suggest a consensus: As is often the case in quality improvement initiatives, improving the quality of care for our patients by developing literature-based protocols for blood transfusion and reducing adverse events will also result in cost savings. I would add, in the spirit of the goals of our Clinical and Translational Science Award, that research on blood transfusion has progressed through the first two translational stages: from "T1" (discovery of blood groups, fractionation and storage methods, etc., translated to individual patient treatment), to "T2" (defining risk groups and hemoglobin targets for translation to optimal clinical practice).

It is now time to progress to the "T3" phase, in which accumulated knowledge on best practices can be disseminated to our physicians, nurses and students, so that known best practices can be achieved across our health-care system in a manner that saves blood, saves money and saves lives.

Forward Together,

David S. Guzick, M.D., Ph.D."

Reference


Key Findings

Patient discharges in the transfused cohort were significantly more likely to have at least one co morbidity than discharges in the non-transfused cohort (54.5% compared to 47.1%). Of the estimated 38.66 million discharges in the United States in 2004, 5.8% (2.33 million) were associated with blood products transfusion. Average length of stay was 2.5 days longer, odds of death were 1.7 times higher, and odds of infection 1.9 times higher for the transfused cohort.

Despite limitations, this study shows that more than 2 million hospital admissions annually are associated with a blood products transfusion and that patients remain at risk of experiencing adverse clinical outcomes. The observation that transfusion recipients experience negative outcomes independent of age, sex, co morbidities, admission type, or DRG assignment warrants further investigation to better identify the appropriateness of current transfusion triggers and to develop and implement more effective approaches to reduce the non-emergent use of blood in hospitalized patients. Additional research to identify transfusion triggers, including patient severity, risk–benefit trade-offs, and the use of blood in elective surgical cases, should be a priority. In a significant number of trauma and urgent cases when uncontrolled haemorrhage is the clinical priority, surgeons often have limited options to rapidly correct blood loss, and therefore, the threshold for transfusion may be low. However, with elective cases, surgeons are likely to have more
options such as the use of haemostatic agents to address blood loss and avoid or reduce the need for transfusion. This is especially important given the persistent challenges associated with maintaining an adequate blood supply. TRALI and incompatibility reactions were not reported for patients identified as transfusion recipients. This finding also warrants further investigation, given that the Joint Commission and the American Association of Blood Banks have established transfusion-specific performance improvement standards, blood use reviews, and reporting requirements for suspected transfusion-related adverse events.

Finally, given that transfusion-related adverse clinical and health-related quality-of-life outcomes may persist after hospital discharge, additional prospective observational studies are needed to assess the long-term health status and quality of life of transfusion recipients. In conclusion, raising provider awareness and recognition of the frequency and potential negative clinical outcomes of blood products transfusion—as an independent predictor or surrogate for blood loss—may yield significant clinical and quality-of-life benefits at the individual patient level. Equally important is the need to encourage providers to adopt strategies and techniques that are more effective at controlling inadequate surgical haemostasis and that may reduce the frequency of blood products transfusions.

Details

The objective of a very large retrospective cohort study in 2004 in the US, Morton, et al., was to enumerate the national frequency of blood products transfusion and associated clinical and health outcomes across the full spectrum of procedures and clinical conditions warranting inpatient care. To the best of our knowledge, no study to date has assessed this. This information is important for many reasons, including the following:

- Increasing provider and patient awareness;
- Encouraging the adoption of novel approaches to minimize intraoperative and early postoperative bleeding, reducing blood transfusions; and
- Most important, improving postoperative outcomes and health-related quality of life.

In this study, the frequency of blood products transfusion, morbidity, mortality, length of stay (LOS), and hospital charges were examined among all hospitalisations (discharges) in the United States in 2004 using the Agency for Healthcare Research and Quality's 2004 Healthcare Cost and Utilization Project Nationwide Inpatient Sample (NIS). The NIS is an all-payer national survey that approximates a 20% multistage sample of inpatient care in the United States. Included in NIS are US community hospitals, which are defined by the American Hospital Association to be “all non-federal, short-term, general, and other specialty hospitals.” Facilities excluded from NIS are: short-term rehabilitation facilities, long-term hospitals, psychiatric hospitals, alcoholism/chemical dependency treatment facilities, and federal facilities (e.g., Veterans Administration hospitals). The final sample for NIS 2004 was drawn from 37 states and includes patient-level data for 8,004,571 discharges from 1004 hospitals. Only inpatient data found in a discharge abstract are available in the NIS, with safeguards to protect the privacy of individual patients, physicians, and hospitals. The NIS does not have unique patient identifiers, and as a result, patients cannot be followed longitudinally. The NIS includes more than 100 clinical and nonclinical data elements for each hospitalization including patient demographics, one principal and up to 14 secondary diagnoses, one principal and up to 14 secondary procedures, admission and discharge status, LOS, primary payer source, total charges, and hospital characteristics.
TABLE 27: TOP 10 PRIMARY PROCEDURE CATEGORIES WITH GREATEST FREQUENCY OF TRANSFUSION

<table>
<thead>
<tr>
<th>Primary Procedure (CCS Procedure Category)</th>
<th>Transfusion Discharges (N = 2,231,419) n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper gastrointestinal endoscopy; biopsy</td>
<td>163,628 (7.3)</td>
</tr>
<tr>
<td>Hip replacement: total and partial</td>
<td>108,495 (4.9)</td>
</tr>
<tr>
<td>Knee arthroplasty</td>
<td>99,455 (4.5)</td>
</tr>
<tr>
<td>Respiratory intubation and mechanical</td>
<td>86,202 (3.9)</td>
</tr>
<tr>
<td>ventilation</td>
<td>74,432 (3.3)</td>
</tr>
<tr>
<td>Treatment; fracture or dislocation of hip</td>
<td>64,240 (2.9)</td>
</tr>
<tr>
<td>and femur</td>
<td>52,173 (2.4)</td>
</tr>
<tr>
<td>Coronary artery bypass graft</td>
<td>48,061 (2.2)</td>
</tr>
<tr>
<td>Other vascular catheterization: not heart</td>
<td>46,433 (2.1)</td>
</tr>
<tr>
<td>Colonoscopy and biopsy</td>
<td>41,676 (1.9)</td>
</tr>
</tbody>
</table>

*Procedures classified per Clinical Classification Software (CCS) for International Classification of Diseases, Ninth Revision, Clinical Modification procedure categorization.


The following outcomes in this Morton, et al. study were evaluated: in-hospital mortality, LOS, postoperative infections, non-infectious transfusion related complications, and total charges. ICD-9-CM diagnosis codes were used to identify postoperative infections and included the following: bacteraemia (790.7), cellulitis and abscess (682), mediastinitis (519.2), osteomyelitis (730.0, 730.2, and 730.9), pneumonia (481, 482, 485, and 486), septicemia (038), and urinary tract infection (599.0). ICD-9-CM diagnosis codes were also used to identify non-infectious transfusion-related complications including TRALI (518.7), anaphylactic shock caused by serum (999.4), other serum reaction (999.5), ABO incompatibility reaction (999.6), and Rh incompatibility reaction (999.7). Additional complications were examined separately from these because they capture non-transfusion-related events in addition to events related to transfusion; thus, the best estimate of transfusion-related complications falls somewhere in between. These included air embolism (999.1), other vascular complications (999.2), other infection (999.3), and transfusion reaction not otherwise specified (999.8).

According to the 2004 NIS database, there were an estimated 38.66 million discharges in the United States in 2004. Approximately 5.8% (2.23 million) of these discharges recorded an ICD-9-CM procedure code for blood products transfusion. The 10 most common CCS categories for procedures performed during the same hospitalization as a transfusion accounted for approximately 10% of all hospitalizations and more than 35% of hospitalizations in the transfused cohort. Among transfusion recipients, the most common orthopaedic, cardiovascular, and colorectal procedures made up 13.7%, 7.2%, and 4.3%, respectively. Hip replacement was the most common procedure associated with transfusion (Figure 43), with more than one quarter (29.8%) of discharges from hip replacement requiring transfusion. Blood products transfusion was also associated with more than 20% of discharges involving each of the following procedures: repair of a fractured or dislocated hip and femur (27.1%), CABG surgery (24.9%), upper gastrointestinal endoscopy with biopsy (22.5%), and knee arthroplasty (20.6%).
FIGURE 43: FREQUENCY OF TRANSFUSION AMONG TOP 10 PROCEDURES WITH GREATEST FREQUENCY OF TRANSFUSION


Blood products transfusion was also associated with more than 20% of discharges involving each of the following procedures: repair of a fractured or dislocated hip and femur (27.1%), CABG surgery (24.9%), upper gastrointestinal endoscopy with biopsy (22.5%), and knee arthroplasty (20.6%).

The overall average age of the discharges was 61.1 years; 44.7% were male. On average, patients who received blood products transfusion were older (mean 66.9 years) in the transfused cohort compared with the non-transfused cohort (59.7 years; \( P < .0001 \)). Almost half (48.5%) of patient discharges were associated with at least 1 comorbidity. Patient discharges in the transfused cohort were significantly more likely to have at least one comorbidity than discharges in the non-transfused cohort (54.5% vs. 47.1%; \( P < .0001 \)). Overall, almost one third (29.1%) had private insurance and two thirds (64.3%) had public insurance. Additionally, 72.6% were designated as emergent or urgent.

Average LOS, mortality, and postoperative infection rates were significantly higher in the transfused cohort than in the non-transfused cohort. Average LOS was 2.5 days longer for the transfused cohort compared with the non-transfused cohort after adjusting for confounders (\( P < .0001 \)). Additionally, total charges were $17,194 higher for the transfused cohort compared with the non-transfused cohort after adjusting for confounders (\( P < .0001 \)). Overall, death occurred in 2.1% of all hospitalizations in 2004 and in 6.4% of the 10 procedure categories most associated with transfusion. Odds of death were 1.7 times higher in the transfused cohort compared with the non-transfused cohort after controlling for age, sex, Charlson comorbidity index, admission type, and DRG (\( P < .0001 \)). The infection rate was also significantly higher for the transfused cohort compared with the non-transfused cohort (0.33% vs. 0.15%; \( P < .0001 \)).

After controlling for confounders, the odds of having at least one postoperative infection was 1.9 times greater for the transfused cohort than for the non-transfused cohort (\( P < \)
The most frequently recorded postoperative infection was pneumonia, whose frequency was 0.12% in the transfused cohort compared with 0.06% in the non-transfused cohort \((P < .0001)\). No discharges with an ICD-9-CM diagnosis code indicating the occurrence of a non-infectious complication of transfusion were identified among the transfused cohort in the analysis. However, minor events may not have been coded in NIS.

