European Commission

Building national programmes of Patient Blood Management (PBM) in the EU

A Guide for Health Authorities

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Abbreviations

ACQSHC	Australian Commission on Quality and Safety in Health Care
ACBSA	Advisory Committee on Blood Safety and Availability in the United States
AR	Anaemia Rate
CCG	Clinical Commissioning Groups (CCG)
CPOE	Computerised physician order entry
DBAC	Data Collection, Benchmarking and Analytics Committee
ICD	International Classification of Disease
JDoH	Jurisdiction's Departments of Health
EPAS	Electronic Patient Administration System
EPHO	Essential Public Health Operations
EU	European Union
FFP	Fresh Frozen Plasma
GRADE	Grading of Recommendations, Assessment, Development and Evaluations
GSC	Guidelines and Standards Committee
FTE	Full time equivalent
HTA	Health Technology Assessment
ICU	Intensive Care Unit
IT	Information Technology
JPAC	Joint United Kingdom Blood Transfusion and Tissue Transplantation Services Professional Advisory Committee
LIS	Laboratory Information System
MoH	Minister of Health
NA	National Authority
NBA	National Blood Authority
NHMRC	National Health and Medical Research Council
NHS	National Health Service
NHSBT	National Health Service Blood and Transplant
PBM	Patient Blood Management
PLT	Platelets
QoL	Quality of Life
RBC	Red Blood Cells
SDH	Social Determinants of Health
TI	Transfusion Index
TIS	Transfusion Information System
TR	Transfusion Rate
TReg	Transfusion Registry
USDHHS	US Department of Health and Human Services
WHA	World Health Assembly
WHO	World Health Organization

1 The Framework for National Authorities to Actively Pursue the Dissemination and Implementation of Patient Blood Management within their Territories

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). 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 a patient-focused, evidence-based and systematic approach to optimize the management of patient and transfusion of blood products for quality and effective patient care. It 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, the use of alternatives to blood transfusion and blood conservation."* (3).

The priorities for action agreed on in this forum were grouped into clinical/hospital, national and international levels (4). Some of the actions requested on the national level are:

- Identify major national clinical needs, and based on these, develop and implement national guidelines on blood use including patient blood management
- Establish a minimum data set that can be captured at each hospital
- Conduct multi-centric studies
    - Patient outcomes
    - Alternatives
- Conduct benchmarking studies to compare practices in different hospitals and clinicians
- Develop educational curriculum
    - Pre-service
    - In-service
    - Post graduate educations (multiple disciplines)
- Focus on outcome research
- Translate - Make available current evidence through desk research - meta analysis
    - Move forward on randomised controlled trials (RCTs)
    - Need more funding for RCTs in Patient Blood Management

Resolution WHA63.12 and the subsequent WHO Global Forum on Patient Blood Management set the framework for National Authorities (NAs) of the 194 WHO Member States to actively support the dissemination and implementation of PBM.

NOTE
Resolution WHA63.12 and the subsequent WHO Global Forum on Patient Blood Management set the framework for National Authorities to actively support the dissemination and implementation of PBM.

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 guide for national authorities, and an equivalent one for hospitals, were delivered to the European Commission under that contract. They have no regulatory or legally–binding status but are intended as tools to support NAs and hospitals 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.

2 The Development of Patient Blood Management across the Globe

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 (5-7). Contrary to the traditional product-focused approach of Optimal Blood Use programmes, PBM takes a patient-focused approach. This is achieved by sustainably correcting anaemia, preventing blood loss and harnessing and optimising the physiological tolerance of anaemia. Thus, unnecessary transfusion is reduced or avoided and patient safety and outcome are improved.

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 (8) 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 nine languages. Subsequently, several national PBM programmes were developed including Better Blood Transfusion in Scotland (9), PBM by NHS Blood and Transplant (NHSBT) in England (10), initiatives in Italy (11, 12) and in four University hospitals in Germany (13).

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 (14). 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 (15-23). 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.

PBM initiatives across the globe have contributed to good practices to treat anaemia, minimize blood loss and avoid unnecessary transfusions while improving patient outcomes. Such results were achieved with the state-wide Western Australia Department of Health PBM program (23), the ONTRraC Blood Conservation Program in Ontario (24), PBM programs of hospital groups and single institutions, but also several programs for specific patient populations (25-35). Studies looking at single PBM modalities, for example anaemia management across different patient populations (36-51) or bleeding management including point-of-care coagulation management in populations with high bleeding risk (52-65), have demonstrated safety, effectiveness and improved outcome.

NOTE
Large government driven PBM initiatives and hospital based PBM programmes are currently expanding. They have demonstrated that unnecessary transfusions can be avoided by correcting anaemia and minimizing blood loss while improving patient outcomes. Numerous studies including randomized controlled trials looking at single PBM modalities have demonstrated safety, effectiveness and improved outcome.

Large observational studies point to the high overall treatment cost associated with transfusion and the cost savings achieved through implementation of PBM in large healthcare systems (23, 24, 66-68). Several randomized controlled trials comparing usual care with single or combined PBM measures demonstrate significant reductions in blood product utilization and other economically relevant factors in the intervention group (37, 39, 52, 55, 61, 62, 69), and Health Technology Assessments (HTA) for some PBM modalities are available (70, 71). Certain PBM measures in certain indications might not be cost-effective (72) or might require additional evidence due to conflicting results (73). The economic aspects of PBM were not within the scope of this contract and are therefore not addressed further in this document.

3 The Opportunity for National Authorities to Improve Patient Outcomes and Safety through Dissemination and Implementation of PBM

Anaemia, major blood loss and transfusions are three independent risk factors for adverse patient outcomes. This section of the report puts the focus on the patient safety and outcome aspects of this triad of independent risk factors and the opportunity for the NAs to address them through pro-actively supporting the dissemination and implementation of PBM.

Anaemia is a global epidemic and accounted for 8.8% of the world's total disability from all conditions in 2010, with iron deficiency anaemia as the most common cause. The anaemia prevalence in Western Europe, Central Europe and Eastern Europe was 11.1%, 15.9% and 15.5% for males and 15.3%, 20.2% and 27.7% for females respectively. (74). In the context of an aging population in the developed world, it is important to note that anaemia prevalence increases with age. In particular, pre-operative anaemia prevalence in various surgical populations is much more pronounced than in the general population (19-75% of elective surgery patients, 24-26% of cardiac surgery patients, 30-40% of non-cardiac surgery patients, 19-38% of orthopaedic surgery patients and 70% of colorectal surgery patients) (75-82).

The evidence strongly suggests that anaemia is an independent risk factor for adverse outcomes including mortality, morbidity (e.g. cardiac, respiratory, urinary tract, wound events, sepsis, and venous thromboembolism), length of hospital stay and postoperative admission to intensive care (81, 83). In addition, the literature and the Australian PBM guidelines state that anaemia is a contraindication for elective surgery (84-86). However, in the vast majority of surgical patients anaemia remains uncorrected. Given the estimated number of more than 74 million major surgeries[1] in Europe (Western Europe with 56.3 million, Central Europe with 5.9 million and Eastern Europe with 12.0 million) (87, 88), it is widely acknowledged that practice change could have a sustainable impact on improved outcomes for millions of patients along with considerable health economic improvements every year.

NOTE

Anaemia is a global epidemic with high prevalence in the aging and surgical population.

The current evidence strongly suggests that anaemia is an independent predictor for adverse outcomes including mortality, morbidity and length of hospital stay and increases cost of care. In addition, guidelines state that anaemia is a contraindication for elective surgery. Practice change towards routine anaemia management in elective surgical patients could have a sustainable impact on improved outcomes for millions of patients along with considerable health economic improvements every year.

[1] Any intervention occurring in a hospital operating theatre involving the incision, excision, manipulation, or suturing of tissue, usually requiring regional or general anaesthesia or sedation

Blood loss is another independent risk factor for adverse outcomes. Severe bleeding events increase mortality and morbidity by up to three times (89-93). However, data show a high variability of surgical blood loss for matched patients (75, 94, 95). Therefore, poorly controlled blood loss represents a serious patient safety issue that should be addressed by blood conservation strategies, including meticulous surgery and a number of evidence-based anaesthesiological measures and techniques. This underlines the importance for NAs to explore all possible avenues to promote the minimisation of patient blood loss as recommended by WHA63.12 " (96). It also supports that the correction of pre-operative anaemia should be a standard of care, because this increases the patients' safety margin in the event of severe bleeding.

A further patient safety issue is the routine phlebotomy practice on wards and ICUs that is not always indicated. The haematopoietic system of a healthy individual produces roughly 40ml of blood per day. However, the total amount of blood phlebotomised in an ICU patient is often a multiple of this volume. A study at the Cleveland Clinic in the U.S. showed that that an average patient-day in the cardio-vascular ICU involved a total volume of about 116 ml of blood drawn (97). Over the entire ICU stay, this sometimes leads to a patient's iatrogenic blood loss equivalent to several units of packed red blood cells (RBCs) (97-102).

NOTE
Blood loss through poorly controlled bleeding or unnecessary iatrogenic causes is another independent predictor for adverse outcomes. It also induces and exacerbates anaemia. Practice change could mitigate risk and therefore improve patient safety.

For decades the default treatment for blood loss and/or anaemia has been allogeneic blood transfusion which is the most common therapeutic intervention in hospitalised patients (103). In settings such as critical bleeding and bone marrow failure, blood transfusion is an essential intervention and is potentially life-saving. However, accumulating evidence shows that particularly in haemodynamically stable patients, transfusion is another independent risk factor for adverse outcomes. For example, some systematic reviews and meta-analyses of randomized controlled trials (graded as 1A evidence) have shown some evidence of increased risks (including infection, cardiac events, re-bleeding and in hospital mortality) from liberal transfusion (Table 1) (104-108). In addition, large numbers of risk-adjusted observational studies have shown an independent dose-response association between transfusion and increased morbidity, length of hospital stay and mortality (109-123). Some of these effects may be attributable to transfusion related immunomodulation (124, 125) and should be considered together with other immunological risks of transfusion, such as immediate and delayed immunological reactions to blood cells (126), transfusion-related lung injury (127) and post-transfusion antibodies/immunological memory, which may compromise future transfusions and pregnancies (126) as well as organ transplantations (128) and haematopoietic stem cell transplantations (129).

Table 1. Meta-analyses comparing outcomes with restrictive vs. liberal transfusion strategies

	Studies	Patients	Reduction in RBC Transfusions (restrictive group)	Hospital Mortality	Infections
Carson et al. 2012 (104)	19	6,264	-39%	-23%	-19%
Rohde et al. 2014 (105)	18	7,593	Not analysed	Not analysed	-12%/-18%*
Salpeter et al. 2014 (107)	3	2,364	-43%#	-26%	-14%
Holst et al. 2015 (106)	31	9,813	-44%	No difference	-27%
Carson et al. 2016 (108)	31	12,587	-43%	No difference°	No difference

* The meta-analysis from Rhode et al. refers to serious infections.

Transfusion rate

° 30-day mortality

Other adverse outcomes due to physiologic influences of blood component transfusions are also observed. In particular cardiac/circulatory overload, which have recently been shown to be more frequent than hitherto thought (130-132). These pose perioperative risk in vascular, transplant and thoracic surgeries, in intensive care patients (133), the elderly, and patients with kidney failure, fluid overload or cardiac failure (134, 135). All of which are frequent transfusion recipients. The summary of the 2014 annual reporting of serious adverse events and reactions (SARE) lists transfusion associated circulatory overload (TACO) as the leading cause of transfusion-related death (see http://ec.europa.eu/health/blood_tissues_organs/docs/blood_sare_2014_en.pdf).

It is challenging to capture fully all these clinical transfusion associated reactions in the current procedures established for haemovigilance. However, in the future there might be possibilities to link incidence data on healthcare associated infections [see https://www.vicniss.org.au] and possibly other adverse outcomes with transfusion and haemovigilance data. Such more comprehensive reporting might accelerate the uptake of PBM.

NOTE

In the setting of critical bleeding and bone marrow failure, blood transfusion is potentially life-saving. However, accumulating evidence shows that in the majority of clinical settings with most patients being haemodynamically stable, transfusion is another independent risk factor for adverse outcomes.

In the future, haemovigilance systems might use opportunities to link incidence data on healthcare associated infections, ischaemic events, mortality and other adverse outcomes with transfusion and haemovigilance data to accelerate the uptake of PBM.

Effective information and education on the current evidence for adverse outcome from anaemia and blood loss, but also on all potential adverse reactions from the transfusion of allogeneic blood components (including the directly infectious, the non-infectious, the immunological, physiological, acute, delayed and long-term adverse events) is equally important for a more rapid dissemination and implementation of PBM. This needs to reach out to the majority of health professionals, including general practitioners, but also to patients. Raising awareness fosters the physician-patient discussion on PBM and better enables informed consent and ultimately patient autonomy.

NOTE

NAs have the opportunity to improve patient outcomes and patient safety through facilitation and coordination of information and education related to all known risks of anaemia, bleeding and transfusion, and to PBM as the new standard of care to largely pre-empt these risks. This approach needs to reach out to health professionals, but also patients, to ensure fully informed consent and patient autonomy.

4 Using the Donabedian Model to Identify Current Quality Gaps in Ensuring PBM as a National Standard of Care

Physicians are responsible for the best possible treatment of the individual patient. Public health authorities are responsible for creating and maintaining a framework under which the community in general can stay healthy (http://www.who.int/healthsystems/publications/hss_key/en/).

By many, the Donabedian Quality Framework (136, 137) is considered the predominant model for quality improvement used in public health settings. It allows grouping each quality measure of a health system under one of three quality categories, namely the quality of:

- structure
- process and
- outcome.

The fundamental concept behind this model is that a good structure leads to improved processes and thus improved results.

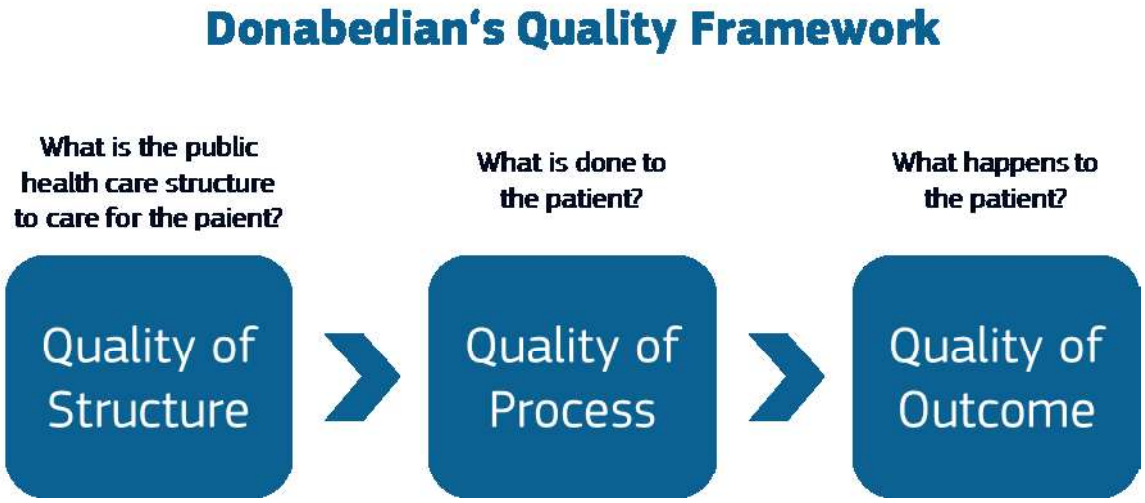

Figure 1. Quality framework with three main dimensions: quality of structure, quality of process and quality of outcome

The first dimension is the adequate quality of healthcare *structure* and is the basic condition to enable an effective continuum of healthcare for the public. It includes timely surveillance and monitoring of issues critical to healthcare, services aimed at the protection and promotion of health as well as the prevention of disease. To sustainably ensure and improve these services, healthcare structures requires governance, human resources, training, education, equipment, technology and facilities. In addition, they require

organisation, including not only management and reporting systems and funding, but also relevant research.

The second dimension is the actual quality of *process* or *care*, asking and evaluating what is actually done to and for patients. The focus here is on the quality of diagnostic and therapeutic services, the quality of prevention and patient preparation, and the quality of patient education, empowerment, autonomy and pathways to establish informed consent.

The third dimension is the quality of *outcomes*. It refers to the consequences of the interaction between patients and the healthcare system. Parameters to measure actual outcomes include, but are not limited to, mortality, morbidity and quality of life, readmission and reoperation rates, average length of hospital stay and patient satisfaction.

