Supporting Patient Blood Management (PBM) in the EU

A Practical Implementation Guide for Hospitals

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E-mail: SANTE-SOHO @ec.europa.eu

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Authors	Hans Gombotz, Axel Hofmann, Astrid Nørgaard and Peter Kastner
Expert reviews	This report was discussed with the experts of the teaching hospitals that were engaged in the European Patient Blood Management project: Kai Zacharowski, Patrick Meybohm, Suma Choorapoikayil (University Hospital Frankfurt, Germany), Astrid Nørgaard, Bo Hempel-Sparsoe (Rigshospitalet - University Hospital Copenhagen, Denmark), Klaus Markstaller, Arno Schiferer, David Baron (General Hospital / University Hospital Vienna, Austria), Branka Golubić Ćepulić, Anđela Babić, Tina Tomić Mahečić (University Hospital Zagreb, Croatia), Ivo Pires, Patrícia Conde, Lucindo Ormonde (University Hospital Santa Maria Lisbon, Portugal) and reviewed by the expert members of the Patient Blood Management project: Philippe Van der Linden (Brugmann University Hospital Brussels, Belgium), Shannon Farmer (Perth, Western Australia), Johann Kurz (Vienna), Jens Meier, Hannes Müller (Johannes Kepler University Linz, Austria).
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Abbreviations

ACD	Anaemia of chronic disease
AIDS	Acquired immunodeficiency syndrome
ALOS	Average length of stay
AR	Adverse reactions
CKD	Chronic kidney disease
CPOE	Computerised physician order entry
EU	European Union
ESA	Erythropoiesis-stimulating agent
FFP	Fresh frozen plasma
Hb	Haemoglobin
HBV	Hepatitis B virus
HCV	Hepatitis C virus
HIV	Human immunodeficiency virus
ICU	Intensive care unit
ICU-ALOS	Average length of stay in intensive care unit
IDA	Iron-deficiency anaemia
INR	International normal ratio
PACU	Post anaesthesia care unit
PBM	Patient Blood Management
POC	Point-of-Care
RBC	Red Blood Cells
TI	Transfusion index
TR	Transfusion rate
TRIM	Transfusion related immunomodulation
WA	Western Australia
WHO	World Health Organization

1 Introduction

1.1 Background

For many physicians and clinicians and across many different specialties, blood transfusion is still considered the first line treatment when facing anaemia and/or blood loss. In the European Union (EU), more than 5 million patients are receiving around 24 million units of blood or blood components each year (Annual Summary of the Reporting of Serious Adverse Reactions and Events, 2015, European Commission[1]). However, a large body of clinical evidence shows that in many clinical scenarios both anaemia and blood loss can be effectively treated with a series of evidence-based measures to better manage and preserve a patient's *own* blood, rather than resorting to a *donor's* blood, thus leading to a significant overall reduction of blood transfusions.

This is why over the last decade the focus in the EU, and elsewhere, has shifted from ensuring safety and quality of blood and blood components (product focused) towards a broader concept that takes a holistic, multi-disciplinary approach to caring for each patient's haematopoietic system in a manner that aims to ensure the best possible outcome (patient-focused). This widely accepted approach is referred to as Patient Blood Management (PBM).

According to the WHO, patient blood management (PBM) is a "patient-focused, evidence based and systematic approach for optimising the management of patients and transfusion of blood products to ensure high quality and effective patient care" (1). In 2010 the World Health Assembly Resolution WHA63.12 endorsed PBM specifically referring to the three-pillar concept *"bearing in mind that patient blood management means that before surgery every reasonable measure should be taken to optimise the patient's own blood volume, to minimise the patient's blood loss and to harness and optimize the patient-specific physiological tolerance of anaemia"* (2). The resolution urges WHO Member States to promote PBM where appropriate. It also requests the Director General of the WHO to provide guidance, training and support to Member States on safe and rational use of blood products and to support the introduction of transfusion alternatives and PBM.

In March 2011 the WHO organised the "Global Forum for Blood Safety: Patient Blood Management" in Dubai, stating in its Concept Paper that "Patient blood management (PBM) is designed to improve patient outcomes through the safe and rational use of blood and blood products and by minimizing unnecessary exposure to blood products. Essential elements of patient blood management include: the prevention of conditions that might otherwise result in the need for transfusion (through health promotion and screening for early detection), appropriate diagnosis and optimal treatment, including the use of alternatives to transfusion, good surgical and anaesthetic techniques and blood conservation." The attendees also sought to assess the current challenges in implementing PBM programmes and to identify mechanisms for improving the impact of PBM programmes (3).

The modern patient blood management (PBM) concept is an evidence-based, multidisciplinary, multi-modal therapeutic approach to individually manage and preserve the patient's own blood in surgical and non-surgical settings (4-6). Contrary to the traditional product-focused approach of Optimal Blood Use programmes, PBM takes a patient-focused approach. This is achieved by sustainably preventing and

correcting anaemia, preventing blood loss and harnessing and optimising the physiological tolerance of anaemia. Thus, unnecessary transfusions are reduced or avoided and patient safety and outcome are improved.

The high prevalence of untreated pre-operative anaemia, the unmet need for improved bleeding management and a liberal transfusion practice, point towards huge potential to improve outcome and avoid millions of transfusions each year (7). This is driven by ongoing patient safety issues such as new and re-emerging risks from infected donor blood, inventory pressures/product shortage leading to delays in surgeries, and above all, the mounting evidence on adverse outcome due to anaemia, blood loss and transfusion (8-10). The findings from a growing number of large observational studies and randomised controlled trials strongly suggest avoiding each unnecessary transfusion to reduce morbidity and mortality (11-16). Thus, in recent years, a growing number of publications support the benefits and cost-effectiveness of PBM. In addition, these issues are increasingly addressed in postgraduate educational and training programmes (17-29).

In the EU, the change in approach from 'product focused' to 'patient focused' first led to an EU Public Health funded project entitled EU Optimal Blood Use (30) which explored blood transfusion processes, making recommendations to ensure the safety, clinical effectiveness and efficiency of blood transfusions. A Manual of Optimal Blood Use was developed by transfusion experts from 18 EU countries and is available in 9 languages. Subsequently, several national PBM programmes were developed including Better Blood Transfusion in Scotland (31), PBM by NHS Blood and Transplant (NHSBT) in England (32), initiatives in Italy (33, 34) and in four University hospitals in Germany (35).

In other parts of the World also, an increasing number of leading organisations and transfusion medicine specialists support the PBM concept, including the American Association of Blood Banks (36). Experience in Australia and New Zealand has shown that, although PBM was first developed in elective surgery, the principles can also be applied to emergency surgery, trauma, medical settings and obstetrics (27, 29, 37-43). Furthermore, the effect of PBM on transfusion utilisation is not confined to red blood cells. Its principles can be extended to pre-empt the transfusion of platelets, fresh frozen plasma and other blood products that also carry risk.

In recognition of the important role of PBM in promoting patient safety and improving clinical outcomes, the European Union (EU) Public Health Programme called for tenders in 2013 for a service contract that would support the progress of PBM in the EU. The contract was awarded to a team led by the AIT Austrian Institute of Technology GmbH.

This PBM Implementation Guide for hospitals was delivered to the European Commission under that contract. An equivalent guide for authorities on developing national PBM programmes was also developed under the contract. These guides have no regulatory or legally–binding status but are intended as tools to support hospitals and authorities in EU Member States in establishing PBM as a standard to improve quality and safety of patient care. In order to ensure appropriate and optimal use of blood and blood components (5, 6), transfusion decisions should always adhere to current evidence-based guidelines, and be taken after careful evaluation of a variety of patient-specific and patient-group-specific factors.

1.2 The purpose of this guide

This PBM implementation guide was developed as a supporting tool for hospitals in the implementation of PBM at the operational level. It has taken inspiration from successfully implemented programmes in different parts of the world, recommending a well-recognised model for introducing change. It is acknowledged that alternative change management models could also be applied successfully.

The guide focuses on how to implement the PBM concept in hospitals in a practical way, building on already recognised best practices (44-47). It does not aim to review the clinical evidence for PBM or to provide clinical PBM guidelines**.** A substantial list of publications that provide the rationale for PBM and that define good clinical practice supporting PBM is included at the end of this document.

This guide is the result of the combined expertise of an international, multidisciplinary team of clinicians and PBM professionals and the collective experience gathered from a 30 month pilot programme for the implementation of PBM in five European teaching hospitals. The final goal is to support PBM as a sustainable standard of care across the EU.

Given the multi-disciplinary and holistic approach required for PBM implementation, the guide is relevant for all medical professionals and organisations involved in caring for patients suffering from anaemia, blood loss and medical conditions that might require transfusion. It should stimulate hospital management to invest greater efforts in the evaluation and treatment of patients with low iron status prior to admission or surgery and should encourage transfusion stakeholders to take a fresh look at their professional fields and discover new opportunities for safely reducing the transfusion rate in their hospitals.

1.3 Utilization of allogeneic blood products in European countries

The utilization of allogeneic blood products in European countries has been analysed and reported in a study conducted as part of the EU-PBM service contract. Overall, a remarkable variability between countries in issuance figures per 1,000 population has been observed. As an example, Figure 1 shows the inter-country variability of RBC units issued per 1,000 population from 2011 and 2012. The median for all countries in 2012 (ES and NO with 2011 data) was 38.8 RBC units issued per 1,000 population with a standard deviation of ±11.9 units. The relative variability of platelet units and fresh frozen plasma units issued lies in the same range.

In many countries (AT, BE, CZ, DK, IE, LU, NL and UK) a continuous reduction in RBC usage can be observed over the past five to ten years. Notably, the Netherlands, although already having the lowest per capita use of all three major allogeneic blood products, still shows a reduction in issuance figures. This may be the result of a successful cultural change towards PBM. According to a survey article published in 2012, the Netherlands has PBM strategies in place, at least for major elective surgery (48); it represents a good example of a country where PBM related measures have been successfully implemented. Ireland has also shown remarkable reductions in terms of RBC issuance resulting from initiatives to improve blood stock management and increased monitoring of usage indicators.

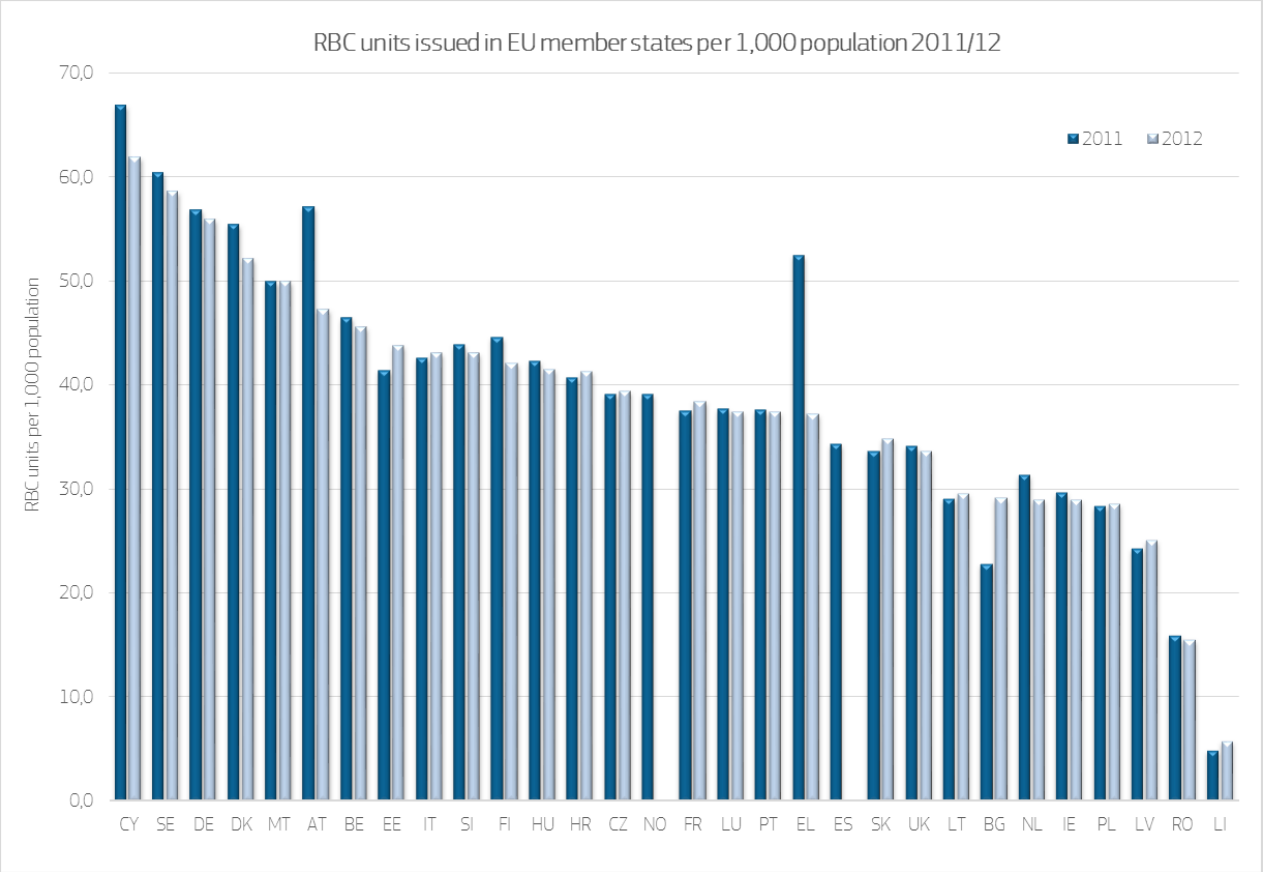

Figure 1. RBC issued per 1,000 population 2011 and 2012 in European countries

The large inter-country transfusion variability per 1,000 population across Europe may be partly explained by different characteristics of national health care systems. However, numerous studies have also shown that significant national and international inter-centre transfusion variability for standard procedures in matched patients is highly prevalent. This variability has been shown also in other parts of the world (49-53). In addition the percentage of RBC units that are transfused to surgical patients is now much lower than for medical patients and suggest that PBM initiatives should increasingly focus on medical patients and in particular on haematology patients (41, 42).

Overall data collected on utilisation show that the implementation of PBM across Europe has the potential to remarkably reduce the usage of allogeneic blood products (29, 54, 55). Based on the international literature, a targeted and careful administration of blood and blood components can be expected to lead to a significant reduction in the usage of allogeneic blood products, and at the same time significantly improve patient safety and outcomes.

2 Stakeholders, their roles and responsibilities in the implementation of PBM at the hospital level

A stakeholder is "one who is involved in or affected by a course of action" (56), "a person, group or organisation that has interest or concern in an organisation" (57) or "a person with an interest or concern in something, especially a business" (58). Stakeholders can be categorised as key, primary and/or secondary stakeholders:

- **Key stakeholders** are individuals or groups who can significantly influence the course of action. They are also described as key players or champions. They develop or have a high level of power and interest in the course of action.
- **Primary stakeholders** are those ultimately involved in or affected by a course of action.
- **Secondary stakeholders** are individuals or groups that have a role in the decision-making in the course of action without being directly impacted or being impacted to a lesser degree.

In general, active stakeholder involvement can have a positive (supportive) or negative (obstructive) impact. Likewise, passive stakeholders can be affected positively or negatively by the course of action.

In a broader sense, a PBM stakeholder is an individual or group involved or affected by establishing PBM as a new paradigm in the field of medicine. When confined to a regional health system or a hospital, a PBM stakeholder is an individual or group involved or affected by establishing PBM as a new standard of care in this particular health system or hospital. For instance the newly appointed head of the department of anaesthesiology and intensive care has identified sufficient support from some of his team members to introduce PBM as the new standard of care. As programme champions they embark on their change management mission, recruiting more clinical staff members. In understanding the need for change and the potential benefits, some orthopaedic or cardio-thoracic surgeons might join as primary stakeholders while others might oppose for various reasons. Whether opposition will be successfully overcome and the new standard will be anchored in the hospital's culture heavily depends on the level of adherence to the change management principles discussed hereafter.

The following section solely relates to stakeholder roles and responsibilities in the implementation of PBM in clinical institutions.

2.1 Key stakeholders in the implementation of PBM at the hospital level

2.1.1 Demanding patients and responding clinicians – key stakeholders of the first blood conservation initiatives

Many of the early Blood Conservation programmes, the predecessors of PBM programmes, were initiated through patients who declined blood transfusions for personal reasons. These patients pro-actively looked for individual physicians offering surgical and/or medical treatment options without the use of allogeneic blood components. Numerous physicians around the world responded favourably to this request and, in some clinical centres, were joined by their colleagues. These small groups began offering their

professional services on a regular basis, thereby establishing the first blood conservation centres (59, 60). Over time, some of these developed further and became large, internationally recognised PBM centres (61-64).

The key stakeholders driving these developments were a specific group of patients with a particular need and individual clinicians that agreed to help them. The approach they developed in the early 1990s is now considered by many professionals to be a standard of care that should be available to all patients facing a medical or surgical intervention with a potentially significant blood loss or being profoundly anaemic (65).

2.1.2 Current and future roles of patients, patient organisations and physicians as key PBM stakeholders

In order to make PBM the new standard of care, it is necessary to build on the early successes of the blood conservation programmes outlined above. The key stakeholders to achieve this goal are primarily clinicians, such as department heads, who both have a professional interest to implement this new method of care and sufficient power to do so (see Table 1). The current evidence on anaemia, blood loss and transfusion as independent predictors for adverse outcomes (19, 20, 66-73), the precautionary principle, and the principle of non-maleficence ('primum non nocere') are compelling reasons to take action to sustainably implement PBM, and to formally and informally disseminate and support the concept within their other spheres of influence. Their primary role is to lead the practice change within their own clinical departments.

Table 1. Roles and responsibilities of key PBM stakeholders

Key PBM stakeholders	Roles and responsibilities
Clinical department heads	• Taking the clinical lead to implement PBM as the hospital's standard of care • Educating peers about PBM • Disseminating PBM guidance based on peer-reviewed evidence • Recruiting more champions • Networking active primary stakeholders • Ensuring continuity and sustainability of PBM
Patient organisations	• Giving patients a "voice" • Publicly formulating the need for PBM to improve patient safety and outcome
Transfusion medicine departments/hospital blood bank heads, blood services	• Taking the clinical lead to implement PBM as the hospital's standard of care • Educating peers about PBM • Disseminating PBM guidance based on peer-reviewed evidence, • Taking the lead in restructuring of hospital blood bank to meet changing transfusion needs • Expanding from transfusion consultation to PBM consultation with appropriate training where necessary

As the evidence for the benefit of PBM and the risk of transfusion are more broadly communicated through secondary PBM stakeholders (e.g. government agencies, media doctors and medical journalists), an increasing number of patients/consumers are likely to seek treatment options without transfusion. Factual (evidence-based) and targeted public communication on transfusion and PBM is required. Once this kind of public information and education reaches critical mass, patients are able to make an informed treatment choice and patient advocacies/organisations can become key stakeholders and push for a rapid clinical implementation of PBM. Patients should be supported and educated in a way that they might be enabled to become key PBM stakeholders. As an example, a fact sheet of the Western Australia Department of Health informs the public about the state's PBM Programme (74).

Actions to be taken

PBM fact sheets and patient information should be issued by public health authorities to help patients get educated on PBM. They should encourage patients facing a medical or surgical intervention to ask their general practitioner questions like:

- Am I anaemic or are my iron levels low? If so, how can it be treated before my procedure?
- Are there any medications, herbal or vitamin supplements I should stop taking before my procedure?

When meeting a specialist, patients should be encouraged to ask:

- Is there a possibility of blood transfusion in my planned procedure?
- Besides the risk of infection, are there other complications from transfusion that I should be aware of?
- What options are available to help me to avoid a transfusion in my procedure?
- If a blood transfusion becomes necessary, can you limit the amount of blood you give me?

2.1.3 Transfusion medicine specialists as key stakeholders at a crossroads

Transfusion medicine specialists and/or laboratory physicians are often the heads or chief administrators of hospital blood banks. The implementation of PBM programmes can lead to significant reductions in the hospitals' blood utilisation. This may have economic consequences for hospital blood banks and regional blood services. Finding themselves at a crossroads, they must either downscale the transfusion medicine department, by adjusting the infrastructure and personnel, or align the department's activities to new activities/services, for instance within the scope of PBM. Blood centres might also choose to consolidate and merge with other centres within certain geographical areas.

As an example the department of anaesthesiology and intensive care at the General Hospital Linz, one of Austria's largest public hospitals, initiated a PBM programme in 2005. Over a period of six years clinicians reduced blood utilisation by 60 - 70% (75) (see 4.3.1 page 45).

