

# Patient Blood Management in the Netherlands: Between practice and evidence

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# Outline

- Introduction
- Blood use in the Netherlands
- What is patient blood management (PBM)?
- Practical implementation of PBM
- Evidence of PBM
- More opportunities for PBM?
- Conclusions

# Introduction

## Inhabitants

Estonia: 1,3 million

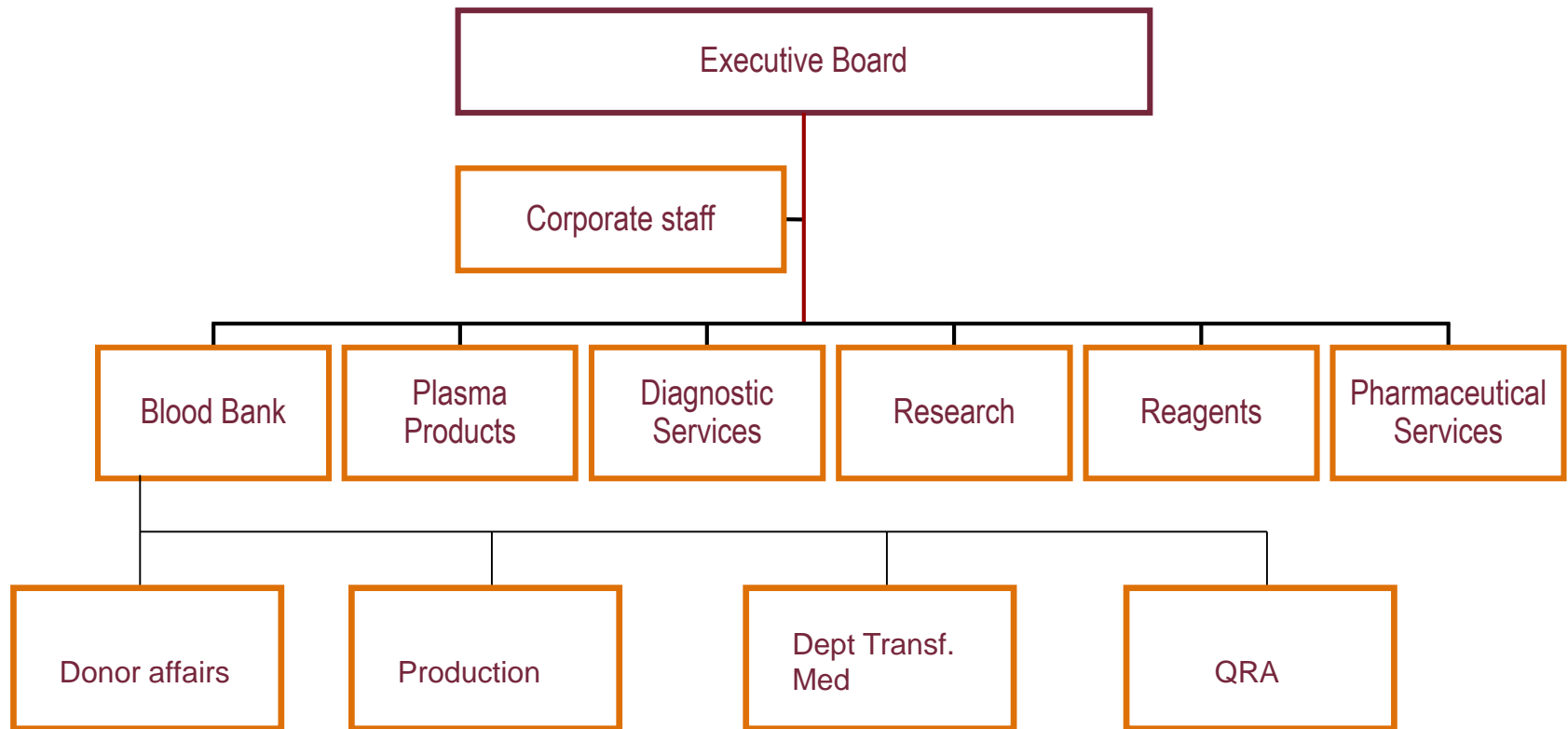
Netherlands: 16,9 million



# Sanquin Blood Supply Foundation

- The only organization in the NL authorized to supply blood (products)
- Not-for-profit
- Approximately 3,000 employees; 5 divisions:
  - **Blood Bank**
  - Plasma Products
  - Diagnostic Services
  - **Research** – Sanquin staff working with / partly employed at academic centers
  - Reagents