In a patient-centric health system, the quality of *outcome* should mainly determine the quality of *structure* and *process*. This is in line with the key components of a well-functioning health system responding in a balanced way to meet a population's needs and expectations as defined by the WHO (http://www.who.int/healthsystems/publications/hss_key/en/).

- Improving the health status of individuals, families and communities
- Defending the population against what threatens its health
- Protecting people against the financial consequences of ill-health
- Providing equitable access to people-centred care.

4.1 The Donabedian Model Points to the NAs as Key Players for Disseminating and Implementing PBM

The three key questions to evaluate the three Donabedian quality dimensions are well suited to identify the weaknesses and quality gaps in ensuring PBM as a new healthcare standard.

First, the question of what happens to the patient when treated according to PBM principles (quality of PBM outcome) is being answered through a large and increasing body of clinical evidence; including many large observational studies, pre-and post-implementation studies, and randomised controlled trials (23-29, 31, 32, 37, 39, 138, 139). They clearly demonstrate that modifying the triad of independent risk factors for adverse outcomes – anaemia, bleeding and transfusion – by applying the three-pillar-concept of PBM significantly reduces adverse patient outcomes. This includes morbidity, mortality, readmission rates, and hospital length of stay at reduced overall cost.

Second, the question of what is and could be done to treat and improve the outcome in anaemic and bleeding patient populations (quality of PBM process) is satisfactorily answered. The EU-PBM pilot project carried out as part of the EU Public Health Programme contract, and numerous PBM programmes described in the literature demonstrate that PBM can be sustainably implemented in single hospitals and even across state wide public hospital systems (24, 138, 139).

Third, the question of what is the healthcare structure that can broadly enable PBM (quality of PBM structure) reveals large structural deficits and obstacles for establishing PBM in daily clinical practice. Despite the compelling scientific evidence in support of PBM and its practicality, it is still far from being implemented routinely as a standard of care. Specific factors limiting the uptake of PBM are:

- Lack of PBM awareness in relevant stakeholder groups
- Lack of prioritising the implementation of PBM given the large potential for improvement of healthcare
- Lack of information to the public at large about the risks of anaemia, bleeding and transfusion
- Lack of PBM information targeted at relevant professional stakeholder groups
- Lack of undergraduate education on PBM and transfusion in both nursing and medical schools
- Lack of postgraduate PBM education and training for nurses, physicians and other health professionals
- Lack of patient education and empowerment
- Lack of research and knowledge of the health consequences of anaemia in the population at risk of being hospitalised, in different patient groups and in particular during postoperative rehabilitation
- Disincentives and missing motivation for healthcare providers to implement PBM
- Lack of coordinated patient care between pre-hospitalisation and hospitalisation phase
- Lack of career perspectives/incentives for clinicians interested in PBM
- Lack of a continuous PBM benchmarking, analytics and reporting system
- No hospital accreditation for PBM
- No PBM certification for clinicians

NOTE
The Donabedian quality framework helps identify quality gaps and points such as structural deficits and obstacles limiting the uptake of PBM as standard of care. It primarily lies in the executive power and public responsibility of the NAs to remove these impediments to fully enable healthcare providers to routinely practise PBM for improving the overall quality of care. PBM needs to be prioritised in order to achieve the full improvement potential in the growing patient population segment at risk.

Usually the Ministry of Health (MoH) takes on the overall responsibility for delivering “the right care in the right place at the right time”. However, in this era of rapidly growing and often changing evidence “right care” is constantly refined and often re-defined. Growing demand for health services influenced by current population dynamics and budgetary constraints pose additional challenges. In this dynamic environment, the chief administrators of the MoH are urged to act as “change managers”. To adjust the healthcare structure and its functionality to newly identified needs, systems managers are required to take the lead through prioritisation, coordination and delegation.

Activities under the governance of the MoH to overcome structural deficits and obstacles limiting the uptake of PBM could include:

- Carrying out tasks under competent departments within the MoH
    - Patient information & education
    - Patient safety measures
    - Health monitoring
    - Disease control
    - Documentation (case history, patient data, outcomes data)
    - Creation/adoption of quality standards and evidence-based clinical guidelines
- Delegating tasks to autonomous administrative bodies such as Healthcare Insurance for billing, coding & funding of PBM related extra- and intramural services, the Medical Council overseeing the standards, conduct and competence of physicians, and other bodies or entities.
- Organising and facilitating trans-sectoral cooperation with other ministries such as the ministry of education (undergraduate curricula when appropriate), ministry of justice (patient rights, medico-legal aspects)
- Liaising with non-governmental organisations (NGOs) such as patient organisations and patient advocates
- Organising and/or outsourcing certain tasks to consultancies and professional organisations or entities such as data collection, benchmarking and analytics.

It primarily lies in the power and public responsibility of NAs to remove these structural impediments in order to fully enable healthcare providers to practice PBM and achieve improved overall outcomes for a large and growing patient population.

In a growing number of countries, public health authorities seek to achieve what is now called the triple aim (140):

1) improving the patient and provider experience of care,
2) improving the health of populations, and
3) reducing the per capita cost of healthcare.

Engaging in the dissemination and implementation of PBM represents a unique opportunity to reach the triple aim on a large scale.

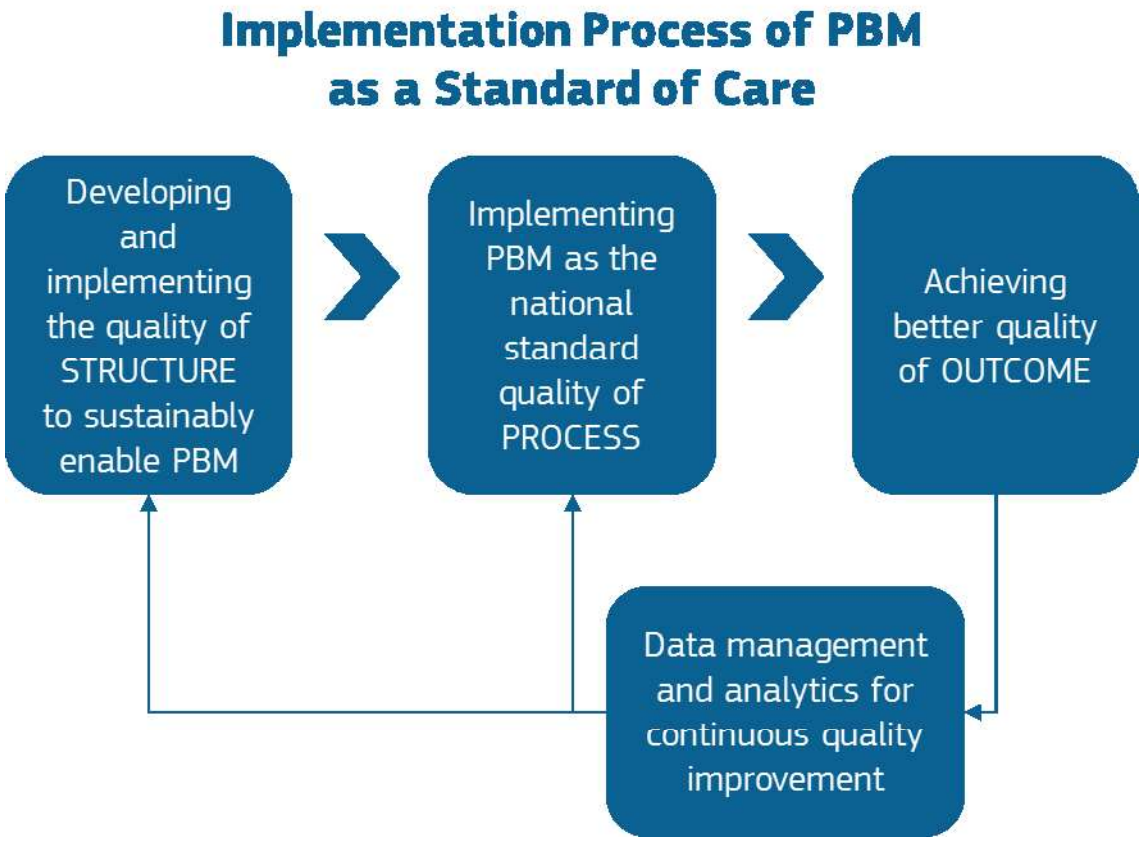

Figure 2. Quality framework and PBM

5 Using the WHO Europe's Scheme of Essential Public Health Operations (EPHO) as a Structural Framework to Disseminate and Implement PBM

The WHO Regional Committee for Europe adopted the European Action Plan for Strengthening the Public Health Capacities and Services and its accompanying resolution (EUR/RC62/R5) (141) in Malta 2012. The action plan outlines in detail the 10 Essential Public Health Operations (EPHOs) (142) which can be applied to capacity building, planning and delivery of services. It proposes 10 avenues of action related to the EPHOs, intended to assist EU Member States in strengthening public health capacities and services in an equitable way across the whole region. Due to the generic and comprehensive methodology recommended, these 10 EPHOs are particularly well suited to be used as a structural framework to disseminate and implement PBM as a standard of care within Europe.

The operations are divided in three main parts:

- Service intelligence,
- Service enabler and
- Service delivery

Service delivery, incorporating the main areas of health protection, health promotion and disease prevention, are informed by robust public health intelligence and enhanced by enablers (Figure 3). Understanding the structure and the 10 EPHOs helps identify what the specific *structural* deficits and obstacles for the uptake of PBM are and how the NAs could overcome them. The most effective and efficient method of delivering these operations is through an integrated approach, rather than through vertically organised programmes.

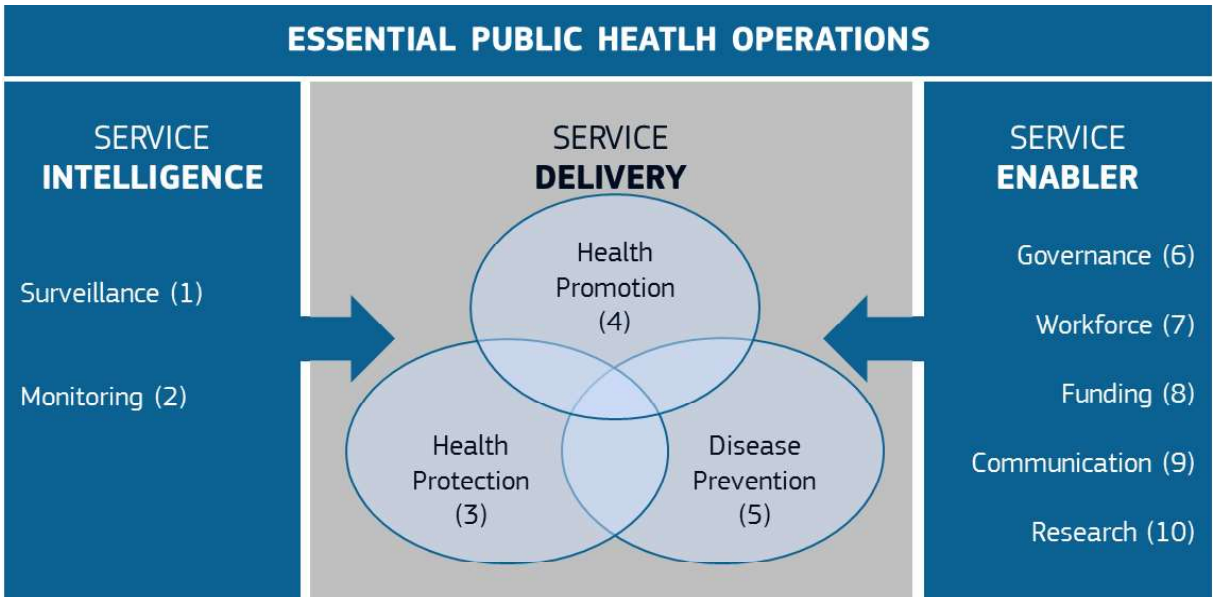

Figure 3. Three main clusters of public health services and related essential operations, adapted from (143)

5.1 Service Intelligence and PBM

5.1.1 Surveillance of anaemia, transfusion and outcome in the hospitalised population

Policy-makers need to have a clear and timely picture of how health is maintained in a given population, and what indicators contribute to or reduce opportunities to be healthy. Surveillance systems have the purpose of fulfilling this task. They are designed to continuously feed information and intelligence to assess health needs, detect trends, respond, plan or adjust activities aimed at improving health and measure their impact.

Why a PBM surveillance system is deemed necessary

Each year an estimated 20 - 40% of all major surgeries in the EU Member States are in patients with uncorrected anaemia (75-82). This often leads to allogeneic blood transfusions and concomitant additional risks that could be pre-empted when applying PBM modalities. Since this ongoing practice has a significant negative impact on patient outcomes across the EU, adequate surveillance measures by NAs to control and mitigate the risk for anaemia and transfusion are strongly recommended.

Surveillance measures recommended to NAs

1. Stepwise introduction of mandatory continuous collection of patient level data on anaemia, transfusion and outcome to measure and guide the implementation of PBM as a standard of care

Most hospitals' electronic patient administration systems (EPAS) routinely capture patient demographics, admission details, ICD diagnoses, procedures and outcome data. They are essential for coding, billing and reimbursement of each single case. Sometimes, these systems also capture whether a patient has been

transfused in the course of the hospitalisation, which allows transfusion rates to be derived for different patient groups. Sometimes EPAS also capture whether patients are anaemic when admitted.

However, patient level data on pre- and postoperative haemoglobin levels, point of care coagulation tests, platelet counts, the number and type of blood components transfused, and other relevant parameters are usually not available on EPAS. This information is usually only found on the hospitals' Laboratory Information System (LIS) and Transfusion Information System (TIS) or transfusion registry (TReg). Usually LIS and TIS/TReg are not automatically linked to EPAS.

The quality of the process of care-data should reflect the relevant patient populations at risk (hospitalized, scheduled for surgery, anaemic, bleeding) and the PBM elements and transfusion process within these populations. In addition, outcome data should be in place to continuously monitor the effect of changes to the process of care (survival, adverse reactions, length of stay, re-admission). NAs should therefore strongly recommend the data linkage between EPAS, LIS and TIS, in order to establish key performance indicators on anaemia, bleeding and adherence to transfusion or preferably PBM guidelines. The developmental stages of electronic data collection and automation between EU Member States might still largely differ in terms of quality, compliance and degree of implementation. Therefore, a stepwise introduction of mandatory continuous collection of patient level data adapted to measure and guide the implementation of PBM is recommendable.

In some EU Member States, a number of key performance indicators (KPIs) are already monitored and analysed by national haemovigilance organisations. A practical and efficient recommendation could be to extend haemovigilance tasks to aggregate and monitor also PBM KPIs, as listed in this Guide.

Step I: Basic Key Performance Indicators (KPIs) (mandatory):

Key measures to provide basic KPIs for inpatients are transfusion rate (TR), transfusion index (TI) and anaemia rate (AR) at admission. TR is the percentage of patients transfused, TI is the number of transfusions per patient and AR is the percentage of anaemic patients. These parameters should be regularly reported to clinical department heads and the hospitals' quality and safety managers. TR, TI and AR should be calculated across all hospitalised patients as well as for subgroups based on demographic data (gender, age), admission details (planned or emergency interventions), ICD diagnostic codes and procedures, and patient outcome information (e.g. complications, nosocomial infection, length of hospital stay and mortality).

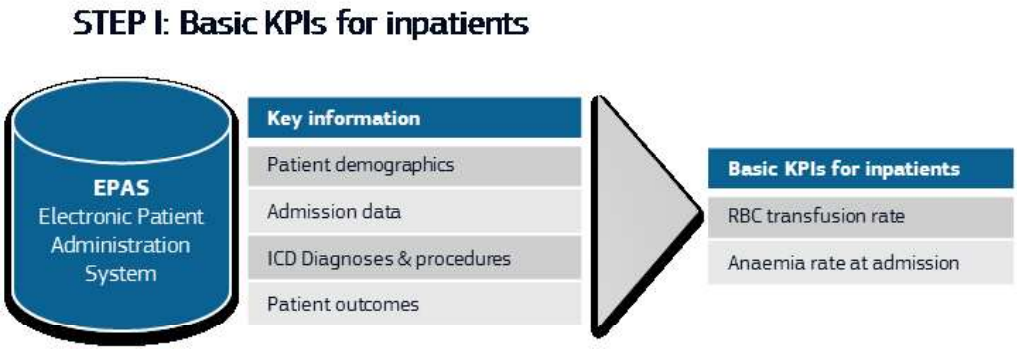

Figure 4. Step I: Mandatory introduction of basic key performance indicators (KPI) for inpatients: RBC transfusion rate, transfusion index and rate of patients admitted with and/or operated with anaemia.