2.2 Primary PBM Stakeholders

Actions to be taken
All primary stakeholders – including patient representatives, physicians, nurses, perfusionists, clinical pharmacists, hospital administrators, IT administrators) should be addressed and actively integrated into the multidisciplinary PBM team as further elaborated in Step 2 – "Form a powerful PBM Group" (see 3.2.2 page 31)

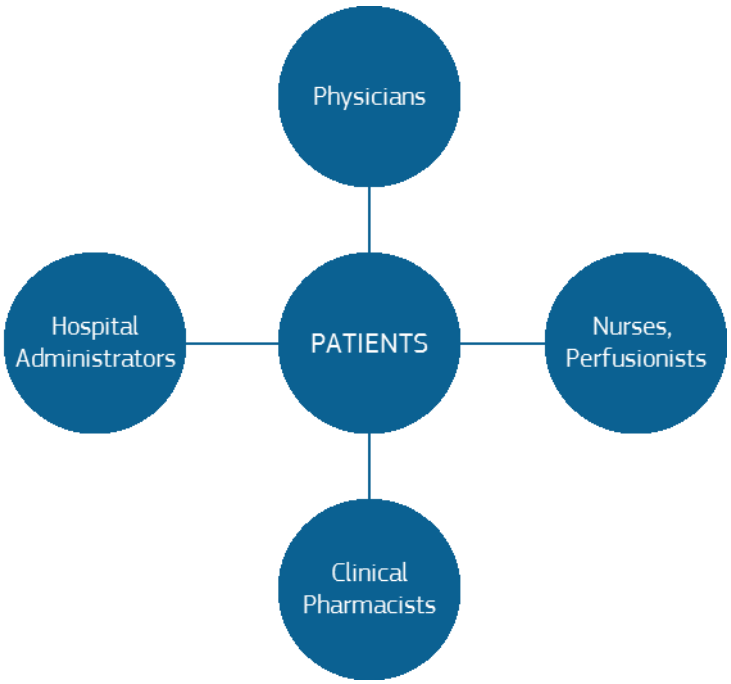

Figure 2. Primary PBM Stakeholders

2.2.1 Patients

Although most patients do not yet have the awareness to take on a role as *key* PBM stakeholders, they are clearly *primary* PBM stakeholders because they are personally affected by PBM as a new standard of care. The most affected patient groups are:

- Bleeding patients
- Anaemic patients
- Iron deficient patients
- Patients at a high risk of major blood loss
- Patients with bleeding disorders

These patients receive the vast majority of RBCs, platelets and FFP. Blood transfusion was the most common procedure performed during hospitalisations in 2011 in the United States; with 2.93 million counts or 94 per 10,000 population (12% of stays with a procedure) (76). Assuming that a similar rate can be applied for the European Union, an estimated 4.8 million acute-care inpatients receive blood

component transfusions. Once educated on why PBM is beneficial for them, a large proportion of patients could become primary PBM stakeholders and pro-actively discuss their PBM options and treatment plan with their general practitioner and clinicians.

2.2.2 Physicians

Physicians are clearly primary PBM stakeholders. They are intimately involved in the course of action because they have to change practice and sometimes behaviour (77). Managing the patient's blood or circulatory system, according to the three-pillar-principle of PBM, requires them to understand and follow peer-reviewed PBM guidelines, and apply related algorithms[1]. This might also necessitate structural changes and additional workflows, i.e. instituting a pre-operative anaemia clinic, a well-established point-of-care coagulation management, routine use of cell-salvage when indicated, etc.

All physicians at an institution should be aware of the PBM implementation process. Physicians who regularly treat patients at risk of or with major blood loss and/or anaemia (and with empirically high blood product prescriptions) are very important stakeholders. Each has the potential of becoming a PBM champion. Department heads have the means and power to make PBM a new standard of care. Those in senior positions can influence and network in favour of PBM.

The following professions regularly deal with patient populations as described under 2.2.1:

- Anaesthesiologists
- Intensive care specialists
- Transfusion medicine specialists/laboratory physicians
- Surgeons
    - cardio-thoracic
    - orthopaedic
    - vascular
    - visceral/abdominal
    - transplant
    - general
    - trauma/emergency
- Internists
    - Haematologists
    - Gastroenterologists
    - CardiologistsOncologists
- Obstetricians and gynaecologists

Although not always the case, anaesthesiologists are often responsible for transfusion decisions in the operating theatre and, over a period of ≤ 4hrs, in the post anaesthesia care unit (PACU). In tertiary hospitals, most blood components are transfused in intensive care units [up to 40% of the total units transfused; unpublished data, Western Australia PBM Project]. Therefore, anaesthesiologists and intensive care specialists are primary stakeholders in the implementation of PBM (in some countries,

[1] see 5 "Identification of good practices in PBM" in deliverable 2 EU-PBM Project – Study and Survey report

anaesthesiologists are also intensive care specialists). Their departments have a central role in implementing PBM across their entire institution. Often a PBM programme's champions/key stakeholders are working in these departments. Pre- and peri-operative anaemia management, (systemic) bleeding management, and measures to optimise oxygenation while reducing metabolic demand are usually in the professional domain of these experts. These treatment modalities represent major elements of the three pillars of PBM. Therefore, these two groups of professionals are strong *primary* PBM stakeholders.

PBM strongly impacts the role of transfusion medicine specialists and/or laboratory physicians in the hospital blood bank (see 2.1.3). In some hospitals they may even represent the *key* PBM stakeholders. This has the advantage that they can restructure their department in the most controlled way. They can also support PBM by promoting and scrutinising strict adherence to transfusion guidelines and a single-unit transfusion policy. They can further support post- and under-graduate PBM education programmes with emphasis on transfusion risks and outcomes. They can also support basic PBM benchmarking of transfusion rates and indices (often hospital information systems and hospital blood bank information systems are not or only partly interfaced; in the early implementation phase of hospital PBM programmes, the electronic hospital blood bank system is sometimes the only available source for: total transfusion numbers, transfusion per ordering physician, pre-transfusion haemoglobin measures, and other important baseline data to measure and monitor the progress of the PBM programme). With the implementation of PBM the hospital blood bank will most likely encounter significant reductions in pre-transfusion testing (cross matching, antibody search, etc.). This decrease in activity might be partly compensated by regularly measuring other laboratory parameters, i.e. iron status of anaemic patients.

Cardio-thoracic, orthopaedic, vascular, visceral/abdominal, general, transplant and trauma/emergency surgery are often associated with high blood loss and high transfusion variability[2]. Surgeons in these fields are *primary* PBM stakeholders. Many still need education on transfusion no longer being the default position, and that the circulatory system/patient's own blood volume should be treated with the same care and diligence as every other body system. Their course of action change is ultimately affected by putting more emphasis on surgical bleeding control that includes a number of modalities from the second pillar of the PBM concept. They might also have to learn that anaemia in many of their elective patients is a contraindication for surgery.

Gastroenterologists are often dealing with anaemic patients due to chronic bleeding. Cardiologists sometimes encounter unintended bleeding events/haemorrhage in the course of percutaneous coronary interventions (PCI). Haematologists and oncologists are regularly dealing with chemotherapy and cancer induced anaemia; oncology patients are often undergoing major surgeries with potentially high blood loss. The course of action of these specialists is ultimately affected by PBM, urging them to apply the precautionary principle and the principle of non-maleficence - primum non nocere -, and not transfusing their patients by default.

[2] see 2.1.5 "Transfusions by specific operations or procedures" in deliverable 2 EU-PBM Project – Study and Survey report

2.2.3 Other health professionals

Due to their close daily working relationship with physicians who are *primary* stakeholders in PBM, a number of other health professionals are also ultimately involved in or affected by the course of action.

- Perfusionists
- Intensive care nurses
- Theatre nurses
- Ward nurses
- Transfusion nurses.

Perfusionists are ultimately affected by facilitating/enabling low-prime perfusion to reduce RBC utilisation. Intensive care nurses and theatre nurses are affected by the protocols for minimisation of iatrogenic blood loss (restricted phlebotomy through smaller samples and reduced sampling frequency). They have to closely monitor and quickly report bleeding events, particularly in coagulopathic patients and patients with increased bleeding tendency. They may also need to get used to the concept of transfusion decision points, looking at symptoms rather than numbers (haemoglobin, haematocrit) (78).

Ward nurses might be affected by new and more restrictive blood ordering schedules. Transfusion nurses are affected by the reduction of transfusion rates, but might monitor intravenous iron infusions instead.

2.2.4 Clinical pharmacists

Clinical pharmacists interact directly with physicians to ensure that the medications prescribed contribute to optimal health outcomes (79). The implementation of PBM ultimately impacts on the clinical pharmacist's portfolio of products, mainly drugs and medications. Purchasing volumes for haematinics, hyperfibrinolytics, and factor concentrates are likely to increase; whereas volumes for RBCs, platelets, FFP and pre-transfusion test assays are likely to drop. As long as all these products are under the same hospital pharmacist's budget control, the overall impact of PBM is expected to be favourable and change management will easily be supported by the pharmacy.

2.2.5 Hospital administrators: Reallocation of resources to improve effectiveness

Hospital administrators and executives are *primary* PBM stakeholders because they are ultimately affected by the course of action. They include the:

- Administrative director
- Chief financial officer (CFO)
- Medical director / Clinical governance
- Medical director
- Nursing director
- Risk and Quality Assurance Manager
- IT Manager

Mastering financial challenges and reaching satisfactory quality and safety levels are top priorities for health executives and hospital administrators. From their perspective, the five most important parameters to control are:

- Cost

- Mortality rates
- Complication rates
- Readmissions
- Average length of stay (ALOS)

An increasing number of studies show significant reductions in mortality, complications, readmissions, ALOS and cost with PBM and blood conservation programmes (19, 28, 35, 80-88). Once hospital administrators have understood the positive impact PBM can have on their institutions' financial results (in addition to improved patient outcomes) – regardless of whether the organisation follows a cost minimisation or a profit maximisation model – they are expected to fully support the change management process (89), and facilitate the following four tasks:

- Providing PBM infrastructure
- Establishing continuous PBM benchmarking and reporting systems
- Instituting PBM related educational programmes
- Proactively offering PBM to medical and surgical patients

Actions to be taken
Based on expected savings of direct and indirect costs from sustainable implementation of PBM the hospital administration should support the PBM guiding coalition with necessary resources.

2.3 Implementation tasks to enable PBM

2.3.1 Providing PBM infrastructure

The PBM infrastructure for a hospital is the basic organisational framework needed to develop and maintain PBM as a standard of care. It includes human resources, equipment and technology, third party services and workspace. This involves decisions and support from all hospital directors and the CFO in their roles as *primary* stakeholders. It requires establishing a:

- PBM organisation with (77, 86)
    - Formal structure (organisational chart)
    - Duties and responsibilities (job descriptions)
    - Multidisciplinary PBM committee (this could be established by reorganising and extending the role of the existing hospital transfusion committee, along with the haemovigilance committee/contacts if they are separate)
    - Full time equivalents (FTEs) and salaries
- Pre-operative anaemia clinic (75, 90, 91)
- Point-of-care bleeding management system (92-94)
- PBM information system (see 2.3.2) (95)
- Computerised physician order entry (CPOE) system for blood components (96-98)
- Microsampling systems (99)
- PBM and transfusion audits (77)

Given the short to mid-term returns on investment, most investments should be made available through reallocation of resources or departmental budgets.

2.3.2 Establishing continuous PBM benchmarking and reporting systems

One of the most important structural PBM measures chief hospital administrators are responsible for is the introduction and implementation of a continuous benchmarking and reporting system. Systematic measurement is essential for improvement (*"If you cannot measure it, you cannot improve it"*, Lord Kelvin). The multidisciplinary PBM committee (see 2.3.1 above) would use the data generated by such a system on an ongoing and continuous basis. During the implementation period, comprehensive support from the IT department is necessary. Depending on the size of the organisation and the PBM programme, the support needed may reach one or even two FTEs over a 12-month period and coordination with the human resources department may be indicated.

In a fully developed PBM benchmarking and reporting system, transfusion data are routinely linked to data from a variety of other domains like: demographic data, patient outcomes data, departmental performance data and sometimes physicians' performance data.

Since most of these data are typically subject to data protection regulations, proper pseudo- or anonymisation is required. From the start, governance and legal requirements as well as aspects of data collection and privacy protection measures must be taken into account. These need to be communicated to and documented for all stakeholders of the benchmarking process. This issue usually requires input and clearance from the legal department, the ethics committee/internal review board and, as far as physician performance data are concerned, support from the human resources department.

Actions to be taken

1. Establishing a continuous reporting system for internal benchmarking.
2. Once the internal information system has reached its operational stage, a subset of the data collected for internal benchmarking should be sent to a cross-institutional benchmarking site to assess the performance as compared to peer programmes in other healthcare organisations.

Stage 1: Measuring transfusion rate (TR) and transfusion index (TI) as an inverse function of PBM
Stage 2: Collecting patient-level data on anaemia and its treatment
Stage 3: Collecting patient-level data on calculated perioperative blood loss
Stage 4: Measuring outcome data comparing patients with transfusion and with PBM

(details see below)

Stage 1: Measuring transfusion rate and index as an inverse function of PBM

The key performance indicators (KPIs) are:

- **Transfusion rate (TR)**: the percentage of transfused patients with a defined patient cohort of patients

- **Transfusion index (TI)**: the mean number of units per transfused patient within a defined cohort of patients

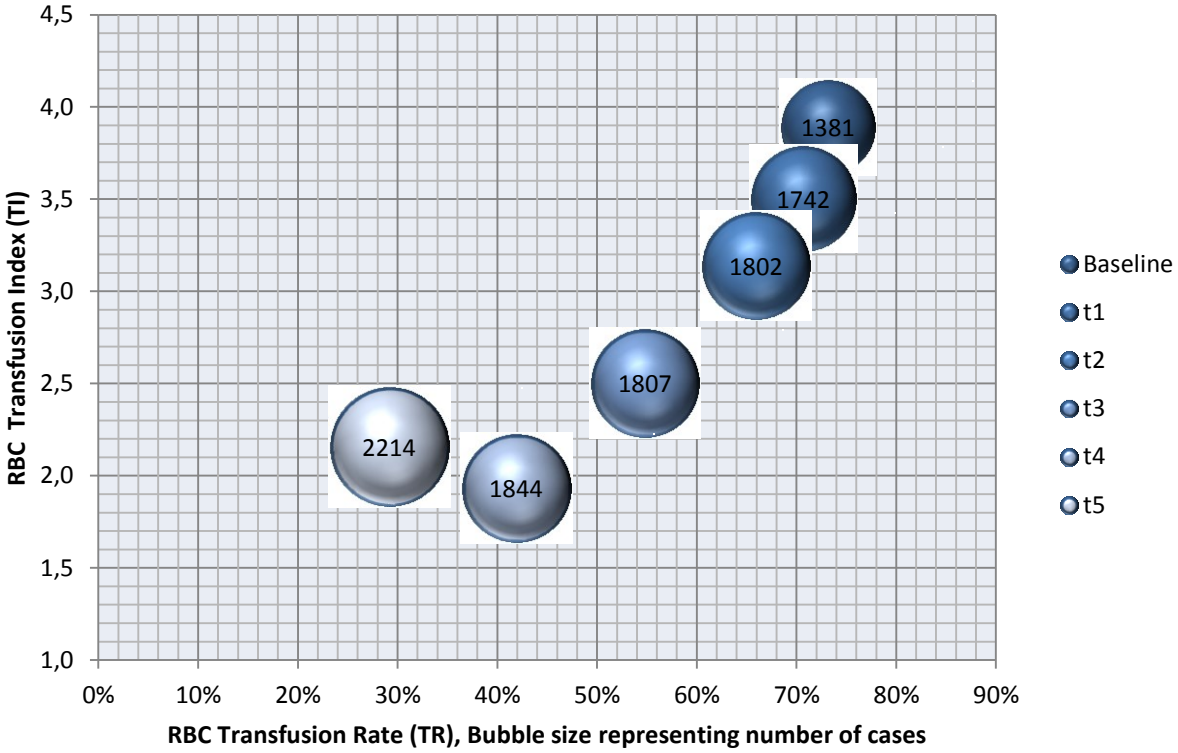

Figure 3. A fictitious example of a dynamic bubble diagram with transfusion rates (TR), transfusion indices (TI) and number of patients in observed cohort. Bubble size represents the number of cases (100, 101).

The literature suggests using bubble diagrams with the relative bubble sizes representing the number of procedure-specific inpatient admissions or patients of a pre-defined cohort; the position of the bubble representing the transfusion rate (TR) on the x-axis and the mean transfusion index (TI) on the y-axis. The different colours help to identify the developmental path over time. The graph can be used per:

- Surgeon
- Prescribing clinician
- Department
- Hospital/hospital system
- State

These KPIs can be monitored for RBCs, platelets, FFP and also for cryoprecipitate (where in use). The reduction of TR and TI can be used as inverse PBM performance indicators.

Stage 2: Collecting patient-level data on anaemia and its treatment

It is also recommended to monitor the incidence and treatment of anaemia prior to surgery, particularly in patients undergoing high risk procedures. Even mild anaemia is an independent predictor of adverse

outcomes (102-106) that should be corrected by treatment modalities of the 1st pillar of PBM. Thus, it is necessary to collect (anonymised) patient-level data on:

- Haemoglobin concentration at the patient's first visit of the pre-op anaemia clinic
- Pre-operative haemoglobin concentration (after anaemia correction)
- Post-operative haemoglobin concentration, preferably between post-op days 3, 4 or 5 (107, 108)

In transfused patients, it is important to capture data on:

- Pre-transfusion haemoglobin concentration
- Post-transfusion haemoglobin concentration

When linked with stage 1 data, over-transfusion and non-compliance with single-unit transfusion policies of clinicians, departments etc. may become apparent. Analogous to this, platelet counts pre- and post-platelet transfusions, and international normal ratios (INR) pre- and post-FFP transfusions should be collected.

In benchmarking these performance indicators, the risk of under-transfusion, as with all risks associated with the implementation of a significant change in practice, should not be ignored and should be monitored. It is acknowledged, however, that the risk of undertransfusion is reportedly significantly less than the risk of overtransfusion (109-119).

Stage 3: Collecting patient-level data on calculated perioperative blood loss

Monitoring the incidence and volume of perioperative blood loss, particularly in procedures with empirically devised high blood volume losses is also recommended. Blood loss is another independent predictor for adverse outcomes (120-126) and should be corrected by treatment modalities of the 2nd PBM pillar. Using the Mercuriali-algorithm (107), perioperative blood loss can be calculated using the following variables:

- Pre-operative circulatory volume derived from body weight and height (127)
- Pre-operative haemoglobin concentration, and
- Post-operative haemoglobin concentration

In transfused patients the result can be corrected for units transfused (from linking with stage 1 data) and in cell-salvaged patients it can be corrected for salvaged volumes. Change of mean calculated blood loss in specific surgical populations over time is an important quality indicator for PBM.

Stage 4: Measuring outcome data comparing patients with transfusion and with PBM

In the final stage of implementing PBM benchmarking and reporting systems, all available data on blood utilisation, anaemia and calculated blood loss should be linked with patient outcome data. Capturing the following outcome parameters is recommended:

- Hospital mortality
- 30-day mortality
- 90-day mortality

- 5-year mortality
- Infection rate
- Pulmonary complication rate
- Hospital acquired anaemia rate
- Readmission rate
- Reoperations
- Composite morbidity
- ALOS
- ICU-ALOS
- Cost

Standardised electronic reporting, regular reviewing and internal auditing of transfusion and PBM benchmark results, helps the key and primary stakeholders to direct the change management process effectively. Such standardised information systems must of course comply with all legal requirements (e.g. data protection). The following points should be clearly defined:

- Who the different recipients are (key PBM stakeholders/champions and on aggregated levels, representatives of clinical departments, hospitals, etc.)
- What the information contents and formats are for each group of recipients
- What the reporting cycles are (for instance monthly or quarterly)
- What the cycles for internal auditing are (e.g. departmental auditing might sometimes be necessary on an ad-hoc basis, otherwise one audit per year might be sufficient).

2.3.3 Supporting PBM related education programmes

Multiple ongoing education strategies are pivotal to bring about practice change and sustained realignment of the hospital's culture. The knowledge base on the impact of anaemia, blood loss and bleeding, transfusion, and PBM is comprehensive and rapidly growing. This is well reflected by the tens of thousands of related PubMed listed articles. It is challenging for PBM stakeholders to keep up with the abundant flow of new information, and to select what might be clinically relevant and important to support the PBM change management process. Therefore, hospital administrators and executives should support continuous educational programmes and initiatives with a PBM focus. These might include:

- Multidisciplinary PBM post- and under-graduate training courses and education/curricula (77).
- Workshops on specific PBM topics (e.g. how to manage different forms of anaemia in pre-operative clinics, point-of-care coagulation management, surgical bleeding management and others)
- Enrolment in PBM e-learning systems (128)
- Development of lectures for nursing schools
- Regularly organising lectures with national and international PBM key opinion leaders

Well-coordinated PBM programmes have education programmes for all stakeholders within the hospital, including physicians, nurses, transfusion medicine specialists, pharmacists, medical controllers, hospital administrators and other non-clinical staff. Some hospitals expand their educational activities even further by annually inviting patients and their families to learn about PBM programmes and the patient benefits.