**TABLE 28: DEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF INPATIENT STAYS AMONG TOP 10 PROCEDURES WITH GREATEST FREQUENCY OF TRANSFUSION**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Overall (N = 4,085,168)</th>
<th>Transfused (N = 785,795)</th>
<th>Nontransfused (N = 3,299,372)</th>
<th>(P) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (standard error)</td>
<td>61.1 (0.36)</td>
<td>66.9 (0.38)</td>
<td>59.7 (0.40)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>1,829,001 (44.7)</td>
<td>323,336 (41.1)</td>
<td>1,505,665 (45.6)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Charlson comorbidity index, n (%)</td>
<td></td>
<td></td>
<td></td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>0</td>
<td>2,103,260 (51.5)</td>
<td>357,784 (45.5)</td>
<td>1,745,476 (52.9)</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>1,122,381 (27.5)</td>
<td>225,485 (28.7)</td>
<td>896,895 (27.2)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>478,485 (11.7)</td>
<td>103,059 (13.1)</td>
<td>375,426 (11.4)</td>
<td></td>
</tr>
<tr>
<td>≥3</td>
<td>381,042 (9.3)</td>
<td>99,467 (12.7)</td>
<td>281,575 (8.5)</td>
<td></td>
</tr>
<tr>
<td>Admission type, n (%)</td>
<td></td>
<td></td>
<td></td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Emergency</td>
<td>1,746,083 (42.7)</td>
<td>339,316 (43.2)</td>
<td>1,406,768 (42.6)</td>
<td></td>
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<tr>
<td>Urgent</td>
<td>1,219,613 (29.9)</td>
<td>223,390 (28.4)</td>
<td>996,223 (30.2)</td>
<td></td>
</tr>
<tr>
<td>Elective</td>
<td>601,400 (14.7)</td>
<td>107,863 (13.7)</td>
<td>493,537 (15.0)</td>
<td></td>
</tr>
<tr>
<td>Other* and missing</td>
<td>518,070 (12.7)</td>
<td>125,227 (14.7)</td>
<td>402,845 (12.2)</td>
<td></td>
</tr>
<tr>
<td>Payer</td>
<td></td>
<td></td>
<td></td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Medicare</td>
<td>2,234,278 (54.7)</td>
<td>502,469 (63.9)</td>
<td>1,731,809 (52.5)</td>
<td></td>
</tr>
<tr>
<td>Private</td>
<td>1,188,805 (29.1)</td>
<td>183,193 (23.3)</td>
<td>1,005,612 (30.5)</td>
<td></td>
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<tr>
<td>Medicaid</td>
<td>391,778 (9.6)</td>
<td>59,583 (7.6)</td>
<td>332,195 (10.1)</td>
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<tr>
<td>Self-pay</td>
<td>142,184 (3.5)</td>
<td>19,212 (2.4)</td>
<td>122,975 (3.7)</td>
<td></td>
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<tr>
<td>Other† and missing</td>
<td>128,122 (3.1)</td>
<td>21,339 (2.7)</td>
<td>106,783 (3.2)</td>
<td></td>
</tr>
</tbody>
</table>

*Other admission type includes other, trauma center, and newborn.

†Other payer includes other and no charge.

TABLE 29: OUTCOMES ASSOCIATED WITH BLOOD TRANSFUSION IN HOSPITALIZED PATIENTS AMONG TOP 10 PROCEDURES WITH GREATEST FREQUENCY OF TRANSFUSION

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Overall (N = 4,085,168)</th>
<th>Transfused (N = 785,795)</th>
<th>Nontransfused (N = 3,299,372)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>262,110 (6.4)</td>
<td>59,356 (7.4)</td>
<td>202,754 (6.1)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>OR (95% CI)</td>
<td>1.7 (1.56-1.85)</td>
<td></td>
<td></td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Length of stay (days)</td>
<td>7.3 (0.10)</td>
<td>9.2 (0.20)</td>
<td>6.8 (0.10)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Total charges</td>
<td>$40,687 ($875)</td>
<td>$55,363 ($17,305)</td>
<td>$37,242 ($7,874)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Incremental change (SE)</td>
<td>$17,194 ($1,273)</td>
<td></td>
<td></td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Infections</td>
<td>7,720 (0.189)</td>
<td>2,606 (0.322)</td>
<td>5,114 (0.155)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>OR of at least 1 (%)</td>
<td>1.9 (1.36-2.55)</td>
<td></td>
<td></td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Pneumonia, n (%)</td>
<td>2,964 (0.073)</td>
<td>958 (0.122)</td>
<td>2,006 (0.061)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Septis, n (%)</td>
<td>2,131 (0.052)</td>
<td>624 (0.105)</td>
<td>1,507 (0.049)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Urinary tract infection, n (%)</td>
<td>1,780 (0.044)</td>
<td>569 (0.072)</td>
<td>1,211 (0.037)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Cellulitis and abscess, n (%)</td>
<td>516 (0.013)</td>
<td>144 (0.018)</td>
<td>372 (0.011)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Bacteremia, n (%)</td>
<td>306 (0.007)</td>
<td>89 (0.011)</td>
<td>217 (0.007)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Osteomyelitis, n (%)</td>
<td>24 (0.001)</td>
<td>24 (0.001)</td>
<td>0 (0.000)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Melenitis, n (%)</td>
<td>0 (0.000)</td>
<td>0 (0.000)</td>
<td>0 (0.000)</td>
<td>&lt;.0001</td>
</tr>
</tbody>
</table>

Abbreviations: OR, odds ratio; CI, confidence interval; SE, standard error.

aAfter controlling for the following: age, sex, comorbidities (e.g., Charlson comorbidity index), type of admission, diagnosis-related group, and payer (for length of stay only); ORs represent odds of the outcome among patients who received a blood transfusion compared with those who did not receive a blood transfusion; incremental change represents the regression coefficient or increase among those patients who received a blood transfusion compared with those who did not receive a blood transfusion.


There are several limitations to this study. First, this analysis is based on identifying blood products transfusion recipients using ICD-9-CM procedure codes that indicate the occurrence of transfusion. For reasons discussed previously, transfusion procedure codes are likely to be underreported. As such, all relevant cases may not have been captured, which would underestimate the true frequency of blood products transfusion in hospitalized patients, affect demographic composition of the study population, and influence other outcome measures of interest such as LOS, postoperative infection rates, and mortality. However, given the extensive sample size, the magnitude and direction of the results reported here are robust, even with the potential for underreporting or misclassification of some transfusion cases.

Second, only data collected in the 2004 NIS database were assessed; these are derived from discharge record abstractions. Thus, detailed and precise information was not available to validate that a blood products transfusion procedure was performed or that a patient actually experienced a negative outcome. Also, cross-sectional survey databases such as NIS do not provide preadmission or post-hospital discharge data. Without these additional data, the nature or severity of blood loss, specific trigger for transfusion, number of units transfused, patient selection bias for endoscopic versus open approach, or link between procedure and timing of transfusion, for example, preoperative, intraoperative, or postoperative, cannot be accurately determined.

Third, autologous is often considered to be a safer blood product with respect to compatibility reactions; however, it still carries the risks of inflammatory reaction and
infection associated with any transfusion. Perioperative autologous transfusion that would largely be a cell saver product may be used extensively in orthopaedic and cardiac procedures and make up a significant portion of the blood products transfusion represented in this study. The negative outcome rates in this study may be conservatively low because of the inclusion of the large number of orthopaedic and cardiac procedures.

Despite these limitations, this Morton, et al. study shows that more than 2 million hospital admissions annually are associated with a blood products transfusion and that patients remain at risk of experiencing adverse clinical outcomes. The observation that transfusion recipients experience negative outcomes independent of age, sex, co morbidities, admission type, or DRG assignment warrants further investigation to better identify the appropriateness of current transfusion triggers and to develop and implement more effective approaches to reduce the non-emergent use of blood in hospitalized patients. Additional research to identify transfusion triggers, including patient severity, risk–benefit trade-offs, and the use of blood in elective surgical cases, should be a priority. In a significant number of trauma and urgent cases when uncontrolled haemorrhage is the clinical priority, surgeons often have limited options to rapidly correct blood loss, and therefore, the threshold for transfusion may be low. However, with elective cases, surgeons are likely to have more options such as the use of haemostatic agents to address blood loss and avoid or reduce the need for transfusion. This is especially important given the persistent challenges associated with maintaining an adequate blood supply. TRALI and incompatibility reactions were not reported for patients identified as transfusion recipients. This finding also warrants further investigation, given that the Joint Commission and the American Association of Blood Banks have established transfusion-specific performance improvement standards, blood use reviews, and reporting requirements for suspected transfusion-related adverse events. Finally, given that transfusion-related adverse clinical and health-related quality-of-life outcomes may persist after hospital discharge, additional prospective observational studies are needed to assess the long-term health status and quality of life of transfusion recipients. In conclusion, raising provider awareness and recognition of the frequency and potential negative clinical outcomes of blood products transfusion—as an independent predictor or surrogate for blood loss—may yield significant clinical and quality-of-life benefits at the individual patient level. Equally important is the need to encourage providers to adopt strategies and techniques that are more effective at controlling inadequate surgical haemostasis and that may reduce the frequency of blood products transfusions.

Reference


Key Findings

Children with severe malaria anaemia received either malarial treatment and whole blood transfusion or malaria treatment alone. There was no significant difference between the
transfused and non-transfused groups although there were significantly more adverse events in the transfused group compared with the non-transfused group.

Details

In two African randomized controlled trials (RCT), Holzer et al. randomised 116 children (aged 2 months to 6 years) with severe malarial anaemia (Hb level between 40 g/L and 57 g/L) to receive either malaria treatment and whole blood transfusion (relatively fresh blood donated by relatives), or malaria treatment alone. Bojang et al. randomised 114 children (aged 6 months to 9 years) with severe malarial anaemia (Hb level between 40 g/L and 50 g/L) to receive either whole blood transfusion or oral iron. Meremikwu and Smith combined the data from these two trials in a Cochrane Collaboration review and meta-analysis. The combined data showed there was no significant difference in mortality between the transfused and non-transfused (RR 0.41; 95% CI, 0.06-2.70; p=0.4). There were, however, significantly more severe adverse events in the transfused group compared with the non-transfused group (RR 8.60; 95% CI, 1.11-66.43; P=0.04).

Reference


Key Findings

Taylor et al. identified transfusion being associated with an adjusted dose-dependent increased risk of nosocomial infection (NI), ICU and hospital length of stay and mortality in 2085 surgical and medical ICU patients. Transfused patients were 6 times more likely to develop infection compared with non-transfused. The authors stated, “Transfused patients with a better prognosis had higher mortality rates, suggesting that transfusions may do more harm than good in ICU patients who have a reasonably good chance of survival.”

Details

Taylor et al. identified transfusion being associated with an adjusted dose-dependent increased risk of nosocomial infection (NI), ICU and hospital LOS and mortality in 2085 surgical and medical ICU patients. Compared with non-transfused patients, the transfused had higher NI rates (14.3% vs. 5.8%; P<.0001), longer ICU LOS (8.2 vs. 3.3 days; P<.0001), longer hospital LOS (18.3 vs. 9.9 days; P<.0001) and higher mortality rates (21.8% vs. 10.2%; P<.0001). Transfused patients were 6 times more likely to develop infection compared with non-transfused. The investigators documented a dose-dependent relationship with the risk of developing infection increasing by 9.7% for every red blood cell unit transfused. Even after adjusting for survival probability, transfused patients had significantly higher NI rates (14.3% vs. 5.8%; P<.0001), longer ICU LOS (8.2 vs. 3.3 days; P<.0001), longer hospital LOS (18.3 vs. 9.9 days; P<.0001), and higher mortality rates (21.8% vs. 10.2%; P<.0001). A sobering finding was after adjusting for patients’ probability of survival (POS), based on Mortality Prediction Model scores, transfused patients who were less severely ill (higher POS quartiles) had significantly higher mortality rates than similar POS non-transfused patients. The authors stated, “Transfused patients with a better prognosis had higher mortality rates, suggesting that transfusions may do more harm than good in ICU patients who have a reasonably good chance of survival.” Leucoreduction resulted in non-significant reduction in NI in this study. The authors also discussed the possible clinical implications of this finding. The cost of NI in the US is estimated to be greater than US$2 billion per annum and worldwide adding US$1,000-4,500 extra cost per patient in ICU from one NI. Bloodstream infections can average $40,000 per survivor.
FIGURE 44: COMPARISON OF TRANSFUSED VERSUS NON TRANSFUSED NOSOCOMIAL INFECTION OUTCOMES


Reference


Key Findings

Zilberberg et al. reported a strong independent relationship between packed red blood cell transfusion and the development of acute respiratory distress syndrome in the ICU (adjusted odds ratio of 2.80). They also identified an adjusted dose-response relationship between increasing packed red blood cell units (PRBCs) transfused and increased risk of acute respiratory distress syndrome (ARDS). Receiving 1 to 2 units of PRBCs was associated with a greater than twofold increase in ARDS, 3 to 4 units with an almost threefold increase, and greater than 4 units with a greater than fivefold increase, compared with patients not exposed to any PRBC transfusions.