Step II: Advanced KPIs (recommended)

After successful implementation of systems to provide basic KPIs, the system should be enhanced by using the individual case identification codes to link EPAS, TIS and LIS. Type and units of blood and blood components (RBC, FFP, PLT, Cryoprecipitate) transfused, laboratory values pre-transfusion, and at admission and discharge should be linked in order to allow automated electronic processing of the following KPIs for blood and blood components (RBC, FFP, PLT, Cryo) per 1.000 discharges. Data coverage (e.g. the percentage of units transfused with a pre-tranfusion trigger within a relevant time frame) should be actively reported for all indicators:

- AR at admission and discharge
- AR prior to elective surgery
- Intraoperative blood loss (external measured bleeding volume)
- Perioperative total blood loss (external and internal) calculated by total red cell mass before and after surgery (preferably at day 5)
- Rate (%) of single RBC units transfused
- Mean RBC transfusion triggers and targets
- Mean pre / post PLT transfusion platelet counts/ platelet function tests
- Mean pre / post FFP transfusion coagulation tests (international normalised ratio (INR)/viscoelastic point of care tests)
- Use of antifibrinolytic medication (tranexamic acid) during certain types of surgery
- Correct management of antithrombotic medication perioperatively (documentation of guideline-compliant medication + monitoring of platelet function tests and/or coagulation tests in high risk patients)
- Utilisation rate of topical haemostatic agents in certain types of surgery
- Utilisation rate of autotransfusion in selected types of surgery

(see additional/complementary information under “Establishing continuous PBM benchmarking and reporting systems” in “Supporting Patient Blood Management (PBM) in the EU A Practical Implementation Guide for Hospitals”)

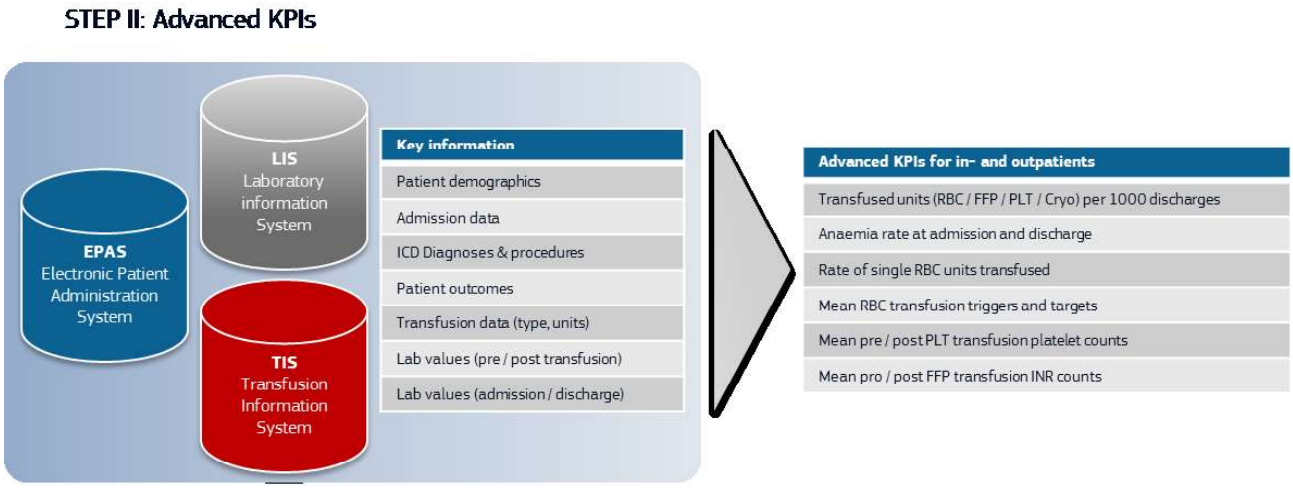

Figure 5. Recommended integration of different data sources to provide advanced KPIs which allow continuous surveillance of the utilisation of blood and blood components (RBC, FFP, PLT, Cryoprecipitate) (144, 145).

NOTE

The mandatory electronic documentation, collection and evaluation of basic patient level KPIs on anaemia, transfusion and outcome and their provision to decision makers, health care professionals and the public are strongly recommended.

Once a basic data system has been implemented, the development of an advanced PBM data system is recommended.

2. Aggregation of collected data for continuous benchmarking, analytics and reporting/feedback to healthcare providers

Benchmarking is a valuable tool used to continuously monitor and evaluate quality of care at different levels. There are two main approaches: continuous measurement of one's own performance (internal) and comparison with best performer's (external) benchmarking. The aim of internal benchmarking is to compare the situation pre- and post-implementation of certain measures, and to monitor the outcome at regular intervals. The aim of external benchmarking is to compare the outcome of institutional procedures and behavioural habits within a typical group of organisations, and to learn about the latest methods and practices of other organisations. Benchmarking programmes are usually implemented either at a regional level initiated by health authorities, or in an institution-initiated model where one site identifies key indicators and invites other institutions to participate. The reliability of the results, both within an institution and between institutions or healthcare systems, strongly relies on the validity of data derived from each source.

For reliable and high quality PBM benchmarking results, it is recommended to set up an automated process for data aggregation by linking EPAS, TIS and LIS based on the individual case identifier and

providing direct data export at regular intervals (monthly or quarterly). PBM reports should include data analyses with standard tables and diagrams. Reports of KPIs should be presented as time series to follow the utilisation of blood and blood components and the association with patient outcome. For clinical department heads, hospital managers, and NAs it is highly recommended to perform an intra- and inter-institutional comparison of KPIs between hospitals with comparable procedures and patient populations.

NOTE
Clinical department heads and hospital administrators must know how patient outcomes and the transfusion practice of their institution changes over time and how this compares with other hospitals. For sustainable and successful implementation of PBM it is highly recommended for NAs to strengthen and encourage their hospitals to participate in national and international benchmarking processes.

5.1.2 Monitoring health hazards

Actively monitoring health problems and hazards in the community is pivotal for health authorities to react in a timely manner when a crisis is developing, setting the right priorities and responding effectively to emergencies. Monitoring the change in health hazards from transfusion during the transition to PBM is useful to demonstrate the need for PBM.

Why monitoring of transfusion variability is indicated

Uncorrected anaemia and poorly controlled bleeding are hazardous for patients and lead to additional hazards due to increased utilisation of allogeneic blood components that could be avoided. Thus, high variability of blood utilisation in matched patient populations is an indicator for sub-optimal quality and safety. Institutions with PBM programmes systematically reduce the described patient risks as indicated by more homogenous and relatively low levels of blood utilisation, while the opposite is observed in those without PBM programmes. Numerous studies have shown transfusion variability for matched patients between 0 and 100%, (75, 94, 146, 147). Although the literature shows that the prevalence of under-transfusion (148) is clearly less than the prevalence of over-transfusion (149-158), transfusion monitoring also helps to detect this risk.

Flagging TR and TI outliers recommended to NAs

To foster quality of care through PBM and prevent unnecessary health hazards, particularly in high-risk populations, it is recommended to routinely flag institutions with TR and TI outliers and to link these results with patient-level data on transfusion thresholds, pre-transfusion anaemia and outcomes, including major morbidity and mortality..

NOTE
Routine monitoring and flagging of institutions with TR and TI outliers and linking these results with patient-level data on transfusion thresholds, pre-transfusion anaemia and patient outcomes will support NAs in fostering PBM, thus preventing health hazards.

Additional benefits from monitoring and addressing high levels of blood utilization:

Reducing blood utilization through PBM and the monitoring of extreme transfusion variability will also reduce the risks from transfusions that are usually monitored by haemovigilance systems such as the small, but remaining risk of transfusion transmitted viral, bacterial and parasitic infections, transfusion-related acute lung injury (TRALI), transfusion associated circulatory overload (TACO), wrong unit transfused and others.

5.2 Service Delivery and PBM

5.2.1 Health protection through PBM

Health protection encompasses activities to ensure conditions for healthy living, avoid conditions for unhealthy living, and protect health. NAs have available a number of instruments to achieve these purposes, including public information and campaigns, specific information, training and education for health professionals, education and empowerment of high-risk patient groups, but also legislation and sanctions.

Intelligence gathered from PBM related surveillance, monitoring (see sections 4.1.1 and 4.1.2) and newly emerging evidence is essential to develop relevant informational and educational contents to protect health. Based on this, single health protective measures might be legislated.

PBM related health protection measures recommended to NAs

For **clinical/academic key opinion leaders** and other PBM **experts:**

- Create a framework to regularly analyse PBM related surveillance and monitoring data and update relevant scientific evidence on the management of anaemia, hypoxia and bleeding.

For the **public at large**:

- Create a framework and develop contents to raise public awareness about anaemia and the advantages of PBM, the importance of maintaining normal iron and haemoglobin levels, and controlling, maintaining and protecting the circulatory volume in health and disease, as well as the risks and benefits of allogeneic transfusions.

For **patients and high-risk groups:**

- Create a framework and develop contents to inform, educate and empower patients and high-risk groups (see 3.2.1 in the "*PBM Implementation Guide for Health Professionals to implement Patient Blood Management as a new standard of care*".) with the aim to achieve fully informed consent and making autonomous decisions on treatments and therapies involving PBM modalities.

- Recommend active and passive patient support from patient advocacies and patient safety groups to disseminate PBM.

For **clinicians, quality and safety managers, hospital administrators and public health representatives:**

- Create a framework and develop materials to inform and educate clinicians, quality and safety managers, hospital administrators and public health representatives on the triad of independent risk factors for adverse outcome and PBM as an evidence-based, safe and cost-effective standard of care.

For the **coordination of framework building, content development, legislation and other activities** see section 4.3.1 Governance.

NOTE

Recommended health protection measures for the NAs :

- To raise public awareness about the risks of anaemia, blood loss and transfusions
- To educate patients in PBM, its treatment modalities with their risks and benefits, and empower them to shared decision-making
- To create a framework for experts to regularly analyse PBM and relevant surveillance and monitoring data
- To create a framework and contents to inform and educate clinicians, quality and safety managers, hospital administrators and public health representatives on PBM as an evidence-based, safe and cost-effective standard of care.

5.2.2 Health promotion including action to address inequity and social determinants of health

The purpose is to promote and improve population health and well-being by reducing inequalities and addressing the broader social and environmental determinants of health.

Why PBM is relevant for health promotion

One of the social determinants of health (SDH) is the social condition that people live in. The anaemia prevalence in Central Europe, and even more so in Eastern Europe, is very high compared to Western Europe (74). At the same time, blood safety levels are lower and blood availability is more restricted in areas with higher anaemia prevalence (159). Another SDH is the patient's gender. Women are more likely to receive allogeneic RBC transfusions and a greater quantity of blood than men. In some patient populations this is also associated with increased mortality in females when compared to matched or comparable male patients (160-162). To some degree, these regional and gender inequalities of patients' health status can be mitigated by instituting PBM as standard of care, and in particular by routinely correcting anaemia pre-operatively (first pillar of PBM).

PBM related health promotion measures recommended to NAs

Anaemia in general, iron deficiency and iron deficiency anaemia could be broadly addressed by a national or international/global health promotion campaign. Introducing and supporting a "World Anaemia Day" could improve health literacy on anaemia, its symptoms, treatment, nutritional aspects and outcome. It would not only raise the awareness within the global society including the healthy and diseased, but also of health professionals. It might also trigger research initiatives and new pharmacological and nutritional

developments. Potential partners to promote and sustain the “World Anaemia Day” could be WHO, United Nations World Food Programme, ICEF, MoHs, the World Bank, select professional societies and foundations.

In addition, national initiatives and measures to raise the awareness for anaemia, its associated health risks and its avoidance might be recommendable and gain international traction when coordinated and organised in parallel by some of the EU Member States.

Integrating PBM and anaemia management into health promotion efforts is indicated. According to a recently published epidemiological study, and despite causing so much disability and mortality, “anaemia, does not receive its requisite attention in many public health spheres. Such inattention may be partly because anaemia is thought of as a by-product of other disease processes rather than as a target for intervention in and of itself“ (74). However, the proper recognition and management of anaemia may improve both the recognition of underlying but overlooked diseases as well as alleviating the consequences of anaemia.

NOTE
Recommended health promotion measures for the NAs:

Increase awareness in the public and amongst health professionals to draw attention to anaemia with its associated risks, social determinants, consequences and its avoidance
Integrate anaemia in the pathways of health promotion

5.2.3 Disease prevention

The purpose of this EPHO is to prevent disease through actions at primary, secondary, tertiary and quaternary levels. Primary prevention aims to prevent hazards and diseases before they might occur. This is done by prevention of exposures to hazards, changing behaviour and patterns that can lead to disease or injury, and increasing resistance to disease or injury in case exposure occurs. Secondary prevention aims to detect early the disease or injury that has already occurred. This often includes screening programmes and regular examinations for certain high-risk populations to detect whether disease has occurred at all. Immediately addressing disease in its earliest stages halts or slows its progress and reduces its immediate and potential long-term impact. Secondary prevention also includes patient-specific strategies to prevent disease recurrence. Tertiary prevention aims to soften the impact of chronic disease or permanent disability. This includes measures to improve quality of life (QoL) by reducing symptoms, improving functional capacity and expanding life expectancy. Quaternary prevention aims to avoid unnecessary or excessive interventions and their consequences.

Most measures to prevent fall within the duties and responsibilities of health professionals and healthcare providers.

Why PBM is relevant for disease prevention

PBM is essentially the practice of preventative medicine. Its rationale lies in the pre-emption of three modifiable risk factors for adverse patient outcomes, namely anaemia, bleeding and transfusion (163).

PBM related disease prevention measures recommended to NAs

Primary prevention

Creating a sense of urgency for PBM as a new evidence-based standard of care through clinical training and education is an important measure of primary prevention. It should emphasise the awareness about anaemia and iron deficiency among clinicians to improve timely recognition and management of these conditions.

Secondary prevention

PBM goes beyond the concept of appropriate use of blood products, because it pre-empts and significantly reduces the need for transfusion by addressing modifiable risk factors that might lead to transfusion long before a transfusion may even be considered (163). This includes routine early pre-operative detection and correction of both anaemia and bleeding disorders as key elements. These measures are associated with significant reduction of morbidity (including nosocomial infection and ischaemic events), mortality, hospital length of stay and the likelihood to be transfused (see section 2). In addition, the timely identification of peri-operative bleeding, its cause and immediate correction ("stop the bleeding first") is part of secondary prevention. Standard use of viscoelastic coagulation testing and targeted therapy in bleeding patients is also considered secondary prevention (164, 165).

Tertiary prevention

Tertiary prevention might be achieved by applying PBM modalities in cancer patients for the improvement of Quality of Life (QoL), disease free survival and the reduction of tumour progression and cancer recurrence (166), and in patients with chronic heart failure with the improvement in fatigue and physical performance (36, 48) as well as reduction in hospital admission rates.

Quaternary prevention

The combination between PBM and the concept of optimal blood use leads to quaternary prevention. PBM reduces or pre-empts transfusion. Optimal blood use, particularly the use of restrictive haemoglobin triggers and single-unit ordering for the non-massively bleeding patient, is a cornerstone of quaternary prevention. This can be achieved by implementing evidence-based transfusion guidelines (e.g. Grading of Recommendations Assessment, Development and Evaluation (GRADE) based guidelines (167) which may be applied internationally. Compliance with guidelines can be enhanced by, for example, (interactive) computerised physician order entry (CPOE) system policies, by regular audits of hospital and department transfusion practices or by automated data capture and analysis (see 8.7 Appendix 7 - Computerized Physician Order Entry Systems (CPOE).

NOTE

Primary disease prevention includes:

- Creating a sense of urgency for PBM as a new evidence-based standard of care through clinical training and education to prevent blood loss and anaemia

Secondary disease prevention includes:

- Routine early pre-operative detection and management of anaemia
- Routine early pre-operative detection and management bleeding disorders
- Timely identification of peri-operative bleeding, its cause and immediate correction
- Standard use of viscoelastic coagulation testing and targeted therapy in bleeding patients

Tertiary disease prevention includes:

- Application of PBM modalities in cancer patients for the improvement of QoL
- Stimulating and/or supporting erythropoiesis in chronically ill patients to pre-empt transfusions
- Application of PBM modalities in patients with chronic heart failure with the improvement in fatigue and physical performance
- Overall reduction in hospital admission rates

Quaternary disease prevention includes:

- Avoid excessive phlebotomy
- Adherence to evidence-based transfusion guidelines, e.g. restrictive indications and single-unit transfusion policy
- Introduce (interactive) CPOE systems policy
- Audit regularly the hospitals' and departments' transfusion practice against guidelines

5.3 Service Enabling and PBM

5.3.1 Assuring governance for the national dissemination and implementation of PBM

Intelligent governance is the necessary condition to ensure policy development that leads to well-functioning, effective public health services. It requires efficient methods, processes and integrated institutions to maintain accountability, quality and equity with taxpayers' money spent. This also includes the availability of well-qualified staff within the NAs and expertise and support from competent stakeholders outside the NAs.