2.3.4 Proactively offering PBM training to medical and surgical patients

Hospitals should communicate their PBM programmes. Hospital administrators and executives should involve the institution's public relations or communications department to develop a communication strategy with a focus on the patient centeredness and the outcomes of PBM.

Actions to be taken

Communication of the PBM programme requires appropriate media channels such as:

- Hospital websites
- Annual report of the hospital with a PBM section
- Press releases
- Downloadable and/or printed materials
- Posters
- Patient information brochures
- PBM newsletters

3 How to implement PBM as a new standard of care

3.1 Introduction

Change in organisations can be of utmost importance, but a high percentage of change projects fail. Various change management models have been developed. Some of them are more general, while others are customised for specific types of organisations including the clinical sector (29, 47, 129-139). John Kotter's eight-step model (140) integrates important elements that are common in change management processes and has been successfully applied to implement the PBM concept at the Western Australia Patient Blood Management Program [2]. Overall, the Kotter model serves as a framework rather than a step-by-step action plan. Kotter's organisational change principles are also incorporated in the IHI-improvement model (141), which may be used to take the implementation further into everyday practice within the hospital department by establishing local improvement teams, larger hospital networks, and using the plan-do-study-act (PDSA) cycle of quality improvement and local data. The eight-step model serves as a template for the implementation of PBM in this EU-PBM guide. The model is based on the avoidance of eight common errors, which usually account for failure of change efforts. Each error has a specific solution, and together these represent the eight-step change model.

These eight errors are (130):

1) allowing too much complacency,
2) failing to create a sufficiently powerful guiding coalition,
3) underestimating the power of vision,
4) under-communicating the vision,
5) permitting obstacles to block the new vision,
6) failing to create short-term wins,
7) declaring victory too soon, and
8) neglecting to anchor changes firmly in the corporate culture.

In this implementation guide, Kotter's eight steps have been adapted to the implementation of the PBM concept with the ultimate goal to alter physicians' behaviour and to improve transfusion culture in the medical setting (Figure 4). This overarching concept determines all the clinical and organisational measures to be taken by and adapted to the particular institution. Since this is a step-by-step strategy, skipping or not completing one step leads to a halt or even regression of the process. On the other hand, moving too quickly to the further steps involves the risk of failure.

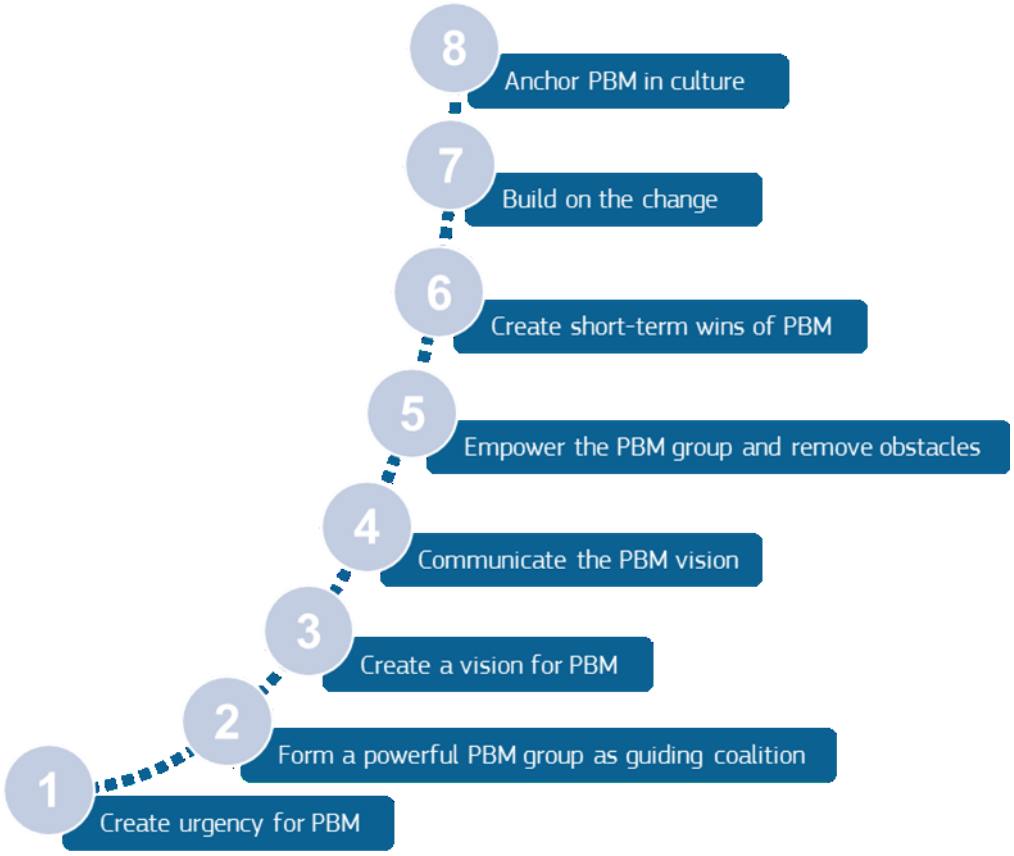

Figure 4. Eight-step PBM implementation strategy according to the Kotter model.

3.2 Managing change from the default transfusion position to PBM

3.2.1 Step 1 - Create urgency for PBM

1) Help others see the need for change and they will be convinced of the importance of acting immediately (J. Kotter).

A failure to develop a sense of urgency leads, almost with certainty, to a failure of the entire change management process. Kotter suggests for a change to be successful that about 75% of the people involved need to "buy into" that change. "Buy in" from frontline staff is especially essential (142). Therefore, devoting a significant amount of time and energy to the first step is an absolute must. The PBM concept, which must be modelled and adapted in accordance with institutional needs by the respective institutional leaders, has to be communicated to all stakeholders concerned. This includes, but is not limited to, nurses, physicians, patient advocates and hospital managers. Tailored to the different needs of the audiences, communication has to be simple, repetitive and bi-directional (from leaders to team members and back).

Striking PBM arguments that may be put forward are: harming patients due to the prevalence of untreated preoperative anaemia (108, 143-147), a lack of attention to proactive bleeding management (148), the often behaviour-based blood ordering schedules (149-152), and the frequent to high

transfusion rates of individual institutions (obtained by benchmarking or comparison to recent literature) (108).

According to the three pillar PBM concept, a minimal set of parameters (Table 2) should be assessed on individual case levels, ideally by directly linking the main data sources (transfusion database, hospital information system, patient data management system) in order to capture and evaluate intra-institutional baseline data such as anaemia prevalence, surgical blood loss, transfusion rate and index. Whenever possible, baseline data should also be compared inter-institutionally. This could help to identify differences in practice and knowledge. This would further lay the foundations for a regular (e.g. monthly) reporting process.

Table 2. Recommended transfusion parameters for internal assessment

Total number of blood and blood components issued • Red blood cells (RBC) • Fresh frozen plasma (FFP) • Factor concentrates • Platelets • Cryoprecipitate
Blood and blood component data per patient (patient level and mean values per indication) • Number of units ordered • Number of units transfused
Transfusion indicators (patient level and mean values per indication) • Anaemia prevalence at hospital admission • Pre- and postoperative haemoglobin. • Pretransfusion haemoglobin. • Perioperative blood loss calculated using the Mercuriali algorithm [161, 378]. • Bleeding assessment - actively bleeding (yes/no).
Parameters to be included in the monthly generated internal PBM report • Transfusion rate for blood and blood components • Transfusion index for RBC and FFP • Total transfusion index for RBC and FFP • Number of components transfused per transfusion episode to monitor single-unit transfusion policies • Responsible person for transfusion.

Additional classical drivers for an urgent change are: increasing transfusion related costs, newly and re-emerging pathogens in the blood pool, remaining disease transmission, increased morbidity and mortality and limited efficacy often associated with transfusion and the objective to reduce risk for potential blood donors (69). Inversely, the definition of expected results and their positive impact on patient outcome underlines the urgent need to implement a PBM concept. Table 3 shows a list of recommended minimal data set for follow-up of patients.

Table 3. Recommended mid- to long-term follow-up of outcome data from all patients (transfused and non-transfused)

Length of stay • in hospital • in intensive care unit
Rate of complications • Readmission rate • Reoperation rate • Infection rate • Others like Transfusion-related acute lung injury (TRALI), acute respiratory distress syndrome (ARDS), etc. • Postoperative iron deficiency rate • Anaemia rate at discharge • Anaemia rate at out-patient follow-up
Mortality rate • in hospital • 30 days / 90 days/ 1-year / 5-year

Additional financing might be required at least at the initiation of the PBM programme. However, the full implementation of PBM substantially reduces hospital treatment costs (19, 153, 154). The following data should be considered for cost effectiveness reasoning:

- Product costs of transfused blood and blood components
- Product costs of discarded and expired blood and blood components
- Product costs for PBM treatment modalities (e.g. erythropoietin, iron)
- Costs for lab tests and diagnostic processes
- Costs of logistics and delivery process

Cost impacts should be calculated following well established methodologies such as those recommended by the National Institute for Clinical Excellence in the UK (Methods guide assessing cost impact) (155).

Introducing an informed consent process for anaemia management including PBM related questions into the pre-operative checklist for surgeons and anaesthesiologists, and PBM curricula for post- and undergraduates also help to create a sense of urgency.

Key points – Step 1

- Communication of the PBM programme through appropriate media channels such as:
- Implementing PBM requires management, but above all, leadership is a key requirement.
- Devoting a significant amount of energy and time to create a sense of urgency is a must.
- Communicating the arguments for the PBM concept and its beneficial effects on patient safety and outcome to all stakeholders - from leadership to frontline staff is critical.
- An immediate sense of urgency should be established by pointing out the main problem (1-3 problems), which are obvious and easy to understand for all major stakeholders. This overall headline message should be strong, clear and short (30 seconds to explain). Beyond this, a differential communication plan is necessary.
- Initially, additional financing might be necessary. However, the full implementation of PBM substantially reduces hospital treatment costs.
- Moving onto the further steps too fast involves the risk of failure.

Table 4. Checklist for step 1: Create urgency for PBM

#	Proposed assessment topics	Result(*)
1.1	Main arguments for the implementation of PBM • Communication strategy including strong arguments (e.g. lower mortality, lower complication rate, shorter length of stay etc. as shown in relevant publications) • Compelling and logical arguments tailored to the audience and the department's specific needs ("heart & brain arguments"). • Communicating current evidence	
1.2	Specially tailored educational information to • clinical directors and co-workers in surgery, nursing and finance…) • hospital managers (and health care providers) • primary care physicians • patients and patient advocates	
1.3	Capture and evaluate intra-institutional PBM related baseline data such as prevalence of anaemia, blood loss, transfusion trigger, transfusion rate and index • Report results to departmental teams and key stakeholders. • Communicate PBM as "gold standard"	
1.4	Compare inter-institutional baseline data such as anaemia prevalence, blood loss, transfusion threshold, transfusion rate and index. • Report (anonymised) results to departmental teams and key stakeholders • Evaluate differences and try to identify practice and knowledge gaps.	

1.5	Informed patient consent for anaemia treatment [3] (39)	
1.6	Adding relevant PBM questions to the preoperative checklists (SOP) of the surgeons and anaesthesiologists	
1.7	Developing and introducing mandatory post- and undergraduate PBM curricula	

(*) +++ strong, ++ moderate, + weak, - none

3.2.2 Step 2 - Form a powerful PBM group as guiding coalition

2) Assemble a group with enough power to lead the change effort, and encourage the group to work as a team (J. Kotter).

A clinical reference group acting as a **guiding coalition,** hereafter called the **PBM group,** with commitment and a heavy influence that is able to work as a **team** *outside* the hierarchy has to be established (the PBM group requires many more members than the PBM committee, however some members of the group might later on also serve in the PBM committee). Support from the hospital managers and directors is also essential for successful teamwork. Above all, simply managing the change is not enough. Teamwork and leadership are preconditions for success. To lead the change, a coalition of influential people whose power is derived from a variety of sources including job title, expertise, reputation and political importance, has to be formed (156, 157). In order to secure inclusion of all relevant specialties and professions, and reduce built-in resistance from major stakeholders, the PBM group should include several clinical specialities where patients are at risk, organisational quality managers, and transfusion medicine specialists, if available, from the in-hospital blood centre. Also, managerial representation should be present (hospital directors, or managers with direct connections to the hospital directors). Such leaders can be found throughout their hospital. A PBM group *without* strong leadership will not have the power required to overcome inertia and resistance against PBM implementation.

The leaders should communicate the special PBM aspects regarding expected results (157), modify their language ("building up" and "breaking down"(158)), support improvisation (159), sell solutions for encompassing change, and engage co-workers through purpose and challenge (160).

As PBM is a multidisciplinary and multi-professional concept, leaders and team members have to be recruited from different departments, professional groups and hierarchical levels. For example, implementation of perioperative PBM without support from leading nurses and surgeons can barely be successful. The impact of multidisciplinary teams is often limited by suboptimal intra-team communication. Perception of the current PBM team climate and teamwork may reveal room for improvement (161, 162). Perioperative PBM scenarios can be managed by a team of PBM trained

[3] "If patients suffer from anaemia, they shall be informed that their surgery related risks can be reduced by treating their anaemia first. Surgery related risks might be an increased transfusion rate, infection risk and anaemic infarct rate and therefore a longer hospital stay. For all elective surgeries a previous anaemia clarification and treatment is highly recommended" (Informed consent, General Hospital Linz, 2016).

anaesthesiologists, surgeons and, if necessary, by intensive care specialists. Other scenarios will benefit from support from haematologists, gastroenterologists, radiologists or specialists from trauma surgery, oncology or diagnostic labs. Also, transfusion medicine specialists may play an important role, particularly if there is a hospital based blood centre, especially since some PBM programmes have been initiated by transfusion specialists. In others, nurses play a key role in establishing and maintaining the PBM project (163, 164).

Once formed, the PBM group should continue to build a sense of urgency within their environment (step 1) and generate their own momentum for change. Potential weaknesses of the PBM coalition should be identified and corrected as soon as possible. All relevant data about utilisation of blood and blood components should be accessible to the PBM team; technical support from the IT-department for professional data management is necessary.

The PBM group should be founded by, merged with or as a minimum supported by the hospitals' transfusion committee.

Key points – Step 2

- Teamwork and leadership are essential for successful and sustainable change management.
- The PBM group should be constituted as a multi-professional and multidisciplinary team.
- The PBM members need to be committed and have enough power and sense of responsibility to lead the change.
- The PBM group should continue to build a sense of urgency and generate the momentum needed for change.
- The PBM group should eventually be merged with the hospitals' transfusion committee.

Table 5. Checklist for step 2: Form a powerful PBM group as guiding coalition

#	Proposed assessment topics	Result(*)
2.1	Main disciplines included (anaesthesia, surgery, transfusion medicine, laboratory, haematology, gastroenterology, pharmacology, quality management)	
2.2	Sufficient number of professionals included (physicians, nurses, perfusionists, hospital management, networkers, quality managers)	
2.3	Leading professionals (key leaders), officially assigned by the hospital providers, included	
2.4	Support from hospital management (including budget for PBM)	
2.5	Support from clinical directors	
2.6	Support from patient advocacy	
2.7	Support from IT-department for data management	

2.8	Use of tools to facilitate the team	
2.9	Emphasis on networking and cross communication within the hospital teams	

(*) +++ strong, ++ moderate, + weak, - none

3.2.3 Step 3 - Create a vision for PBM

3) Create a vision to help direct the change effort, and develop strategies for achieving that vision (J. Kotter).

Vision (mission statement) plays a key role in producing the necessary change. The vision should emphasise the importance of PBM implementation and should motivate team members through empathy, envisioning and empowerment. Without vision-guided decision-making, the implementation effort can easily dissolve into a number of confusing and incompatible projects, which are time consuming and may go in the wrong direction or nowhere at all.

Without a clear direction in mind, a suggestion for change has no context. Mission statements should create a link between the vision and the more specific recommendations. To be more precise, the vision of PBM implementation should be the result of group discussions based on recent literature and the current hospital circumstances. The obligatory use of scientific evidence represents a continuous basis to continuously evolve PBM. All proposed ideas and solutions should be linked to an overall vision that is easy to understand and remember (158). Eventually, the entire PBM staff should be able to describe this vision within five minutes or less.

The vision of PBM implementation is: improved patient safety and optimal clinical outcome can be achieved when the optimisation and preservation of a patient's own blood takes priority over the transfusion of donor blood.

Exemplary vision statements in favour of PBM:

- "We prevent and treat anaemia to improve outcome and safe lives!"
- "PBM is the gold standard to improve patient safety and outcome"

In addition, strategies to execute the vision should be defined and include timelines as well as milestones. These strategies should closely follow the PBM concept and should be based on the personnel and medical resources of the institution.

Key points – Step 3

- PBM implementation should follow a vision that is clear, easy to understand, communicate and remember.
- The vision should serve as an umbrella for the different PBM modalities.
- Principles to create a vision
    - encompass all staff members and all patients

- be positive
- do not provoke fear

- Vision plays a key role in producing useful change and may inspire large numbers of people.
- PBM vision should be executed in a way that is based on the current scientific evidence and the current and future resources of the hospital and of the regional health care system.

Table 6. Checklist for step 3: Create a vision for PBM

#	Proposed assessment topics	Result(*)
3.1	Vision of the PBM Group formulated and consented	
3.2	Vision in line with the current evidence and the available resources of the hospital	
3.3	Vision supported by relevant stakeholders	
3.4	Strategies for executing the PBM (vision) developed	
3.5	Each strategy should have milestones defined and be executed within a given time frame (road map and timelines)	
3.6	Strategies should include a stakeholder mapping for the environment (level of interest/power level)	

(*) +++ strong, ++ moderate, + weak, - none

3.2.4 Step 4 - Communicating the PBM vision

4) Make sure as many as possible understand and accept the vision and the strategy (J. Kotter).

Implementing PBM requires that all people involved are willing to co-operate. Once people see the potential benefits of the PBM concept and believe that expected results are really possible they will support it (157). For that reason the PBM leading group and hospital directors should use continuous and multi-channel communication to capture the team's hearts and minds. Each opportunity for communication should be used. However, communication must be tailored to the special needs of the team members and come in both words and actions. "The talk has to be walked", i.e. what is done is more important than what is said. Behaviour inconsistent with verbal communication undermines change efforts significantly. Also, all stakeholders' concerns and anxieties must be addressed and discussed.

Expected strategies, results and how their performance is measured should be communicated. For example, if a baseline evaluation shows a significantly higher perioperative blood loss compared to other institutions, the goal to reduce perioperative blood loss by PBM must be unmistakeably formulated. Also, evidence-based modalities of how to achieve it, like with the use of antifibrinolytics (165-170), minimal invasive surgery (171, 172) etc., must be clearly communicated to the target audience.

As a result of this "communication campaign" each member of the departments involved should be motivated by the benefits of PBM implementation, thus leading to a positive attitude towards this concept. Measures of intervention should be deliberately chosen to reach maximum effectiveness and sustainability (see Appendix 1 – Methods of intervention).

Key points – Step 4

- Lead by example.
- Talk often and credibly about the vision of PBM implementation.
- Use every occasion to launch reminders, such as portal, screen saver, tweets, social media, and posters.
- Communicate PBM within different channels.
- Address key members' concerns and anxieties openly and honestly.
- Announce well-defined goals and monitor their accomplishment.
- Anchor PBM to the education programme.
- Include health authorities.

Table 7. Checklist for step 4: Communicate the PBM vision

#	Proposed assessment topics	Result(*)
4.1	Meetings, lectures and workshops are held	
4.2	PBM is communicated through the hospitals' homepage, intranet and other suitable channels	
4.3	Guidelines, literature and other information material are provided in print and electronically (apps etc.)	
4.4	Target audiences are familiar with PBM concept	
4.5	Lead by example (with sufficient number of leaders)	

(*) +++ strong, ++ moderate, + weak, - none

3.2.5 Step 5 - Empower the PBM group and remove obstacles

5) Remove obstacles to change, change systems or structures that seriously undermine the vision, and encourage risk-taking and non-traditional ideas, activities, and actions (J. Kotter).

The driving forces behind the project need to be strengthened while the resisting forces need to be weakened. The team leaders should have their jobs and responsibilities clearly defined. Also, they should have the competence and resources necessary to make the expected changes possible. As a consequence,

to empower the team, signal involvement including support of change and deployment of resources by (senior) leaders is recommended (157). Innovation, risk-taking, and improvisation should be encouraged, since they provide new ways for enabling the change, especially when resources (time, material, staffing) are limited. Benchmarking comparing not only institutions but also physicians may highlight specific problems and provide solutions.