Details

Zilberberg et al. subsequently conducted a sub-group analysis of the CRIT study to evaluate the association between packed red blood cell (PRBC) transfusion and acute respiratory distress syndrome (ARDS) in critically ill patients. The investigators focused on patients who did not have ARDS on admission, but developed ARDS during their ICU stay. After adjusting for multiple confounding factors, the authors reported a strong independent relationship between PRBC transfusion and the development of ARDS in the ICU (adjusted odds ratio of
2.80). Sighting reports estimating ARDS results in 3.6 million inpatient days of care annually and results from this study demonstrating that ARDS was associated with increased duration of ventilatory support, increased ICU and hospital length of stay and mortality, the authors suggest that their “findings should give physicians pause when considering transfusion” in at risk patients.

Reference


Key Findings

Amato A, and Pescatori M conducted a meta-analysis which aimed to evaluate the role of perioperative blood transfusions (PBT) on colorectal cancer recurrence. This was accomplished by validating the results of a previously published meta-analysis (Amato 1998); and by updating it to December 2004. Amato and Pescatori concluded that the updated meta-analysis confirmed the previous findings. All analyses support the hypothesis that PBT have a detrimental effect on the recurrence of curable colorectal cancers. However, since heterogeneity was detected and conclusions on the effect of surgical technique could not be drawn, a causal relationship cannot still be claimed. Carefully restricted indications for PBT seem necessary.

Details

The improvement of renal allograft survival by pre-transplantation transfusions alerted the medical community to the potential detrimental effect of transfusions in patients being treated for cancer. Amato A, and Pescatori M, conducted a meta-analysis which aimed to evaluate the role of perioperative blood transfusions (PBT) on colorectal cancer recurrence. This was accomplished by validating the results of a previously published meta-analysis (Amato 1998); and by updating it to December 2004. Published papers were retrieved using Medline, EMBASE, the Cochrane Library, controlled trials web-based registries, or the CCG Trial. The search strategy used was: {colon OR rectal OR colorectal} WITH {cancer OR tumour OR neoplasm} AND transfusion. The tendency not to publish negative trials was balanced by inspecting the proceedings of international congresses.

Patients undergoing curative resection of colorectal cancer (classified either as Dukes stages A-C, Astler-Coller stages A-C2, or TNM stages T1-3a/N0-1/M0) were included if they had received any amount of blood products within one month of surgery. Excluded were patients with distant metastases at surgery, and studies with short follow-up or with no data. A specific form was developed for data collection. Data extraction was cross-checked, using the most recent publication in case of repetitive ones. Papers’ quality was ranked using the method by Evans and Pollock. Odds ratios (OR, with 95% confidence intervals) were computed for each study, and pooled estimates were generated by RevMan (version 4.2). When available, data were stratified for risk factors of cancer recurrence.

The findings of the 1998 meta-analysis were confirmed, with small variations in some estimates. Updating it through December 2004 led to the identification of 237 references. Two-hundred and one of them were excluded because they analysed survival (n=22), were repetitive (n=26), letters/reviews (n=66) or had no data (n=87). Thirty-six studies on 12,127 patients were included: 23 showed a detrimental effect of PBT; 22 used also multivariable analyses, and 14 found PBT to be an independent prognostic factor. Pooled estimates of
PBT effect on colorectal cancer recurrence yielded overall OR of 1.42 (95% CI, 1.20 to 1.67) against transfused patients in randomized controlled studies. Stratified meta-analyses confirmed these findings, also when stratifying patients by site and stage of disease. The PBT effect was observed regardless of timing, type, and in a dose-related fashion, although heterogeneity was detected. Data on surgical techniques was not available for further analysis.

Amato and Pescatori concluded that the updated meta-analysis confirmed the previous findings. All analyses support the hypothesis that PBT have a detrimental effect on the recurrence of curable colorectal cancers. However, since heterogeneity was detected and conclusions on the effect of surgical technique could not be drawn, a causal relationship cannot still be claimed. Carefully restricted indications for PBT seem necessary.

Reference


Key Findings

In a multi-centre prospective observational study of 8004 consecutive patients undergoing isolated coronary artery bypass graft (CABG) surgery the Northern New England Cardiovascular Disease Study Group sought to address the question of whether the morbidity and mortality associated with haemodilution anaemia in CABG surgery with cardiopulmonary bypass is due to the anaemia or the red blood cell transfusions used to treat the anaemia. The authors conclude that haemodilution anaemia during cardiopulmonary bypass is associated with an increased risk of low-output heart failure, however, management of that anaemia with red blood cell transfusion is independently associated with an increased risk of low-output heart failure.

Details

In a multi-centre prospective observational study of 8004 consecutive patients undergoing isolated coronary artery bypass graft (CABG) surgery the Northern New England Cardiovascular Disease Study Group sought to address the question of whether the morbidity and mortality associated with haemodilution anaemia in CABG surgery with cardiopulmonary bypass (as shown in an earlier study is due to the anaemia or the red blood cell transfusions used to treat the anaemia. The primary outcome measure in this study was low-output heart failure (LOF). The authors explain that they used this measure because it is a good indicator of the outcome of intraoperative management. They also chose to analyse patients transfused with only 1 or 2 red blood cell units in order to minimise the confounding effect of more heavily transfused patients which may reflect management of active bleeding rather than routine anaemia. The investigators compared patients who received red blood cell transfusions (1 or 2 units) with patients receiving no red blood cell transfusions. They also analysed anaemia and outcome in nadir haematocrit (HCT) groups (HCT ≤20, 21 to 22, 23 to 24 and ≥25). In each nadir HCT group there were patients managed with and without red blood cell transfusions. Overall, both anaemia and red blood cell transfusion was associated with an increased risk of LOF. The risk of LOF was increased almost twofold in the transfused patients compared with those not transfused (12.4% vs. 6.8% respectively). After adjusting for all factors known to influence patient outcomes, both anaemia and red blood cell transfusion were still risk factors for LOF. Between each nadir HCT group there was a 10% increased risk of LOF. Red blood cell transfusion was associated
with a 27% increased risk compared with no transfusion. The authors conclude that
haemodilution anaemia during cardiopulmonary bypass is associated with an increased risk of
LOF, however, management of that anaemia with red blood cell transfusion is independently
associated with an increased risk of LOF.

Reference

Rogers, Mary A.M., et al. Hospital variation in transfusion and infection after cardiac

Key Findings

Rogers, Mary A.M., et al. assessed hospital variation in blood use and outcomes in cardiac
surgery patients. They concluded that allogeneic blood transfusion was associated with an
increased risk of infection at multiple sites, suggesting a system-wide immune response.
Hospital variation in transfusion practices after coronary artery bypass grafting was
considerable indicating that quality efforts may be able to influence practice and improve
outcomes.

Details

Rogers, Mary A.M., et al. assessed hospital variation in blood use and outcomes in cardiac
surgery patients. They evaluated outcomes in 24,789 Medicare beneficiaries in the state of
Michigan, USA, who received coronary artery bypass graft surgery from 2003 to 2006. Using
a cohort design, patients were followed from hospital admission to assess transfusions, in-
hospital infection and mortality, as well as hospital readmission and mortality 30 days after
discharge. Multilevel mixed-effects logistic regression was used to calculate the intra-
hospital correlation coefficient (for 40 hospitals) and compare outcomes by transfusion
status.

Overall, 30% (95 CI, 20% to 42%) of the variance in transfusion practices was attributable to
hospital site. Allogeneic blood use by hospital ranged from 72.5% to 100% in women and
49.7% to 100% in men. Allogeneic, but not autologous, blood transfusion increased the odds
of in-hospital infection 2.0-fold (95% CI 1.6 to 2.5), in-hospital mortality 4.7-fold (95% CI 2.4
to 9.2), 30-day readmission 1.4-fold (95% CI 1.2 to 1.6), and 30-day mortality 2.9-fold (95% CI
1.4 to 6.0) in elective surgeries. Allogeneic transfusion was associated with infections of the
genitourinary system, respiratory tract, bloodstream, digestive tract and skin, as well as
infection with *Clostridium difficile*. For each 1% increase in hospital transfusion rates, there
was a 0.13% increase in predicted infection rates. Rogers et al. concluded that allogeneic
blood transfusion was associated with an increased risk of infection at multiple sites,
suggesting a system-wide immune response. Hospital variation in transfusion practices after
coronary artery bypass grafting was considerable indicating that quality efforts may be able
to influence practice and improve outcomes.

Reference

Wu, W.C., et al., Blood transfusion in elderly patients with acute myocardial infarction. N

Key Findings

Wu et al. assessed the benefit of transfusion in anaemic elderly patients with myocardial
infarction by analysing a United States Medicare/Medicaid database of 234,769 patients.
Univariate analysis demonstrated that transfusion was associated with decreased 30-day
mortality in patients admitted with a haemoglobin value ≤ 100 g/L, and a trend toward
improved survival up to a haemoglobin value of 110 g/L. However, patients transfused with a haemoglobin value >110 g/L had an increased mortality. No multivariate or propensity score matching was performed and the <100 g/dL group had twice the number of do-not-resuscitate (DNR) orders, more diabetes and fewer aggressive cardiology and cardiac surgery interventions compared with the higher haemoglobin groups, resulting in considerable debate over the relevance of the findings of this study.

Details

To assess the benefit of transfusion in anaemic elderly patients with myocardial infarction (MI) Wu et al. analysed a United States Medicare/Medicaid database of 234,769 admitted over a one-year period with a primary diagnoses of acute MI. After exclusions 78,769 patients 65 years of age or older were grouped into different haematocrit/haemoglobin groups for evaluation. 50% of the evaluation group were anaemic (defined as a haemoglobin value less than 13 g/L). 4.7% of the entire evaluable group received a blood transfusion. Univariate analysis demonstrated that transfusion was associated with decreased 30-day mortality in patients admitted with a haemoglobin value ≤ 100 g/L, and a trend toward improved survival up to a haemoglobin value of 110 g/L. However, patients transfused with a haemoglobin value >110 g/L had an increased mortality. No multivariate or propensity score matching was performed and the <100 g/dL group had twice the number of do-not-resuscitate (DNR) orders, more diabetes and fewer aggressive cardiology and cardiac surgery interventions compared with the higher haemoglobin groups, resulting in considerable debate over the relevance of the findings of this study.

Reference


Key Findings

A study subsequent to Wu (see above) of patients with myocardial infarction came to a different conclusion. Rao et al. analysed data from three large international randomised controlled trials involving 24,111 patients with acute coronary syndrome. After multivariate and propensity analysis, adjusting for timing of events, bleeding, type of infarction, nadir haemoglobin and procedure, blood transfusion was associated with a 3.94 times increased risk for 30-day mortality. When examined by haemoglobin levels, the investigators found an association between transfusion and increased 30-day mortality at a mean haemoglobin > 83 g/L. The adjusted increased hazard (odds ratio) for death was 168.64 for a mean haemoglobin level of 100 g/L and 291.64 for mean nadir haemoglobin of 117 g/L. They found no association between transfusion and increased mortality and, conversely, no benefit, in patients with a mean haemoglobin < 83 g/L.

Details

A study subsequent to Wu (see above) of patients with MI came to a different conclusion. Rao et al. analysed data from three large international randomised controlled trials involving 24,111 patients with acute coronary syndrome. Whereas Wu et al. excluded patients younger than 65 years, those with bleeding within 48 hours of admission, and those who underwent cardiac surgery, Rao et al. included all patients, regardless of age, bleeding events, or interventions. Ten per cent of patients underwent at least one blood transfusion. The investigators found that patients who underwent transfusion had a significantly higher unadjusted rate of 30-day death (8.00% vs. 3.08%; P<.001), myocardial infarction (MI) (25.16% vs. 8.16%; P<.001), and combined death/MI (29.24% vs. 10.02%; P<.001) compared
with patients who did not undergo transfusion. After multivariate and propensity analysis, adjusting for timing of events, bleeding, type of infarction, nadir haemoglobin and procedure, blood transfusion was associated with a 3.94 times increased risk for 30-day mortality. When examined by haemoglobin levels, the investigators found an association between transfusion and increased 30-day mortality at a mean haemoglobin > 83 g/L. The adjusted increased hazard (odds ratio) for death was 168.64 for a mean haemoglobin level of 100 g/L and 291.64 for mean nadir haemoglobin of 117 g/L. They found no association between transfusion and increased mortality and, conversely, no benefit, in patients with a mean haemoglobin < 83 g/L.