Governance to disseminate and establish PBM as a standard practice in public health

1. Create, institute and empower a National PBM Steering Committee

PBM is a multi-facetted and complex public health issue that requires support from more than a single group of stakeholders. Strong leadership and good coordination is necessary to effectively disseminate and implement PBM as a new standard of care across the health system. Within the EU Member States, the MoH might directly or indirectly organise and empower a committee of chief administrators and experts to administer and steer this process. Such a recommendation is in line with resolution WHA63.12 and the subsequent WHO Global Forum on Patient Blood Management setting the framework for NAs to have a role in assessing, policy making, and assurance related to the dissemination and implementation of PBM.

Ideally, the "National PBM Steering Committee" should be formed with representation from select MoH departments, the public health insurance system, the National Medical Association, the quality and safety agency, the centre of disease control and the public hospital trusts (including representation from administration, finance, quality and safety, legal, information technology (IT) and finance departments).

NOTE

Creating, instituting and empowering a National PBM Steering Committee provides a strong driver for the successful dissemination and implementation of PBM as a new standard of care.

Establishing the inter-sectoral link between the MoH and the relevant ministries of Education and Research might be helpful to support the integration of PBM teaching modules into under- and post-graduate curricula of the various health professions (see Appendix 3 – Proposed content of PBM Curricula).

Participation of ministries responsible for research along with public research institutions fosters the integration of PBM research (see 5.3.5).

Table 2. List of National Authorities (NAs)

List of National Authorities (NAs)
Ministry of Health
Social and public health insurance
National Medical Association
Quality and safety agency
Centre for disease control
Public hospital trusts including representation from administration, finance, quality and safety, legal, information technology (IT) and medical controlling
Ministries of Education and Research (inter-sectoral activities)
Public research institutions

Good strategic planning and evidence-based policy development aimed at measurable health goals and public health activities at national, regional and local levels require the linkage and participation of stakeholders outside the NAs. This includes key opinion leaders in the field of PBM and official delegates from professional societies representing clinicians who particularly deal with a high prevalence of anaemia and moderate to severe blood loss, pharmacists, nurses, perfusionists, laboratory physicians, transfusion medicine specialists and general practitioners. Due to the strong emphasis on the surveillance and monitoring (see 5.1.1 and 5.1.2) of PBM KPIs, benchmark and data analysts should also be integrated. Concerning the medico-legal aspects and patient rights and empowerment, the participation of medico-legal experts, ethicists, patient rights experts, patient advocacies and patient representation is advisable.

Table 3. List of external stakeholders in support of the PBM governance and policy development process

List of External Stakeholders Partnering in Support of the PBM Governance and Policy Development Process
Key opinion leaders in the field of PBM
Official delegates from professional societies representing clinicians who particularly deal with a high prevalence of anaemia and moderate to severe blood loss, pharmacists, nurses, perfusionists, laboratory physicians, transfusion medicine specialists and general practitioners.
Benchmark and data analysts
Epidemiologists
Medico-legal experts
Ethicists
Patient rights experts
Patient advocacies
Patient representatives

To change and adapt the current healthcare structure to the needs of PBM, the Steering Committee would then institute and authorise a number of necessary committees, subcommittees and temporary task forces (Figure 6). It would also ensure that all communication channels deemed useful to disseminate all relevant information for the various target audiences and the public at large would be fully utilised.

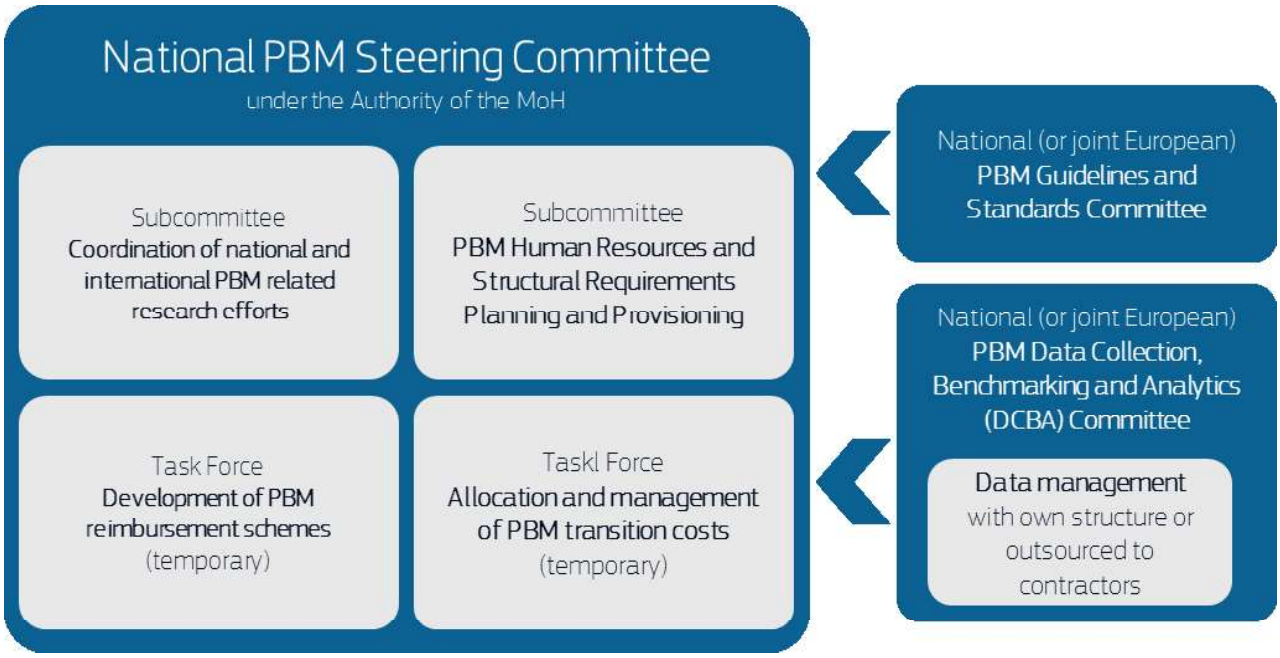

Figure 6. PBM Governance Structure

2. Establish a multi-professional PBM Guidelines and Standards Committee

Establishing a multi-professional PBM Guidelines and Standards Committee (GSC) is necessary and in line with the recommendation from the 2011 WHO *Global Forum for Blood Safety: Patient Blood Management* to ensure the application of concurrent and evidence-based PBM modalities.

It would be the responsibility of the National PBM Steering Committee to institute the GSC and to make available the resources for the development and regular updating of the guidelines and standards. This GSC should seek the input from the professional groups listed in table 4. This must happen through a formalised process and involve the coordination with the respective professional societies, professional bodies, associations and institutions.

Table 4. List of professions with needed input on the creation of PBM guidelines

Recommended professions giving input for the creation and updating of PBM guidelines and standards
Anaesthesiologists
Burns specialists
Cardiologists
Cardio-thoracic surgeons
Clinical haematologists
General practitioners
General surgeons
Gynaecologists and obstetricians
Hospital pharmacists
Intensive care specialists

Internal medicine specialists
Laboratory physicians
Neonatologists
Neurosurgeons
Oncologists
Orthopaedic surgeons
Patient advocates
Patient rights experts
Paediatricians (haematology, oncology)
Transfusion medicine specialists
Trauma surgeons
Urologists
Vascular surgeons
Visceral surgeons

To create synergies, GSCs of the different EU Member States might jointly develop PBM guidelines and standards and seek the professional input from various European professional societies. It could be useful to seek cooperation with the National Blood Authority (NBA), Australia and European NAs. The NBA has sponsored the development of the world's first comprehensive set of National PBM guidelines under the auspices of the National Health and Medical Research Council (NHMRC) in Australia (see section 6). The NBA is now aimed at regularly updating these guidelines that are in accordance with WHA63.12. Following the GRADE methodology (or similar), the NBA PBM guideline and other guidelines achieving sufficient scores using the AGREE tool, evidence based recommendations (GRADE) may be directly exchanged between countries.

3. Establish a National PBM Data Collection, Benchmarking and Analytics Committee

In line with three recommendations from the 2011 WHO *Global Forum for Blood Safety: Patient Blood Management,* namely to 1) establish a minimum PBM data set captured at each hospital, 2) conduct benchmarking studies to compare practices in different hospitals and clinicians, and 3) focus on outcome research, the National PBM Steering Committee should institute a National PBM Data Collection, Benchmarking and Analytics Committee (DBAC). This committee could outsource the actual data collection and management to qualified contractors. DBAC could also become part of a joint European effort. This would allow for continuous inter-country benchmarking and pan-European outcomes research with a large and fast growing database.

4. Create a Subcommittee for PBM Human Resources and Structural Requirements Planning and Provision

Fully enabling PBM requires sufficient facilities, a standard set of devices and equipment, IT and foremost a skilled workforce. To quantify these requirements mid and long-term, the National PBM Steering Committee could create a subcommittee with responsibility for PBM Human Resources and Structural Requirements Planning. Input from the GSC's findings and results from the DBAC would allow for better planning.

5. Create a Subcommittee for the Proposition and Coordination of National and International PBM research efforts

In accordance with the recommendation from the 2011 WHO *Global Forum for Blood Safety: Patient Blood Management* to focus on related outcomes research, including multi-centric studies and "to move forward on randomised controlled trials", the National PBM Steering Committee could create a subcommittee to foster, initiate and coordinate national and international PBM research programmes.

6. Create Task Forces for the Allocation and the Management of PBM Transformation Funds and the Development of PBM Reimbursement Schemes

Accumulating evidence shows that PBM is associated with significant reductions of average length of hospital stay, complications, costs and transfusions (138). The favourable cost-effectiveness of PBM is a compelling argument for its implementation. However, some initial capital investments have to be made to enable the transformation or conversion from the old to the new standard of care before returns will be realised. A task force under the supervision of the PBM Steering Committee could carry out the planning and management of these financial requirements.

Some PBM modalities are not adequately reflected in the reimbursement schemes of public health insurances, for instance the routine detection and management of pre-operative anaemia. A task force under the PBM Steering Committee and with representation from clinical experts, hospital administrators and public health insurance could be established to resolve such disparities.

7. Ensure PBM related communication

The PBM Steering Committee should ensure and organise the timely and well-coordinated communication of PBM related matters, under its governance or in support of it, to all relevant stakeholders and the public at large.

5.3.2 Workforce, equipment and facilities enabling PBM

Following the logic of the Donabedian quality framework, the *structural* quality is currently missing to fully enable PBM in the healthcare systems of most EU Member States (see 4.1).

Ensuring the three fundamental elements to build structure

As for each work process, the three fundamental elements of structure are a qualified and trained workforce, necessary equipment/technology, and appropriate facilities.

1. Planning and providing a sufficient PBM workforce and its education

Identification of hospitals and medical departments for implementation activities and ensuring a sufficient workforce starts with staff requirement planning. The Subcommittee for PBM Human Resources and Structural Requirements Planning and Provision should carry out this task.

Based on each hospital's own empirical data for different patient populations, procedures with the highest blood utilisation should be identifiable. In order for the Subcommittee to pragmatically derive quantitative PBM staff requirements, it should combine this information and the identification of the hospitals with the biggest overall use of blood components, and then apply the Pareto principle or the so-called "80 to 20 rule":

- Selecting the top 20% of all hospitals in the country in terms of their absolute blood component utilisation would probably account for around 80% of the national utilisation. The necessary data could be supplied by the haemovigilance authorities or the DBAC. All their anaesthesia departments, intensive care units, pharmacies, and quality and safety departments would require a workforce skilled in PBM.
- Identifying the procedure codes in the selected hospitals (in many institutions this will include at least orthopaedic, cardio-thoracic and abdominal procedures) would account for approximately 80% of the hospitals' total blood utilisation. All clinical departments responsible for these procedures would be identified along with the personnel requiring training and skills in PBM. All relevant data could be supplied by the hospitals' own information system.

With this approach, a relatively small fraction of hospital departments will cover approximately two thirds of the national PBM caseload. The criteria for how NAs, or their respective representatives, can best choose hospitals or hospital departments eligible for PBM programmes is simply based on the Pareto rule, combining the data of hospitals and procedures with maximum blood utilisation. How to estimate the required number of staff is demonstrated by the following example:

Generic example for how to estimate clinical PBM staff and training requirements across national health systems

A country with approximately 200 hospitals reports a total annual RBC utilisation of 300,000 RBC units. Applying the Pareto rule, the 40 biggest of these hospitals (20%) with an estimated 20 clinical departments each or 800 departments in total are expected to use 240,000 units (80%). Applying the Pareto rule once more, 160 of these departments are expected to use 192,000 RBC units or 64% of the country's overall utilisation. To ensure appropriate PBM, the following staff with a minimum PBM skill set and a certain level of seniority is required:

- 160 clinical specialists (one per department)
- 160-320 nurses (one to two per department)
- 40 hospitals pharmacists (one per hospital)
- 40 transfusion medicine specialists (one per hospital)
- 40 quality and safety managers (one per hospital)

For the vast majority of this staff, practice change following educational measures will be sufficient to enable PBM. However, each of the 40 hospitals would need at least one clinical lead for PBM with 0.25 – 0.5 FTE, one PBM coordinator with 0.25 – 0.5 FTE and one clinical nurse coordinator with 0.5 – 1.0 FTE.

Job descriptions for clinical PBM leads, PBM coordinator and clinical PBM nurse coordinators are in the appendix of this document (see 0 page 68).

Ensuring a competent workforce requires staff education and evaluation. This task should also fall under the responsibility of the Subcommittee for PBM Human Resources and Structural Requirements Planning and Provision. The recommendation from the *2011 WHO Global Forum on Patient Blood Management* was to develop educational curricula for both under- ("pre-service") and post-graduates of multiple disciplines. This includes physicians, nurses, pharmacists and quality and safety managers. Proposals for the design of PBM curricula and training courses are in the appendix of this document. PBM certification for clinical PBM leads, PBM nurse coordinators and the hospital's quality and safety managers should become mandatory.

A number of interactive PBM e-learning courses and educational video clips are offered by different professional institutions (see 0

Appendix 4 - List of PBM related e-learning courses). Some of the material is freely available and can be easily integrated in under- and postgraduate curricula (see 8.3 Appendix 3 - Proposed content of PBM curricula).

PBM training and education for post-graduates could also be an integral part of the exchange programmes for clinicians organised by The European Hospital and Healthcare Federation (HOPE) (168). Throughout EU countries, HOPE seeks to promote improvements in the health of citizens, a uniformly high standard of hospital care, and to foster efficiency, effectiveness and humanity in the organisation and operation of hospital services and of the health systems within which they function.

NOTE

Planning for and providing sufficient PBM workforce and its education encompasses:

- Undergraduate PBM education (nurses, physicians and other health professionals)
- Postgraduate PBM education (nurses, physicians and other health professionals)
- PBM job descriptions and recruitment plans
- PBM certification for clinical leads, nurse coordinators and quality and safety managers
- PBM exchange programmes for clinicians (HOPE programme)

2. Providing necessary equipment and technology for PBM

Based on the guidelines and standards recommended by the GSC, and possibly on HTAs in some of the EU Member States, the Subcommittee should also plan and ensure that each hospital with a PBM programme has the necessary state-of-the-art technology available to fully enable PBM. This might include the procurement of equipment for routine microsampling (particularly in ICUs), non-invasive tissue oxygenation monitoring, minimised circuits in heart-lung machines, viscoelastic coagulation testing at the point-of-care, cell-salvage, administration of haematinics in the pre-operative setting (e.g. infusion chairs), and laboratory devices for the routine pre-operative testing of anaemia, iron-deficiency and coagulation-disorder related parameters. It might also include CPOE software for managing quaternary disease prevention (see 5.2.3).

NOTE

Enabling PBM might include the standard provision of:

- Routine microsampling equipment
- Non-invasive tissue oxygenation monitoring devices
- Minimised circuits in heart-lung machines
- Equipment for viscoelastic coagulation testing at the point-of-care (POC)
- Cell-salvage machines

- Infusion chairs
- Laboratory devices
- Software

3. Providing hospital facilities for PBM

Most PBM modalities can be applied during hospitalisation, particularly those grouped under the second and third pillar of PBM. However, routine detection and treatment of pre-operative anaemia and coagulation disorder requires dedicated space on hospital sites. This includes patient reception, waiting areas and treatment rooms. Therefore, the Subcommittee should ensure public hospitals with PBM programmes have dedicated premises.