In many cases the obstacles may be very real and change cannot happen without addressing barriers, since one well-placed blocker can stop the entire change effort. Therefore, time and strategies to remove obstacles are necessary. Do not waste time ("death by delay") In the first place, obstacles have to be identified continuously and be quickly bypassed or removed to get the organisation in line with the PBM concept. Barriers are mostly intertwined and may be structural, cultural and psychological. According to Kotter, "*occasionally, the roadblocks are only in people's heads and the challenge is to convince them that no external barriers exist* "[4]. For example, long-standing traditional transfusion habits, which have seldom been evaluated, are still frequently discussed. Whereas, the quick and positive results yielded by PBM with regard to the degree of anaemia and transfusion are rarely discussed. To couple information and clinical experience is a powerful way to get the attention of busy physicians ("see, feel, change" approach) (131). Implementing and continuously using electronic intra- and inter-institutional benchmarking and reporting systems between physicians and between departments are strongly recommended ("data is power"). A mentoring programme could also be helpful. It is advisable to concentrate on the supporters and not waste too much time with those who are resistant to change ("don't waste time and energy!") (173).

Organisational obstacles, amongst others, are lack of resources and interdisciplinary communication, absence of incentives, and insufficient periods between referral to the anaesthesia department for preoperative assessment and the operation date. If structural barriers relate to functions that impact behaviour, trying to influence behaviour won't work unless the structure is changed. For example, a functioning preoperative clinic needs sufficient staff and work space.

Key points - Step 5

- Define clear roles and responsibilities for leaders.
- Encourage innovation and improvisation.
- Encourage leadership power and competence.
- Recognise and reward people for making change happen (incentives).
- Identify and quickly remove or bypass obstacles (human or otherwise).
- Concentrate on supporters and do not waste too much time and energy with "no nos"(174).

[4] Kotter, John P. Leading Change. Boston: Harvard Business School P, Chapter I - Transforming Organizations: Why Firms Fail

Table 8. Checklist for step 5: Empower the PBM group and remove obstacles

#	Proposed assessment topics	Result(*)
5.1	Identify behavioural and organisational obstacles (human or otherwise)	
5.2	Implement electronic benchmarking and reporting systems to continuously measure transfusion and patient level outcome data. Have a first version of the database including minimal dataset ready as early as possible	
5.3	Establish ongoing PBM training for all relevant staff	
5.4	Duties and responsibilities of leaders clearly defined	
5.5	Personnel and technical support recruited	
5.6	Team members incentivised (e.g. publications)	
5.7	Official empowerment from hospital administration / management obtained	

(*) +++ strong, ++ moderate, + weak, - none

3.2.6 Step 6 - Create short-term wins of PBM

6) Plan for achievements that can easily be made visible, follow-through with those achievements and recognise and reward employees who were involved (J. Kotter).

Nothing motivates more than success. However, real change takes time and complex projects, like PBM implementation, are at risk of losing momentum if there are no short-term goals to meet and celebrate. Generating short-term wins increases the chance that PBM implementation will not only be continued, but also completed by the staff (130, 174). Short-term wins mean short-term targets ("low hanging fruits"), which should be implemented within a reasonable time frame (three to 12 months depending on the type of modality). Short-term modalities are effective when they are inexpensive, easy to understand, and visible to many with little room for failure. They should be part of the PBM concept and be implemented without the help from any critics of PBM and results should be unambiguous. It is advisable to start with the easiest one and employees who help to meet the targets should be rewarded (public acknowledgment, participation in meetings etc.). In short, failure of implementing easy goals can hurt the entire PBM initiative.

Characteristics of effective short-term win strategies (175)

- **Measurable** - Select short-term with convincing improvements (not vague and fuzzy).
- **Visible** - People need to see real evidence of the progress to validate the change effort.
- **Timely** - Ideally first results should appear within three months (partial or progressive results are also valid).
- **Relevant to stakeholders** - Ensure the improvements are valuable to the majority of the stakeholders.

- **Relevant to the situation** - Wins should provide a test of the vision and change plan against real conditions so they provide useful information to learn from.

Proposed PBM modalities for easy wins are the following:

- optimising blood-ordering schedules to avoid unnecessary logistics, lab tests, control measures and blood samples (176),
- reducing amount of phlebotomies (micro sampling, reduced number of lab tests) (177, 178),
- reducing transfusion index by using a single unit strategy (179),
- checking for blood count and iron status to detect preoperative anaemia on time (146, 180, 181),
- calculating blood loss for benchmarking (182),
- starting a transfusion database for continuous monitoring of blood use (183),
- irradiating washed blood to increase utilisation of autologous blood (184),
- using restrictive/symptomatic transfusion thresholds/triggers to avoid unnecessary transfusions (84),
- using antifibrinolytics to reduce perioperative blood loss (170),
- maintaining perioperative normothermia (185),
- using other modalities appropriate for the individual institution (e.g. patient questionnaire) (100)

Key points – Step 6

- Take some time to work through the various needs of your stakeholders and categorise these needs by 'importance to the stakeholder' and 'ease of implementation'.
- Select only one or two easily achievable short term measures.
- Select short-term goals carefully, because failure to reach them compromises the PBM initiative as a whole.
- Define short-term targets and clear results (e.g. reduction of RBC usage).
- Include an implementation timeline (do not waste time).
- Complete selected short-term measures in less than 12 months.
- Reward people who help to meet the targets.

Table 9. Checklist for step 6: Create short-term wins of PBM

	Proposed assessment of short-term winning measures	Result(*)
6.1	Revised blood ordering schedules	
6.2	Micro sampling (smaller volumes, less frequent)	
6.3	Implementation of a single unit ordering and transfusion strategy	
6.4	Preoperative anaemia management • Introduction of patient information about options for preoperative anaemia treatment (where appropriate), web-based and/or paper form (39) • Preoperative screening for anaemia and iron status	

6.5	Preoperative check for coagulation and expected blood loss (e.g. Mercuriali algorithm to calculate expected blood loss and post-operative haematocrit)	
6.6	Standard use of antifibrinolytics	
6.7	Irradiation of salvaged blood in surgical cancer patients	
6.8	Applying restrictive/symptomatic transfusion thresholds/triggers	
6.9	Other hospital specific easy wins (patient questionnaire)	

(*) +++ strong, ++ moderate, + weak, - none

3.2.7 Step 7 - Build on the change

7) Use increased credibility to change systems, structures, and policies that don't fit the vision, also hire, promote, and develop employees who can implement the vision, and finally reinvigorate the process with new projects, themes, and change agents (J. Kotter).

The complex efforts of PBM implementation risk losing momentum if there are no short-term goals to meet and celebrate. Without short-term wins, too many team members will give up or even actively resist. However, easy wins are only the beginning of what has to be done to achieve sustainable PBM implementation. Each success is a chance to build on what went right and to set further goals for PBM implementation (by removing barriers, by getting more resources, etc.).
To suggest after an easy win the project is mostly done would be a severe mistake, because new approaches are fragile and have a tendency towards regression until they sink deep into the culture. Therefore, it is mandatory to analyse not only the objectives achieved, but also which further improvements need to be accomplished.
PBM team members must continue to focus on new PBM implementation modalities to keep momentum going. This means, with the idea of continuous improvement and adaptation in mind, they should consolidate the gains achieved and produce even more change along the three pillars of PBM (186). The PBM team should find workarounds and solutions to overcome still existing behavioural, structural and organisational obstacles. It is important to gradually expand the PBM concept across the entire hospital.

Key points – Step 7

- Consolidate and celebrate successful short-term wins.
- Continue to focus on PBM parameters and set further goals (continuous improvement).
- Regular workarounds.
- Expand PBM across the entire hospital.
- Continuously monitor key parameters via a database and communicate the results to all clinicians.

Table 10. Checklist for step 7: Build on the change (Never let up)

#	Proposed assessment topics	Result(*)
7.1	Consolidate and complete the implementation of the three-pillar strategy (e.g. preoperative anaemia treatment if Hb < WHO threshold or if expected blood loss is likely to make patient anaemic)	
7.2	Continue with workarounds and solutions to overcome behavioural, structural and organisational obstacles	
7.3	Implement a database for the continuous monitoring of parameters	
7.4	Internal auditing of transfusion practice on a regular basis	
7.5	Reporting and evaluating results and achievements with hospital staff and management	
7.6	Motivate hospital staff to attend lectures and study publications	
7.7	Continuous improvement, rethinking strategies and goals	
7.8	Rewards and incentives for successful PBM team members	
7.9	Include project management / timeline / milestones / benchmark *cycles*	

7.10	Set up a framework using stepwise indicator systems to follow changes
	• Structure indicators (examples)
	  o establishing the PBM team
	  o patient flow for cardiac surgery
	• Process indicators (examples)
	  o using more tranexamic acid
	  o higher rate of single unit ordering
	• Outcome indicators (examples)
	  o lower transfusion rate
	  o lower transfusion index
	  o lower rate of complications
	  o lower rate of patients with anaemia	

(*) +++ strong, ++ moderate, + weak, - none

3.2.8 Step 8 - Anchor PBM in culture

8) Articulate the connections between the new behaviours and organisational success, and develop the means to ensure leadership development and succession (J. Kotter).

The PBM concept should become an integral part of and be deeply anchored in the hospital's culture. Otherwise, it might become the subject of degradation as soon the pressure associated with the change

efforts is removed. Therefore, success stories showing the positive results of PBM implementation have to be frequently communicated to the entire hospital staff and at scientific meetings. For example, significant reduction of the transfusion rate in combination with better outcome and increased patient safety. Success stories should also be published. Moreover, not only should the key members' contributions to the change process be publicly recognised, but also the frustrations they experienced acknowledged and discussed.

To give PBM a solid place in hospital culture, PBM leaders and hospital directors should continue to support PBM implementation. This includes the existing PBM team as well as new staff. One bad succession decision (for example not considering PBM in the training of new staff members or not providing necessary resources) can undermine a decade of hard work. Anchoring PBM also requires that sufficient time be taken to ensure the next generation of PBM team members really do internalise this new approach. Therefore, the PBM concept must be part of the staff's training and education programme.

Key points – Step 8

- PBM should be part of the hospital's culture.
- The PBM team has clear competences and responsibilities.
- PBM is an intrinsic part of the staff's training and education programme.
- Internal reporting on outcome indicators is supported by direct data access to transfusion database, hospital information system and patient data management system.

Including specific criteria related to PBM to a national hospital accreditation programme::

- Level 1 - Start of PBM implementation based on the EU-PBM Guide (Step 1)
- Level 2 - First results based on easy win measures (Step 1 to 6)
- Level 3 - Full implementation of PBM (Step 1 to 8) → EU-PBM Excellence centres

Table 11. Checklist for step 8: Anchor PBM in culture

#	Proposed assessment topics	Result(*)
8.1	Three pillar strategy anchored as part of the hospital's culture	
8.2	PBM patient level benchmarking and reporting processes by procedure, clinician and department are in place and fully automated	
8.3	Routine reporting of key parameters to clinical directors and the hospital management in place (mortality, complications, readmissions, length of stay and cost)	
8.4	Conducting clinical studies and producing (multidisciplinary) publications	
8.5	PBM certification from national hospital accreditation programme	

(*) +++ strong, ++ moderate, + weak, - none

3.3 PBM Implementation steps (Matrix)

The matrix summarises actions supporting each step according the Kotter model and could be used to build a customised action plan or checklist for a hospital.

Table 12. Summary of actions supporting each implementation step according to the Kotter model

	(1) Establish urgency for PBM	(2) Form a powerful PBM group	(3) Create a vision for PBM	(4) Communicate the PBM Vision within the hospital	(5) Empower the team and remove obstacles	(6) Generate short-term wins	(7) Build on the change	(8) Anchor PBM in culture
1	Putting together main arguments for the implementation of PBM Preparing communication strategy with compelling and logical arguments Effectively communicating current evidence	Including main disciplines (anaesthesia, surgery, transfusion medicine, laboratory, haematology, gastroenterology, pharmacology, quality management)	Formulating and consenting the vision of the PBM Group	Organizing and conducting meetings, lectures and workshops	Identifying behavioural, organisational, financial and infrastructural obstacles	Revising blood ordering schedules	Consolidating and completing the implementation of the three-pillar strategy (e.g. Preoperative anaemia treatment if Hb < WHO threshold or if expected blood loss is likely)	Anchoring three pillar strategy as part of the hospital's culture
2	Specially tailoring educational contents to • clinical directors and department heads in surgery, internal medicine, nursing, pharmacy, controlling, finance, and IT • hospital managers and health care providers • primary care physicians • patients and patient advocates	Including sufficient number of professionals from multiple disciplines (physicians, nurses, perfusionists, hospital managers, networkers, quality managers)	Ensuring vision is in line with the current evidence and the available resources of the hospital	Communicating PBM through the hospitals' homepage, intranet and other suitable channels	Implementing electronic benchmarking and reporting systems to continuously measure transfusion and patient level outcome data. Having a first version of the database including minimal dataset ready as early as possible	Introducing microsampling (smaller volumes, less frequent)	Continuing with workarounds and solutions to overcome behavioural, structural and organisational obstacles	Having fully automating benchmarking and reporting processes by procedure, clinician and department in place
3	Capturing and evaluating intra-institutional PBM related baseline data such as prevalence of anaemia, blood loss, transfusion trigger, transfusion rate and index • Reporting results to departmental teams and key stakeholders. • Communicate PBM as "gold standard"	Officially assigning leading professionals by the hospital executives (key leaders)	Ensuring stakeholders support of PBM vision	Providing guidelines, literature and other suitable information materials in print and electronically	Establishing ongoing PBM training for all relevant staff	Implementing a single unit ordering and transfusion policy	Expanding the database for the continuous monitoring of key parameters.	Routinely reporting of key parameters to clinical directors and the hospital management

	(1) Establish urgency for PBM	(2) Form a powerful PBM group	(3) Create a vision for PBM	(4) Communicate the PBM Vision within the hospital	(5) Empower the team and remove obstacles	(6) Generate short-term wins	(7) Build on the change	(8) Anchor PBM in culture
4	Comparing inter-institutional baseline data such as anaemia prevalence, blood loss, transfusion threshold, transfusion rate and index. • Reporting results to departmental teams and key stakeholders • Evaluating differences and trying to identify practice and knowledge gaps.	Ensuring support from hospital management (including budget for PBM)	Developing strategies tor communicate and execute the PBM vision	Ensuring target audiences are familiar with PBM concept	Clearly defining duties and responsibilities of leaders	Installing preoperative anaemia management • Patient information about options for preoperative anaemia treatment • Preoperative screening for anaemia and iron status	Regularly conducting internal audits of transfusion/PBM practice	Conducting clinical studies and producing (multidisciplinary) publications
5	Introducing informed consent for anaemia treatment	Ensuring support from clinical directors	Defining milestones and setting timelines to execute strategies (road map and timelines)	Leading by example (sufficient number of team leaders necessary)	Recruiting personnel and technical support	Preoperative check for coagulation and expected blood loss (e.g. Mercuriali algorithm to calculate expected blood loss and post-operative haematocrit)	Reporting and discussing results and achievements with hospital staff and management	Attaining PBM certification from national hospital accreditation programme
6	Adding relevant PBM questions to the preoperative checklists (SOP) of the surgeons and anaesthesiologists	Ensuring support from patient advocacy	Strategies should include a stakeholder mapping for the environment (power level and interest/support level)		Incentivising team members (e.g. publications)	Making use of antifibrinolytics a standard	Motivating hospital staff to attend lectures and study publications	
7	Developing and introducing mandatory post- and undergraduate curricula	Ensuring support from IT-department for data management			Obtaining official empowerment from hospital administration / management	Making irradiation of salvaged blood a standard in surgical cancer patients	Continuously improving, rethinking strategies and goals	
8		Giving tools to facilitate the team			Obtaining official empowerment from clinical director	Applying restrictive/symptomatic transfusion thresholds/triggers	Rewarding and incentivising successful PBM team members	
9		Emphasising networking and cross communication within the departments and hospital teams				Identifying other hospital specific easy wins (patient questionnaire)	Including project management / timeline / milestones / Benchmark cycles	
10							Setting up a framework using stepwise indicator systems to follow changes • Structure indicators • Process indicators • Outcome indicators • lower rate of patients with anaemia	

4 Examples of successful PBM initiatives

4.1 Western Australia Department of Health: The world's first state-wide PBM programme

In 2008, the Western Australia Department of Health initiated a 5-year project to implement a sustainable health-system-wide PBM programme with the aim to improve patient outcomes while reducing costs (187). Clinically, the programme was structured on the three pillar/nine-field matrix of PBM (40, 75, 188). Kotter' eight step model was applied and multiple strategies were employed to bring about a cultural change from a blood-product focus to a patient focus. At the start of the programme, the State of Western Australia (WA) already had one of the lowest red blood cell issuance rates per 1,000 population in the developed world (31.8 RBC per 1,000 population). The programme identified reasons and drivers for practice change (189, 190). From 2008 to 2015, issuance for RBCs in WA progressively decreased to 19.4 units per 1,000 population. During the same years, despite an increasing volume of hospital admissions, total issuance of RBC in the entire state decreased from 70,143 to 50,529. The study is the world's largest to date in the field of PBM. It included 605,046 patients admitted to Western Australia's four major adult tertiary-care hospitals over six years, with results showing:

- 28% reduction in hospital mortality
- 15% reduction in average hospital length of stay
- 21% decrease in hospital-acquired infections
- 31% decrease in the incidence of heart attack or stroke.

The use of blood products reduced by 41% during the study period, representing a cost saving of $18.5 million. However, gross savings, which include the cost of administering transfusions in the hospitals, is estimated to be between $80-100 million (188).

4.2 OnTRAC: A provincial PBM programme in Canada

In 2002 the Ministry of Health and Long-term Care of Ontario developed a provincial blood conservation programme (86, 191). A medical director and a project administrator were appointed, along with programme nurse coordinators in 23 hospitals. OnTRAC started with focus on three targeted procedures: knee and hip arthroplasty, and elective coronary artery bypass graft (CABG) surgery. Later on in the project implementation radical prostatectomy was included as an additional procedure. Initial results at 12 months demonstrated an overall 24% reduction in blood use for total knee arthroplasty, 14% reduction for AAA, and 23% reduction for CABG surgery. Additionally, patients who were transfused received fewer units. Non-transfused patients had lower postoperative infection rates ($p<0.05$) and length of stay ($p<0.0001$); and a multivariate analysis showed transfusion as an independent predictor of increased length of stay. The investigators concluded: "Implementation of the programme 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, data at 18 and 24 months showed there was an overall reduction in the number of patients receiving RBC transfusion (192). In 2014 the authors reported overall cost savings for the four targeted procedures of 39.5 million dollar to the health care system by consequently try to lose less and to

save/give back patients' blood. The cost of the programme itself was $3,257,000 (86, 191). In the context of these high quality and outcomes gains at reduced cost, the authors stated that the slow adoption of the concept is due to "the traditional concept that blood products are an effective and safe therapeutic intervention", but continue "this needs to be replaced by the new concept that transfusion of blood products represents an undesirable outcome" (86). Changing practice needs data on current transfusion rates and practices. It has been shown that a key component is to treat pre-operative anaemia and this requires seeing patients early. Among others difficulties the following have been encountered in the program: governmental emphasis on shorter wait times for surgery (sometimes precluding the possibility of appropriate anaemia treatment), costs and accessibility to blood conservation measures, and sometimes difficulty in recruiting physician and administrative champions. The OnTRAC team acknowledges the cardinal role of the medical directors when they were able to identify one in each hospital.

4.3 Institutional programmes

4.3.1 General Hospital Linz (Austria)

The 900-bed General Hospital in Linz performs about 27,000 surgical procedures per year. Although it was one of the institutions with the lowest transfusion rate in the Austrian Benchmark Study, a patient blood management project was initiated in 2008. In addition to lectures and workshops in co-operation with all departments, several measures have been taken to reduce allogeneic blood transfusions with the ultimate goal to improve patient outcome and safety. Over a period of six years clinicians reduced blood utilisation by 60 - 70% (75). The General Hospital Linz (Austria) reported a reduction of RBC utilisation of more than 40% after the implementation of PBM (with a reduction of 75% in the department of anaesthesiology and intensive care, 77% in the department of orthopaedics and 57% in the general surgery department (193). By the end of 2014, an overall reduction of almost 70% in red blood cell concentrates has been achieved. Unfortunately, due to limited financial and logistical resources, the effect on patient outcome could not be evaluated.