# Organization





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graph TD; BB[Blood Bank] --> DA[Donor Affairs]; BB --> P[Production]; BB --> QRA[Quality and Regulatory Affairs]; BB --> DTM[Dept. Transfusion Medicine];
```

Blood Bank

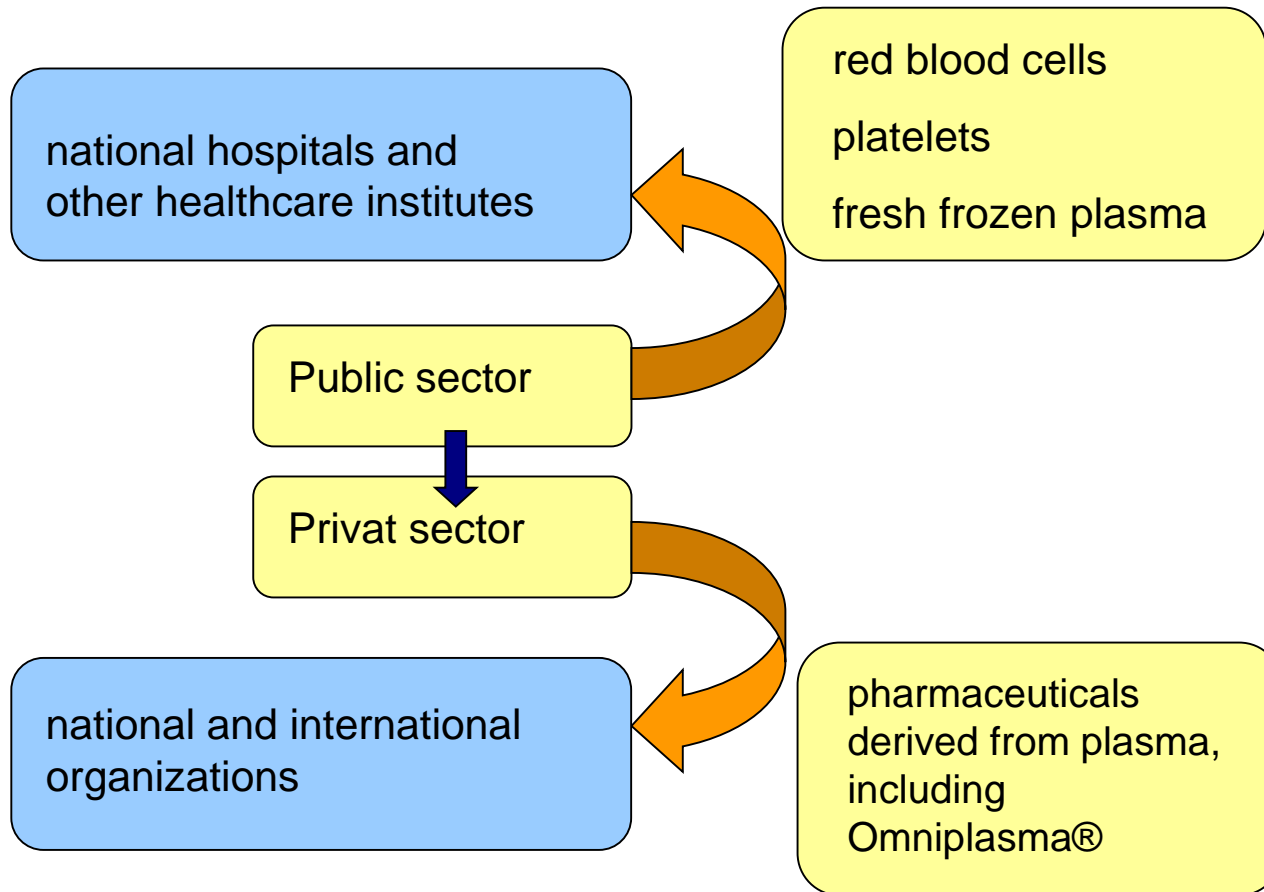
Donor Affairs

Production

Quality and  
Regulatory Affairs

Dept. Transfusion  
Medicine

# Sanquin



3000 employees; 400,000 donors



## Hospitals

- 90 hospitals
  - 8 university hospitals
- Each hospital has its own transfusion laboratory and performs compatibility tests