Reference


Key Findings

In an effort to minimise the confounding contribution of injury and shock to outcome, Croce et al. evaluated the association between delayed transfusion and serious respiratory complications in a cohort of ICU patients with less severe blunt trauma who received no transfusion within the initial 48 hours after admission. They found blood transfusion was still an independent predictor of serious adverse outcome. The authors concluded, “This study demonstrates that transfusions are not innocuous and that aggressive pursuit of transfusion substitutes is warranted.”

Details

In an effort to minimise the confounding contribution of injury and shock to outcome, Croce et al. evaluated the association between delayed transfusion and serious respiratory complications (ventilator-associated pneumonia [VAP], acute respiratory distress syndrome [ARDS]) and death in a cohort of ICU patients with less severe (ISS <25) blunt trauma who received no transfusion within the initial 48 hours after admission. Of the 5,260 patients who met study criteria, 778 (15%) received delayed transfusion. Logistic regression analysis identified delayed transfusion as being independently associated with VAP, ARDS and death. In a subgroup analysis of younger patients (age <50), with even less injury (ISS <16, Glasgow Comma Score [GCS] >11, chest Abbreviated Injury Scale [AIS] <3), and minimal shock (base excess ≥ 5.0 mEq/L), blood transfusion was still an independent predictor of serious adverse outcome. The authors concluded, “This study demonstrates that transfusions are not innocuous and that aggressive pursuit of transfusion substitutes is warranted.”

Reference


Key Findings

Dunne et al. in a study of 9539 trauma patients found that blood transfusion within the first 24 hours was an independent predictor of systemic inflammatory response syndrome (SIRS) as well as mortality, ICU admission, and ICU length of stay. Patients who received blood transfusion in the first 24 hours after trauma had a significantly increased risk of SIRS compared to those not transfused.
Details

Dunne et al. in a study of 9539 trauma patients found that blood transfusion within the first 24 hours was an independent predictor of systemic inflammatory response syndrome (SIRS) as well as mortality, ICU admission, and ICU LOS. Patients who received blood transfusion in the first 24 hours after trauma had a significantly increased risk of SIRS (relative risk ratios 2.1 to 5.4 for SIRS scores 1–4) compared to those not transfused. Multinomial logistic regression analysis revealed that after controlling for age, ISS, GCS, gender, and race blood transfusion was an independent predictor of SIRS, (OR 2.43, 95% CI 1.99–2.95; p <0.0001). Transfused patients had significantly increased mortality rates (22.2% vs. 1.4%, p <0.0001), increased ICU admission rates (57.4% vs. 7.4%; p <0.0001), and increased ICU LOS (16.8 vs. 9.9, p < 0.00001) compared to non-transfused patients. Transfused patients also had significantly increased hospital LOS (14.5 vs. 2.555 days, p <0.00001) compared to non-transfused patients. After controlling for other factors that affect trauma outcome, including age, ISS, GCS, race, and gender, transfused patients had a fourfold increased risk of mortality (OR 4.23, 95% CI 3.07–5.84, p <0.0001) and a greater than fourfold increased risk of ICU admission (OR 4.62, 95% CI 3.84–5.55, p <0.0001) compared to non-transfused patients. In addition, linear regression analysis revealed blood transfusion to be an independent risk factor for ICU LOS (5.2 days longer ICU LOS for the transfused group; p <0.0001) and hospital LOS (7.3 days longer hospital LOS for the transfused group; p <0.0001).

Reference


Key Findings

Given the greater postoperative mortality rate in women compared to men following coronary artery bypass graft (CABG) surgery, Rogers and colleagues investigated whether the higher transfusion rate in women may contribute to the gender-different mortality. They found women were 3.4 times more likely to be transfused than men and received a significantly greater number of units. Women were 1.5 times more likely to die within 100 days of surgery than men. However, when adjusted for blood transfusion, there was no longer a significant difference in the mortality between men and women – suggesting blood transfusion being a risk factor for mortality. The authors conclude that this study suggests the increased mortality in women following CABG surgery is likely due to their increased receipt of blood transfusion.

Details

Given the greater postoperative mortality rate in women compared to men following coronary artery bypass graft (CABG) surgery, Rogers and colleagues investigated whether the higher transfusion rate in women may contribute to the gender-different mortality. Of the 9,218 patients included in the study 74.8% received an allogeneic blood transfusion. This study confirmed that women are more likely to be transfused than men (88.2% vs. 66.7%). After adjusting for variables (age, race, 30 co morbidities and urgency of admission) women were 3.4 times more likely to be transfused than men and received a significantly greater number of units. Patients who received blood had a significantly increased infection rate compared with those not receiving blood (14.6% vs. 4.9%). The infection rate in patients receiving autologous blood only (n=90) was 5.6%. Compared with non-transfused, the risk of transfused patients developing a specific site infection increased 6.8 times for septicaemia, 3.5 times for respiratory tract, 2.3 times for urinary tract, 2.4 times for digestive tract, 3.6
times for heart and 3.7 times for device-related. The authors also found a dose-dependent relationship, with the infection rate increasing with the number of units transfused (1-4 U = 13.6%, 5-9 U = 25.3%, 50-99 U = 30.8%). The 100-day mortality rate was 9.4% for transfused patients compared with 1.5% in those not transfused. After adjusting for variables, transfused patients were 5.6 times more likely to die within 100 days of surgery compared with those not transfused. Women were 1.5 times more likely to die within 100 days of surgery than men. However, when adjusted for blood transfusion, there was no longer a significant difference in the mortality between men and women – suggesting blood transfusion being a risk factor for mortality. The authors conclude that this study suggests the increased mortality in women following CABG surgery is likely due to their increased receipt of blood transfusion.

Reference


Key Findings

Murphy, G.J., et al. aimed to quantify associations of transfusion with clinical outcomes and cost in patients having cardiac surgery. They concluded that red blood cell transfusion in patients having cardiac surgery is strongly associated with both infection and ischemic postoperative morbidity, hospital stay, increased early and late mortality, and hospital costs.

Details

Murphy, G.J., et al. aimed to quantify associations of transfusion with clinical outcomes and cost in patients having cardiac surgery. They concluded that red blood cell transfusion in patients having cardiac surgery is strongly associated with both infection and ischemic postoperative morbidity, hospital stay, increased early and late mortality, and hospital costs. Clinical, haematology, and blood transfusion databases were linked with the UK population register. Additional hematocrit information was obtained from intensive care unit charts. Composite infection (respiratory or wound infection or septicaemia) and ischemic outcomes (myocardial infarction, stroke, renal impairment, or failure) were pre-specified as co-primary end points. Secondary outcomes were resource use, cost, and survival. Associations were estimated by regression modelling with adjustment for potential confounding. All adult patients having cardiac surgery between April 1, 1996, and December 31, 2003, with key exposure and outcome data were included (98%). Adjusted odds ratios for composite infection (737 of 8516) and ischemic outcomes (832 of 8518) for transfused versus non-transfused patients were 3.38 (95% confidence interval [CI], 2.60 to 4.40) and 3.35 (95% CI, 2.68 to 4.35), respectively. Transfusion was associated with increased relative cost of admission (any transfusion, 1.42 times [95% CI, 1.37 to 1.46], varying from 1.11 for 1 U to 3.35 for _9 U). At any time after their operations, transfused patients were less likely to have been discharged from hospital (hazard ratio [HR], 0.63; 95% CI, 0.60 to 0.67) and were more likely to have died (0 to 30 days: HR, 6.69; 95% CI, 3.66 to 15.1; 31 days to 1 year: HR, 2.59; 95% CI, 1.68 to 4.17; _1 year: HR, 1.32; 95% CI, 1.08 to 1.64).
Reference


Key Findings

Dr Jacque Lacroix and colleagues report on their 2007 international multicenter Transfusion Requirements in the Pediatric Intensive Care Unit (TRIPICU) Study, a trial, described by the authors of the accompanying editorial, as having implications for understanding the role of such transfusions in all critically ill patients. The investigators compared a liberal versus a restrictive transfusion threshold in stable critically ill children. Results showed that the restrictive transfusion threshold resulted in a 44% reduction in the number of red blood cell transfusions and a 96% reduction in the number of patients exposed to any transfusion when compared with the liberal threshold. This was achieved without any increase in measured adverse outcomes. The authors conclude that a restrictive transfusion threshold in stable critically ill children in ICU can be used safely to reduce transfusion exposure. They caution, however, on applying this finding to other patient groups. After commenting on this trial and reviewing the results of three other randomized trials evaluating transfusion triggers, Drs Howard Corwin and Jeffery Carson in their editorial conclude that the overall evidence does not support liberal use of transfusion in critically ill patients. They state, “Red-cell transfusion should no longer be regarded as ‘may help, will not hurt’ but, rather, should be approached as ‘first do no harm.”

Details

Dr Jacque Lacroix and colleagues report on their 2007 international multicenter Transfusion Requirements in the Pediatric Intensive Care Unit (TRIPICU) Study, a trial, described by the authors of the accompanying editorial, as having implications for understanding the role of such transfusions in all critically ill patients. The investigators compared a liberal versus a restrictive transfusion threshold in stable critically ill children. Six hundred and thirty seven eligible patients between the ages of 3 days and 14 years were randomized to one of the two groups: 317 to the liberal transfusion threshold group (hemoglobin level of 9.5 g/dL) and 327 to the restrictive transfusion threshold group (hemoglobin level of 7 g/dL). They compared the two groups with regard to both the total number of transfusions per patient and the proportion of patients who avoided transfusions. All blood used in the study was pre-storage leukocyte-reduced. The primary outcome measure was a composite of death and multiple-organ-dysfunction syndrome. Secondary outcomes included sepsis, infections, transfusion reactions, adverse events and intensive care unit (ICU) and hospital length of stay. Results showed that the restrictive transfusion threshold resulted in a 44% reduction in the number of red blood cell transfusions and a 96% reduction in the number of patients exposed to any transfusion when compared with the liberal threshold. This, the authors report, was achieved without any increase in measured adverse outcomes. Both primary and secondary outcome measures were not significantly different between groups. The authors note that this result, in relation to adverse outcomes, differs from the only large randomized controlled trial comparing a liberal versus a restrictive transfusion strategy in critically ill adult patients, a study in which organ failure, other complications and in-hospital mortality were significantly higher in the liberal group compared with the restrictive group. The authors present possible factors contributing to the different outcome findings. The authors conclude that a restrictive transfusion threshold in stable critically ill children in ICU can be used safely to reduce transfusion exposure. They caution, however, on applying this finding to other patient groups. After commenting on this trial and reviewing the results of three
other randomized trials evaluating transfusion triggers, Drs Howard Corwin and Jeffery Carson in their editorial conclude that the overall evidence does not support liberal use of transfusion in critically ill patients. They state, “Red-cell transfusion should no longer be regarded as ‘may help, will not hurt’ but, rather, should be approached as ‘first do no harm.”

Reference


Key Findings

The objective of the 2010 Transfusion Requirements After Cardiac Surgery (TRACS) study by Hajjar, Ludhmila A., et al. was to define whether a restrictive perioperative red blood cell transfusion strategy was as safe as a liberal strategy in patients undergoing elective cardiac surgery. The study found that, Independent of transfusion strategy, the number of transfused red blood cell units was an independent risk factor for clinical complications or death at 30 days. The authors concluded that, among patients undergoing cardiac surgery, the use of a restrictive perioperative transfusion strategy compared with a more liberal strategy resulted in non-inferior rates of the combined outcome of 30-day all-cause mortality and severe morbidity.