Pillar I

One of the most important steps for the success was the implementation of a premedication outpatient clinic and the establishment of a diagnostic pathway. The diagnostic pathway was developed in consultation with surgical colleagues and included timely assignment of patients and standardised treatment of preoperative anaemia. At the beginning, this was only possible in some surgical specialities. However, the emerging success of this approach led to the commitment of more and more surgical partners. As a consequence, more than 80% of patients are currently sent to the premedication outpatient clinic before surgery. The introduction of a standardised operating procedure (SOP) for PBM resulted in the award of an Austrian quality management certificate. Furthermore, surgical partners recognised PBM as a trademark and organised PBM meetings to work out instructional material for their professions. By gaining broad acceptance the need for further necessary changes were accepted and PBM implementation became easier.

Moreover, adequate preparation of patients was improved. More and more patients received intravenous iron and erythropoietin after passing through the diagnostic pathway. In 2014, a total of 888 g of intravenous iron was administered. This corresponds to an iron rate of 0.033 g/surgical procedure; whereas, during the same time period, the transfusion rate declined to 0.22 RBC per surgical procedure.

Pillar II
Since surgical partners anticipated blood-free or blood-sparing techniques as a valuable goal, several measures were adopted to minimise perioperative blood loss: increased usage of cell salvage, application of local haemostyptics, usage of small circuits for cardiopulmonary bypass, and modern surgical approaches (minimal invasive) in order to minimise damage to surrounding tissues.

Pillar III
From 2008-2014, the transfusion trigger was reduced from 10 g/dl to 7 g/dl. However, this did not result in a significant decline of the mean haemoglobin concentration during a hospital stay. In the same time period the transfusion rate declined significantly (about 70%).

4.3.2 Implementing PBM at the Landesklinikum Gänserndorf-Mistelbach (Austria)

The Landesklinikum Gänserndorf-Mistelbach (Austria) participated in the first and second Austrian PBM benchmark trial conducted by the Austrian Ministry of Health. At the hospital about 29,400 in-patients are treated in 12 departments per year. After the head of anaesthesia and intensive care unit received the first PBM benchmark report the hospital management decided to disclose the results and to start a PBM programme. Out of 18 participating centres the Landesklinikum Gänserndorf-Mistelbach had the highest RBC transfusion rate with 8.648 transfused RBC in 2004. After an external audit by PBM experts in 2005 a PBM implementation team was installed. Immediate implementation of “short term win” actions resulted in reduced RBC utilisation although the number of in-hospital patients increased. In 2006 the total number of RBC units declined by 35% to 5,694. In a six years follow-up period the overall transfusion rate for RBC was reduced from 6.7% to 4.8% and the transfusion index was reduced from 4,5% to 3,8% (5).

5 References

1. WHO. World Health Organization - Global Forum for Blood Safety: Patient Blood Management - Concept paper, Available from: http://www.who.int/bloodsafety/events/gfbs_01_pbm_concept_paper.pdf, 2011, (last access 11/07/2016).
2. WHA. 63.12 - Sixty-Third World Health Assembly , Agenda item 11.17, 21 May 2010 - Availability, safety and quality of blood products 2010, Available from: http://apps.who.int/gb/ebwha/pdf_files/WHA63/A63_R12-en.pdf (last access: 11/07/2016).
3. Shander A, Isbister J, Gombotz H. Patient blood management: the global view. Transfusion. 2016;56 Suppl 1:S94-S102.
4. Gombotz H. Patient Blood Management: A Patient-Orientated Approach to Blood Replacement with the Goal of Reducing Anemia, Blood Loss and the Need for Blood Transfusion in Elective Surgery. Transfusion medicine and hemotherapy : offizielles Organ der Deutschen Gesellschaft fur Transfusionsmedizin und Immunhamatologie. 2012;39(2):67-72.
5. Gombotz H, Zacharowski K, Spahn DR. Patient Blood Management: Georg Thieme Verlag Stuttgart-New york; 2016.
6. Goodnough LT, Shander A. Blood management. ArchPatholLab Med. 2007;131(5):695-701.
7. Musallam KM, Tamim HM, Richards T, Spahn DR, Rosendaal FR, Habbal A, et al. Preoperative anaemia and postoperative outcomes in non-cardiac surgery: a retrospective cohort study. The Lancet. 2011;378(9800):1396-407.
8. Goodnough LT, Brecher ME, Kanter MH, AuBuchon JP. Transfusion medicine. Second of two parts--blood conservation. The New England journal of medicine. 1999;340(7):525-33.
9. Goodnough LT, Brecher ME, Kanter MH, AuBuchon JP. Transfusion medicine. First of two parts--blood transfusion. The New England journal of medicine. 1999;340(6):438-47.
10. von Heymann C, Kaufner L, Sander M, Spies C, Schmidt K, Gombotz H, et al. Does the severity of preoperative anemia or blood transfusion have a stronger impact on long-term survival after cardiac surgery? The Journal of thoracic and cardiovascular surgery. 2016.
11. Willems A, Van Lerberghe C, Gonsette K, De Ville A, Melot C, Hardy JF, et al. The indication for perioperative red blood cell transfusions is a predictive risk factor for severe postoperative morbidity and mortality in children undergoing cardiac surgery. Eur J Cardiothorac Surg. 2014;45(6):1050-7.
12. Perel P, Clayton T, Altman DG, Croft P, Douglas I, Hemingway H, et al. Red blood cell transfusion and mortality in trauma patients: risk-stratified analysis of an observational study. PLoS medicine. 2014;11(6):e1001664.
13. Paone G, Likosky DS, Brewer R, Theurer PF, Bell GF, Cogan CM, et al. Transfusion of 1 and 2 units of red blood cells is associated with increased morbidity and mortality. The Annals of thoracic surgery. 2014;97(1):87-93; discussion -4.
14. Goodnough LT, Maggio P, Hadhazy E, Shieh L, Hernandez-Boussard T, Khari P, et al. Restrictive blood transfusion practices are associated with improved patient outcomes. Transfusion. 2014;54(10 Pt 2):2753-9.
15. Walsh M, Garg AX, Devereaux PJ, Argalious M, Honar H, Sessler DI. The association between perioperative hemoglobin and acute kidney injury in patients having noncardiac surgery. Anesthesia and analgesia. 2013;117(4):924-31.
16. Restellini S, Kherad O, Jairath V, Martel M, Barkun AN. Red blood cell transfusion is associated with increased rebleeding in patients with nonvariceal upper gastrointestinal bleeding. Alimentary pharmacology & therapeutics. 2013;37(3):316-22.
17. Gross I, Shander A, Sweeney J. Patient blood management and outcome, too early or not? BestPractResClinAnaesthesiol. 2013;27(1):161-72.
18. Isbister JP. The three-pillar matrix of patient blood management - an overview. BestPractResClinAnaesthesiol. 2013;27(1):69-84.
19. Kotze A, Carter LA, Scally AJ. Effect of a patient blood management programme on preoperative anaemia, transfusion rate, and outcome after primary hip or knee arthroplasty: a quality improvement cycle. British Journal of Anaesthesia. 2012;108(6):943-52.
20. Leahy MF, Roberts H, Mukhtar SA, Farmer S, Tovey J, Jewlachow V, et al. A pragmatic approach to embedding patient blood management in a tertiary hospital. Transfusion. 2014;54(4):1133-45.

21. Shander A, Hofmann A, Isbister J, Van AH. Patient blood management - The new frontier. BestPractResClinAnaesthesiol. 2013;27(1):5-10.
22. Shander A, Javidroozi M, Perelman S, Puzio T, Lobel G. From bloodless surgery to patient blood management. MtSinai J Med. 2012;79(1):56-65.
23. So-Osman C, Nelissen RG, Koopman-van Gemert AW, Kluyver E, Poll RG, Onstenk R, et al. Patient blood management in elective total hip- and knee-replacement surgery (part 2): a randomized controlled trial on blood salvage as transfusion alternative using a restrictive transfusion policy in patients with a preoperative hemoglobin above 13 g/dl. Anesthesiology. 2014;120(4):852-60.
24. So-Osman C, Nelissen RG, Koopman-van Gemert AW, Kluyver E, Poll RG, Onstenk R, et al. Patient blood management in elective total hip- and knee-replacement surgery (Part 1): a randomized controlled trial on erythropoietin and blood salvage as transfusion alternatives using a restrictive transfusion policy in erythropoietin-eligible patients. Anesthesiology. 2014;120(4):839-51.
25. Spahn DR. Anemia and patient blood management in hip and knee surgery: a systematic review of the literature. Anesthesiology. 2010;113(2):482-95.
26. Theusinger OM, Stein P, Spahn DR. Applying 'Patient Blood Management' in the trauma center. Curr Opin Anaesthesiol. 2014;27(2):225-32.
27. Vamvakas EC. Reasons for moving toward a patient-centric paradigm of clinical transfusion medicine practice. Transfusion. 2013;53(4):888-901.
28. Moskowitz DM, McCullough JN, Shander A, Klein JJ, Bodian CA, Goldweit RS, et al. The impact of blood conservation on outcomes in cardiac surgery: is it safe and effective? AnnThoracSurg. 2010;90(2):451-8.
29. Verdecchia NM, Wisniewski MK, Waters JH, Triulzi DJ, Alarcon LH, Yazer MH. Changes in blood product utilization in a seven-hospital system after the implementation of a patient blood management program: A 9-year follow-up. Hematology. 2016;21(8):490-9.
30. The Optimal Blood Use Website, Available from: http://www.optimalblooduse.eu/, (last access: 11/07/2016).
31. Dalrymple K, Watson D. Ten years of transfusion practitioners and better blood transfusion in Scotland. Nursing management. 2014;20(10):27-30.
32. JPAC. Joint United Kingdom (UK) Blood Transfusion and Tissue Transplantation Services Professional Advisory Committee: Patient Blood Management. Available from: http://www.transfusionguidelines.org.uk/uk-transfusion-committees/national-blood-transfusion-committee/patient-blood-management (last access: 11/07/2016).
33. Guerra R, Velati C, Liumbruno GM, Grazzini G. Patient Blood Management in Italy. Blood Transfus. 2016;14(1):1-2.
34. Vaglio S, Prisco D, Biancofiore G, Rafanelli D, Antonioli P, Lisanti M, et al. Recommendations for the implementation of a Patient Blood Management programme. Application to elective major orthopaedic surgery in adults. Blood Transfus. 2016;14(1):23-65.
35. Meybohm P, Fischer DP, Geisen C, Muller MM, Weber CF, Herrmann E, et al. Safety and effectiveness of a Patient Blood Management (PBM) program in surgical patients--the study design for a multi-centre prospective epidemiologic non-inferiority trial. BMC health services research. 2014;14:576.
36. AABB. Advancing Transfusion and Cellular Therapies Worldwide: Patient Blood Management, Available from: http://www.aabb.org/pbm/Pages/default.aspx (last access: 11/07/2016).
37. Haas T, Goobie S, Spielmann N, Weiss M, Schmugge M. Improvements in patient blood management for pediatric craniosynostosis surgery using a ROTEM((R)) -assisted strategy - feasibility and costs. Paediatr Anaesth. 2014;24(7):774-80.
38. Gombotz H, Hofman A, Rehak P, Kurz J. [Patient blood management (part 2). Practice: the 3 pillars]. Anasthesiologie, Intensivmedizin, Notfallmedizin, Schmerztherapie : AINS. 2011;46(7-8):466-74.
39. Gombotz H, Hofmann A, Rehak P, Kurz J. [Patient blood management (part 1) - patient-specific concept to reduce and avoid anemia, blood loss and transfusion]. Anasthesiologie, Intensivmedizin, Notfallmedizin, Schmerztherapie : AINS. 2011;46(6):396-401.
40. Isbister JP. The three-pillar matrix of patient blood management--an overview. Best practice & research Clinical anaesthesiology. 2013;27(1):69-84.
41. Tinegate H, Pendry K, Murphy M, Babra P, Grant-Casey J, Hopkinson C, et al. Where do all the red blood cells (RBCs) go? Results of a survey of RBC use in England and North Wales in 2014. Transfusion. 2016;56(1):139-45.

42. Fillet AM, Desmarets M, Assari S, Quaranta JF, Francois A, Pugin A, et al. Blood products use in France: a nationwide cross-sectional survey. Transfusion. 2016.
43. Meybohm P, Herrmann E, Steinbicker AU, Wittmann M, Gruenewald M, Fischer D, et al. Patient Blood Management is Associated With a Substantial Reduction of Red Blood Cell Utilization and Safe for Patient's Outcome: A Prospective, Multicenter Cohort Study With a Noninferiority Design. Ann Surg. 2016;264(2):203-11.
44. Armstrong K, Kendall E. Translating knowledge into practice and policy: the role of knowledge networks in primary health care. The HIM journal. 2010;39(2):9-17.
45. Bero LA, Grilli R, Grimshaw JM, Harvey E, Oxman AD, Thomson MA. Closing the gap between research and practice: an overview of systematic reviews of interventions to promote the implementation of research findings. The Cochrane Effective Practice and Organization of Care Review Group. Bmj. 1998;317(7156):465-8.
46. Gagliardi AR, Brouwers MC. Integrating guideline development and implementation: analysis of guideline development manual instructions for generating implementation advice. Implement Sci. 2012;7:67.
47. Grol R, Grimshaw J. From best evidence to best practice: effective implementation of change in patients' care. Lancet. 2003;362(9391):1225-30.
48. Shander A, Van Aken H, Colomina MJ, Gombotz H, Hofmann A, Krauspe R, et al. Patient blood management in Europe. Br J Anaesth. 2012;109(1):55-68.
49. Gombotz H, Rehak PH, Shander A, Hofmann A. The second Austrian benchmark study for blood use in elective surgery: results and practice change. Transfusion. 2014.
50. Bennett-Guerrero E, Zhao Y, O'Brien SM, Ferguson TB, Jr., Peterson ED, Gammie JS, et al. Variation in use of blood transfusion in coronary artery bypass graft surgery. JAMA. 2010;304(14):1568-75.
51. Likosky DS, Al-Attar PM, Malenka DJ, Furnary AP, Lehr EJ, Paone G, et al. Geographic variability in potentially discretionary red blood cell transfusions after coronary artery bypass graft surgery. J Thorac Cardiovasc Surg. 2014.
52. Rogers M, Blumberg N, Saint S, Langa K, Nallamothu B. Hospital variation in transfusion and infection after cardiac surgery: a cohort study. BMC Medicine. 2009;7(1):37.
53. Stover EP, Siegel LC, Body SC, Levin J, Parks R, Maddi R, et al. Institutional variability in red blood cell conservation practices for coronary artery bypass graft surgery. Institutions of the MultiCenter Study of Perioperative Ischemia Research Group. J CardiothoracVascAnesth. 2000;14(2):171-6.
54. Bruun MT, Pendry K, Georgsen J, Manzini P, Lorenzi M, Wikman A, et al. Patient Blood Management in Europe: surveys on top indications for red blood cell use and Patient Blood Management organization and activities in seven European university hospitals. Vox Sang. 2016.
55. Van der Linden P, Hardy JF. Implementation of patient blood management remains extremely variable in Europe and Canada: the NATA benchmark project: An observational study. European journal of anaesthesiology. 2016;33(12):913-21.
56. Merriam-Webster Dictionary. Available from: http://www.merriam-webster.com/dictionary/stakeholder (last access: 11/07/2016).
57. Business Dictionary, Available from: http://www.businessdictionary.com/ (last access:11/07/2016).
58. Oxford Dictionaries, available from: http://www.oxforddictionaries.com/de/definition/englisch_usa/stakeholder (last access: 11/07/2016).
59. Helm RE, Rosengart TK, Gomez M, Klemperer JD, DeBois WJ, Velasco F, et al. Comprehensive multimodality blood conservation: 100 consecutive CABG operations without transfusion. Ann Thorac Surg. 1998;65(1):125-36.
60. Green JA. Blood conservation in cardiac surgery: the Virginia Commonwealth University (VCU) experience. J Cardiothorac Vasc Anesth. 2004;18(4 Suppl):18S-23S.
61. The Institute for Patient Blood Management and Bloodless Medicine and Surgery at Englewood Hospital: Englewood Hospital and Medical Center; 2015 [Available from: http://www.englewoodhospital.com/esvw1.asp.
62. Anästhesiologie und operative Intensivmedizin: Allgemeines Krankenhaus der Stadt Linz; 2015 [Available from: http://www.linz.at/akh/1411.asp.
63. The Center for Bloodless Medicine and Surgery: Johns Hopkins Medicine; 2015 [Available from: http://www.hopkinsmedicine.org/bloodless_medicine_surgery/.
64. Patient Bood Management Program Eastern Maine Medical Center; 2015 [Available from: http://www.emmc.org/blood_management.aspx.
65. The National Patient Blood Management (PBM) Collaborative: Australian Commission on Safety and Quality in Health Care; 2015 [Available from: http://www.safetyandquality.gov.au/national-priorities/pbm-collaborative/.

66. Isbister JP, Shander A, Spahn DR, Erhard J, Farmer SL, Hofmann A. Adverse blood transfusion outcomes: establishing causation. TransfusMedRev. 2011;25(2):89-101.
67. Farmer SL, Towler SC, Leahy MF, Hofmann A. Drivers for change: Western Australia Patient Blood Management Program (WA PBMP), World Health Assembly (WHA) and Advisory Committee on Blood Safety and Availability (ACBSA). BestPractResClinAnaesthesiol. 2013;27(1):43-58.
68. Marik PE, Corwin HL. Efficacy of red blood cell transfusion in the critically ill: a systematic review of the literature. Crit Care Med. 2008;36:2667-74.
69. Hofmann A, Farmer S, Shander A. Five drivers shifting the paradigm from product-focused transfusion practice to patient blood management. Oncologist. 2011;16 Suppl 3:3-11.:3-11.
70. Rohde JM, Dimcheff DE, Blumberg N, Saint S, Langa KM, Kuhn L, et al. Health care-associated infection after red blood cell transfusion: a systematic review and meta-analysis. JAMA : the journal of the American Medical Association. 2014;311(13):1317-26.
71. Hofmann A, Farmer S, Towler SC. Strategies to preempt and reduce the use of blood products: an Australian perspective. Curr Opin Anaesthesiol. 2012;25(1):66-73.
72. Villanueva C, Colomo A, Bosch A, Concepci+›n M, Hernandez-Gea V, Aracil C, et al. Transfusion Strategies for Acute Upper Gastrointestinal Bleeding. New England Journal of Medicine. 2013;368(1):11-21.
73. Carson JL, Carless PA, Hebert PC. Transfusion thresholds and other strategies for guiding allogeneic red blood cell transfusion. CochraneDatabaseSystRev. 2012;4:CD002042. doi: 10.1002/14651858.CD002042.pub3.:CD002042.
74. Lamhaut L, Apriotesei R, Combes X, Lejay M, Carli P, Vivien BÆ. Comparison of the Accuracy of Noninvasive Hemoglobin Monitoring by Spectrophotometry (SpHb) and HemoCue-Æ with Automated Laboratory Hemoglobin Measurement. Anesthesiology. 2011;115(3).
75. Gombotz H, Hofmann A. [Patient Blood Management : three pillar strategy to improve outcome through avoidance of allogeneic blood products]. Anaesthesist. 2013;62(7):519-27.
76. Most Frequent Procedures Performed in U.S. Hospitals, 2011 Rockville, MD, United States: HCUP Home. Healthcare Cost and Utilization Project, Agency for Healthcare Research and Quality (AHRQ), U.S. Department of Human Services; 2015 [Available from: http://www.hcup-us.ahrq.gov/reports/statbriefs/sb165.jsp.
77. Leahy MF, Roberts H, Mukhtar SA, Farmer S, Tovey J, Jewlachow V, et al. A pragmatic approach to embedding patient blood management in a tertiary hospital. Transfusion. 2013.
78. Koch CG. Tolerating anemia: taking aim at the right target before pulling the transfusion trigger. Transfusion. 2014;54(10 Pt 2):2595-7.
79. About Clinical Pharmacists: American College of Clinical Pharmacy; 2015 [Available from: http://www.accp.com/about/clinicalpharmacists.aspx.
80. Farmer SL TK, Hofmann A, Semmens J, Mukhtah SA, Prosser G, et al. A Programmatic Approach to Patient Blood Management – reducing transfusions and improving patient outcomes. The Open Anesthesiology Journal. 2015;9:1-11.
81. Frank SM, Wick EC, Dezern AE, Ness PM, Wasey JO, Pippa AC, et al. Risk-adjusted clinical outcomes in patients enrolled in a bloodless program. Transfusion. 2014;54(10 Pt 2):2668-77.
82. Pattakos G. Outcome of patients who refuse transfusion after cardiac surgery: A natural experiment with severe blood conservation. Archives of Internal Medicine. 2012;172(15):1154-60.
83. Gross I, Seifert B, Hofmann A, Spahn DR. Patient blood management in cardiac surgery results in fewer transfusions and better outcome. Transfusion. 2015;55(5):1075-81.
84. Goodnough LT, Maggio P, Hadhazy E, Shieh L, Hernandez-Boussard T, Khari P, et al. Restrictive blood transfusion practices are associated with improved patient outcomes. Transfusion. 2014.
85. Anthes E. Evidence-based medicine: Save blood, save lives. Nature. 2015;520(7545):24-6.
86. Freedman J. The ONTraC Ontario program in blood conservation. Transfusion and apheresis science : official journal of the World Apheresis Association : official journal of the European Society for Haemapheresis. 2014;50(1):32-6.
87. Froessler B, Palm P, Weber I, Hodyl NA, Singh R, Murphy EM. The Important Role for Intravenous Iron in Perioperative Patient Blood Management in Major Abdominal Surgery: A Randomized Controlled Trial. Ann Surg. 2016;264(1):41-6.
88. Mehra T, Seifert B, Bravo-Reiter S, Wanner G, Dutkowski P, Holubec T, et al. Implementation of a patient blood management monitoring and feedback program significantly reduces transfusions and costs. Transfusion. 2015;55(12):2807-15.