NOTE

Enabling PBM includes the standard provision of:

- Patient reception and waiting areas for pre-operative/pre-hospitalisation optimisation
- Treatment areas for pre-operative/pre-hospitalisation patient optimisation

5.3.3 Organisation and Funding of PBM

Efficient, effective and responsive healthcare services require appropriate organisation and financing.

Specific organisational and funding needs for PBM

1. Creating a template for the in-hospital PBM organisation

A national template for the in-hospital PBM organisation needs to be developed using the available workforce, equipment and facilities specific to PBM. This should be done under the direction of each EU Member States' PBM Steering Committee and the respective Subcommittee for PBM Human Resources and Structural Requirements Planning and Provision. This corresponds to the recommendations from the *Supporting Patient Blood Management (PBM) in the EU – A Practical Implementation Guide for Hospitals.* Following the Kotter model for change management as an integral part of the PBM Implementation Guide, it is essential to "create a clinical (PBM) reference group as a guiding coalition" and to "empower the PBM team".

The job descriptions with tasks and responsibilities for the PBM clinical lead, the PBM coordinator and the PBM nurse coordinator as well as the recommendations for tasks and responsibilities of the hospitals' PBM committees serve as a general direction for integrating and anchoring the PBM organisation into the

hospitals' overall organisational structure (see 8.6 Appendix 6 - Organisation of the hospital's PBM committee).

2. Funding in-hospital PBM organisation and its clinical implementation

The evidence clearly demonstrates the cost-effectiveness of PBM programmes, generating multiple returns of investment within short- to mid-term planning horizons (24, 30, 138, 169, 170). The significant reduction and pre-emption of blood component utilisation, related laboratory work, and numerous pre, - intra- and post-transfusion services allows immediate reallocation of financial resources already budgeted and provided for within the public health system (66, 67, 169, 171, 172). However, even under such favourable preconditions, the reallocation of available funds may need to be authorised and stipulated by NAs.

Based on proposals produced by the Task Force for the Allocation and the Management of PBM Transformation Funds, the Steering Committee should secure the necessary resources. The provision of financial means to build the in-hospital PBM structure and organisation is also in line with the change management recommendations of the PBM Implementation Guide, namely to "empower the PBM team".

3. Developing a reimbursement scheme for PBM services during the pre-hospitalisation phase

Most PBM treatment modalities are provided intramurally, i.e. for hospitalised patients. Related costs are accounted for by the hospital and reimbursed by the public health insurance system. However, fully effective correction of anaemia, a measure representing the 1st pillar of PBM in elective surgery patients, is required several weeks ahead of the intended procedure. In terms of adequate reimbursement, this poses a structural challenge in many health systems of the EU Member States. Therapeutic measures performed by hospital departments above a certain number of days prior to the patients' hospitalization (e.g. more than five days in Germany) are not reimbursed by the public health insurance. Therefore, these patients would seek extramural care and see their general practitioner or family doctor to get their anaemia treated. However, general practitioners are not always inclined to treat their patients' pre-operative anaemia, because their standard reimbursement scheme is not sufficient to cover the treatment cost.

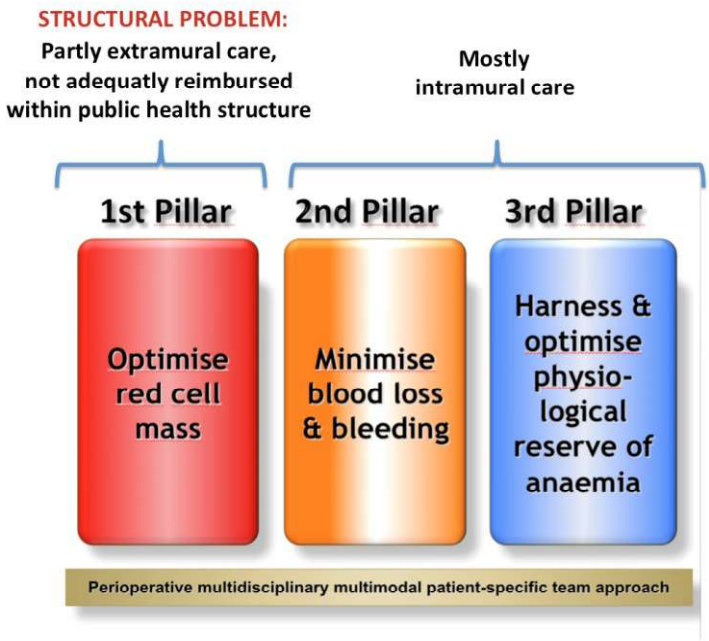

Figure 7. Three pillar PBM concept (adapted from (163, 173))

To close this gap, it seems necessary to develop appropriate reimbursement schemes for fully integrated PBM services during the pre-hospitalisation phase. This may fall under the responsibility of the Task Force for the Development of PBM Reimbursement Schemes under the supervision of the National PBM Steering Committee.

5.3.4 PBM communication

According to the WHO's Regional Office for Europe, NAs in public health should use modern communication methods and technologies to support leadership and advocacy for community engagement and empowerment. Communication for public health should improve health literacy and status of individuals and populations. It must also enhance their capacity to access, understand and use information to reduce risk, prevent disease, promote health, and utilise health services (174).

Ensuring PBM specific communication to both health professionals and the public at large

In terms of its multi-modality and multi-professionalism, PBM is a rather complex concept. To move more quickly from policy to practice, the general public, and more importantly many health professionals, including both in-hospital clinicians, general practitioners, and health administrators need to be familiarised with this practice. Therefore, to accelerate the dissemination and sustainable implementation of PBM, NAs might specifically target the professional audiences. Education is needed on the role of PBM in primary, secondary and tertiary disease prevention, and on the role of transfusion avoidance in quaternary disease prevention. The NAs' channels would primarily be electronic, including the MoH's and their agencies' web-portals. Press releases, circulars and statistical briefs as well as symposia sponsored by the MoH should also be considered.

The general public could be addressed through the MoH's and patient advocacies' electronic portals, but also indirectly through press releases. Leaflets, flyers and posters could be distributed in hospitals, medical practices and other public health institutions.

To improve health literacy on the burden and avoidance of anaemia, a "World Anaemia Day" might address the public. This could be organised as a concerted action of NAs around the world.

NOTE

NAs might provide the following communication contents and channels:

- PBM webpage section for patients, health professionals and health administrators
- PBM online courses for health professionals
- PBM and anaemia management fact sheets
- PBM alert systems for health professionals
- PBM press releases and other PR activities

See 7.1 Appendix 1 - List of PBM-related web-links (last access: 13/04/2016)

A key document to be electronically provided and communicated by NAs and patient advocacies is a PBM fact sheet to educate anaemic patients and patients undergoing surgery or any other procedure with a potentially clinically significant blood loss. This evidence-based document should use layperson's terms to educate patients on PBM treatment modalities. This enables and empowers patients to reach a fully informed consent with their treating physicians before the intervention.

NOTE

NAs should provide and distribute a PBM fact sheet for anaemic patients and patients planning to undergo a procedure with the risk of a potentially significant blood loss. This enables and empowers patients to reach a fully informed consent with their treating physicians before the intervention.

5.3.5 PBM research

In its support in improving the quality of healthcare, the WHO's Regional Office for Europe emphasises: "Current research is designed to enhance the role of the patient in reducing safety risks within three priority themes of blood transfusion, hospital infections and hand hygiene. In addition, a fourth theme is to improve communication during patient handovers" (175). Research implies that PBM might have a significant role in improving outcome through reducing the exposure to transfusion, thus reducing the risk of TTI and also hospital-acquired infections (104-107). Due to the multi-modality and multi-

professionalism of PBM, more research might be needed to answer more specific questions and close evidence-gaps.

With the DBAC commissioning “Big PBM Data Management” and the Coordination of National and International PBM Research Efforts, the NAs are in a good position to monitor clinical and scientific progress to improve evidence-informed PBM policy making. By supporting research, the NAs are also in line with the recommendations from the 2011 WHO *Global Forum for Blood Safety: Patient Blood Management*, to conduct and fund RCTs, to make meta-analyses, to make current evidence available through desk research, and to translate research into practice (4) (see 5.3.1 Assuring governance for the national dissemination and implementation of PBM).

PBM related research topics include but are not limited to

1. Population health and risks:

Anaemia occurrence and risk factors (age, gender, social factors, nutrition, behaviour)
Iron deficiency and iron deficiency anaemia
Antithrombotics use and bleeding risk in surgery
Transfusion outcomes and alternatives in “overlooked” patient groups (children, elderly, chronic diseases with transfusion).

2. Techniques and technologies:

Surgical techniques to minimize bleeding
Technologies to minimize other iatrogenic blood loss (e.g. non-invasive methods for measuring anaemia and oxygenation and circulation)
Next generation volume expanders.

3. Direct and derived effects of PBM implementation:

Impact on LOS, infection, mortality and readmission
Reduction of iron deficiency and anaemia prevalence,
Improvement of QoL, functional ability and self-care in connection with PBM, e.g. after surgery in the elderly.

6 Summary Table of the EU-PBM Strategy to Help National Authorities to Disseminate and Implement PBM in Hospitals across the EU

Following the template of the WHO Europe, table 5 summarizes 10 essential public health operations (EPHOs) split into three groups, namely service intelligence, service delivery and service enabler in connection with PBM.

Each EPHO contains a package of activities that can be pursued and/or supported by NAs to disseminate and implement PBM in their respective health systems and hospital.

The asterisks behind each activity indicate whether the NA should consider the facilitation, information, recommendation, incentives, control/inspection, legislation or enforcement in connection with the described activity.

Table 5. Summary Table: EU-PBM Strategy to help National Authorities to disseminate and implement PBM in hospitals across the EU

	Essential Public Health Operation (EPHO)							
	Activity	Facilitation	Information	Recommendation	Incentives	Control/Inspection	Legislation	Enforcement
A	**Intelligence**							
1.	Surveillance							
	Continuously collect patient level data on anaemia, transfusion and outcome to measure and guide the implementation of PBM as a standard of care							
	• Mandate the collection of basic key performance indicators (step 1)					x	x	x
	• Recommend and support the collection of advanced performance indicators (step 2)	x	x	x	x			
	• Recommend and support the collection of comprehensive performance indicators (step 3)	x	x	x	x			
	Aggregate collected data for continuous benchmarking, analytics and feedback to health care providers						x	x
2.	Monitoring							

	Recommend the monitoring and flagging of too liberal blood component utilisation to prevent health hazards	x	x	x				
	Mandate dose-dependent outcome monitoring in transfused patients					x	x	x
	• Non-transfusion transmitted infectious adverse reactions (nosocomial and others)					x	x	x
	• Non-infectious adverse reactions					x	x	x
	• Mortality					x	x	x
	Link monitoring for hospitals' quality improvement with blood utilisation data					x	x	x
	Activity	Facilitation	Information	Recommendation	Incentives	Control/Inspection	Legislation	Enforcement
B	Service							
3.	Health protection							
	Create a framework of clinical and academic key opinion leaders to translate the findings from national/European PBM surveillance and monitoring data as well as from newly emerged scientific evidence into practice improvement	x	x	x				
	Develop information and education materials for clinicians, quality and safety managers and hospital administrators	x	x	x				
	Create a framework to raise public awareness about PBM benefits	x	x	x				
	Create a framework and develop contents to inform, educate and empower patients and high-risk groups that might benefit from PBM.	x	x	x				
	• Mandate comprehensive patient education on the risks of PBM modalities, including potential immediate and delayed adverse events		x				x	x
	• Mandate comprehensive patient education on the risks of transfusion therapies including all non-transfusion transmitted infectious risks (immunological/TRIM), all non-infectious or physiological risks, all known donor-borne pathogenic risks, and the potential existence of unknown donor-borne pathogenic risks		x				x	x
	Pro-actively link PBM stakeholders to maximise benefits	x	x	x				
4.	Health promotion							
	Support and pursue the idea of a World Anaemia Day	x	x	x				
	Take iron deficiency and iron deficiency anaemia awareness	x	x	x				

	measures							
5a	Primary disease prevention							
	Create a sense of urgency for PBM as a new evidence-based standard of care through professional training and education	x	x	x	x			
	Alert general practitioners of the importance of anaemia management	x	x	x				
5b	Secondary disease prevention							
	Routine early pre-operative detection and correction of anaemia	x	x	x	x			
	Routine early pre-operative detection and correction bleeding disorders	x	x	x	x			
	Timely identification of peri-operative bleeding, its cause and immediate correction	x	x	x				
	Standard use of viscoelastic coagulation testing and targeted therapy in bleeding patients	x	x	x				
5c	Tertiary disease prevention							
	Apply PBM modalities in cancer patients for the improvement of QoL	x	x					
	Stimulate erythropoiesis in chronically ill patients to pre-empt transfusions	x	x					
	Apply PBM modalities in patients with chronic heart failure with the improvement in fatigue and physical performance	x	x	x				
5d	Quaternary disease prevention							
	Avoid excessive phlebotomy	x	x	x				
	Mandate a single-unit transfusion policy	x	x	x	x			
	CPOE systems policy	x	x	x				
	Audit regularly the hospitals' and departments' transfusion practice	x	x					
	Activity	Facilitation	Information	Recommendation	Incentives	Control/Inspection	Legislation	Enforcement
C	Enabler							
6	Governance							
	Create and Institute a National PBM Steering Committee under the authority of the MoH		x				x	x
	Establish a multi-professional PBM Guidelines and Standards Committee		x				x	x

	Establish a National PBM Data Collection, Benchmarking and Analytics Committee		x				x	x
	Create a Subcommittee for PBM Human Resources and Structural Requirements Planning and Provision	x	x	x				
	Create a Subcommittee for the Proposition and Coordination of National and International PBM research efforts	x	x	x				
	Create Task Forces for the Allocation and the Management of PBM Transformation Funds and the Development of PBM Reimbursement Schemes	x	x	x				
	Ensure PBM related communication	x	x					
7	Workforce, equipment and facilities							
	Provide sufficient PBM workforce	x	x	x	x			
	Provide PBM job descriptions and recruitment plan	x	x	x	x			
	Provide sufficient PBM education	x	x	x	x			
	• Undergraduate PBM education (nurses, physicians and other health professionals)	x	x	x	x			
	• Postgraduate PBM education (nurses, physicians and other health professionals)	x	x	x	x			
	• PBM exchange programs for clinicians (HOPE program)	x	x	x	x			
	Introduce PBM clinician certification program	x	x	x				
	Introduce PBM hospital accreditation program	x	x	x				
	Provide necessary equipment and technology for PBM	x	x	x	x			
	• Routine microsampling equipment	x	x	x	x			
	• Non-invasive tissue oxygenation monitoring devices	x	x	x	x			
	• Minimised circuits in heart-lung machines	x	x	x	x			
	• Equipment for viscoelastic coagulation testing at the point-of-care (POC)	x	x	x	x			
	• Cell-salvage machines	x	x	x	x			
	• Infusion chairs and equipment for the administration of haematinics	x	x	x	x			
	• Laboratory devices	x	x	x	x			
	• Software	x	x	x	x			
	Provide hospital facilities for PBM							
	• Patient reception and waiting areas for pre-operative/pre-hospitalisation patient optimisation	x	x	x	x			
	• Treatment areas for pre-operative/pre-hospitalisation optimisation	x	x	x	x			

8	Organisation & Funding							
	Use and nationally adapt existing templates for the in-hospital PBM organisation			x			x	
	• Systematically identify PBM target hospitals	x						
	• Use a validated PBM implementation methodology	x	x	x				
	Organise reallocation of funds and resources towards PBM	x	x	x	x			
	Provide funds for the PBM implementation	x	x	x	x			
	Close gap between provider and payer ("reimbursement gap") for pre-op anaemia management and patient preparation		x				x	x
	(Co)finance the (Joint European) multidisciplinary PBM guidelines development and continuous guidelines re-evaluation process	x	x	x	x			
9	Communication							
	Provide PBM webpage sections for patients, health professionals and health administrators	x						
	Provide PBM online courses for health professionals	x						
	Provide PBM and anaemia management fact sheets	x						
	Provide PBM alert systems for health professionals	x						
	Provide PBM press releases and other PR activities	x						
10	Research							
	Conduct studies on PBM related issues regarding	x	x	x				
	• Population health and risks	x	x	x				
	• Techniques and technologies	x	x	x				
	• Patient outcomes	x	x	x				
	• Cost-effectiveness	x	x	x				
	Fund the conducting of such studies	x	x	x				
	Use the nationally available PBM data (see EPH01 and 2) for population based studies	x	x	x				

7 Past and Current PBM Activities of NAs in the Developed World

The leading country with NAs proactively supporting PBM is Australia with the Australian Commission on Quality and Safety in Health Care (ACQSHC), the National Blood Authority (NBA) and the Jurisdiction's Departments of Health (JDoH) taking on their responsibilities. The ACQSHC has declared PBM a top national priority. The NBA has made the dissemination and implementation of PBM one of their core responsibilities, with a comprehensive set of electronically accessible information and educational instruments and materials. These include a series of six PBM guidelines developed under the oversight of the NHMRC, covering massive bleeding, peri-operative, intensive care, medical, obstetrics and maternity, neonatal and paediatric settings. The DoHs of all Australian Jurisdictions have made available PBM information and materials for health professionals, administrators and patients.