Details

The objective of the 2010 Transfusion Requirements After Cardiac Surgery (TRACS) study by Hajjar, Ludhmila A., et al. was to define whether a restrictive perioperative red blood cell transfusion strategy was as safe as a liberal strategy in patients undergoing elective cardiac surgery. The TRACS study, a prospective, randomized, controlled clinical non-inferiority trial was conducted between February 2009 and February 2010 in an intensive care unit at a university hospital cardiac surgery referral centre in Brazil. Consecutive adult patients (n=502) who underwent cardiac surgery with cardiopulmonary bypass were eligible; analysis was by intention-to-treat. Patients were randomly assigned to a liberal strategy of blood transfusion (to maintain a hematocrit_30%) or to a restrictive strategy (hematocrit_24%). Composite end point of 30-day all-cause mortality and severe morbidity (cardiogenic shock, acute respiratory distress syndrome, or acute renal injury requiring dialysis or hemofiltration) occurring during the hospital stay. The non-inferiority margin was predefined at –8% (i.e., 8% minimal clinically important increase in occurrence of the composite end point). Haemoglobin concentrations were maintained at a mean of 10.5 g/dL(95% confidence interval [CI], 10.4–10.6) in the liberal-strategy group and 9.1 g/dL (95% CI, 9.0–9.2) in the restrictive-strategy group (P=.001). A total of 198 of 253 patients (78%) in the liberal-strategy group and 118 of 249 (47%) in the restrictive-strategy group received a blood transfusion (P=.001). Occurrence of the primary end point was similar between groups (10% liberal vs 11% restrictive; between-group difference, 1% [95% CI, –6% to 4%]; P=.85). Independent of transfusion strategy, the number of transfused red blood cell units was an independent risk factor for clinical complications or death at 30 days (hazard ratio for each additional unit transfused, 1.2 [95% CI, 1.1–1.4]; P=.002). Hajjar, Ludhmila A., et al. concluded that, among patients undergoing cardiac surgery, the use of a restrictive perioperative transfusion strategy compared with a more liberal strategy resulted in non-inferior rates of the combined outcome of 30-day all-cause mortality and severe morbidity.
Reference


Key Findings

Jeschke and colleagues investigated the association between allogeneic blood transfusion and infection and mortality in severely burned paediatric patients. Even after adjusting for the known effects of increased total body surface area burn and inhalation injury on sepsis, the authors conclude that receiving >20 units of red blood cells significantly increased the risk of sepsis. Of interest the investigators included weight as a covariate and report that it appears that the total amount of red blood cells transfused determined the risk, not the relative amount, that is, red blood cells given per kilogram.

Details

Jeschke and colleagues investigated the association between allogeneic blood transfusion and infection and mortality in severely burned paediatric patients. Their retrospective cohort study included 277 patients admitted to their institution from 1997 to 2004 with a burn >30% total body surface area (TBSA). The study’s design attempted to include only transfusions that were given before patients became clinically infected or septic. Patients were stratified into groups by small, medium and large TBSA burns (<40%, 40-60% and >60% respectively) and whether or not they had inhalation injury. Groups were further divided according to whether they received “low” or “high” amounts of blood products and by the number of operations. Results showed that there was no significant increase in sepsis in patients with small burns given either low or high amounts of blood. In patients with large burns the risk of developing infection increased from 8% in the low red blood cell transfusion group (<20 units) to 58% in the high red blood cell group (>20 units). In large burn patients the mortality rate was 6% when receiving low amounts of blood and 30% when receiving high amounts (odds ration [OR] = 6.79). In the large burn group with inhalation injury the mortality rate was 11% in the low red blood cell group and 72% in the high red blood cell group (OR=11.6). Even after adjusting for the known effects of increased TBSA burn and inhalation injury on sepsis, the authors conclude that receiving >20 units of red blood cells significantly increased the risk of sepsis. Of interest the investigators included weight as a covariate and report that it appears that the total amount of red blood cells transfused determined the risk, not the relative amount, that is, red blood cells given per kilogram.

Reference


Key Findings

Marik et al. conducted a prospective, controlled, interventional study in 1993 to determine the effect of red blood cell transfusion on gastrointestinal and whole-body oxygen uptake in a multidisciplinary intensive care unit of a tertiary care teaching hospital. They concluded that they had failed to demonstrate a beneficial effect of red blood cell transfusion on measured systemic oxygen uptake in patients with sepsis. Patients receiving old transfused red blood cells developed evidence of splanchnic ischemia. They postulated that the poorly
deformable transfused red blood cells cause microcirculatory occlusion in some organs, which may lead to tissue ischemia in some organs.

Details

Marik et al. conducted a prospective, controlled, interventional study in 1993 to determine the effect of red blood cell transfusion on gastrointestinal and whole-body oxygen uptake in a multidisciplinary intensive care unit of a tertiary care teaching hospital. Twenty-three critically ill patients with sepsis undergoing mechanical ventilation were the subjects of the study. Systemic oxygen uptake was measured by indirect calorimetry and calculated by the Fick method. Gastric intramucosal pH as measured by tonometry was used to assess changes in splanchnic oxygen availability. Measurements were made prior to transfusion of 3 U of packed red blood cells. These measurements were then repeated immediately following transfusion, as well as 3 and 6 hours later. There was no increase in systemic oxygen uptake measured by indirect calorimetry in any of the patients studied for up to 6 hours post-transfusion (including those patients with an elevated arterial lactate concentration). However, the calculated systemic oxygen uptake increased in parallel with the oxygen delivery in all the patients. More importantly, they found an inverse association between the change in gastric intramucosal pH and the age of the transfused blood (r=-.71; P<.001). In those patients receiving blood that had been stored for more than 15 days, the gastric intramucosal pH consistently decreased following the red blood cell transfusion.

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Reference


Key Findings

Stored red cells undergo progressive structural and functional changes over time. Koch, C.D., et al. tested the hypothesis that serious complications and mortality after cardiac surgery are increased when transfused red cells are stored for more than two weeks. They concluded that, in patients undergoing cardiac surgery, transfusion of red cells that had
been stored for more than two weeks was associated with a significantly increased risk of postoperative complications as well as reduced short-term and long-term survival.

Details

Stored red cells undergo progressive structural and functional changes over time. Koch, C.D., et al. tested the hypothesis that serious complications and mortality after cardiac surgery are increased when transfused red cells are stored for more than two weeks. They examined data from patients given red-cell transfusions during coronary-artery bypass grafting, heart-valve surgery, or both between June 30, 1998, and January 30, 2006. A total of 2872 patients received 8802 units of blood that had been stored for 14 days or less (“newer blood”), and 3130 patients received 10,782 units of blood that had been stored for more than 14 days (“older blood”). Multivariable logistic regression with propensity-score methods was used to examine the effect of the duration of storage on outcomes. Survival was estimated by the Kaplan–Meier method and Blackstone’s decomposition method. The median duration of storage was 11 days for newer blood and 20 days for older blood. Patients who were given older units had higher rates of in-hospital mortality (2.8% vs. 1.7%, P = 0.004), intubation beyond 72 hours (9.7% vs. 5.6%, P<0.001), renal failure (2.7% vs. 1.6%, P = 0.003), and sepsis or septicemia (4.0% vs. 2.8%, P = 0.01). A composite of complications was more common in patients given older blood (25.9% vs. 22.4%, P = 0.001). Similarly, older blood was associated with an increase in the risk-adjusted rate of the composite outcome (P = 0.03). At 1 year, mortality was significantly less in patients given newer blood (7.4% vs. 11.0%, P<0.001).

Koch, C.D., et al. concluded that, in patients undergoing cardiac surgery, transfusion of red cells that had been stored for more than two weeks was associated with a significantly increased risk of postoperative complications as well as reduced short-term and long-term survival.

Reference


Key Findings

Tsai, A.G., et al. reviewed the experimental evidence showing systemic and microvascular effects of blood transfusions instituted to support the organism in extreme haemodilution and haemorrhagic shock, focusing on the use of fresh vs. stored blood as a variable. The question: “What does a blood transfusion remedy?” was analysed in experimental models addressing systemic and microvascular effects showing that oxygen delivery is not the only function that must be addressed. They concluded that that fresh blood is intrinsically a better resuscitation fluid than older, stored blood in the animal model systems in which it has been carefully studied.

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Tsai, A.G., et al. reviewed the experimental evidence showing systemic and microvascular effects of blood transfusions instituted to support the organism in extreme haemodilution and haemorrhagic shock, focusing on the use of fresh vs. stored blood as a variable. The question: “What does a blood transfusion remedy?” was analysed in experimental models addressing systemic and microvascular effects showing that oxygen delivery is not the only function that must be addressed. In extreme haemodilution and haemorrhagic shock blood
transfusions simultaneously restore blood viscosity and oxygen carrying capacity, the former being critically needed for re-establishing a functional mechanical environment of the microcirculation, necessary for obtaining adequate capillary blood perfusion. Increased oxygen affinity due to DPG depletion is shown to have either no effect or a positive oxygenation effect, when the transfused red blood cells (RBCs) do not cause additional flow impairment due to structural malfunctions including increased rigidity and release of haemoglobin. Tsai, A.G., et al. conclude that that fresh blood is intrinsically a better resuscitation fluid than older, stored blood in the animal model systems in which it has been carefully studied. It is also apparent that blood transfusions are called for to restore oxygen carrying capacity, while one of the major problems is deficient microvascular perfusion and function. In fact it is questionable whether a blood transfusion is the optimal remedy for re-establishing tissue perfusion in an organism subjected to haemodilution and haemorrhage, or both. A precise understanding of the mechanisms involved in blood transfusion may be intrinsically impossible, because blood composition per se is a moving target. Distinguishing between “fresh” and “old” RBCs overlooks that the distribution of RBC age in the circulation is presumed to be approximately Gaussian, with an average centred at their circulatory half-life, therefore even “fresh” blood has a fraction of RBCs at the end of their cycle. Experimental studies in transfusion studies have presently addressed the question and provide preliminary answer to: What is the problem that must be remedied when a blood transfusion is called for? We propose that oxygen is only one part of the problem, and that microscopic perfusion is the other component. Remarkably their relative importance is not yet established, however there is evidence that adequate restoration of microvascular perfusion deficiency in anemia and haemorrhagic resuscitation may be as efficacious as restoring oxygen carrying capacity, therefore potentially significantly reducing the use of blood. Although experimental studies seldom reproduce emergency and clinical conditions, nonetheless they serve to explore fundamental physiological mechanisms in the microcirculation that cannot be directly studied in humans.

Reference


Key Findings

An abstract entitled Blood Transfusion Increases Hospital Acquired Septicaemia by O’Mara et al., from the Hunter New England Health Service, Australia was presented at the 52nd ASH Annual Meeting and Exposition, December 4-7, 2010, Orlando, Florida. The abstract said the study showed there was a statistically significant increase in septicaemia following red cell transfusion. The null hypothesis was rejected. The data base was examined by the age of red cells transfused and its effect on nosocomial septicaemia. There was a statistically significant effect of older blood on the rate of septicaemia.
52ND ASH ANNUAL MEETING AND EXPOSITION, DECEMBER 4-7, 2010,
Orange County Convention Center, Orlando, Florida

346 Blood Transfusion Increases Hospital Acquired Septicaemia

Poster Session: Basic Science and Clinical Practice in Blood Transfusion: Poster II
Monday, December 6, 2010, 6:00 PM-8:00 PM
Hall A3/A4 (Orange County Convention Center), Poster Board III-125

Stephen Kenneth O’Mara, BSc., MBBS, FRACP, FRCPA\(^1\), John Ferguson, MBBS, FRACP, FRCPA\(^2\) and Michael Manolis, Assoc.Dip.HealthScience, Tech.Cert.Path\(^3\)

\(^1\)Haematology and Clinical Governance, Hunter New England Health, Tamworth, Australia

\(^2\)Infectious diseases, Hunter Area Pathology service, Newcastle, Australia

\(^3\)Transfusion Laboratory, Hunter Area Pathology service, Newcastle

The rate of septicaemia was measured following blood transfusion in patients admitted to hospital greater than 48 hours. The data was collected prospectively and analysed retrospectively. The aim of the analysis was to disprove that red cell transfusion increased the rate of hospital acquired septicaemia. Data was extracted on patients who had a transfusion and an episode of septicaemia between 1999 and 2008 at a university teaching hospital, John Hunter Hospital, Newcastle, Australia (JHH). The database contained information on 20161 transfusion events of 102,600 units of packed red cells. The septicaemia database contained 8375 patients with blood culture proven septicaemia.