89. Spahn DR, Theusinger OM, Hofmann A. Patient blood management is a win-win: a wake-up call. British journal of anaesthesia. 2012;108(6):889-92.
90. Radia D, Momoh I, Dillon R, Francis Y, Cameron L, Fagg TL, et al. Anemia management: development of a rapidaccess anemia and intravenous iron service. Risk management and healthcare policy. 2013;6:13-22.
91. Kendoff D, Tomeczkowski J, Fritze J, Gombotz H, von Heymann C. [Preoperative anemia in orthopedic surgery : Clinical impact, diagnostics and treatment.]. Der Orthopade. 2011.
92. Mishra PK, Thekkudan J, Sahajanandan R, Gravenor M, Lakshmanan S, Fayaz KM, et al. The role of point-of-care assessment of platelet function in predicting postoperative bleeding and transfusion requirements after coronary artery bypass grafting. Ann Card Anaesth. 2015;18(1):45-51.
93. Mallett SV, Armstrong M. Point-of-care monitoring of haemostasis. Anaesthesia. 2015;70 Suppl 1:73-7, e25-6.
94. Karkouti K, McCluskey SA, Callum J, Freedman J, Selby R, Timoumi T, et al. Evaluation of a Novel Transfusion Algorithm Employing Point-of-care Coagulation Assays in Cardiac Surgery: A Retrospective Cohort Study with Interrupted Time-Series Analysis. Anesthesiology. 2015;122(3):560-70.
95. Mukhtar SA, Leahy MF, Koay K, Semmens JB, Tovey J, Jewlachow J, et al. Effectiveness of a patient blood management data system in monitoring blood use in Western Australia. Anaesth Intensive Care. 2013;41(2):207-15.
96. Rothschild JM, McGurk S, Honour M, Lu L, McClendon AA, Srivastava P, et al. Assessment of education and computerized decision support interventions for improving transfusion practice. Transfusion. 2007;47(2):228-39.
97. Zuckerberg GS, Scott AV, Wasey JO, Wick EC, Pawlik TM, Ness PM, et al. Efficacy of education followed by computerized provider order entry with clinician decision support to reduce red blood cell utilization. Transfusion. 2015.
98. Goodnough LT, Shieh L, Hadhazy E, Cheng N, Khari P, Maggio P. Improved blood utilization using real-time clinical decision support. Transfusion. 2013.
99. Fischer DP, Zacharowski KD, Meybohm P. Savoring every drop - vampire or mosquito? Crit Care. 2014;18(3):306.
100. Gombotz H, Zacharowski K, Spahn D. Patient Blood Management: Thieme Stuttgart-New York-Dehli-Rio de Janeiro; 2016. 264 p.
101. Yazer MH, Waters JH. How do I implement a hospital-based blood management program? Transfusion. 2012;52(8):1640-5.
102. Musallam KM, Tamim HM, Richards T, Spahn DR, Rosendaal FR, Habbal A, et al. Preoperative anaemia and postoperative outcomes in non-cardiac surgery: a retrospective cohort study. Lancet. 2011.
103. Spahn DR. Anemia and patient blood management in hip and knee surgery: a systematic review of the literature. Anesthesiology. 2010;113(2):482-95.
104. Beattie WS, Karkouti K, Wijeysundera DN, Tait G. Risk associated with preoperative anemia in noncardiac surgery: a single-center cohort study. Anesthesiology. 2009;110(3):574-81.
105. Dunne JR, Malone D, Tracy JK, Gannon C, Napolitano LM. Perioperative anemia: an independent risk factor for infection, mortality, and resource utilization in surgery. The Journal of surgical research. 2002;102(2):237-44.
106. Shander A, Knight K, Thurer R, Adamson J, Spence R. Prevalence and outcomes of anemia in surgery: a systematic review of the literature. Am J Med. 2004;116 Suppl 7A:58S-69S.
107. Mercuriali F, Inghilleri G. Proposal of an algorithm to help the choice of the best transfusion strategy. Curr Med Res Opin. 1996;13(8):465-78.
108. Gombotz H, Rehak PH, Shander A, Hofmann A. Blood use in elective surgery: the Austrian benchmark study. Transfusion. 2007;47(8):1468-80.
109. Lienhart A, Auroy Y, Pequignot F, Benhamou D, Warszawski J, Bovet M, et al. Survey of anesthesia-related mortality in France. Anesthesiology. 2006;105(6):1087-97.
110. Lucas DJ, Ejaz A, Spolverato G, Kim Y, Gani F, Frank SM, et al. Packed red blood cell transfusion after surgery: are we "overtranfusing" our patients? Am J Surg. 2016;212(1):1-9.
111. Mair B, Agosti SJ, Foulis PR, Hamilton RA, Benson K. Monitoring for undertransfusion. Transfusion. 1996;36(6):533-5.
112. Hibbs SP, Nielsen ND, Brunskill S, Doree C, Yazer MH, Kaufman RM, et al. The impact of electronic decision support on transfusion practice: a systematic review. Transfus Med Rev. 2015;29(1):14-23.
113. Hibbs S, Miles D, Staves J, Murphy MF. Is undertransfusion a problem in modern clinical practice? Transfusion. 2014.

114. Shander A, Fink A, Javidroozi M, Erhard J, Farmer SL, Corwin H, et al. Appropriateness of allogeneic red blood cell transfusion: the international consensus conference on transfusion outcomes. Transfus Med Rev. 2011;25(3):232-46 e53.
115. Butler CE, Noel S, Hibbs SP, Miles D, Staves J, Mohaghegh P, et al. Implementation of a clinical decision support system improves compliance with restrictive transfusion policies in hematology patients. Transfusion. 2015;55(8):1964-71.
116. Jairath V, Kahan BC, Logan RF, Travis SP, Palmer KR, Murphy MF. Red blood cell transfusion practice in patients presenting with acute upper gastrointestinal bleeding: a survey of 815 UK clinicians. Transfusion. 2011;51(9):1940-8.
117. Barr PJ, Donnelly M, Cardwell CR, Parker M, Morris K, Bailie KE. The appropriateness of red blood cell use and the extent of overtransfusion: right decision? Right amount? Transfusion. 2011;51(8):1684-94.
118. Nuttall GA, Stehling LC, Beighley CM, Faust RJ, American Society of Anesthesiologists Committee on Transfusion M. Current transfusion practices of members of the american society of anesthesiologists: a survey. Anesthesiology. 2003;99(6):1433-43.
119. Saxena S, Wehrli G, Makarewicz K, Sartorelli J, Shulman IA. Monitoring for underutilization of RBC components and platelets. Transfusion. 2001;41(5):587-90.
120. Shander A. Financial and clinical outcomes associated with surgical bleeding complications. Surgery. 2007;142(4 Suppl):S20-5.
121. Vivacqua A, Koch CG, Yousuf AM, Nowicki ER, Houghtaling PL, Blackstone EH, et al. Morbidity of bleeding after cardiac surgery: is it blood transfusion, reoperation for bleeding, or both? The Annals of thoracic surgery. 2011;91(6):1780-90.
122. Christensen MC, Krapf S, Kempel A, von Heymann C. Costs of excessive postoperative hemorrhage in cardiac surgery. The Journal of thoracic and cardiovascular surgery. 2009;138(3):687-93.
123. Spence RK, Carson JA, Poses R, McCoy S, Pello M, Alexander J, et al. Elective surgery without transfusion: influence of preoperative hemoglobin level and blood loss on mortality. Am J Surg. 1990;159(3):320-4.
124. Stokes ME, Ye X, Shah M, Mercaldi K, Reynolds MW, Rupnow MF, et al. Impact of bleeding-related complications and/or blood product transfusions on hospital costs in inpatient surgical patients. BMC Health Serv Res. 2011;11:135.
125. Ye X, Lafuma A, Torreton E, Arnaud A. Incidence and costs of bleeding-related complications in French hospitals following surgery for various diagnoses. BMC Health Serv Res. 2013;13(1):186.
126. Alstrom U, Levin LA, Stahle E, Svedjeholm R, Friberg O. Cost analysis of re-exploration for bleeding after coronary artery bypass graft surgery. Br J Anaesth. 2012;108(2):216-22.
127. Nadler SB, Hidalgo JH, Bloch T. Prediction of blood volume in normal human adults. Surgery. 1962;51(2):224-32.
128. BloodSafe eLearning Australia: South Australian Department of Health and Ageing 2014 [Available from: https://www.bloodsafelearning.org.au.
129. Barker ER. Use of diffusion of innovation model for agency consultation. Clinical nurse specialist CNS. 1990;4(3):163-6.
130. Kotter JP. What leaders really do. Harvard business review. 1990;68(3):103-11.
131. Silversin J, Kornacki MJ. Implementing change: from ideas to reality. Family practice management. 2003;10(1):57-62.
132. Berwick DM. Disseminating innovations in health care. JAMA : the journal of the American Medical Association. 2003;289(15):1969-75.
133. W. B. Managing Transitions: Cambridge, MA, Perseus Books; 2003.
134. E S. Organizational culture and leadership (3rd Ed): San Francisco, CA Jossey-Bass; 2004.
135. Boyatzis RE AK. The ideal self as the driver of intentional change. J Manag Dev. 2006;25:18.
136. Campbell RJ. Change management in health care. The health care manager. 2008;27(1):23-39.
137. Reinhardt AC, Keller T. Implementing interdisciplinary practice change in an international health-care organization. International journal of nursing practice. 2009;15(4):318-25.
138. Stoller JK. Implementing change in respiratory care. Respiratory care. 2010;55(6):749-57.
139. Michie S, Abraham C, Eccles MP, Francis JJ, Hardeman W, Johnston M. Strengthening evaluation and implementation by specifying components of behaviour change interventions: a study protocol. Implement Sci. 2011;6:10.
140. John K. Kotter International, Cambridge U.S. Website: Available from: http://www.kotterinternational.com/the-8-step-process-for-leading-change/ (last access: 11/07/2016).

141. Institute for Healthcare Improvement, Cambridge U.S. Website, Avialbale from: http://www.ihi.org/resources/Pages/HowtoImprove/default.aspx, (last access: 11.07.2016)
142. Hatler CW, Mast D, Corderella J, Mitchell G, Howard K, Aragon J, et al. Using evidence and process improvement strategies to enhance healthcare outcomes for the critically ill: a pilot project. Am J Crit Care. 2006;15(6):549-55.
143. Beattie WS, Karkouti K, Wijeysundera DN, Tait G. Risk associated with preoperative anemia in noncardiac surgery: a single-center cohort study. Anesthesiology. 2009;110(3):574-81.
144. Carrascal Y, Maroto L, Rey J, Arevalo A, Arroyo J, Echevarria JR, et al. Impact of preoperative anemia on cardiac surgery in octogenarians. Interact Cardiovasc Thorac Surg. 2010;10(2):249-55.
145. Dunkelgrun M, Hoeks SE, Welten GM, Vidakovic R, Winkel TA, Schouten O, et al. Anemia as an independent predictor of perioperative and long-term cardiovascular outcome in patients scheduled for elective vascular surgery. AmJ Cardiol. 2008;101(8):1196-200.
146. Miceli A, Romeo F, Glauber M, de Siena PM, Caputo M, Angelini GD. Preoperative anemia increases mortality and postoperative morbidity after cardiac surgery. Journal of cardiothoracic surgery. 2014;9:137.
147. Patel MS, Carson JL. Anemia in the preoperative patient. MedClinNorth Am. 2009;93(5):1095-104.
148. Reed MJ, Lone N, Walsh TS. Resuscitation of the trauma patient: tell me a trigger for early haemostatic resuscitation please! Crit Care. 2011;15(2):126.
149. Mundy GM, Hardiment K, Revill J, Birtwistle SJ, Power RA. Do we really need to routinely crossmatch blood before primary total knee or hip arthroplasty? Acta OrthopScand. 2004;75(5):567-72.
150. Palmer T, Wahr JA, O'Reilly M, Greenfield ML. Reducing unnecessary cross-matching: a patient-specific blood ordering system is more accurate in predicting who will receive a blood transfusion than the maximum blood ordering system. AnesthAnalg. 2003;96(2):369-75, table.
151. Richardson NG, Bradley WN, Donaldson DR, O'Shaughnessy DF. Maximum surgical blood ordering schedule in a district general hospital saves money and resources. AnnRColl Surg Engl. 1998;80(4):262-5.
152. Rogers BA, Johnstone DJ. Audit on the efficient use of cross-matched blood in elective total hip and total knee replacement. AnnRColl Surg Engl. 2006;88(2):199-201.
153. Cohn CS, Welbig J, Bowman R, Kammann S, Frey K, Zantek N. A data-driven approach to patient blood management. Transfusion. 2013:10.
154. Spahn DR, Theusinger OM, Hofmann A. Patient blood management is a win-win: a wake-up call. Br J Anaesth. 2012;108(6):889-92.
155. National Institute for Health and Clinical Excellence, Assessing Cost impact - Methods guide August 2011, https://www.nice.org.uk/Media/Default/About/what-we-do/Into-practice/Costing_Manual_update_050811.pdf (last access: 12/08/2016).
156. Choi J. A motivational theory of charismatic leadership: Envisioning, empathy, and empowerment Journal of Leadership and Organizational Studies. 2006;13(1):24-43.
157. Cowley B. Why change succeeds: An organization self-assessment. Organization Developement Journal. 2007;25(1):25-30.
158. Brower H, Fiol, C.M., Emrich,C. The language of leaders. Journal of Leadership studies. 2007;1(3):67-80.
159. Leybourne S. Managing improvisation within change management: Lessons from UK financial services. The Services Industries Journal 2006;26(1):73-95.
160. Van Dam KO, S. Daily work contexts and resistance to organisational change: The role of leader-member exchange, developement climate, and change process. Applied Psychology: An Internal Review. 2008;57(2):313-34.
161. Makary MA, Sexton JB, Freischlag JA, Holzmueller CG, Millman EA, Rowen L, et al. Operating room teamwork among physicians and nurses: teamwork in the eye of the beholder. J Am Coll Surg. 2006;202(5):746-52.
162. Thomas EJ, Sexton JB, Helmreich RL. Discrepant attitudes about teamwork among critical care nurses and physicians. Crit Care Med. 2003;31(3):956-9.
163. Gallagher T, Darby S, Vodanovich M, Campbell L, Tovey J. Patient blood management nurse vs transfusion nurse: is it time to merge? British Journal of Nursing. 2015;24(9):492-5.
164. Shander A, Javidroozi M. Blood conservation strategies and the management of perioperative anaemia. Current opinion in anaesthesiology. 2015;28(3):356-63.
165. Faraoni D, Willems A, Melot C, De HS, Van der Linden P. Efficacy of tranexamic acid in paediatric cardiac surgery: a systematic review and meta-analysis. EurJCardiothoracSurg. 2012;42(5):781-6.
166. Fawzy H, Elmistekawy E, Bonneau D, Latter D, Errett L. Can local application of Tranexamic acid reduce post-coronary bypass surgery blood loss? A randomized controlled trial. J CardiothoracSurg. 2009;4:25.

167. Henry D, Carless P, Fergusson D, Laupacis A. The safety of aprotinin and lysine-derived antifibrinolytic drugs in cardiac surgery: a meta-analysis. CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne. 2009;180(2):183-93.
168. Hutton B, Joseph L, Fergusson D, Mazer CD, Shapiro S, Tinmouth A. Risks of harms using antifibrinolytics in cardiac surgery: systematic review and network meta-analysis of randomised and observational studies. Bmj. 2012;345:e5798.
169. Koster A, Borgermann J, Zittermann A, Lueth JU, Gillis-Januszewski T, Schirmer U. Moderate dosage of tranexamic acid during cardiac surgery with cardiopulmonary bypass and convulsive seizures: incidence and clinical outcome. British journal of anaesthesia. 2013;110(1):34-40.
170. Irisson E, Hemon Y, Pauly V, Parratte S, Argenson JN, Kerbaul F. Tranexamic acid reduces blood loss and financial cost in primary total hip and knee replacement surgery. Orthopaedics & traumatology, surgery & research : OTSR. 2012;98(5):477-83.
171. Black EA, Campbell RK, Channon KM, Ratnatunga C, Pillai R. Minimally invasive vein harvesting significantly reduces pain and wound morbidity. Eur J Cardiothorac Surg. 2002;22(3):381-6.
172. Markar SR, Kutty R, Edmonds L, Sadat U, Nair S. A meta-analysis of minimally invasive versus traditional open vein harvest technique for coronary artery bypass graft surgery. Interactive cardiovascular and thoracic surgery. 2010;10(2):266-70.
173. Kotter JP. Leading Change: Why transformation efforts fail. Harvard business review. 1995;March - April 1995.
174. Kotter JP, Schlesinger LA. Choosing strategies for change. Harvard business review. 1979;57(2):106-14.
175. Guide to Leading Organisational Change, The University of Queensland, Australia, https://www.hr.uq.edu.au/step-6 (last access: 2016/08/21).
176. Katz RI, Dexter F, Rosenfeld K, Wolfe L, Redmond V, Agarwal D, et al. Survey study of anesthesiologists' and surgeons' ordering of unnecessary preoperative laboratory tests. Anesthesia and analgesia. 2011;112(1):207-12.
177. Chapman K, Chivers S, Gliddon D, Mitchell D, Robinson S, Sangster T, et al. Overcoming the barriers to the uptake of nonclinical microsampling in regulatory safety studies. Drug discovery today. 2014;19(5):528-32.
178. Dillen L, Loomans T, Van de Perre G, Versweyveld D, Wuyts K, de Zwart L. Blood microsampling using capillaries for drug-exposure determination in early preclinical studies: a beneficial strategy to reduce blood sample volumes. Bioanalysis. 2014;6(3):293-306.
179. Naylor JM, Adie S, Fransen M, Dietsch S, Harris I. Endorsing single-unit transfusion combined with a restrictive haemoglobin transfusion threshold after knee arthroplasty. Qual Saf Health Care. 2010;19(3):239-43.
180. Scrascia G, Guida P, Caparrotti SM, Capone G, Contini M, Cassese M, et al. Incremental Value of Anemia in Cardiac Surgical Risk Prediction With the European System for Cardiac Operative Risk Evaluation (EuroSCORE) II Model. The Annals of thoracic surgery. 2014;98(3):869-75.
181. Jans O, Jorgensen C, Kehlet H, Johansson PI, Lundbeck Foundation Centre for Fast-track H, Knee Replacement Collaborative G. Role of preoperative anemia for risk of transfusion and postoperative morbidity in fast-track hip and knee arthroplasty. Transfusion. 2014;54(3):717-26.
182. H.Rehak P. Calculation of the transfusion probability - The Mercuriali Algorithm. In: H. Gombotz KZ, D.R. Spahn, editor. Patient blood management: Thieme Publisher Stuttgart., New York, Dehli, Rio; 2016. p. 65 - 71.
183. A. Hofmann SF. Key role of benchmarking processes in PBM. In: H. Gombotz KZ, D.R. Spahn, editor. Patient Blood Management: Thiem Stuttgart-New York-Dehli-Rio; 2016. p. 40 - 53.
184. Hansen E, Bechmann V, Altmeppen J. Intraoperative blood salvage in cancer surgery: safe and effective? TransfusApherSci. 2002;27(2):153-7.
185. Esnaola NF, Cole DJ. Perioperative normothermia during major surgery: is it important? Adv Surg. 2011;45:249-63.
186. Gershengorn HB, Kocher R, Factor P. Management strategies to effect change in intensive care units: lessons from the world of business. Part II. Quality-improvement strategies. Annals of the American Thoracic Society. 2014;11(3):444-53.
187. Western Australia Patient Blood Management Programme - Website, Available from: http://ww2.health.wa.gov.au/Corporate%20search%20results?searchStr=pbm&site=current (last access: 11/07/2016).
188. Leahy MF, Hofmann A, Towler S, Trentino KM, Burrows SA, Swain SG, et al. Improved outcomes and reduced costs associated with a health-system-wide patient blood management program: a retrospective observational study in four major adult tertiary-care hospitals. Transfusion. 2017.