In 2011, the Advisory Committee on Blood Safety and Availability (ACBSA) in the United States (US) organised an expert meeting under the auspices of the Department of Health and Human Services (USDHHS) to address the potential role of PBM (http://nih.granicus.com/ViewPublisher.php?view_id=22). The USDHHS began collecting data on the penetration of PBM across the US. Its latest Blood Collection and Utilization Survey Report (2011) dedicated a section to PBM.

Within the EU, the NAs of some EU Member States have taken action, reflecting resolution WHA63.12.

Austria

Several years before resolution WHA63.12, the Austrian Federal Ministry of Health had already initiated activities that led to a heightened awareness of PBM. In 2003, it issued a call for tender to conduct the first prospective observational Austrian Benchmark Study on Blood Utilisation across randomly selected public hospitals. This initiative was a landmark effort that not only confirmed the high prevalence of extreme inter-institutional transfusion variability for matched elective surgical patients, but was also the world's first study to quantify the relative impact of predictors for transfusion in the elective setting (75, 94). The results showed that 97.4% of all transfusion events are predicted by the patients' level of anaemia and blood loss, and the clinician's thresholds triggering transfusions ("transfusion trigger"). These important findings laid the foundations for PBM. To study the effect of the first Benchmark Study on blood utilisation, the Austrian Federal MoH funded a follow-up study that included the same hospitals with approximately the same number of elective surgical patients and the same indications.

Denmark

The Danish Health Authorities run the Danish Transfusion Database, in which utilisation of blood components is bench marked between hospitals and regions. In 2014, the Danish Health Authorities published the first GRADE-based transfusion guideline (National Klinisk Retningslinje for blodtransfusion af 19. Juni 2014 (176)). It highlights the lack of evidence for beneficial health effects of liberal transfusion and stresses the need for future PBM. This guideline recommends monitoring transfusion KPI's as recommended in this report (e.g. transfusion rates & index, pre-transfusion haemoglobin) and a

subcommittee has defined that it should done on a national level, per region, hospital and for selected surgical procedures by means of the Danish Transfusion Database. The five regions in Denmark responsible for running the public hospitals have launched a common quality improvement initiative in 2015 called "Patient Blood Management in the Danish Regions" based on the WHO principles, in which guideline-adherent transfusion practice, improved perioperative bleeding control and preoperative anaemia management is endorsed.

Italy

In 2013, under the national program of self-sufficiency for blood and blood products, the Ministry of Health issued the recommendation to. "*define and promote the application of multidisciplinary evidence-based approaches, to improve patient outcomes in a sustainable way by means of maintaining haemoglobin concentration, optimising haemostasis and minimizing blood loss. To identify patients at risk of transfusion, and to define plans for their clinical management (patient blood management) to reduce or eliminate the need for allogeneic transfusion, and reducing related risks and costs*" (Gazzetta Ufficiale della Repubblica Italiana, n. 292 del 13 dicembre 2013, Ministero della Salute, decreto 29 ottobre 2013, Allegato A).

In 2014, the Ministry of Health issued the following recommendation: *"With reference to the medical and surgical diagnostic and therapeutic pathways with major transfusion impact, during 2013, the Centro Nazionale Sangue (National Blood Centre), initiated together with technical-scientific collaborations, a national project for the promoting of the implementation of multidisciplinary and multimodal approaches to the patient blood management, by identifying patients at risk of transfusion (particularly in elective surgery patients) and defining management plans to reduce or eliminate the need for allogeneic transfusion by means of a) maintaining haemoglobin concentration, b) optimising haemostasis and where applicable, c) minimizing blood loss. The development of the pilot project in orthopaedic surgery is expected to be rolled out during 2014"* (Gazzetta Ufficiale della Repubblica Italiana, n. 265 del 14 novembre 2014, Ministero della Salute, decreto 24 settembre 2014, Allegato A). In the same year, the National Blood Centre (Centro Nazionale Sangue), initiated the national "PBM-Italy" program at the *Instituto Ortopedico Rizzoli* (Bologna) and at the *Azienda Ospedaliero-Universitaria Pisana*. Starting in the field of major elective orthopaedic surgery, the program promotes the implementation of multidisciplinary and multimodal PBM approaches including the early identification and management of patients at risk of transfusion

In 2015, the Ministry of Health issued the following decree: *"In order to prevent avoidable transfusions, specific programs (PBM) are defined and implemented in our national territory, with particular reference to the preparation of patients for elective surgical treatments, based on guidelines to be issued by the National Blood Centre to be endorsed within six months from the enactment of this decree"* (Gazzetta Ufficiale della Repubblica Italiana, n. 300 del 28 dicembre 2015, Ministero della Salute, decreto 2 novembre 2015, Art.25 (5)).

According to the premise of the National Program for Plasma and Plasma Derivatives for 2016-2020, a trend in Italy is observed "*following the adoption of policies and patient blood management (PBM) aimed at implementing methods and tools to ensure the appropriate management, both organizationally and clinically, of the individual patient's blood, in order to improve outcomes*" (Gazzetta Ufficiale della

Repubblica Italiana, n. 9 del 12 gennaio 2017, Ministero della Salute, Decreto 2 diciembre 2016, Allegato A).

United Kingdom

In 2013, the National Health Service (NHS) in England conducted a survey in all NHS Trusts in England on their preparedness for PBM and their current activities. The response rate was 98%. One of the NHS's official websites now has a full section on PBM and anaemia management with educational material, algorithms and toolkits for health professionals. The site also offers information for patients (177). The National Health Services Blood and Transplant (NHSBT) currently employ a clinical director for PBM. The unit's special focus is on the North-West Pre-operative Anaemia Project, where a large working group from trusts in the North West of England drive the implementation of pre-op anaemia management in every day practice. Pilot sites are in the process of implementing pathways based on regional algorithms (178). A PBM measuring tool is being implemented in two of the participating hospitals. Clinical Commissioning Groups (CCG) - NHS organisations set up by the Health and Social Care Act in 2012 to organise the delivery of NHS services to the public - are discussing large-scale commissioning and design of anaemia management pathways with the Greater Manchester Elective Orthopaedic group. Bolton Trust has developed an Anaemia Management in Primary Care Pathway (179).

The National Blood Transfusion Committee's PBM recommendations were prepared following the Future of Blood Transfusion Conference. The recommendations are supported by NHS and NHSBT. On its website, the Joint United Kingdom Blood Transfusion and Tissue Transplantation Services Professional Advisory Committee (JPAC) features a section on PBM (180).

8 Appendix:

8.1 Appendix 1 – List of PBM-related web-links (last access: 13/04/2016)

Table 6. List of PBM-related web-links

National PBM guidelines		
PBM programmes and initiatives in the public sector		
Australia	Australian Commission on Quality and Safety of Health Care	http://www.safetyandquality.gov.au/national-priorities/pbm-collaborative/
Australia	Queensland	https://www.health.qld.gov.au/clinical-practice/guidelines-procedures/patient-safety/blood-management/blood-product/default.asp
Australia	South Australia	https://bloodsafelearning.org.au/course/patient-blood-management-pbm/
Australia	Victoria	https://www2.health.vic.gov.au/hospitals-and-health-services/patient-care/speciality-diagnostics-therapeutics/blood-matters
Australia	Western Australia	http://ww2.health.wa.gov.au/Articles/N_R/Patient-Blood-Management-tools-templates-and-resources
Europe	European Union Patient Blood Management	http://www.europe-pbm.eu
Italy	Centro Nazionale Sangue, Ministero della Salute	http://www.centronazionalesangue.it/notizie/patient-blood-management
United Kingdom	National Health Service	http://hospital.blood.co.uk/patient-services/patient-blood-management/
Teaching hospital with PBM programmes		
Austria	Kepler Universitätsklinikum Linz, Austria	https://www.kepleruniklinikum.at/versorgung/kliniken/anaesthesiologie-und-intensivmedizin/wir-ueber-uns/
Germany	Universitätsklinikum Frankfurt	http://www.kgu.de/kliniken-institute-zentren/einrichtungen-des-klinikums/kliniken/zaw/anaesthesiologie-intensivmedizin-und-schmerztherapie/forschung/patient-blood-management.html http://www.patientbloodmanager.de
Switzerland	University Hospital Zürich	http://www.anaesthesie.usz.ch/fachwissen/seiten/patient-blood-management.aspx
United States	Eastern Maine Medical Center, Bangor, ME	https://www.emmc.org/Patient-Blood-Management.aspx
United States	Englewood Hospital and Medical Center, Englewood, NJ	https://www.englewoodhospital.com/ms_bloodless_home.asp
United States	Johns Hopkins Hospital, Center for Bloodless Medicine and Surgery, Baltimore, MD	http://www.hopkinsmedicine.org/bloodless_medicine_surgery
PBM foundations		
IFPBM	International Foundation for Patient Blood Management	http://www.ifpbm.org
Societies, institutions and networks with a PBM Focus		
ANEMO	Anaemia Working Group Italy	http://www.anemo.it

AWGE	Anaemia Working Group Espana	http://softwarecorp.es/awgeportal
AWGP	Anaemia Working Group Portugal	http://www.awgp.pt
German PBM Network	University Hospital Frankfurt	http://www.patientbloodmanagement.de
NATA	Network for the Advancement of Transfusion Alternatives	http://www.nataonline.com
SABM	Society for the Advancement of Blood Management	http://www.sabm.org
Societies, institutions and networks with a focus on anaemia management		
EORTC	European Organization for the Research and Treatment of Cancer	http://www.eortc.org/investigators/guidelines/eortc-guidelines/
KDIGO	Clinical Practice Guideline for Anaemia in Chronic Kidney Disease	http://kdigo.org/home/guidelines/anemia-in-ckd/
Selected transfusion guidelines including sections on PBM		
Denmark	Sundhedsstyrelsen: National klinisk retningslinje om indikation for transfusio med blodkomponenter	https://sundhedsstyrelsen.dk/da/udgivelser/2014/~/media/EEA1EA90C15E4A97B9E786D2850B3664.ashx
France	Haute Autorité de Santé; Agence nationale de sécurité du médicament et des produits de santé: Recommendation de bonne pratique, Transfusion de globules rouges homologues: produits, indications, alternatives	http://www.has-sante.fr/portail/upload/docs/application/pdf/2015-02/transfusion_de_globules_rouges_homologues_-_produits_indications_alternatives_-_recommandations.pdf
Italy	Italian National Blood Centre; Recommendations for the implementation of a Patient Blood Management programme. Application to elective major orthopaedic surgery in adults	http://www.bloodtransfusion.it/scarica.aspx?tipo=A&id=002922&riv=000106
United Kingdom	Joint United Kingdom (UK) Blood Transfusion and Tissue Transplantation Services Professional Advisory Committee	http://www.transfusionguidelines.org.uk/uk-transfusion-committees/national-blood-transfusion-committee/patient-blood-management
Transfusion medicine societies, transfusion services and related institutions with PBM activities		
AABB	American Association of Blood Banks	http://www.aabb.org/pbm/Pages/default.aspx
ARCBS	Australian Red Cross Blood Service	http://www.transfusion.com.au/transfusion_practice/patient_blood_management
ISBT	International Society for Blood Transfusion	http://www.isbtweb.org/working-parties/clinical-transfusion/
SIMTI	Italian Society of Transfusion Medicine and Immunohaematology	http://www.simti.it/

8.2 Appendix 2 - List of specialities known to be high blood users

Over the last three decades a number of studies have described how transfusions of blood components are distributed across patient age groups, international classification of disease codes (ICD-codes), and specialities, and utilized for surgical patients, respectively. This section summarises the frequency of utilization based on these categories.

- **Transfusions by age group**

The literature shows that approximately half of all Red Blood Cell (RBC) transfusions are used in the age group >65 years (table 7) and the ratio is growing due to current population dynamics (171, 181). A cross-sectional study conducted by Vamvakas et al. looked at all residents of a United States county who received transfusions from 1989 to 1992. The incidence of RBC transfusion was 42.9 units / 1,000 population per year and varied from 12.1 units in those less than 41 years old compared to 254.2 units in those older than 65 years. Patients over 65 years old represented 54.3% of all patients transfused, receiving 53.3% of all RBCs transfused (182). Wells et al. conducted a population based prospective observational study on RBC transfusion over two 14 day periods in October 1999 and June 2000. The 18 National Health Service (NHS) hospitals in north England[1] included in the study, showed the age group >70 years received 47% of the 9,774 RBC transfusions. A further population based study by Cobain et al. in Western Australia, with a total of 50,605 RBC units transfused during the financial year 2001/2002, showed a rate of 47.9% for the same age group (183, 184). A similar population based study, conducted in the Danish county of Fuenen, showed patients >70 years received 55.4% of 25,553 RBC transfusions (185, 186). A database analysis from Finland by Palo et al., including all transfused patients from four university and five central hospital districts (managing 63% of Finnish inpatient episodes) in 2002 and 2003, showed that 51.6% of all transfusion recipients were over 64 years of age (187). A population based cross-sectional study was conducted for all in-hospital RBC transfusions in the German federal state of Mecklenburg-Pomerania in 2005. Of all transfusions, 62.1% were given to patients 65 years of age or older (181). The PROTON study by Borkent-Raven et al., covering 28% of the total blood use in the Netherlands from 1996 to 2005, showed that recipients of 65 years and older received 57.6% of RBCs (188).

Table 7. Red blood cell (RBC) utilisation by old-age patient groups

Study	Country or region	Year(s) of data collection	Patient age (years)	Share of RBC transfusions
Vamvakas et al. (182)	USA	1989-1992	>65	53.3%
Wells et al. (183)	north England	1999, 2000	>70	47%
Cobain et al. (184)	Western Australia	2001-2002	>70	47.9%
Titlestad et al. (186)	Fuenen, Denmark	2002	>70	55.4%
Palo et al. (187)	Finland	2002-2003	>64	51.6%
Greinacher at al.(181)	Germany, Mecklenburg-Pomerania	2005	>64	62.1%
Borkent-Raven et al. (188)	Netherlands	1996-2005	>64	57.6%

[1] Wells at al. use in the original paper the wording "north England" ("*The north of England is a geographically well defined region …*")

The overall analysis, of these and a number of other studies, shows that current population dynamics in most developed countries will lead to an increasing demand for RBC transfusions in the old-age patient group if transfusion patterns remain unchanged (171, 181, 189). This is supported by another study from Borkent-Raven et al. They developed mathematical models to predict the demand for RBC units in the Netherlands. One model is based on demography only and predicts an increase of 23% in RBC demand from 2008 to 2015. The second model, however, incorporates trends in clinical RBC use based on what the authors called "optimal or restricted blood use", predicting a decrease of RBC demand by 8% over the same period (190). The impact of the old-age patient group on blood utilisation is also clearly demonstrated by Ali et al. with computerised data collection on all potentially[1] transfused patients covering ≈70% of all blood usage in Finland. The data, for the period from 2002 to 2006, show 70- to 80-year-olds had an eightfold higher RBC consumption than 20- to 40-year-olds (191).

- **Transfusions by ICD codes**

The Dutch PROTON study, with 290,043 transfused patients, analysed the utilisation of 2,405,012 blood components (1,720,075 RBCs) by ICD-9 primary discharge diagnoses (188). A similar study was conducted in 45 hospitals in central Ontario from September 1991 to August 1992 with approximately 26,800 transfused patients who received a total volume of 101,116 RBCs (192). The population based study conducted in the Danish county of Fuenen captured 25,553 RBCs transfusions by ICD-10 codes (185, 186). These studies show that approximately three quarters of all RBC transfusions were used in patients of five main groups of ICD diagnoses (ICD-9 lists at total of 19 main groups and ICD-10 a total of 22 main groups): neoplasms, diseases of the circulatory system, diseases of the digestive system, injury, poisoning and other consequences of external causes including trauma, and diseases of the blood and blood forming organs (table 8).