Blood was issued using a computerised cross matching system. Analysis of the issuing of blood found no bias in the age of blood issued based on age, sex, number of units or by year of issue. All patients having a septicaemic event recorded following transfusion were analysed and compared to septicaemia occurring in all admissions greater than 48hrs in which no transfusion occurred. All patients who were diagnosed with septicaemia in the 6 months prior to transfusion were excluded as were patients who received five or more units of packed red cells to exclude the bias from the sickest patients. All patients whose septicaemia occurred greater than 16 days after transfusion were excluded as were patients whose septicaemia occurred before the second day after transfusion. A total of 258 patients were reviewed to test the hypothesis (Table 1).

There was a statistically significant increase in septicaemia following red cell transfusion. The null hypothesis was rejected. The data base was examined by the age of red cells transfused and its effect on nosocomial septicaemia. There was a statistically significant effect of older blood on the rate of septicaemia. Packed red cells transfused less than 14 days of age had no effect on the septicaemia rate. Blood that was 14-28 days of age increased the rate of nosocomial septicaemia by 1.65. Red Cells that were between 29 and 35 days of age increased the rate of septicaemia by 2.5 times. Blood that was between 36 and 42 days of age increased the rate by approximately 4.4 times, with the absolute risk of developing septicaemia within 15 days being approximately 4% (Table 2). The time course of septicaemia was examined for patients receiving at least one unit of 28 day old blood. It was
found that the risk of sepsis lasted less than 15 days p<0.001. The conclusion of our analysis suggests that packed red cells older than 14 days increase the risk of septicemia in hospitalised patients, this effect continues to rise until 42 days post collection.

Table 1

<table>
<thead>
<tr>
<th>N</th>
<th>Odds Ratio(CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cases of nosocomial septicemia</td>
<td>1684</td>
</tr>
<tr>
<td>Admissions greater than 48 hours</td>
<td>175,325</td>
</tr>
<tr>
<td>Prior to exclusions</td>
<td>790</td>
</tr>
<tr>
<td>All transfusions</td>
<td>790</td>
</tr>
<tr>
<td>No previous sepsis</td>
<td></td>
</tr>
<tr>
<td>Study Group</td>
<td>258</td>
</tr>
<tr>
<td>Less than 5 units Transfusion.</td>
<td>258</td>
</tr>
<tr>
<td>No previous sepsis.</td>
<td>258</td>
</tr>
<tr>
<td>Septicaemia &gt;2 days &lt;16days</td>
<td>258</td>
</tr>
<tr>
<td>2.02</td>
<td>(1.92-2.12)</td>
</tr>
</tbody>
</table>

Table 2

<table>
<thead>
<tr>
<th>Age of oldest red cell pack</th>
<th>Less than 15 days of age</th>
<th>15 to 28 days of age</th>
<th>29-35 days of age</th>
<th>36-42 days of age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percentage transfused</td>
<td>24%</td>
<td>49%</td>
<td>14%</td>
<td>12%</td>
</tr>
<tr>
<td>Number of transfusions &lt; 5 units</td>
<td>3524</td>
<td>7161</td>
<td>2115</td>
<td>1802</td>
</tr>
<tr>
<td>Septicaemia observed</td>
<td>33</td>
<td>102</td>
<td>52</td>
<td>71</td>
</tr>
<tr>
<td>Odds ratio</td>
<td>0.98</td>
<td>1.54</td>
<td>2.55</td>
<td>4.4</td>
</tr>
<tr>
<td>Confidence Interval.</td>
<td>0.65-1.31</td>
<td>1.34-1.74</td>
<td>2.26-2.84</td>
<td>4.16-4.64</td>
</tr>
</tbody>
</table>

Disclosures: No relevant conflicts of interest to declare

References


Key Findings

The Saline versus Albumin Fluid Evaluation (SAFE) study which was published in May 2004 looked at the use of albumin. The SAFE Investigators issued a subsequent report in 2007 of a post hoc follow-up study of patients with traumatic brain injury who were enrolled in the SAFE study. The study was a collaboration of the Australian and New Zealand Intensive Care Society Clinical Trials Group, the Australian Red Cross Blood Service, and The George Institute for International Health. The SAFE Investigators concluded that, in patients in the ICU, use of either 4% albumin or normal saline for fluid resuscitation results in similar outcomes at 28 days.

Following the conduct of a post hoc follow-up study in 2007 of patients with traumatic brain injury who were enrolled in the study, they concluded that fluid resuscitation with albumin was associated with higher mortality rates than was resuscitation with saline.

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The SAFE Study was a collaboration of the Australian and New Zealand Intensive Care Society Clinical Trials Group, the Australian Red Cross Blood Service, and The George Institute for International Health. The SAFE Investigators concluded that, in patients in the ICU, use of either 4% albumin or normal saline for fluid resuscitation results in similar outcomes at 28 days.

The study which was published in May 2004 noted that, “It remains uncertain whether the choice of resuscitation fluid for patients in intensive care units (ICUs) affects survival”. They conducted a multicentre, randomized, double-blind trial to compare the effect of fluid resuscitation with albumin or saline on mortality in a heterogeneous population of patients in the ICU. The SAFE Investigators randomly assigned patients who had been admitted to the ICU to receive either 4% albumin or normal saline for intravascular-fluid resuscitation during the next 28 days. The primary outcome measure was death from any cause during the 28-day period after randomization.

Of the 6997 patients who underwent randomization, 3497 were assigned to receive albumin and 3500 to receive saline; the two groups had similar baseline characteristics. There were 726 deaths in the albumin group, as compared with 729 deaths in the saline group (relative risk of death, 0.99; 95 per cent confidence interval, 0.91 to 1.09; P=0.87). The proportion of patients with new single-organ and multiple-organ failure was similar in the two groups (P=0.85). There were no significant differences between the groups in the mean (±SD)
numbers of days spent in the ICU (6.5±6.6 in the albumin group and 6.2±6.2 in the saline group, P=0.44), days spent in the hospital (15.3±9.6 and 15.6±9.6, respectively; P=0.30), days of mechanical ventilation (4.5±6.1 and 4.3±5.7, respectively; P=0.74), or days of renal-replacement therapy (0.5±2.3 and 0.4±2.0, respectively; P=0.41).

The study identified six predefined subgroups: patients with and without trauma, with and without severe sepsis, and with and without acute respiratory distress syndrome (ARDS). As a previous meta-analysis had suggested that trauma patients resuscitated with colloid solutions had higher mortality than those resuscitated with crystalloid solutions, trauma was a stratification variable in the study. Patients with severe sepsis and ARDS were identified at baseline to determine whether the increased capillary permeability to albumin seen in those conditions resulted in a treatment effect that differed from that seen in the study patients without those conditions. Within the predefined subgroups there was limited evidence of a treatment effect favouring saline in patients with trauma, and favouring albumin in patients with severe sepsis. The possibly detrimental effect of albumin in patients with trauma was limited to patients with evidence of traumatic brain injury, namely those patients admitted to the ICU as a result of trauma who had a documented, unsedated Glasgow Coma Scale score less than 14 and evidence of brain injury on cerebral computed tomography.

The investigators cautioned that such subgroup differences frequently occur by chance, and the accompanying editorial advised cautious interpretation of the subgroup findings. Thus, the study demonstrated that, in this heterogeneous population of adult ICU patients, albumin can be considered safe, without demonstrating any clear efficacy advantage over saline.

The SAFE Investigators subsequent report in 2007 noted that the Saline versus Albumin Fluid Evaluation study suggested that patients with traumatic brain injury resuscitated with albumin had a higher mortality rate than those resuscitated with saline. Following the conduct of a post hoc follow-up study of patients with traumatic brain injury who were enrolled in the study, they concluded that fluid resuscitation with albumin was associated with higher mortality rates than was resuscitation with saline.

Reference


Key Findings

Wong et al randomised 30 hospitals in Canada to either a blood conservation algorithm (BCA) or usual care (UC) in patients undergoing total hip replacement surgery and found that the blood conservation algorithm resulted in a significant overall 10.4% reduction in the allogeneic blood transfusion rate.

Details

Wong et al randomised 30 hospitals in Canada to either a blood conservation algorithm (BCA) or usual care (UC) in patients undergoing total hip replacement surgery and found that the blood conservation algorithm resulted in a significant overall 10.4% reduction in the allogeneic blood transfusion rate. The investigators developed a blood conservation algorithm involving patient and health care provider education, a treatment plan for erythropoietin (EPO) or preoperative autologous donation (PAD) based on preoperative
haemoglobin levels, and intra- and postoperative transfusion guidelines. Sixty consecutive patients at each participating institution undergoing primary elective total hip arthroplasty during the study period were evaluated. Results demonstrated that the mean allogeneic blood transfusion rate for the UC group of hospitals was 26.1% compared with 16.5% in the BCA group (P=0.02). For patients with a preoperative Hb level between 100 and 130 g/L, a group known to be at greater risk of transfusion, the mean transfusion rate was 47.6% in the UC group versus 24.6% in the BCA group (P=0.002). Cell salvage was used in 1.3% of patients in the BCA group compared with 19.6% in the UC group. Recombinant human erythropoietin (rHuEPO) use was significantly higher in the BCA group compared with the UC group (20.1% vs. 0.6%) while PAD use did not differ between groups (27.1% vs. 25.8%). Of interest, while the baseline Hb levels and intraoperative blood loss did not differ significantly between groups, the BCA group’s mean postoperative Hb nadir was significantly higher compared with the UC group (9.41 g/dL vs. 9.09 g/dL; P=0.04). The investigators suggest that the absolute relative risk reduction in allogeneic transfusion seen in this study may be a conservative estimate of the algorithm’s effect as the study was conducted on an intent-to-treat basis and all patients were evaluated, including those not managed according to the algorithm. They cite an example one hospital that applied the algorithm in only 19.6% of their patients during the study period.

Reference


Key Findings

A landmark Austrian national study benchmarked transfusion practice and evaluated blood conservation strategies in 18 hospitals. This study found wide variations in transfusion practice across participating hospitals and identified predictors of red blood cell transfusion that support the three-pillar concept of blood conservation as a means of reducing transfusions namely, 1) correct anemia prior to surgery, 2) minimize perioperative blood loss, and 3) adopt a lower transfusion trigger. They estimate that adequate preoperative management of anemia in their patient population may have reduced transfusion by 50%. As blood loss was the main predictor of transfusion, methods to minimize blood loss are highlighted as important blood conservation strategies. The authors also estimate from their benchmarking that, if the transfusion rates of the one third of the hospitals that reported the lowest blood usage were matched overall, a reduction in transfusion of up to 60% could be achieved. The investigators also identified blood ordering procedures as another area for potential cost and product savings. Crossmatching was performed routinely in all but one center. Sixty-one percent of crossmatched blood was not transfused. A more patient-specific blood ordering system, they suggest, could result in significant savings.