189. Hofmann A, Farmer S, Shander A. Five drivers shifting the paradigm from product-focused transfusion practice to patient blood management. The oncologist. 2011;16 Suppl 3:3-11.
190. Farmer SL, Towler SC, Leahy MF, Hofmann A. Drivers for change: Western Australia Patient Blood Management Program (WA PBMP), World Health Assembly (WHA) and Advisory Committee on Blood Safety and Availability (ACBSA). Best Pract Res Clin Anaesthesiol. 2013;27(1):43-58.
191. Freedman J, Luke K, Monga N, Lincoln S, Koen R, Escobar M, et al. A provincial program of blood conservation: The Ontario Transfusion Coordinators (ONTraC). Transfusion and apheresis science : official journal of the World Apheresis Association : official journal of the European Society for Haemapheresis. 2005;33(3):343-9.
192. Freedman J, Luke K, Escobar M, Vernich L, Chiavetta JA. Experience of a network of transfusion coordinators for blood conservation (Ontario Transfusion Coordinators [ONTraC]). Transfusion. 2008;48(2):237-50.
193. Patient Blood Management. 1st Edition ed. Stuttgart, New York: Georg Thieme Verlag; 2013.
194. Rossaint R, Bouillon B, Cerny V, Coats TJ, Duranteau J, Fernandez-Mondejar E, et al. The European guideline on management of major bleeding and coagulopathy following trauma: fourth edition. Crit Care. 2016;20:100.
195. Kozek-Langenecker SA, Afshari A, Albaladejo P, Santullano CA, De Robertis E, Filipescu DC, et al. Management of severe perioperative bleeding: guidelines from the European Society of Anaesthesiology. Eur J Anaesthesiol. 2013;30(6):270-382.

6 Appendix 1 – Methods of intervention

Consistently effective interventions

- Reminders (manual or computerised)
- Interventions which are multifaceted (a combination that includes two or more of the following: audit and feedback, reminders, local consensus processes, promotion)
- Education through interactive meetings (participation of healthcare providers in workshops that include discussion or/and practice)

Interventions of variable effectiveness

- Audit and feedback (or any summary of clinical performance)
- Support of local opinion leaders (practitioners identified by their colleagues as influential)
- Local consensus processes (inclusion of participating practitioners to ensure that they are in agreement that the chosen clinical problem is important and the approach to managing the problem is appropriate)
- Patient mediated interventions (any intervention aimed at changing the performance of healthcare providers for which specific information was sought from or given to patients)

Interventions that have limited effect

- Solitary educational materials are not sufficient (distribution of recommendations for clinical care, including clinical practice guidelines, audio-visual materials, and electronic publications)
- Didactic educational meetings when held out of context (such as lectures)

Available protocols and guidelines

Table 13. Available protocols and guidelines

Method	Topic of the guideline	Available from	Last access
Patient Blood Management in general			
	National Blood Authority, Australia	https://www.blood.gov.au/pbm-guidelines	11/07/2016
	Joint United Kingdom (UK) Blood Transfusion and Tissue Transplantation Services Professional Advisory Committee	http://www.transfusionguidelines.org/uk-transfusion-committees/national-blood-transfusion-committee/patient-blood-management	11/08/2016

	AABB - Advancing Transfusion and Cellular Therapies Worldwide	http://www.aabb.org/pbm/Pages/default.aspx	11/08/2016
	Society for Blood Management (SABM)	https://www.sabm.org/	11/08/2016
	Recommendations for the implementation of a Patient Blood Management programme. Application to elective major orthopaedic surgery in adults	http://www.bloodtransfusion.it/articolo.aspx?idart=002922&idriv=000106	11/08/2016
Blood salvage			
	National Institute for Health and Care Excellence (NICE) - Intraoperative blood cell salvage in obstetrics	https://www.nice.org.uk/guidance/ipg144	11/07/2016
	Royal Cornwall Hospital - Clinical Guideline for Intraoperative Cell Salvage	http://www.rcht.nhs.uk/DocumentsLibrary/RoyalCornwallHospitalsTrust/Clinical/Anaesthetics/ClinicalGuidelineNtraoperativeCellSalvage.pdf	11/07/2016
Maintaining normothermia			
	US Normothermia Guidelines	US Normothermia Guidelines	11/07/2016
	University of Pennsylvania Health System	http://www.uphs.upenn.edu/surgery/Education/trauma/SCCS/protocols/Normothermia_Tipsheet.pdf	11/07/2016
	ASPAN's Evidence-Based Clinical Practice Guideline for the Promotion of Perioperative Normothermia	http://www.aspan.org/Clinical-Practice/Clinical-Guidelines/Normothermia	11/07/2016
Anaesthesiological techniques			
	Controlled Hypotension – A Guide to Drug Choice	http://link.springer.com/article/10.2165/00003495-200767070-00007	11/07/2016
Management of severe bleeding			
	The European guideline on management of major bleeding and coagulopathy following trauma: fourth edition (194)	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4828865/	13/09/2016
	Management of severe perioperative bleeding: Guidelines from the European Society of Anaesthesiology (195)	https://www.esahq.org/guidelines/guidelines/published	13/09/2016

7 Appendix 2 – Further reading

- Al Ghwass, M.M., et al., Iron deficiency anemia in an Egyptian pediatric population: a cross-sectional study. Ann Afr Med, 2015. 14(1): p. 25-31.
- Ali, A., M.K. Auvinen, and J. Rautonen, The aging population poses a global challenge for blood services. Transfusion, 2010. 50(3): p. 584-8.
- Al-Refaie, W.B., et al., Blood transfusion and cancer surgery outcomes: a continued reason for concern. Surgery, 2012. 152(3): p. 344-54.
- Amato, A. and M. Pescatori, Perioperative blood transfusions for the recurrence of colorectal cancer. Cochrane Database Syst Rev, 2006(1): p. CD005033.
- Amrein, K., et al., Adverse events and safety issues in blood donation--a comprehensive review. Blood Rev, 2012. 26(1): p. 33-42.
- Amrein, K., et al., Apheresis affects bone and mineral metabolism. Bone, 2010. 46(3): p. 789-95.
- Anand, I., et al., Anemia and Its Relationship to Clinical Outcome in Heart Failure. Circulation, 2004. 110(2): p. 149-154.
- Anand, I.S., Anemia and chronic heart failure implications and treatment options. J Am.Coll.Cardiol., 2008. 52(7): p. 501-511.
- Ania, B.J., et al., Incidence of anemia in older people: an epidemiologic study in a well defined population. J Am Geriatr Soc, 1997. 45(7): p. 825-31.
- Bach, V., et al., Prevalence and possible causes of anemia in the elderly: a cross-sectional analysis of a large European university hospital cohort. Clin Interv Aging, 2014. 9: p. 1187-96.
- Baele, P., et al., The Belgium BIOMED Study about transfusion for surgery. Acta Anaesthesiol Belg, 1998. 49(4): p. 243-303.
- Baele, P.L., et al., Guidelines for the transfusion of red cells. Acta Clin Belg., 2008. 63(5): p. 301-312.
- Baele, P.L., et al., The SANGUIS Study in Belgium: an overview of methods and results. Safe and good use of blood in surgery. Acta Chir Belg., 1994. 94(2): p. 69-74.
- Beale, E., et al., Blood transfusion in critically injured patients: a prospective study. Injury, 2006. 37(5): p. 455-65.
- Beghe, C., A. Wilson, and W.B. Ershler, Prevalence and outcomes of anemia in geriatrics: a systematic review of the literature. Am J Med, 2004. 116 Suppl 7A: p. 3s-10s.
- Bell, M.L., et al., Does preoperative hemoglobin independently predict short-term outcomes after coronary artery bypass graft surgery? Ann.Thorac.Surg., 2008. 86(5): p. 1415-1423.
- Bennett, C.L., et al., Venous Thromboembolism and Mortality Associated With Recombinant Erythropoietin and Darbepoetin Administration for the Treatment of Cancer-Associated Anemia. JAMA: The Journal of the American Medical Association, 2008. 299(8): p. 914-924.
- Beutler, E. and C. West, Hematologic differences between African-Americans and whites: the roles of iron deficiency and alpha-thalassemia on hemoglobin levels and mean corpuscular volume. Blood, 2005. 106(2): p. 740-5.
- Beutler, E. and J. Waalen, The definition of anemia: what is the lower limit of normal of the blood hemoglobin concentration? Blood, 2006. 107(5): p. 1747-1750.
- Blajchman, M.A. and E.C. Vamvakas, The continuing risk of transfusion-transmitted infections. N Engl J Med, 2006. 355(13): p. 1303-5.
- Bochicchio, G.V., et al., Outcome analysis of blood product transfusion in trauma patients: a prospective, risk-adjusted study. World J Surg, 2008. 32(10): p. 2185-9.
- Brabin, L., B.J. Brabin, and S. Gies, Influence of iron status on risk of maternal or neonatal infection and on neonatal mortality with an emphasis on developing countries. Nutr Rev, 2013. 71(8): p. 528-40.
- Bracey, A.W., et al., Lowering the hemoglobin threshold for transfusion in coronary artery bypass procedures: effect on patient outcome. Transfusion, 1999. 39(10): p. 1070-7.
- Brecher, M.E., T. Monk, and L.T. Goodnough, A standardized method for calculating blood loss. Transfusion., 1997. 37(10): p. 1070-1074.

- Brittenham, G.M., Iron balance in the red blood cell donor. Dev Biol (Basel), 2005. 120: p. 77-82.
- Brittenham, G.M., Iron deficiency in whole blood donors. Transfusion, 2011. 51(3): p. 458-61.
- Budnitz, D.S., et al., Emergency hospitalizations for adverse drug events in older Americans. N Engl J Med, 2011. 365(21): p. 2002-12.
- Cable, R.G., et al., Iron deficiency in blood donors: the REDS-II Donor Iron Status Evaluation (RISE) study. Transfusion, 2012. 52(4): p. 702-11.
- Caro, J.J., et al., Anemia as an independent prognostic factor for survival in patients with cancer: a systemic, quantitative review. Cancer, 2001. 91(12): p. 2214-21.
- Carson, J.L., et al., Effect of anaemia and cardiovascular disease on surgical mortality and morbidity. Lancet., 1996. %19;348(9034): p. 1055-1060.
- Carson, J.L., et al., Liberal or Restrictive Transfusion in High-Risk Patients after Hip Surgery. New England Journal of Medicine, 2011. 365(26): p. 2453-2462.
- Carson, J.L., et al., Liberal or restrictive transfusion in high-risk patients after hip surgery. The New England journal of medicine, 2011. 365(26): p. 2453-62.
- Carson, J.L., et al., Mortality and morbidity in patients with very low postoperative Hb levels who decline blood transfusion. Transfusion, 2002. 42(7): p. 812-818.
- Carson, J.L., P.A. Carless, and P.C. Hebert, Transfusion thresholds and other strategies for guiding allogeneic red blood cell transfusion. Cochrane.Database.Syst.Rev., 2012. 4:CD002042. doi: 10.1002/14651858.CD002042.pub3.: p. CD002042.
- Churchhouse, A.M., et al., Does blood transfusion increase the chance of recurrence in patients undergoing surgery for lung cancer? Interact Cardiovasc Thorac Surg, 2012. 14(1): p. 85-90.
- Ciesla, D.J., et al., A 12-year prospective study of postinjury multiple organ failure: has anything changed? Arch Surg, 2005. 140(5): p. 432-8; discussion 438-40.
- Cohn, C.S., et al., A data-driven approach to patient blood management. Transfusion, 2014. 54(2): p. 316-22.
- Corwin, H.L. and J.L. Carson, Blood transfusion--when is more really less? N Engl J Med, 2007. 356(16): p. 1667-9.
- Curley, G.F., et al., Transfusion Triggers for Guiding RBC Transfusion for Cardiovascular Surgery: A Systematic Review and Meta-Analysis. Crit Care Med, 2014.
- Curry, N., et al., Trauma-induced coagulopathy--a review of the systematic reviews: is there sufficient evidence to guide clinical transfusion practice? Transfusion medicine reviews, 2011. 25(3): p. 217-231 e2.
- Custer, B. and J.S. Hoch, Cost-effectiveness analysis: what it really means for transfusion medicine decision making. Transfus Med Rev, 2009. 23(1): p. 1-12.
- De, S.L., et al., Preoperative anemia in patients undergoing coronary artery bypass grafting predicts acute kidney injury. J Thorac.Cardiovasc.Surg., 2009. 138(4): p. 965-970.
- den Elzen, W.P., et al., Effect of anemia and comorbidity on functional status and mortality in old age: results from the Leiden 85-plus Study. CMAJ., 2009. 181(3-4): p. 151-157.
- den Elzen, W.P.J., et al., Effect of anemia and comorbidity on functional status and mortality in old age: results from the Leiden 85-plus Study. Canadian Medical Association Journal, 2009. 181(3-4): p. 151-157.
- Denas, G., et al., Major bleeding in patients undergoing PCI and triple or dual antithrombotic therapy: a parallel-cohort study. J Thromb Thrombolysis, 2013. 35(2): p. 178-84.
- Directive 2002/98/EC of the European Parliament and of the Council. 2002, European Parliament and Council. p. 11.
- Doodeman, H.J., et al., The effect of a preoperative erythropoietin protocol as part of a multifaceted blood management program in daily clinical practice (CME). Transfusion, 2013. 53(9): p. 1930-9.
- Du Pont-Thibodeau, G., K. Harrington, and J. Lacroix, Anemia and red blood cell transfusion in critically ill cardiac patients. Ann Intensive Care, 2014. 4: p. 16.
- Dunne, J.R., et al., Allogenic blood transfusion in the first 24 hours after trauma is associated with increased systemic inflammatory response syndrome (SIRS) and death. Surg Infect (Larchmt), 2004. 5(4): p. 395-404.
- Dunne, J.R., et al., Blood transfusion is associated with infection and increased resource utilization in combat casualties. Am Surg, 2006. 72(7): p. 619-25; discussion 625-6.
- Dunne, J.R., et al., Perioperative anemia: an independent risk factor for infection, mortality, and resource utilization in surgery. J Surg.Res., 2002. 102(2): p. 237-244.

- Dyke, C., et al., Universal definition of perioperative bleeding in adult cardiac surgery. J Thorac Cardiovasc Surg, 2014. 147(5): p. 1458-1463.e1.
- English, M., et al., Blood transfusion for severe anaemia in children in a Kenyan hospital. Lancet, 2002. 359(9305): p. 494-5.
- Engoren, M., et al., The independent effects of anemia and transfusion on mortality after coronary artery bypass. Ann Thorac Surg, 2014. 97(2): p. 514-20.
- Estcourt, L. J., et al. "Restrictive versus liberal red blood cell transfusion strategies for people with haematological malignancies treated with intensive chemotherapy or radiotherapy, or both, with or without haematopoietic stem cell support." Cochrane Database Syst Rev 1: Cd011305, 2017.
- Favrat, B., et al., Evaluation of a single dose of ferric carboxymaltose in fatigued, iron-deficient women--PREFER a randomized, placebo-controlled study. PLoS One, 2014. 9(4): p. e94217.
- Ferraris, V.A., et al., Perioperative blood transfusion and blood conservation in cardiac surgery: the Society of Thoracic Surgeons and The Society of Cardiovascular Anesthesiologists clinical practice guideline. Ann Thorac Surg., 2007. 83(5 Suppl): p. S27-S86.
- Fink, A., et al., The International Consensus Conference on Transfusion Outcomes. Transfusion, 2009. 29: p. 2254.
- Frank, S.M., et al., Risk-adjusted clinical outcomes in patients enrolled in a bloodless program. Transfusion, 2014. 54(10 Pt 2): p. 2668-77.
- Frank, S.M., et al., Risk-adjusted clinical outcomes in patients enrolled in a bloodless program. Transfusion, 2014.
- Freedman, J., et al., Experience of a network of transfusion coordinators for blood conservation (Ontario Transfusion Coordinators [ONTraC]). Transfusion, 2008. 48: p. 237-250.
- Gaskell, H., et al., Prevalence of anaemia in older persons: systematic review. BMC Geriatr, 2008. 8: p. 1.
- Global, regional, and national age-sex specific all-cause and cause-specific mortality for 240 causes of death, 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet, 2015. 385(9963): p. 117-71.
- Gombotz, H. and H. Knotzer, Preoperative identification of patients with increased risk for perioperative bleeding. Curr Opin Anaesthesiol, 2013. 26(1): p. 82-90.
- Goodnough, L.T. and A. Shander, Patient blood management. Anesthesiology., 2012. 116(6): p. 1367-1376.
- Goodnough, L.T., et al., Detection, Evaluation, and Management of Anemia in the Elective Surgical Patient. Anesthesia Analgesia, 2005. 101(6): p. 1858-1861.
- Greinacher, A., et al., Implications of demographics on future blood supply: a population-based cross-sectional study. Transfusion, 2010.
- Gross, I., et al., Patient blood management in cardiac surgery results in fewer transfusions and better outcome. Transfusion, 2015.
- Gupta, P.K., et al., Preoperative Anemia Is an Independent Predictor of Postoperative Mortality and Adverse Cardiac Events in Elderly Patients Undergoing Elective Vascular Operations. Ann Surg., 2013.
- Guralnik, J.M., et al., Prevalence of anemia in persons 65 years and older in the United States: evidence for a high rate of unexplained anemia. Blood, 2004. 104: p. 2263-2268.
- Haagsma, J., et al., Review of disability weight studies: comparison of methodological choices and values. Population Health Metrics, 2014. 12(1): p. 20.
- Hajjar La, V.J., Transfusion requirements after cardiac surgery: The tracs randomized controlled trial. JAMA: The Journal of the American Medical Association, 2010. 304(14): p. 1559-1567.
- Hajjar, L.A., et al., Transfusion requirements after cardiac surgery: the TRACS randomized controlled trial. JAMA, 2010. 304(14): p. 1559-67.
- Halabi, W.J., et al., Blood transfusions in colorectal cancer surgery: incidence, outcomes, and predictive factors: an American College of Surgeons National Surgical Quality Improvement Program analysis. Am J Surg, 2013. 206(6): p. 1024-33.
- Hare, G.M., J. Freedman, and C. David Mazer, Review article: risks of anemia and related management strategies: can perioperative blood management improve patient safety? Can J Anaesth, 2013. 60(2): p. 168-75.
- Hasin, T., et al., Prevalence and prognostic significance of transient, persistent, and new-onset anemia after acute myocardial infarction. Am J Cardiol., 2009. 104(4): p. 486-491.