Table 8. Red blood cell (RBC) utilisation by ICD code

ICD diagnosis, main group	Chiavetta et al. (192) Canada ICD-9 (1991-1992)	Borkent-Raven et al. (188) Proton Netherlands ICD-9 (1996-2005)	Titlestad et al. (185, 186) Fuenen/Denmark ICD-10 (2002)
Neoplasms	26.7%	22.2%	25.7%
Diseases of the circulatory system	16.2%	21.5%	14.5%
Diseases of the digestive system	17.9%	9.8%	15.5%
Injury, poisoning and other consequences of external causes (incl. trauma)	13.4%	10.5%	9.7%
Diseases of the blood and blood-forming organs	4.9%	8.6%	11.1%
Diseases of the musculoskeletal system and connective tissue	5.4%	5.3%	3.5%
Diseases of the genitourinary system	3.8%	3.8%	3.2%
Pregnancy, childbirth (and puerperium)	2.3%	3.7%	1,5%
Symptoms, signs and ill-defined conditions	-	3.3%	3.3%

[1] In the original article the wording "potentially" is used but not explained by the authors

Diseases of the respiratory system	2.9%	2.4%	2.9%
Infectious and parasitic diseases	-	1.3%	2.0%
Endocrine, nutritional, metabolic, immunity diseases	-	1.1%	1.8%
All other diagnostic categories	6.5%	6.5%	5.3%
Total	100,0%	100,0%	100,0%

The database analysis from Finland, by Palo et al., captured the number of transfused patients and the combined number of transfused blood components (RBCs, platelets and FFP) by ICD-10 codes (187). In general, this analysis did not differentiate by the type of component. However, for malignant diseases of the blood and blood-forming organs (C81-C96) as a subgroup of neoplasms (main diagnostic group II of the ICD-10 system), the utilisation of each type of component was singled out with 7.4% for RBCs, 46.2% for platelets and 3.0% for FFP. These data indicate that the large majority of RBCs utilised in patients with neoplasms might be in the group with solid tumours rather than haematological malignancies. This distinction is important, because patients with solid tumours, as the primary diagnosis, often require surgical procedures with specific PBM measures.

- **Transfusions by broad categories by operations or procedures**

Chiavetta et al. captured 101,116 RBC transfusions by broad procedure category according to the Canadian Classification of Diagnostic, Therapeutic, and Surgical Procedures (CCP), a classification system used in Canada until 2004 (192). Three of the first four categories involve visceral/abdominal, cardio-thoracic and orthopaedic surgeries, but the study does not specify and quantify the interventions.

Table 9. Relative numbers of RBCs transfused by operations or procedures

Chiavetta et al. (192) Canada, Categories by Canadian Classification of Diagnostic (CCP)	1991-1992
Digestive system and abdominal region	20.1%
Cardiovascular system	15.8%
Diagnostic and therapeutic procedures	15.2%
Musculoskeletal system	14.7%
Haemic and lymphatic systems	4.3%
Respiratory system	3.6%
Female genital organs	3.3%
Urinary tract	2.6%
Male genital organs	2.3%
Nervous system	1.9%
Obstetric procedures	1.5%
Other	1.8%
no procedures	12.9%
Total	100.0%

The database analysis from Finland, by Palo et al., captured the combined number of all blood components including RBCs, platelets and FFP (a total of 137,530 units in 2003 and 127,286 in 2002)

used for patients undergoing operations. The Nordic Medico-Statistical Committee (NOMESCO) Classification of Surgical Procedures (NCSP) (version 1.7) of the Nordic Centre for Classification of Health Care was used (187). Again, three of the first four categories involve visceral/abdominal, cardio-thoracic and orthopaedic surgeries. However, the ranking is different from the Canadian study by Chiavetta et al.; this is because all blood components are accounted for, not only RBCs.

Table 10. Relative numbers of blood components (RBCs, platelets, FFP) transfused by main operation

Derived from Palo et al. (187) Finland, Categories by Nordic Medico-Statistical Committee (NOMESCO)	2002	2003
Musculoskeletal system	28.0%	26.7%
Digestive system and spleen	20.7%	19.6%
Heart and major thoracic vessels	18.7%	18.0%
Peripheral vessels and lymphatic system	9.1%	9.4%
Obstetric procedures	3.5%	4.5%
Urinary system, male genital organs and retroperitoneal space	4.2%	4.3%
Skin	4.0%	4.1%
Nervous system	3.9%	4.2%
Chest wall, pleura, mediastinum, diaphragm, trachea, bronchus, and lung	5.0%	6.8%
Female genital organs	2.9%	2.5%
Total	100.0%	100.0%

- **Transfusions by specific operations or procedures**

Only two studies were identified giving transfusion figures by specific procedures or surgical interventions. Wells et al. (north England) showed that of all 3,982 surgically transfused RBC units, the five leading surgical procedures were total hip replacement (446 RBC units transfused), abdominal surgery (430 units (excluding colorectal surgery)), coronary artery bypass grafting (398 units), colorectal surgery (267 units) and urology (254 units) (Table 11).

Table 11. Relative numbers of transfused RBCs by specific procedure

Derived from Wells et al. (183) North England Specific procedure		1999/2000
Medicine		51.6%
	Anaemia	*23.2%*
	Haematology	*15.5%*
	Gastrointestinal bleed	*10.8%*
	Other	*1.5%*
	Neonatal top up/ exchange transfusion	*0.6%*
Orthopaedics and trauma		13.8%
	Total hip replacement	*4.6%*
	Fractured neck of femur	*1.8%*

	Total knee replacement	*1.6%*
	Road traffic accident	*1.4%*
	Other	*4.4%*
General surgery		9.5%
	Abdominal	*4.4%*
	Colorectal	*2.7%*
	Other	*2.4%*
Cardiothoracic surgery		6.2%
	Coronary artery bypass-grafting	*4.1%*
	Other	*2.1%*
Vascular surgery		4.6%
	Emergency repair aortic aneurysm	*2.3%*
	Other	*2.3%*
Urology		2.6%
Transplant		1.7%
Neurosurgery		1.2%
Ear, nose, and throat		0.6%
Plastic surgery		0.5%
Obstetrics and gynaecology		6.2%
	Gynaecology	*3.1%*
	Obstetrics	*3.1%*
No clinical details		1.4%

In the second study, Cobain et al. (Western Australia) used diagnosis related groups (DRGs) to identify diseases and procedures with the highest blood utilisation. Of all 50,605 RBCs transfused during the study period, 6,991 units were used in orthopaedic DRGs, 5,453 units were used in cardiovascular DRGs, 4,814 in trauma and 133 in hepatic/biliary DRGs. Other DRGs were haematology with 10,494 units, followed by 7,111 in gastroenterology, 2,760 in gynaecology/obstetrics, 2,548 in renal, 1,622 in respiratory, 1,047 in infection and the remainder in all other DRGs [3] (Table 12).

Table 12. Red blood cell (RBC) utilisation by specific procedure or DRG

Derived from Cobain et al. [3] Western Australia DRG		2001/2002
Medical (predominantly)		45.1%
	Haematology	*20.7%*
	Gastroenterology	*14.1%*
	Renal	*5.0%*
	Respiratory	*3.2%*
	Infection	*2.1%*

Surgical (predominantly)		36.0%
	Cardiovascular	*10.8%*
	Other orthopaedics	*7.0%*
	Hip replacement	*4.9%*
	Knee replacement	*1.9%*
	Trauma (tracheostomy + ventilation/craniotomy)	*9.5%*
	Hepatic/biliary	*1.9%*
Obstetrics / gynaecology		5.5%
all other DRGs		13.4%

- **Transfusions utilised for surgical patients**

Several studies analysed the distribution of transfusions across different patient populations (Table 13). A transfusion survey in 12 Central Virginia Hospitals in 1986 showed that 66% of patients transfused had some type of surgery (193). Brien et al. conducted an audit of blood component therapy based on charts of patients admitted over 8 months in 1986-87, in a Canadian general teaching hospital. With 520 transfusion episodes and a total of 1,218 RBCs transfused, the authors showed that 56% of all units were administered to surgical patients (194). Another Canadian study, in a 219-bed teaching hospital in March 1992, used hospital blood bank records to show that 69% of all units given were to surgical patients (195). The study by Wells et al. showed that 40.7% of all RBC transfusions were used for surgical indications, 51.6% for medical indications, and 6.3% for obstetric or gynaecological indications (183). The study from Finland, by Ali et al., found that 55% of RBCs were used for surgical diagnoses or interventions; whereas, the remainder were used for conservative treatments. The authors did not specify usage by surgical speciality, but found 16% of all blood was used for treatment of cardiac and circulatory system diseases (ICD-10 classes I00-I99) (191). The database analysis from Finland showed that 51.2% of all blood units were transfused in connection with surgical operations (187). The study group from Mecklenburg-Pomerania showed that of all in-hospital RBC transfusions, 37.4% were given to medical patients, 35.1% to surgical patients, 24.6% to critically ill or emergency patients (combined medical and surgical patients), 0.7% to paediatric patients, and 2.2% could not be classified. The procedures were not specified (196).

Table 13. Red blood cell (RBC) utilisation of surgical population

Study	Country or region	Year(s) of data collection	Share of surgical RBC transfusions
Cook and Epps (193)	USA	1986	66%
Brien et al. (194)	Canada	1986-87	56%
Ghali et al. (195)	Canada	1992	69%
Wells et al. (183)	north England	1999, 2000	47%
Ali et al. (191)	Finland	2002-2006	55%
Palo et al. (187)	Finland	2002-2003	51.2%
Greinacher et al. (181)	Germany, Mecklenburg-Pomerania	2005	35.1% + an unspecified share from critically ill or emergency patients

Bruun et al. (139)	Europe	2016	36%
Tinegate et al. (22)	England and North Wales	2016	27%
Fillet et al. (140)	France	2016	34% + an unspecified share of patients

In a European survey by Bruun et al. (197), on average, 61% of red cell units were transfused for medical indications, 36% for surgical indications and 3% for gynaecological or obstetric indications. In a study conducted by Tinegate et al. (22), 27% were transfused for surgical and and 6% for obstetric/gynecologic indications. A recent study conducted in France by Fillet et al. (198) showed that that 34% of patients had a transfusion in a surgical context, whereas the context for 44.8% of patients was not specified.

8.3 Appendix 3 – Proposed content of PBM curricula

Table 14. Proposed content of PBM curricula

1.	Definition, history and aims of PBM
	Learning Objectives: Understand the principles of the new PBM paradigm and the structure of the curriculum. Topics: • General overview and explanation of the multidisciplinary three-pillar strategy and its multimodality. The main goals of PBM are the prevention and treatment of anaemia, the avoidance and minimisation of blood loss, and the optimisation and harnessing of the physiological tolerance of anaemia • Relevance of PBM for conservative medicine and surgery. PBM was first developed in elective surgery but the principles can be applied to emergency surgery, trauma management, and other medical settings. • History and description of the paradigm shift from product-related transfusion medicine to blood-sparing ("bloodless") treatment concepts to comprehensive patient blood management. • PBM includes not only the avoidance of RBC transfusions, but of the transfusion of all allogeneic blood components. • Overview of the curriculum.
2.	Reasons for the urgent implementation of PBM in modern health systems: Drivers for change
	Learning Objectives: Understand the main drivers for the paradigm shift from product focussed transfusion medicine towards PBM Topics: • Outcome of transfusion and PBM modalities • Lack of evidence for the benefit of transfusion in many patient populations • The risk of known, re-emerging and newly emerging pathogens in transfusions of allogeneic blood components relative to the risks of PBM. • The physiological and non-infectious risks of allogeneic blood component transfusions • The growing gap between donor blood supply and demand for blood components • Cost and cost-effectiveness of transfusions versus PBM modalities • Ethics, patient education and patient empowerment
3.	Status quo of PBM in international comparison
	Learning Objectives: Get an overview of the international progress in the dissemination and implementation of PBM and better understand the reasons for failure and success Topics: • International comparison of KPIs derived from surveillance and monitoring data on PBM and transfusions • Analysis and assessment of the differences in structure, process and outcomes related to PBM (Donabedian Quality Framework)
4.	Applying an effective methodology to implement PBM in hospitals

	Learning Objectives: Understand the main challenges and obstacles for culture change and how to overcome them methodologically; understand how to lead change. Topics: • Introduction into the theory of paradigm change, culture change and change management on the background of transfusion being behaviour driven • How to conduct a local SWOT analysis before embarking on the PBM implementation project; focus on the strength and weaknesses of the hospital's patient information system • Establish a pre-implementation baseline with KPIs • How to apply Kotter's eight steps change management model • Learn from case histories: success stories of a full implementation of PBM in various institutions and health systems.
5.	Organising a routine PBM program in hospitals
	Learning Objectives: Understand the infrastructural and organisational needs to run a routine PBM program in a hospital Topics: • Educational measures, administrative and organisational steps to be taken to sustainably run PBM as a standard of care in hospitals or hospital systems. • Interdisciplinary PBM coordination within the hospital • Infrastructural needs and adjustments to run PBM as a standard of care in hospitals or hospital systems o Patient access o Patient logistics o Facilities o Technical standards
6.	PBM treatment modalities following the three pillar concept
6.1	Role of the 1st pillar: optimizing the patient's own red cell mass
	Learning Objectives: Understand the anaemia risk and its role as an independent predictor of adverse outcome; understand the importance of the 1st pillar and its treatment modalities to modify the anaemia risk Topics: • Understanding anaemia and iron deficiency o Definition and aetiology of the different forms of anaemia o Prevalence of anaemia and iron deficiency in the general population o Prevalence of anaemia and iron deficiency in patient populations o Anaemia and its burden of disease • Identification of risk groups, pathophysiological consequences and the negative impact of a anaemia throughout the perioperative period • Estimate the risk of anaemia and the risk of transfusion (required red cell mass) Participants should be able to assess the patient specific anaemia and transfusion risk for the patient as accurately as possible: preoperative investigation, risk scores, retrospective databases. Learning how to apply the Mercuriali algorithm. • Avoid diagnostic and interventional blood loss Blood samples and blood loss during interventional procedures constitute a significant risk of anaemia. Participants will

	learn to minimize blood loss by reducing the diagnostic inspections to the extent necessary and to choose appropriate approach for diagnostic. This is particularly important in children and adults with low body weight. • Detection and correction of anaemia and iron deficiency: o Diagnosis of anaemia: Laboratory methods/parameters for detection and for differential diagnosis of various forms of anaemia. Participants should be able to clarify pre-existing forms of anaemia in the situation and undertake appropriate treatments o Treatment of Anaemia: Guidelines for treatment with iron, vitamin B12, folate and erythropoietin. Participants should be able to handle at least simple forms of anaemia, such as iron deficiency anaemia with a standardized treatment plan. o PBM in septic anaemic patients • Calculation of the required red cell mass: A method of estimating the necessary preoperative erythrocyte mass (type of surgery and patients related parameters, creating a risk scores, calculation by means of the Mercuriali algorithm), determination of the patient-specific tolerable blood loss. Participants should be able to assess the appropriate transfusion risk for the patient as accurately as possible.
6.2	Role of the 2nd pillar: minimising blood loss and bleeding
	Learning Objectives: Understand the risk of bleeding and blood loss as an independent predictor of adverse outcome; understand the importance of the 2nd pillar and its treatment modalities to modify the bleeding risk Topics: • Poorly controlled blood loss in specific procedures and its impact on outcome • Avoidance of diagnostic and interventional blood loss • Perioperative coagulation management: Diagnosis of coagulation disorders with special emphasis on point of care methods, compliant treatment of pre- and perioperative occurring coagulation disorders. Role of normothermia and temperature management. Participants should be able to recognize coagulation-related bleeding risks and to treat without increasing patient's risk. • Methods for reducing blood loss o Surgical methods: Surgical techniques with minimal blood loss, storage techniques, use of special equipment (e.g. argon beamer), use of local anticoagulants, Damaged Control Surgery. Participants should be able to recognize the importance of surgical techniques to minimize blood loss and exert corresponding influence on the surgical procedure. o Anaesthetic Methods: Normovolaemic haemodilution, hypotensive anaesthesia, regional anaesthesia, temperature management. Participants should have knowledge of anaesthesia, which are associated with lower blood loss. o Retransfusion of autologous blood: Possibilities and indications for reinfusion of autologous blood (washed, unwashed, intra- and postoperative), re-transfusion in tumour patients, in patients infected and in obstetrics. Participants should be able to apply the methods, indications and contraindications of autologous transfusion of shed blood in accordance with the guidelines. o Drug therapy: Recognizing and avoiding coagulation disorders, prophylactic therapy with antifibrinolytic agents. Participants should be familiar with the use of medications to reduce blood loss • Timely management of re-bleeding: Participants should be able to recognize the extent and risks of postoperative bleeding and to treat them accordingly.
6.3	Role of the 3rd pillar: optimising the physiological tolerance of anaemia
	Learning Objectives: Understand the physiology of profound anaemia and the treatment options to harness and optimise physiological reserves to

	cope with it Topics: • Methods to increase anaemia tolerance: identification and treatment of anaemia induced comorbidities, improving the circulatory status, improvement in lung function, myocardial ischemia treatment, treatment of arrhythmias, etc. • Optimised ventilation and the role of oxygen dissolved in the circulatory system • Optimised fluid management and the role of capillary density
7.	Physiologic transfusion thresholds and single-unit transfusion policy
	Learning Objectives: Understand the difference between PBM and optimal blood use Topics: • Explain the difference between PBM and optimal blood use ("optimal blood use begins where PBM is exhausted or fails") • Explain the advantage of physiological transfusion triggers over numerical triggers • Show the importance of a single-unit transfusion policy • Show the role of interactive computerised physician order entry systems for the transfusion of blood components • Show the importance of benchmarking physician-level KPIs for transfusion
8.	Medico-legal issues in PBM
	Learning Objectives: Understand the medico-legal implications of the patient's self-determination or autonomy Topics: • Define what a competent adult patient is and explain what his/her patient rights are, and how they are protected • Define what a mature minor patient is and explain what his/her patient rights are, and how they are protected • Explain what an advanced patient directive is, and how this directive has to be honoured • Explain the importance of a hospital-wide policy on an informed consent that documents in writing the discussion on PBM treatment modalities, their risks and benefits, as well as on transfusion and its risks and benefits