Details

A landmark Austrian national study benchmarked transfusion practice and evaluated blood conservation strategies in 18 hospitals. This study found wide variations in transfusion practice across participating hospitals and identified predictors of red blood cell (RBC) transfusion that support the three-pillar concept of blood conservation as a means of reducing transfusions. The study was a prospective observational study involving 18 randomly selected centers. Data was collected via a Web-based data capture system on consecutive patients at participating hospitals undergoing total knee replacement (TKR), total hip replacement (THR), hemicolectomy and coronary artery bypass graft (CABG) surgery. Of the 5326 patients captured, 3622 were finally included in the analysis (in
addition to patients not meeting study criteria, hemicolecotomy patients were excluded from analysis due to the small numbers). The study found high inter-centre variability in RBC transfusion in patients undergoing identical procedures. The percentage of patients transfused in centres ranged from 16 to 85% in THR, 12 to 87% in TKR and 37 to 63% in CABG. There was also a significant variation between centers in the number of units that transfused patients received. Overall, 53% of patients received a 2-unit transfusion, reflecting what the investigators suggest may be a transfusion habit. Postoperative haemoglobin (Hb) levels in the transfused patients were found to be higher than what is now generally employed. A large inter-centre variability in mean calculated blood loss was also observed, a variation the investigators state is difficult to explain. Additionally, there was considerable variation in the use of blood conservation strategies. Statistical analysis revealed lowest pre- and postoperative Hb and perioperative relative blood loss as the main predictors of transfusion. Overall, 19% of patients were anaemic the day before surgery. The authors suggest that the findings of this study support the three-pillar concept of blood conservation as a means of reducing transfusion namely, 1) correct anemia prior to surgery, 2) minimize perioperative blood loss and, 3) adopt a lower transfusion trigger. They estimate that adequate preoperative management of anemia in their patient population may have reduced transfusion by 50%. As blood loss was the main predictor of transfusion, methods to minimise blood loss are highlighted as important blood conservation strategies. The authors also estimate from their benchmarking that, if the transfusion rates of the one third of the hospitals that reported the lowest blood usage were matched overall, a reduction in transfusion of up to 60% could be achieved. The investigators also identified blood ordering procedures as another area for potential cost and product savings. Crossmatching was performed routinely in all but one center. Sixty-one percent of crossmatched blood was not transfused. A more patient-specific blood ordering system, they suggest, could result in significant savings.

Reference


Key Findings

In the United Kingdom, the (UK NHS) Health Service Circular Better Blood Transfusion Safe and Appropriate Use of Blood (HSC 2007/001) was issued in November 2007, detailing the actions required of NHS Trusts, NHS Blood & Transplant and clinicians to improve transfusion practice. It included an action plan and an ongoing programme for Better Blood Transfusion to be implemented in each Trust by November 2008, when the first national audit of compliance would be undertaken. The Report of the 2008 audit provides an excellent and encouraging example of the outcomes that can be achieved in national programs to improve transfusion practice and appropriate use in a consistent, effective way. The Executive Summary of the 2008 Audit Report is set out below:

Details

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### Background
The Health Service Circular Better Blood Transfusion Safe and Appropriate Use of Blood (HSC 2007/001) was issued in November 2007, detailing the actions required of NHS Trusts, NHS Blood & Transplant (NHSBT) and clinicians to improve transfusion practice. It included an action plan and an ongoing programme for Better Blood Transfusion to be implemented in each Trust by November 2008, when the first national audit of compliance would be undertaken.

### Methods
The survey was carried out in December 2008 and January 2009, and used an online tool for the first time for a Better Blood Transfusion survey. One collated response was requested from the Hospital Transfusion Team (HTT) in each Trust or Independent hospital. A PDF version of the survey was made available to download from the survey website to help facilitate discussion between members of the HTT before submitting a combined online response.

### Results
153/166 (92%) NHS Trusts and 33/59 (56%) of Independent hospitals responded to the survey. This was comparable to the 2004 and 2006 surveys, largely due to the efforts of the NHSBT Transfusion Nurse Liaison and Patients Clinical Teams in encouraging hospitals to complete returns. The key results included:

- 148/153 (97%) of NHS Trusts reported they had a Hospital Transfusion Committee which met at least 3 times/year.
- 85/152 (56%) of NHS Trusts have a lead consultant for transfusion with dedicated sessions for blood transfusion in their job plan, compared to 48% in the previous survey, indicating that 44% of HTTs do not have a lead consultant with sufficient time for involvement in transfusion activities.
- 146/152 (96%) of NHS Trusts have a Transfusion Practitioner, and this percentage is unchanged from the last survey in 2006. 26% of Trusts have 1.5WTE or greater number of Transfusion Practitioners in post.
- 149/153 (97%) of NHS Trusts reported they have a clear reporting line to senior Trust management, but 26% have not developed an action plan for transfusion safety and quality and 36% do not make an annual report to senior management as recommended in the Better Blood Transfusion action plan.
- 135/151 (89%) of NHS Trusts reported that their medical staff receive training in transfusion at their induction and at regular interval thereafter. The equivalent figure for nurses was 96%, phlebotomists 93%, and porters 79%. These figures are improved in comparison to the figures for regular training in the survey in 2006, which asked
- Participation in local and national audit has all increased. For example, 145/152 (95%) of NHS Trusts had carried out at least one local audit of transfusion in the last 12 months. 135/153 (88%) of the Trusts had participated in the national audit of bedside practice carried out by the Royal College of Physicians/NHSBT national comparative audit of blood transfusion programme in 2008. This audit found evidence of improved bedside practice, but there were still too many patients (3%) with inadequate identification i.e. without wristbands, and too many patients (10%) not being adequately monitored during transfusions.

- NHS Trusts were asked about progress with compliance with the National Patient Safety Agency (NPSA) Safer Practice Notice 14 Right Patient Right Blood. 147/152 (97%) reported they had started to implement an action plan for training and competency assessment, but only 12% have assessed 50% or more of their staff, which is a requirement by May 2009. Only 126/152 (83%) of NHS Trusts indicated that they were not using a compatibility report or the patients’ notes as part of the pre-transfusion bedside check. Only 59% had appraised the use of bar code patient identification and blood tracking. Only 13 Trusts were administering >10% of transfusions using bedside IT, and only 5 Trusts were taking >10% of blood samples for transfusion using electronic patient identification at the time of the survey.

- 143/152 (94%) of NHS Trusts have both laboratory accreditation from Clinical Pathology Accreditation (CPA) accreditation and participate in the National External Quality Assessment service (NEQAS) scheme. 141/152 (93%) have a certificate of compliance from the Medicines and Healthcare and products Regulatory Authority (MHRA) compared to 83% in 2006, and 86/153 (56%) have been inspected by MHRA compared to 21% in 2006.

- 96/152 (63%) of NHS Trusts have a blood conservation strategy but only 44 NHS Trusts have implemented a blood conservation strategy.

- The number of NHS Trusts with policies for blood usage was little changed from 2006, e.g. the use of red cell transfusions in surgery (58% in 2006 and 61% in 2008) and critical care (70% in 2006 and 67% in 2008), and the use of platelet transfusions in haematology (78% in 2006 and 74% in 2008).

- 98/152 (64%) of NHS Trusts have established local protocols to empower blood transfusion laboratory staff to query clinicians about the appropriateness of requests for transfusion against local guidelines for blood use.

- 135/150 (90%) of NHS Trusts reported they have written procedures for the prescription and administration for anti-D, and 124/149 (83%) indicated they have procedures for the traceability of anti-D.

- 147/150 (98%) of Trusts provide patients with written information, usually in the form of NHSBT information leaflets, but only 16% Trusts estimated that more than 50% of
transfused patients actually receive written patient information (these estimates were much higher in Independent Hospitals).

- 49% of NHS Trusts estimated they anticipated an increase in blood usage and 51% anticipated a decrease. Reasons for an increase included increased workload, increased complexity of care, and an ageing population. Reasons for a decrease included greater use of cell salvage, an increase in the use of electronic issue of blood, and implementation of lower blood count thresholds for transfusion.

- 143/147(97%) for NHS Trusts indicated that NHSBT provides a support network for HTCs and HTTs, for the provision of clinical and specialist advice, information and sharing of good practice. Specific comments were provided about what NHSBT does well and what it could improve. There was evidence of regional variation in the responses to most of the questions. The national and regional results are available on the National Blood Transfusion Committee section of www.transfusionguidelines.org.uk.

Conclusions

There has been good progress in the implementation of some but not all of the recommendations in the action plan of the HSC 2007/001 Better Blood Transfusion Safe and Appropriate Use of Blood. NHS Trusts indicated that key factors preventing implementation were inadequate staff for the HTT, transfusion is not a high priority for NHS Trusts and Strategic health Authorities, and compliance with the UK Blood Safety and Quality Regulations and the NPSA SPN 14 are significant competing demands for the HTT and blood transfusion laboratory staff. Key factors which would assist implementation included additional staff for the HTT, strengthening of the role of the HTT within NHS Trusts, and funding for electronic blood tracking.

The detailed results have been provided to Regional Transfusion Committees for wider dissemination in a format to allow comparison with other Regions. This information should be used to plan further local and regional initiatives to implement the Better Blood Transfusion action plan and improve transfusion practice.

Reference


Key Findings

Irving, et al studied iron management processes at six Australian dialysis units varying in size and locality. The study evaluated the outcomes of and barriers to implementing standard guidelines (Caring for Australasians with renal impairment [CARI]), using iron management in patients having dialysis. Irving found that there was considerable variability among the units in achievement of haemoglobin and iron targets. Implementation barriers included lack of knowledge, lack of awareness of or trust in the CARI guideline, inability to implement the guideline, and inability to agree on a uniform unit protocol. Factors associated with achieving the CARI guideline targets included nurse-driven iron management protocols, use of an iron management decision aid, fewer nephrologists per dialysis unit, and a “proactive”
actively keeping iron levels within target range) rather than “reactive” (only reacting if iron levels are out of the range) protocol.

Details

Irving, et al studied iron management processes at six Australian dialysis units varying in size and locality. The study evaluated the outcomes of and barriers to implementing standard guidelines (Caring for Australasians with renal impairment [CARI]), using iron management in patients having dialysis. The main outcome measures were the processes for assessing indices of iron stores and iron supplementation and comparison with target indices in the CARI guidelines.

Irving, et al found that there was considerable variability among the units in achievement of haemoglobin and iron targets, with 25%–32% of patients achieving haemoglobin targets of 110–120 g/L, 30%–68% achieving ferritin targets of 300–800 μg/L, and 65%–73% achieving transferrin saturation targets of 20%–50%. Implementation barriers included lack of knowledge, lack of awareness of or trust in the CARI guideline, inability to implement the guideline, and inability to agree on a uniform unit protocol. Factors associated with achieving the CARI guideline targets included nurse-driven iron management protocols, use of an iron management decision aid, fewer nephrologists per dialysis unit, and a “proactive” (actively keeping iron levels within target range) rather than “reactive” (only reacting if iron levels are out of the range) protocol.

The results of the Irving, et al study showed that the proportion of patients who were within or outside CARI target iron parameters for each unit were significantly different across the dialysis units. Also, each unit varied on each of the steps in the process pathway for iron management depending on local protocols. Further, practices differed widely from the CARI guideline and between the units. Most units agreed with the CARI guideline on the lower margin of the range for iron stores, but there was a tendency for all units in their local adaptation of the guideline to adopt a lower level for the upper limit for iron stores. Units also varied widely in the frequency with which iron studies were undertaken, as well as whether oral or intravenous iron therapy was administered and what dosages were used. Finally, the process for iron management was different for each unit. All units had a written iron protocol, but not all units complied with their protocol. Each staff member interviewed was aware of the CARI guidelines and the iron guideline disseminated in March 2000. Not all were aware that the website carries updates.

The Irving, et al study found that passive dissemination of the CARI guidelines in March 2000 resulted in awareness of the iron guideline, but also found significant variation in implementation of the guideline across the six dialysis units examined. All units had an iron management process in place; however, the variability of the levels achieved for the iron indices is a measure of the effectiveness of the process. An effective process seemed to depend on the strength of a unit’s local protocol and the staff available to drive the protocol processes.

In the Irving, et al study, identification of barriers was made at seven different levels of the organisations using the National Institute for Clinical Studies barrier tool. The “NICS Barrier Tool” was developed by the National Institute of Clinical Studies (NICS) to help health professionals identify the barriers to applying evidence and changing practice within

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Australian health care settings. The tool can be adapted for the particular situation. As an illustration, the ‘NICS Barrier Tool’ includes an example of the barrier tool being used to identify barriers to influenza vaccination in ‘at risk’ groups.

Research into effective methods for implementing clinical practice guidelines lags behind the research methods involved in producing guidelines. The Irving, et al study highlights the possible barriers to implementing the CARI guideline for iron, and shows that, in order to truly gain an understanding of which guideline implementation methods are most successful, controlled-intervention observational studies and completion of the quality cycle, with critical review of the achievement of targets, should be undertaken in renal medicine.