- Hebert, P.C., et al., A multicenter, randomized, controlled clinical trial of transfusion requirements in critical care. Transfusion Requirements in Critical Care Investigators, Canadian Critical Care Trials Group. N Engl J Med, 1999. 340(6): p. 409-17.
- Herman, C.R., et al., Clopidogrel increases blood transfusion and hemorrhagic complications in patients undergoing cardiac surgery. Ann Thorac Surg, 2010. 89(2): p. 397-402.
- Hill, G.E., et al., Allogeneic blood transfusion increases the risk of postoperative bacterial infection: a meta-analysis. J Trauma, 2003. 54(5): p. 908-14.
- Hofmann, A., et al., Economic considerations on transfusion medicine and patient blood management. Best Pract Res Clin Anaesthesiol, 2013. 27(1): p. 59-68.
- Hogervorst, E., et al., Tolerance of intraoperative hemoglobin decrease during cardiac surgery. Transfusion, 2014.
- Inghilleri, G., Prediction of transfusion requirements in surgical patients: a review. Transfusion Alternatives in Transfusion Medicine, 2010. 11(1): p. 10-19.
- Jauregui-Lobera, I., Iron deficiency and cognitive functions. Neuropsychiatr Dis Treat, 2014. 10: p. 2087-95.
- Jin, B., et al., A meta-analysis of erythropoiesis-stimulating agents in anaemic patients with chronic heart failure. European Journal of Heart Failure, 2010. 12(3): p. 249-253.
- Kapetanakis, E.I., et al., Effect of clopidogrel premedication in off-pump cardiac surgery: are we forfeiting the benefits of reduced hemorrhagic sequelae? Circulation, 2006. 113(13): p. 1667-74.
- Karkouti, K., et al., Low hematocrit during cardiopulmonary bypass is associated with increased risk of perioperative stroke in cardiac surgery. Ann.Thorac.Surg., 2005. 80(4): p. 1381-1387.
- Karkouti, K., et al., Risk Associated With Preoperative Anemia in Cardiac Surgery: A Multicenter Cohort Study. Circulation, 2008. 117(4): p. 478-484.
- Karkouti, K., et al., The independent association of massive blood loss with mortality in cardiac surgery. Transfusion, 2004. 44(10): p. 1453-62.
- Karkouti, K., et al., The influence of baseline hemoglobin concentration on tolerance of anemia in cardiac surgery. Transfusion., 2008. 48(4): p. 666-672.
- Karkouti, K., et al., The influence of perioperative coagulation status on postoperative blood loss in complex cardiac surgery: a prospective observational study. Anesth Analg, 2010. 110(6): p. 1533-40.
- Karthik, S., et al., Reexploration for bleeding after coronary artery bypass surgery: risk factors, outcomes, and the effect of time delay. Ann Thorac Surg, 2004. 78(2): p. 527-34; discussion 534.
- Kassebaum, N.J., et al., A systematic analysis of global anemia burden from 1990 to 2010. Vol. 123. 2014. 615-624.
- Keller-Stanislawski, B., et al., Frequency and severity of transfusion-related acute lung injury--German haemovigilance data (2006-2007). Vox Sang., 2010. 98(1): p. 70-77.
- Koch, C.G., et al., Hospital-acquired anemia: Prevalence, outcomes, and healthcare implications. Journal of Hospital Medicine, 2013. 8(9): p. 506-512.
- Korte, W., et al., Peri-operative management of antiplatelet therapy in patients with coronary artery disease. Joint position paper by members of the working group on Perioperative Haemostasis of the Society on Thrombosis and Haemostasis Research (GTH), the working group on Perioperative Coagulation of the Austrian Society for Anesthesiology, Resuscitation and Intensive Care (OGARI) and the Working Group Thrombosis of the European Society for Cardiology (ESC). Thromb.Haemost., 2011. 105(5): p. 743-749.
- Kulier, A., et al., Impact of Preoperative Anemia on Outcome in Patients Undergoing Coronary Artery Bypass Graft Surgery. Circulation, 2007. 116(5): p. 471-479.
- Kulier, A., H. Gombotz, and E. Stubenvoll, Erythropoietin in patients undergoing coronary artery bypass graft surgery. Clin Investig, 1994. 72(6 Suppl): p. S19-24.
- Lackritz, E.M., et al., Effect of blood transfusion on survival among children in a Kenyan hospital. Lancet, 1992. 340(8818): p. 524-8.
- Lacroix, J., et al., Transfusion strategies for patients in pediatric intensive care units. N Engl J Med, 2007. 356(16): p. 1609-19.
- Lamberts, M., et al., Bleeding after initiation of multiple antithrombotic drugs, including triple therapy, in atrial fibrillation patients following myocardial infarction and coronary intervention: a nationwide cohort study. Circulation, 2012. 126(10): p. 1185-93.

- Lance, M.D., et al., Perioperative dilutional coagulopathy treated with fresh frozen plasma and fibrinogen concentrate: a prospective randomized intervention trial. Vox Sang, 2012. 103(1): p. 25-34.
- Landi, F., et al., Anemia status, hemoglobin concentration, and mortality in nursing home older residents. J.Am.Med.Dir.Assoc., 2007. 8(5): p. 322-327.
- LaPar, D.J., et al., Blood product conservation is associated with improved outcomes and reduced costs after cardiac surgery. J Thorac Cardiovasc Surg, 2013. 145(3): p. 796-803; discussion 803-4.
- Laub, R., et al., Specific protein content of pools of plasma for fractionation from different sources: impact of frequency of donations. Vox Sang, 2010. 99(3): p. 220-31.
- Levi, M., E. Eerenberg, and P.W. Kamphuisen, Bleeding risk and reversal strategies for old and new anticoagulants and antiplatelet agents. J Thromb Haemost, 2011. 9(9): p. 1705-12.
- Levi, M., Epidemiology and management of bleeding in patients using vitamin K antagonists. J Thromb Haemost, 2009. 7 Suppl 1: p. 103-6.
- Levy, J.H., et al., Fibrinogen and hemostasis: a primary hemostatic target for the management of acquired bleeding. Anesth Analg, 2012. 114(2): p. 261-74.
- Levy, J.H., et al., Multidisciplinary approach to the challenge of hemostasis. Anesth Analg, 2010. 110(2): p. 354-64.
- Lindenfeld, J., Prevalence of anemia and effects on mortality in patients with heart failure. Am Heart J, 2005. 149(3): p. 391-401.
- Linder, B.J., et al., The impact of perioperative blood transfusion on survival after nephrectomy for non-metastatic renal cell carcinoma (RCC). BJU Int, 2013.
- Lippi, G., M. Franchini, and E.J. Favaloro, Thrombotic complications of erythropoiesis-stimulating agents. Semin.Thromb.Hemost., 2010. 36(5): p. 537-549.
- Lipsic, E., P. van der Meer, and D.J. van Veldhuisen, Erythropoiesis-stimulating agents and heart failure. Cardiovasc Ther, 2011. 29(4): p. e52-9.
- Liu, L., et al., Perioperative allogenenic blood transfusion is associated with worse clinical outcomes for hepatocellular carcinoma: a meta-analysis. PLoS One, 2013. 8(5): p. e64261.
- Liumbruno, G.M., et al., Patient blood management: a fresh look at a new approach to blood transfusion. Minerva Anestesiol, 2014.
- Maki, T., Optimizing blood usage through benchmarking. Transfusion, 2007. 47: p. 145S-148S.
- Malone, D.L., et al., Blood transfusion, independent of shock severity, is associated with worse outcome in trauma. J Trauma, 2003. 54(5): p. 898-905; discussion 905-7.
- Maluenda, G., et al., The clinical significance of hematocrit values before and after percutaneous coronary intervention. Am Heart J., 2009. 158(6): p. 1024-1030.
- Mannucci, P.M. and M. Levi, Prevention and treatment of major blood loss. N Engl J Med, 2007. 356(22): p. 2301-11.
- Manzano-Fernandez, S., et al., Increased major bleeding complications related to triple antithrombotic therapy usage in patients with atrial fibrillation undergoing percutaneous coronary artery stenting. Chest, 2008. 134(3): p. 559-67.
- Martinsson, A., et al., Anemia in the general population: prevalence, clinical correlates and prognostic impact. Eur J Epidemiol, 2014. 29(7): p. 489-98.
- McCann, J.C. and B.N. Ames, An overview of evidence for a causal relation between iron deficiency during development and deficits in cognitive or behavioral function. Am J Clin Nutr, 2007. 85(4): p. 931-45.
- McClellan, W.M., et al., Prevalence and severity of chronic kidney disease and anemia in the nursing home population. J.Am.Med.Dir.Assoc., 2010. 11(1): p. 33-41.
- McLean, E., et al., Worldwide prevalence of anaemia, WHO Vitamin and Mineral Nutrition Information System, 1993-2005. Public Health Nutr, 2009. 12(4): p. 444-54.
- McQuilten, Z.K., et al., Transfusion practice varies widely in cardiac surgery: Results from a national registry. J Thorac Cardiovasc Surg, 2014. 147(5): p. 1684-1690.e1.
- Mercuriali, F. and M. Intaglietta, Proposal of an algorithm to help the choice of the best transfusion strategy. Curr.Med.Res.Opin., 1996. 13(13): p. 465-478.
- Milman, N., et al., Iron status in 358 apparently healthy 80-year-old Danish men and women: relation to food composition and dietary and supplemental iron intake. Ann.Hematol., 2004. 83(7): p. 423-429.

- Milman, N., et al., Iron status in Danish men 1984-94: a cohort comparison of changes in iron stores and the prevalence of iron deficiency and iron overload. Eur J Haematol., 2002. 68(6): p. 332-340.
- Milman, N., et al., Iron status in Danish women, 1984-1994: a cohort comparison of changes in iron stores and the prevalence of iron deficiency and iron overload. Eur J Haematol, 2003. 71(1): p. 51-61.
- Miyashita, T., et al., An analysis of risk factors of perioperative bleeding in surgical repair of abdominal aortic aneurysm. Journal of Cardiovascular Surgery, 2000. 41(4): p. 595-599.
- Moore, F.A., E.E. Moore, and A. Sauaia, Blood transfusion. An independent risk factor for postinjury multiple organ failure. Arch Surg, 1997. 132(6): p. 620-4; discussion 624-5.
- Morton, J., et al., Frequency and outcomes of blood products transfusion across procedures and clinical conditions warranting inpatient care: an analysis of the 2004 healthcare cost and utilization project nationwide inpatient sample database. Am J Med Qual, 2010. 25(4): p. 289-96.
- Moskowitz, D.M., et al., The impact of blood conservation on outcomes in cardiac surgery: is it safe and effective? Ann.Thorac.Surg., 2010. 90(2): p. 451-458.
- Munoz, M., et al., Efficacy and safety of intravenous iron therapy as an alternative/adjunct to allogeneic blood transfusion. Vox Sanguinis, 2008. 94(3): p. 172-183.
- Munoz, M., J.A. Garcia-Erce, and A.F. Remacha, Disorders of iron metabolism. Part II: iron deficiency and iron overload. J Clin Pathol, 2011. 64(4): p. 287-96.
- Murphy, C.L. and J.J. McMurray, Approaches to the treatment of anaemia in patients with chronic heart failure. Heart Fail.Rev., 2008. 13(4): p. 431-438.
- Murphy, G.J., et al., Liberal or Restrictive Transfusion after Cardiac Surgery. New England Journal of Medicine, 2015. 372(11): p. 997-1008.
- Murray, C.J. and A.D. Lopez, Mortality by cause for eight regions of the world: Global Burden of Disease Study. Lancet, 1997. 349(9061): p. 1269-76.
- Murray, D.J., et al., Coagulation changes during packed red cell replacement of major blood loss. Anesthesiology., 1988. 69(6): p. 839-845.
- Na, H.S., et al., Effects of intravenous iron combined with low-dose recombinant human erythropoietin on transfusion requirements in iron-deficient patients undergoing bilateral total knee replacement arthroplasty. Transfusion., 2011. 51(1): p. 118-124.
- Napolitano, L.M., et al., Clinical practice guideline: red blood cell transfusion in adult trauma and critical care. Crit Care Med, 2009. 37(12): p. 3124-57.
- Nguyen, P.H., et al., Multicausal etiology of anemia among women of reproductive age in Vietnam. Eur J Clin Nutr, 2015. 69(1): p. 107-13.
- Niles, S.E., et al., Increased mortality associated with the early coagulopathy of trauma in combat casualties. J Trauma., 2008. 64(6): p. 1459-1463.
- Norgaard, A., et al., Monitoring compliance with transfusion guidelines in hospital departments by electronic data capture. Blood Transfus, 2014: p. 1-11.
- Nusselder, W.J., et al., The relation between non-occupational physical activity and years lived with and without disability. J Epidemiol Community Health, 2008. 62(9): p. 823-8.
- Ozawa, S., Patient blood management: use of topical hemostatic and sealant agents. Aorn j, 2013. 98(5): p. 461-78.
- Patel, K.V., Epidemiology of anemia in older adults. Semin Hematol, 2008. 45(4): p. 210-7.
- Patel, K.V., Epidemiology of anemia in older adults. Semin.Hematol., 2008. 45(4): p. 210-217.
- Peterson, P.N., et al., Association of longitudinal measures of hemoglobin and outcomes after hospitalization for heart failure. Am Heart J, 2010. 159(1): p. 81-9.
- Piazza, G., et al., Anticoagulation-associated adverse drug events. Am J Med, 2011. 124(12): p. 1136-42.
- Pietersz, R.N., et al., Prophylactic platelet transfusions. Vox Sang, 2012. 103(2): p. 159-76.
- Pollitt, E., The developmental and probabilistic nature of the functional consequences of iron-deficiency anemia in children. J Nutr, 2001. 131(2s-2): p. 669s-675s.
- Qvist, N., et al., Recombinant human erythropoietin and hemoglobin concentration at operation and during the postoperative period: reduced need for blood transfusions in patients undergoing colorectal surgery--prospective double-blind placebo-controlled study. World J Surg., 1999. 23(1): p. 30-35.
- Ranucci, M., et al., Impact of preoperative anemia on outcome in adult cardiac surgery: a propensity-matched analysis. Ann Thorac.Surg., 2012. 94(4): p. 1134-1141.

- Ranucci, M., et al., Major bleeding, transfusions, and anemia: the deadly triad of cardiac surgery. Ann Thorac Surg, 2013. 96(2): p. 478-85.
- Rasmussen, K.M. and R.J. Stoltzfus, New evidence that iron supplementation during pregnancy improves birth weight: new scientific questions. Am J Clin Nutr, 2003. 78(4): p. 673-4.
- Riva, E., et al., Association of mild anemia with hospitalization and mortality in the elderly: the Health and Anemia population-based study. Haematologica., 2009. 94(1): p. 22-28.
- Roeloffzen, W.W., et al., Thrombocytopenia affects plasmatic coagulation as measured by thrombelastography. Blood Coagul.Fibrinolysis., 2010. 21(5): p. 389-397.
- Rohde, J.M., et al., Health care-associated infection after red blood cell transfusion: a systematic review and meta-analysis. JAMA, 2014. 311(13): p. 1317-26.
- Rosengart, T.K., et al., Open heart operations without transfusion using a multimodality blood conservation strategy in 50 Jehovah's Witness patients: implications for a "bloodless" surgical technique. J Am.Coll.Surg., 1997. 184(6): p. 618-629.
- Sabatine, M.S., et al., Association of hemoglobin levels with clinical outcomes in acute coronary syndromes. Circulation., 2005. 111(16): p. 2042-2049.
- Salisbury, A.C., et al., Incidence, correlates, and outcomes of acute, hospital-acquired anemia in patients with acute myocardial infarction. Circ Cardiovasc Qual Outcomes, 2010. 3(4): p. 337-46.
- Salpeter, S.R., J.S. Buckley, and S. Chatterjee, Impact of more restrictive blood transfusion strategies on clinical outcomes: a meta-analysis and systematic review. Am J Med, 2014. 127(2): p. 124-131.e3.
- Samolyk, K.A., State-of-the-art blood management in cardiac surgery. Semin.Cardiothorac.Vasc.Anesth., 2009. 13(2): p. 118-121.
- Sattur, S., et al., The influence of anemia after percutaneous coronary intervention on clinical outcomes. Clin Cardiol., 2009. 32(7): p. 373-379.
- Scott, S.N., et al., The effects of epoetin alfa on transfusion requirements in head and neck cancer patients: a prospective, randomized, placebo-controlled study. Laryngoscope., 2002. 112(7 Pt 1): p. 1221-1229.
- Shander, A., et al., Activity-based costs of blood transfusions in surgical patients at four hospitals. Transfusion, 2010. 50(4): p. 753-65.
- Shander, A., et al., What is really dangerous: anaemia or transfusion? Br J Anaesth, 2011. 107 Suppl 1: p. i41-59.
- Shavelle, R.M., R. MacKenzie, and D.R. Paculdo, Anemia and mortality in older persons: does the type of anemia affect survival? Int.J.Hematol., 2012. 95(3): p. 248-256.
- Shavit, L., et al., Preoperative Hemoglobin and Outcomes in Patients with CKD Undergoing Cardiac Surgery. Clin J Am Soc Nephrol, 2014. 9(9): p. 1536-44.
- Silverberg, D.S., et al., The role of correction of anaemia in patients with congestive heart failure: a short review. Eur J Heart Fail, 2008. 10(9): p. 819-23.
- Singh, A.K., et al., Correction of anemia with epoetin alfa in chronic kidney disease. N Engl J Med., 2006. 355(20): p. 2085-2098.
- Smith, G.A., et al., Oral or parenteral iron supplementation to reduce deferral, iron deficiency and/or anaemia in blood donors. Cochrane Database Syst Rev, 2014. 7: p. CD009532.
- Sowade, O., et al., Avoidance of allogeneic blood transfusions by treatment with epoetin beta (recombinant human erythropoietin) in patients undergoing open-heart surgery. Blood., 1997. 89(2): p. 411-418.
- Stauder, R. and S.L. Thein, Anemia in the elderly: clinical implications and new therapeutic concepts. Haematologica, 2014. 99(7): p. 1127-30.
- Stoltzfus, R.J., Rethinking anaemia surveillance. Lancet, 1997. 349(9067): p. 1764-6.
- Stowell, C.P., et al., An open-label, randomized, parallel-group study of perioperative epoetin alfa versus standard of care for blood conservation in major elective spinal surgery: safety analysis. Spine (Phila Pa, 1976. %2009 Nov 1;34(23): p. 2479-2485.
- Stramer, S.L., et al., Emerging infectious disease agents and their potential threat to transfusion safety. Transfusion, 2009. 49 Suppl 2: p. 1S-29S.
- Terrovitis, J.V., et al., Anemia in heart failure: pathophysiologic insights and treatment options. Future.Cardiol., 2009. 5(1): p. 71-81.
- Transfusion, M.o.t.E.C.P.A.o.B., Guide to the preparation, use and quality assurance of blood components. 2013.
- Trentino, K.M., et al., Increased hospital costs associated with red blood cell transfusion. Transfusion, 2014.

- Triulzi, D.J., Transfusion-related acute lung injury: current concepts for the clinician. Anesth.Analg., 2009. 108(3): p. 770-776.
- Unsworth-White, M.J., et al., Resternotomy for bleeding after cardiac operation: a marker for increased morbidity and mortality. Ann Thorac Surg, 1995. 59(3): p. 664-7.
- Use of blood products for elective surgery in 43 European hospitals. The Sanguis Study Group. Transfus.Med, 1994. 4(4): p. 251-268.
- Vamvakas, E.C. and M.A. Blajchman, Transfusion-related mortality: the ongoing risks of allogeneic blood transfusion and the available strategies for their prevention. Blood, 2009. 113(15): p. 3406-17.
- van Straten, A.H.M., et al., Preoperative Hemoglobin Level as a Predictor of Survival After Coronary Artery Bypass Grafting: A Comparison With the Matched General Population. Circulation, 2009. 120(2): p. 118-125.
- Vanasse, G.J. and N. Berliner, Anemia in Elderly Patients: An Emerging Problem for the 21st Century. ASH Education Program Book, 2010. 2010(1): p. 271-275.
- Vaucher, P., et al., Effect of iron supplementation on fatigue in nonanemic menstruating women with low ferritin: a randomized controlled trial. CMAJ, 2012. 184(11): p. 1247-54.
- Vlaar, A.P., et al., The practice of reporting transfusion-related acute lung injury: a national survey among clinical and preclinical disciplines. Transfusion., 2009.
- Volkova, N. and L. Arab, Evidence-based systematic literature review of hemoglobin/hematocrit and all-cause mortality in dialysis patients. Am J Kidney Dis, 2006. 47(1): p. 24-36.
- Wang, H., et al., Age-specific and sex-specific mortality in 187 countries, 1970-2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet, 2012. 380(9859): p. 2071-94.
- Wang, T., et al., Perioperative blood transfusion is associated with worse clinical outcomes in resected lung cancer. Ann Thorac Surg, 2014. 97(5): p. 1827-37.
- Weiss, G. and L.T. Goodnough, Anemia of chronic disease. N Engl J Med, 2005. 352(10): p. 1011-23.
- Wells, A.W., et al., Where does blood go? Prospective observational study of red cell transfusion in north England. BMJ, 2002. 325(7368): p. 803.
- Weltert, L., et al., Preoperative very short-term, high-dose erythropoietin administration diminishes blood transfusion rate in off-pump coronary artery bypass: a randomized blind controlled study. J Thorac Cardiovasc Surg., 2010. 139(3): p. 621-626.
- Wiersum-Osselton, J.C., T. Marijt-van der Kreek, and W.L. de Kort, Donor vigilance: what are we doing about it? Biologicals, 2012. 40(3): p. 176-9.
- Wong, C. J., et al. A cluster-randomized controlled trial of a blood conservation algorithm in patients undergoing total hip joint arthroplasty. Transfusion. 2007. 47(5): p. 832-841.
- World Health Organization. Nutritional anaemias. Report of a WHO Scientific Group. Technical Report Series, 1968. 405.
- Yao, H.S., et al., Intraoperative Allogeneic Red Blood Cell Transfusion in Ampullary Cancer Outcome after Curative Pancreatoduodenectomy: A Clinical Study and Meta-Analysis. World J Surg, 2008.
- Yoo, Y.C., et al., Effect of single recombinant human erythropoietin injection on transfusion requirements in preoperatively anemic patients undergoing valvular heart surgery. Anesthesiology., 2011. 115(5): p. 929-937.
- Zakai, N.A., et al., A Prospective Study of Anemia Status, Hemoglobin Concentration, and Mortality in an Elderly Cohort: The Cardiovascular Health Study. Archives of Internal Medicine, 2005. 165(19): p. 2214-2220.
- Zakai, N.A., et al., Hemoglobin decline, function, and mortality in the elderly: the cardiovascular health study. Am.J.Hematol., 2013. 88(1): p. 5-9.
- Zilberberg, M., et al., Anemia, transfusions and hospital outcomes among critically ill patients on prolonged acute mechanical ventilation: a retrospective cohort study. Critical Care, 2008. 12(2): p. R60.

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