8.4 Appendix 4 – List of PBM related e-learning courses

Interactive learning programs for PBM, optimal blood use and related topics	
Australian Governments, the National Blood Authority (NBA), the Australian Red Cross Blood Service (Blood Service) and the Australian and New Zealand Society of Blood Transfusion (ANZSBT)	https://bloodsafelearning.org.au/
International Society for Blood Transfusion (ISBT)	http://academy.isbtweb.org/isbt/2014/seoul/53470/james.isbister.the.three-pillar.matrix.of.patient.blood.management.html?f=p14m1s474344
National Health Service, U.K.	http://www.rdehospital.nhs.uk/patients/services/e-learning/e-learning.html
University Hospital Frankfurt, Germany	https://www.pbmanager.com/

8.5 Appendix 5 – Job descriptions for PBM workforce in a hospital

Clinical lead for PBM (0.25 – 0.50 FTEs)	
Responsibilities	
1.	Responsible for the clinical PBM program through professional, goal-oriented leadership and continuous improvement of the program.
2.	Controls blood management and transfusion KPIs across all relevant hospital departments.
3.	Directs the development of strategies, processes, protocols, algorithms and guidelines.
4.	Leads a multi-disciplinary team of experts for sustainable hospital-wide implementation of PBM, coordinates and supports the activities of the PBM representatives of the departments.
5.	Fosters PBM research and establish a network with international experts.
Tasks	
1.	Provides centralised management and propagate in cooperation with the PBM representatives of each department the multidisciplinary program of PBM.
2.	Is chair of PBM .committee
3.	Sets the development of evidence-based guidelines and their sustainable implementation with interest in best practice and communicates the related content so that it uniformly improves patient outcomes by PBM programs.
4.	Monitor and analyse compliance / implementation of the PBM program by continuously screening benchmarking data and feedback and organize the needed information from all parties involved.
5.	Develops and continuously improves, together with the PBM coordinator, strategies resulting from the benchmarking process (treatment protocols, guidelines, standards, methods).
6.	Ensures that appropriate training programs, in accordance with PBM, are developed for the clinical staff and implemented. Regulates the teaching of indication, handling and documentation of blood products.
7.	Integrates the PBM approach into quality management system of the hospital, particularly regarding staffing, technical and organizational features, with the aim of continuous improvement of the quality of care for patients.
8.	Initiates research projects (internal and in cooperation with external expert specialists) to continuous improve PBM.
9.	Represents the PBM program to relevant professional associations, congresses, conferences, public appearances and similar.
10.	Is aware about recent publications in the field of PBM and passes this information further (Education and Knowledge Management).
11.	Cooperates closely with medical / clinical directors of PBM in other hospitals.
Selection criteria	
1.	Senior physician with very good practical experience and good scientific background in the understanding and treatment of bleeding and anaemia and in PBM.
2.	Postgraduate qualification and professional experience.
3.	Well-developed interpersonal and communication skills, written and orally.
4.	Pronounced analytical and conceptual thinking.
5.	Experience in organizing and conducting clinical research.
6.	Leadership at the senior management level.
Desirable qualifications	

1.	Wide range of experience in healthcare.
2.	Knowledge in financing of health care.

PBM coordinator (0.25 – 0.5 FTEs)	
Responsibilities	
1.	Improves patient welfare through implementation and further development of PBM program.
2.	Changes methods of treatment, nursing, laboratory work and related fields.
3.	Improves clinical standards, monitoring, developing methods and change management are main tasks.
Tasks	
1.	Directs and coordinates a multidisciplinary team to implement PBM program.
2.	Provides clinical leadership in collaboration with the medical director of PBM and consultancy in the fields of nursing, laboratory work and related fields of medicine with regard to PBM both inside and outside of the health system.
3.	Initiates and analyses research.
4.	Initiates, implements and evaluates the best practice methods and provides feedback to the field of PBM both inside and outside the health system to ensure the best possible patient care.
5.	Develops and promotes evidence-based guidelines, standards, protocols and manuals in accordance with the legal, technical and economic requirements.
6.	Provides advice, guidance and ensure professional patient care.
7.	Develops and manages a comprehensive anaemia management program as an integral part of the PBM (system for complete detection and correction of anaemia) and ensure an ongoing evaluation / optimization of these processes (pre-operative ambulance).
8.	Offers expertise to a wide range of workers in the health sector and patients and ensures that patients are well informed and decisions are well-founded (including refusal / acceptance of blood transfusions).
9.	Develops innovative approaches and methods to solve complex problems in the field of PBM both within and outside the health system.
10.	Is a member of the multidisciplinary PBM committee (similar to the concept of a transfusion committee).
11.	Develops social component and leadership qualities actively further to promote the PBM program optimally.
12.	Detects and installs when needed new positions for the implementation of the PBM project and formulate job descriptions for those new positions.
13.	Contributes to the recruitment and cares about the introduction of new staff in the organization.
14.	Develops and implements business plans and strategies to optimal use the available personal, financial and structural resources (IT, knowledge, external expertise) effectively that are in accordance with the department and institution aims.
15.	Implements and ensures ongoing performance management.
16.	Designs, implements and evaluates education and training programs within and outside the health system.
17.	Is responsible for the dissemination of new, relevant information regarding the PBM within and outside the health system.
18.	Is involved in public relations. Submit reports for various public places or toward patient complaints and excitations and other initiatives and requests that are required.
19.	Possesses basic knowledge in change management and applies appropriate strategies to promote the PBM program both within and outside the health system.
Selection criteria	
1.	Senior physician with practical experience and good scientific background in bleeding, anaemia and PBM.
2.	Management experience in a clinical speciality.
3.	Well-developed interpersonal and communication skills.
4.	Expertise and know-how in conjunction with PBM / transfusion medicine, also in emergency medicine.

5.	Expertise in the field of human resource development (human resources).
6.	Expertise and skills in terms of research and ongoing development of methods and best practices.
7.	Is on recent track of legal and regulatory requirements.
Desirable qualifications	
1.	Wide range of experience in healthcare.
2.	Knowledge in financing of health care.

Clinical PBM nurse coordinator (0.5 – 1.0 FTEs)	
Responsibilities	
1.	Assures that tasks planed by the PBM medical leader and coordinator are organised and carried out.
2.	Provides leadership and expertise.
3.	Communicates progress to the PBM medical and coordinator.
Tasks	
1.	Networks among multidisciplinary staff in the healthcare field to assist in making change happen within typical clinical practice in the field of PBM and transfusion.
2.	Directs and assist in the creation and formation of policy and procedure in the field of PBM.
3.	Acts as an intermediary between regulatory agencies and the PBM staff
4.	Is responsible for continuous evaluation of PBM competency in all areas of performance including target key performance indicators (KPIs).
5.	During implementation phase, works with the PBM implementation board as well as the PBM staff in the completion and process documentation of the PBM program with the intent of expansion to other geographic areas or states.
6.	Leads and coordinates PBM nurses and multidisciplinary team to implement the PBM program.
7.	Provides clinical leadership and consultancy to nursing, medical, laboratory and allied health care professionals, and providers in the area of PBM both within and external to the hospitals/health service.
8.	In collaboration with the PBM medical leader and coordinator, initiates and analyses research, including blood utilization data and benchmarking, to determine clinical best practice.
9.	Initiates, implements and evaluates best practice activities and provides feedback in order to support the delivery of appropriate clinical care in the area of PBM both within and external to the hospitals/health service.
10.	Develops, implements and promotes evidence based standards, policies, protocols and guidelines that are compliant with relevant professional, industrial and legislative requirements, which influence PBM both internal and external to the hospitals/health service.
11.	Provides advanced, complex patient/client care as well as expert consultancy and guidance both within and external to the hospitals/health service.
12.	Leads and develops a peri-intervention anaemia/iron deficiency detection, evaluation management program
13.	Provides expert consultancy service for a broad range of customers and health professionals, including facilitating the requirements for informed consent/refusal for blood transfusion.
14.	Is a member of the multidisciplinary representative Patient Blood Management Committee.
15.	Provides leadership in the coordination and implementation of quality improvement activities.
16.	Contributes to the formulation of staffing profiles according to analysis of clinical needs and available resources. Operates within the allocated/available budgets for the area of responsibility.
17.	Implements and maintains performance management activities, where applicable.
18.	Leads and develops education and training programs both within and external to the hospitals/health service.
19.	Regularly disseminates information on clinical research in the area of PBM both within and external to the hospitals/health service.
20.	Provides a public relations function for the area including where relevant investigation and report preparation for ministerial, enquiries and consumer complaints.

Selection criteria	
1.	Eligibility for registration as registered nurse.
2.	Knowledge and ability to provide leadership in a complex health service environment and influences the achievement of objectives for the area of responsibility.
3.	Knowledge and application of physical, financial and human resource principles at a senior nursing level.
4.	Ability to contribute effectively as a member of a nursing leadership team and to influence and implement change.
5.	Knowledge and application of quality improvement initiatives.
6.	Well-developed communication, consultation and negotiation skills.
7.	Expert with clinical/professional knowledge in area of transfusion and/or PBM in an acute setting.
8.	Expert knowledge and application of research and best practice principles.
9.	Current knowledge of legislative and regulatory requirements in the areas of equal opportunity, disability services and occupational safety & health, and how these impact on employment, people management and service delivery.
Desirable qualifications	
1.	Possession of or significant progression toward the attainment of a postgraduate qualification in area of specialty.
2.	Demonstrated knowledge of project management.

8.6 Appendix 6 – Organisation of the hospital's PBM committee

Table 15. Functions and role of the PBM committee

Functions of the Patient Blood Management Committee
Function: As a multidisciplinary representative committee that takes the lead in developing, implementing, evaluating and progressing the program. Members of the committee act as role-models for other healthcare professionals in the program. They address key questions in relation to the functioning of the program, take the lead in the implementation of guidelines and assist in the adherence to guidelines. They assist with the development and evaluation of the benchmarking and monitoring databases, education initiatives and research projects.
The Committee's role is to: • Communicate and promote the PBM program vision throughout the institution • Facilitate the change management • Provide forum for discussion and facilitate communication • Provide departmental leadership • Facilitate development and review of protocols, policies, procedures and guidelines • Monitor compliance/ provide feedback on gains and areas for improvement • Collect data (baseline, monitoring, feedback, improvement) • Benchmark outcomes • Initiate educational needs and opportunities • Produce educational materials (including newsletters, brochures, hospital website) • Interact actively with the hospital administration • Develop and review operational policies and protocols • Develop and carry out quality improvement activities • Act as a resource and provide direction • Recommend, develop and review education programs • Initiate proposals for research and clinical trials. • Compile data for analysis Representation • PBM Medical Director (Chair) • PBM Coordinator • PBM nurse coordinator • Medical Administration. • Surgery (representatives from major surgical specialties) • Anaesthesia/Intensive Care • Haematology/Oncology • Emergency medicine • General medicine • Transfusion medicine • OBGYN • Paediatrics and neonatology • Nursing (theatre, ICU and ward) • Pharmacy • Quality and safety management • Chief hospital administration

Table 16. Reorganising transfusion committee to PBM committee (Adapted from Shulman and Saxena (199))

Transfusion Committee*		PBM Committee
The committee chair is a physician who is knowledgeable in transfusion medicine.	→	The committee chair is a physician who is knowledgeable in PBM.
Committee meetings are documented by minutes that are submitted to medical and executive leadership for their review and approval, and which are protected from inappropriate 'discovery'. Each committee member should sign a confidentiality agreement.	→	Committee meetings are documented by minutes that are submitted to medical and executive leadership for their review and approval, and which are protected from inappropriate 'discovery'. Each committee member should sign a confidentiality agreement.
Appropriate policies define institutional transfusion practices. Physicians and nursing services must be aware of these policies and abide by them.	→	Appropriate policies define institutional anaemia/transfusion practices. Physicians and nursing services must be aware of these policies and abide by them.
Audits for compliance with local policies and procedures assess the entire transfusion process, including transfusion practices within the operating room.	→	Audits for compliance with local policies and procedures assess the entire transfusion process, including transfusion practices within the operating room.
Adverse events, incidents and errors are investigated	→	Adverse events, incidents and errors are investigated to prevent extensive blood loss and inappropriate transfusion
Product losses are monitored to show products expired under direct control of the laboratory (inside laboratory loss) versus outside the laboratory due to improper ordering or handling (outside laboratory loss).		
Operational effectiveness of the laboratory service is reviewed, e.g., response times for emergency requests.		
Results of external proficiency testing and accreditation surveys are reviewed.	→	Results of in-/adequate transfusion rate is reviewed.
Quality indicators that address adverse patient events, processes and quality of care, hospital service and operations, and effectiveness and safety of services are monitored after transfusion (such as the functioning of blood warmers).	→	Quality indicators that address optimal patient outcome, processes and quality of care, hospital service and operations, and effectiveness and safety of services are monitored after adherence to the principles of PBM (such as blood sparing techniques).
Medical errors (with or without an adverse outcome) and adverse patient events related to transfusion are tracked, analysed for causes, categorized and reviewed for sentinel events, (e.g., acute fatal haemolytic transfusion reactions or other transfusion related fatality).		
Product contamination is reported to the blood product supplier and other local, state and/or federal agencies as required by policy and/or statute.		
There is a mechanism for involving the medical staff in performance improvement activity including feedback and learning throughout the hospital.	→	There is a mechanism for involving the medical staff in performance improvement activity including feedback and learning throughout the hospital.
There is an integrated plan for the management of blood shortages, including planning for the management of patients based on predetermined categories (e.g., patients in need of immediate resuscitation, patients in need of urgent surgical support, non-surgical patients who are anaemic, scheduled but non-emergent surgical patients).	→	There is an integrated plan for the management of blood shortages, including planning for the management of patients based on predetermined categories (e.g., patients in need of immediate resuscitation, patients in need of urgent surgical support, non-surgical patients who are anaemic, scheduled but non-emergent surgical patients).

8.7 Appendix 7 – Computerized Physician Order Entry Systems (CPOE)

Table 17. Expansion of clinical software for clinical decision support system in the scope of optimal blood use

Type	Intervention	Reference
Real time electronic audit	Traceability of blood products, compliance with guidelines	(200)
Blood conservation algorithm	Decision making tool	(201)
Monitor-feedback program	Registration of blood products and corresponding laboratory values of patient to verify appropriate usage of blood	(30)
Monitor compliance guidelines	Optimise transfusion trigger	(202)
Clinical decision support system	Provides all institutional RBC transfusion guidelines and the patients recent haemodynamic data in a single easy to use format	(203)
Clinical decision support system	Clinicians need to specify the indication for transfusion in case the most recent laboratory results display no indication for transfusion	(154)
Maximum surgical blood order schedule	Identify specific procedures with very low transfusion rates, for which preoperative blood orders for typing and red cell antibody screening or a type and crossmatch were considered unnecessary	(204)
Clinical decision support via electronic medical records	Alert triggered when a provider orders RBCs in a patient with pre-transfusion haemoglobin level above a set threshold	(205)

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