Passive dissemination of the CARI iron guideline raised awareness of the guideline, but Irving, et al said that improving iron management and patient outcomes would take commitment to change within the renal care team, an agreed iron protocol with a decision support aid, a working process for iron management, and skills improvement for renal nursing staff. Factors affecting iron management and barriers to change are numerous. For successful guideline implementation, a strategy to overcome these barriers in individual units should be planned and executed.

Possible barriers to successful implementation of the iron guideline were identified by Irving, M.J. et al as follows:
Nephrologist:
- Lack of awareness or knowledge of a guideline
- Lack of knowledge regarding iron requirements
- Lack of “trust” in the guideline
- Lack of ability to implement the guideline in own practice

Renal nurse:
- Lack of awareness or knowledge of guideline
- Lack of knowledge regarding iron requirements
- Has to follow/wait for instruction from nephrologist regarding iron management
- Possible increased workload
- Following up home dialysis patients

Patient:
- Not accepting iron as important
- Side effects from prescribed treatments
- Comorbid conditions may take precedence
- May be a home dialysis patient

Unit level issues:
- Large numbers of nephrologists working within the one dialysis unit
- Lack of agreement on iron targets among nephrologists
- Lack of effective iron protocol available for staff to follow
- Lack of care plan available for staff to follow for iron management

Management issues:
- May not realise that iron management is an issue
- Unaware of the reduction in relative cost of anaemia management with epoetin, by provision of adequate iron

Infrastructure issues:
- Increased nursing time to check laboratory results of iron studies
- Lack of computerised results
- Laboratories do not automatically send blood test results to dialysis units; nurses are required to access results for their patients
- Iron measurements come from a range of laboratories with different ordering processes and accessibility of results

Guideline:
- Lack of evidence for dosage requirements for iron management

Reference
Key Findings

A study by Grol said that the development and implementation of (evidence-based) clinical practice guidelines is one of the promising and effective tools for improving the quality of care. However the study noted that many guidelines are not used after dissemination. Further, implementation activities frequently produce only moderate improvement and it is therefore important to study specific guideline programs in detail to learn from their successes and failures.

Details

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- more than 70 evidence-based guidelines have been set in a rigorous procedure and have been spread via a variety of strategies. Knowledge and acceptance of the guidelines in the target group are high. In particular, a multifaceted approach with written (scientific journal, support materials) and personal approaches (local consensus discussions, contact with colleagues, outreach visits by peers) seems to be effective in the dissemination;

- the guideline recommendations are followed in on average 67% of the decisions, but there is a large variation between different physicians and between different guidelines;

- specific strategies designed to handle possible obstacles to implementation are needed to improve adherence. Specific implementation projects showed the importance of a ‘diagnostic analysis of the target group and target setting before the start of the implementation.’

Grol concluded that, ‘(the) program to implement a guideline should be well designed, well prepared, and preferably pilot tested before use. Such a program should be built into the normal channels and structures for improving care. More research into the details of implementation is needed to better understand the critical determinants of change in practice.’

Reference


Key Findings

A study in general practices in Norway by Flottorp et al looked at the challenges facing translation of clinical practice guidelines into actual practice. A process evaluation of a
cluster randomized trial of tailored interventions (antibiotic prescriptions, use of laboratory tests and use of telephone consultations) to support the implementation of guidelines for sore throat and urinary tract infection was undertaken to evaluate how the interventions were received and to understand why practices did or did not change. The study found little or no change in the main outcomes but there was great variation between practices in the extent of change in these outcomes.

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Data for the process evaluation were collected from the 120 practices that completed the trial. Multiple methods were used: observations, semi-structured telephone interviews, a postal survey and data extracted from electronic medical records. Flottorp et al investigated factors that might explain a lack of change, including: agreement with the guidelines; communication within each practice; degree of participation in the project; taking time to discuss the guidelines and their implementation; use of the components of the interventions; and routines for telephone consultations. Possible explanatory factors were explored in relation to variation in change and the overall extent of change in rates of use of antibiotics, laboratory tests and telephone consultations.

Sixty-three per cent of practices agreed with the guidelines. Only 35% reported having regular meetings, and 33% discussed the project before its start, although 75% reported agreement about participating within the practice. Only 33% reported meeting to discuss the guidelines. Use of the components of the interventions ranged from 11% for the increased fee for telephone consultations to 48% for the computerized decision support. Forty-four per cent reported problems with telephone routines. No single factor explained the observed variation in the extent of change across practices.

Flottorp et al concluded that inadequate time, resources and support were the most salient factors that might explain a lack of change. Problems with internal communication and telephone routines were important contributing factors in many practices.

Reference


Key Findings

In Australia, in early 2008, the National Institute of Clinical Studies (NICS) Stroke Clinical Reference Group was formed to develop an acute stroke care resource for use in emergency departments (EDs) in Australian hospitals. The NICS reference group used a care bundle approach to develop a guideline implementation tool based on specific recommendations
from the 2007 National Stroke Foundation (NSF) *Clinical guidelines for acute stroke management* relevant for ED care.

The reference group decided, by consensus, not to include thrombolysis and stroke unit care in the care bundle, as the necessary resources to support these are not universally available. However, the reference group believes that an emphasis on the first component of the bundle — a rapid initial stroke screen — could lead to earlier referral to stroke specialists and rapid access to computed tomography or magnetic resonance imaging to confirm the diagnosis and develop a management plan that would consider thrombolysis if clinically appropriate. This illustrates how the components of the care bundle may trigger additional best practice recommendations as a natural consequence and establish joint clinical decision making with other disciplines to improve patient care.

**Details**

In Australia, in early 2008, the National Institute of Clinical Studies (NICS) Stroke Clinical Reference Group was formed to develop an acute stroke care resource for use in emergency departments (EDs) in Australian hospitals — the account of the development and initial implementation of this tool was published by Weeraratne, JI et al in October 2010. The NICS reference group used a care bundle approach to develop a guideline implementation tool based on specific recommendations from the 2007 National Stroke Foundation (NSF) *Clinical guidelines for acute stroke management* relevant for ED care. Although these guidelines were already available, there are well known barriers to guideline implementation in the ED. These include increasing demand and acuity, and the broad diversity of clinical presentations.

The nine member NICS reference group was a collaborative between stroke and ED specialists, pre-hospital providers and managers of state-based stroke networks, with additional guidance from the NSF. The reference group used a Delphi process to reach consensus. In December 2009, the NICS released two documents — the *Emergency department stroke and TIA care bundle: information and implementation package* and the accompanying *Summary for clinicians*. These are available on the National Health and Medical Research Council (NHMRC) website (http://www.nhmrc.gov.au/nics/programs/emergency/stroke_tia.htm).

Care bundles have already been shown to improve guideline compliance and lead to improved patient outcomes in several settings, including the ED. A care bundle is


made up of a small number of best-practice recommendation components, is not as comprehensive as a guideline, and aims to identify critical recommendations relating to areas in which there is a significant practice gap or to act as a trigger to other best practice\textsuperscript{55}.

The NICS care bundle was designed to bring together several components to help clinicians provide quality care to adult patients who present to the ED with suspected stroke or transient ischaemic attack (TIA) by reducing morbidity and mortality and optimising patient outcomes (see Box 1 below). The criteria for a component’s inclusion in the care bundle were determined by the model developed by the Institute for Healthcare Improvement in the United States\textsuperscript{56}:

- each component must be based on sound evidence;
- the delivery of each component must need improvement;
- the delivery of each component must be achievable in terms of universally available resources;
- no component should be a major source of controversy; and
- the delivery of each component must be measurable.

The reference group decided, by consensus, not to include thrombolysis and stroke unit care in the care bundle, as the necessary resources to support these are not universally available\textsuperscript{57}. However, the reference group believes that an emphasis on the first component of the bundle — a rapid initial stroke screen — could lead to earlier referral to stroke specialists and rapid access to computed tomography or magnetic resonance imaging to confirm the diagnosis and develop a management plan that would consider thrombolysis if clinically appropriate\textsuperscript{58}. This illustrates how the components of the care bundle may trigger additional best practice recommendations as a natural consequence and establishes joint clinical decision making with other disciplines to improve patient care (see boxed text below).

At the time of publishing their Editorial in the MJA, the NICS clinical reference group was planning to collaborate with key stakeholders later in 2010 to evaluate the effectiveness of the care bundle, both as a format for providing specific guideline recommendations to a target audience and in terms of the impact on stroke care in the ED. Also, by that time, an


implementation plan and auditing tool had also been developed to assist in the uptake of the recommendations in the care bundle.
1 Components of the NICS care bundle

- Rapid initial stroke screen (grade C; level II)*
- ABCD² assessment¹ for suspected TIA (grade B; level II)
- Urgent‡ CT or MRI (grade A; level I)
- Nil by mouth until bedside swallow screen (within 24 hours) for stroke (grade C; level I)
- Aspirin as soon as possible,§ if haemorrhage excluded (grade A; level I): 150–300 mg one-time loading unless contraindicated
- Physiological monitoring and treatment
- Neurological status (grade C; levels II and III-2): regular monitoring to establish baseline and identify change
- Blood glucose (grade B; level II): cautious treatment of markedly elevated blood glucose levels; early, intensive maintenance of euglycaemia is not recommended. Avoid hypoglycaemia
- Blood pressure (consensus): cautious lowering by no more than 10%–20% if extremely high (≥ 220/120mmHg); monitor for neurological deterioration
- Hydration status (grade B; level II): maintain euvolement

NICS = National Institute of Clinical Studies. TIA = transient ischaemic attack. CT = computed tomography. MRI = magnetic resonance imaging. * Evidence-based grades and levels as per 2007 National Stroke Foundation clinical guidelines. † A seven-point score calculated from age, blood pressure, clinical features, duration of symptoms, and diabetes status. ‡ “Urgent” means as soon as possible, but certainly within 24 hours. § “As soon as possible” means within 48 hours. ¶ Recommended best practice based on clinical experience and expert opinion.
2 Application of the NICS care bundle*

Case study 1: a 68-year-old man presents to a hospital emergency department (ED), having woken with marked weakness of his left arm. Enquiry establishes that he was fine when he went to bed 7 hours earlier. The patient’s blood pressure (BP) at triage is 186/99 mmHg. The triage nurse is concerned that the patient is having a stroke.

Case study 2: a 74-year-old woman with a history of type 2 diabetes mellitus and hypertension presents to a metropolitan tertiary hospital ED. She is unable to speak and has no strength in her right arm or right leg. Her friend states that the symptoms started only 2 hours ago. The patient’s BP is 170/95 mmHg; her heart rate is 80 beats/min and the heart is in sinus rhythm; and her blood glucose level is 9 mmol/L.

The following care is provided for these patients, consistent with the use of the care bundle:

- as part of the patient’s assessment, and based on clinical findings, conduct a rapid initial stroke screen using a validated stroke screening tool to determine whether the patient is likely to have had a stroke. If a stroke is suspected, promptly refer the patient for expert stroke management — this may include referral to a stroke unit, or thrombolytic treatment (which is likely for the patient in case study 2);
- order an urgent computed tomography (CT) scan of the brain;
- ensure no oral intake until the patient undergoes a swallow screen for dysphagia;
- maintain hydration via intravenous or nasogastric fluids;
- administer aspirin (150 mg) within 48 hours if the brain CT scan excludes haemorrhage (if the patient in case study 2 proceeds to thrombolysis, delay aspirin treatment until 24 hours after thrombolysis);
- monitor the patient’s neurological status, blood glucose level, BP and hydration status to prevent further deterioration.

NICS = National Institute of Clinical Studies. *The NICS care bundle was written for the care of stroke patients while in the ED. If the patient is transferred out of the ED early in his or her care, it is anticipated that the remaining components of the bundle will still be provided in the new setting.◆
## Price Assumptions for Blood Demand Model

### PRICE INCREASES

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### Scenario Data Tables

**Projected Nominal Outlays by Scenario ($M)**

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<th>IVlg Medium</th>
<th>IVlg High</th>
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