- Sanquin: reference laboratory



2 Sanquin  
production sites



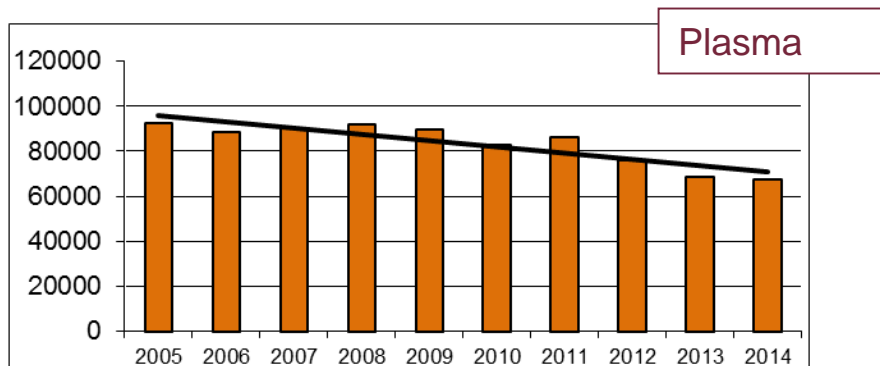
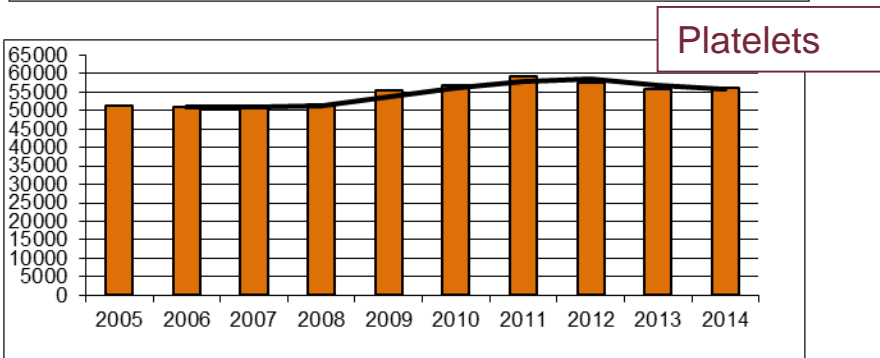
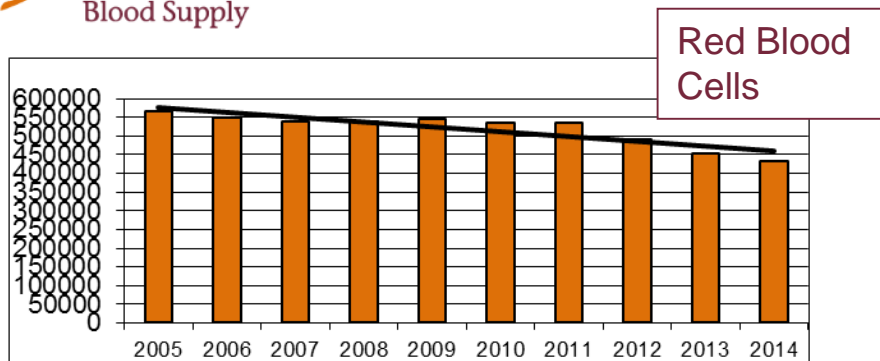
7 issuing depts.



hospital transfusion  
laboratory

# Blood use in the Netherlands

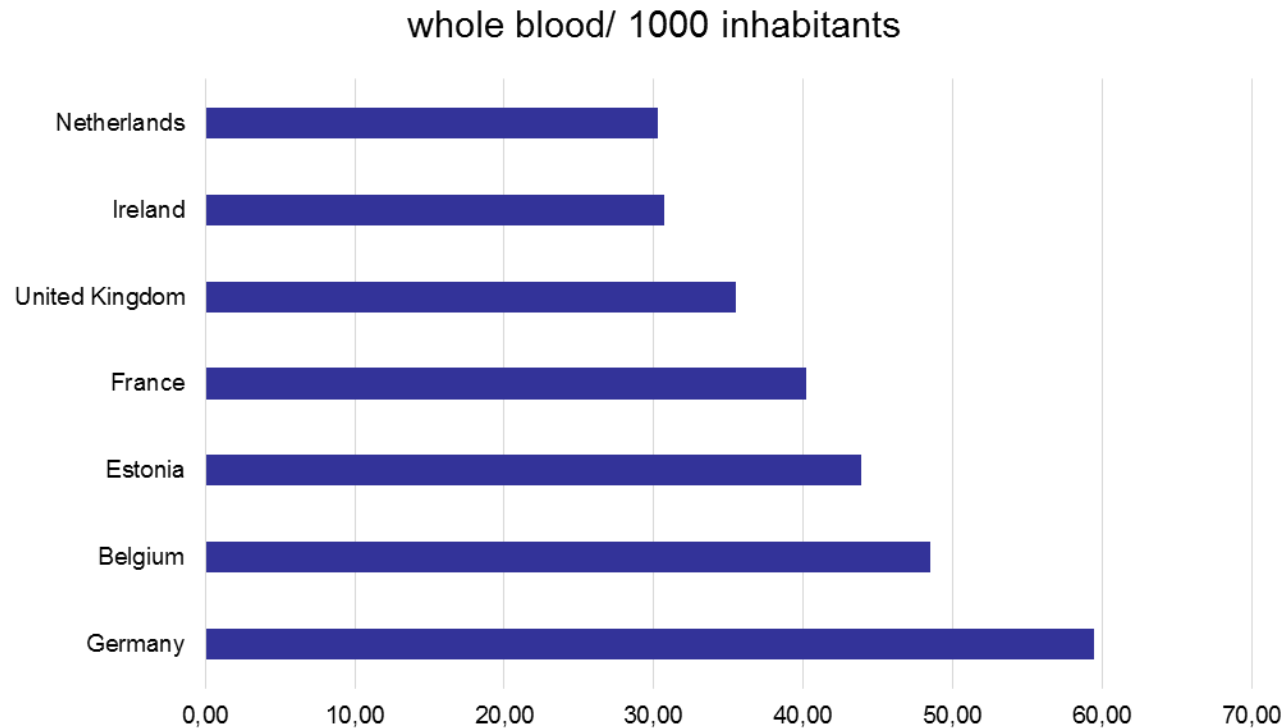
# Number of blood transfusions in the Netherlands



## Blood products (2014)

- 433,500 red blood cells (↓ 26%)
- 56,000 platelets (↑10%)
- 67,600 plasma (↓ 27%)

# Benchmark Europe EDQM 2012



## Possible reasons for declined (red) blood use

- National guideline “Blood Transfusion” (2004, 2011 revised version) including Patient Blood Management
- Quality Act for Health Care institutes and national hemovigilance office “TRIP” (Transfusion and Transplantation Reactions In Patients; founded 2001)
- Benchmark blood use between Dutch Hospitals organized by Sanquin
- Reimbursement system for blood products in the Netherlands
- Cost reduction health care -> hospitals have to economize (6%) and quality indicators Dutch Society of Surgeons -> concentration of care

# What is Patient Blood Management (PBM)?

## **Patient Blood Management definition**

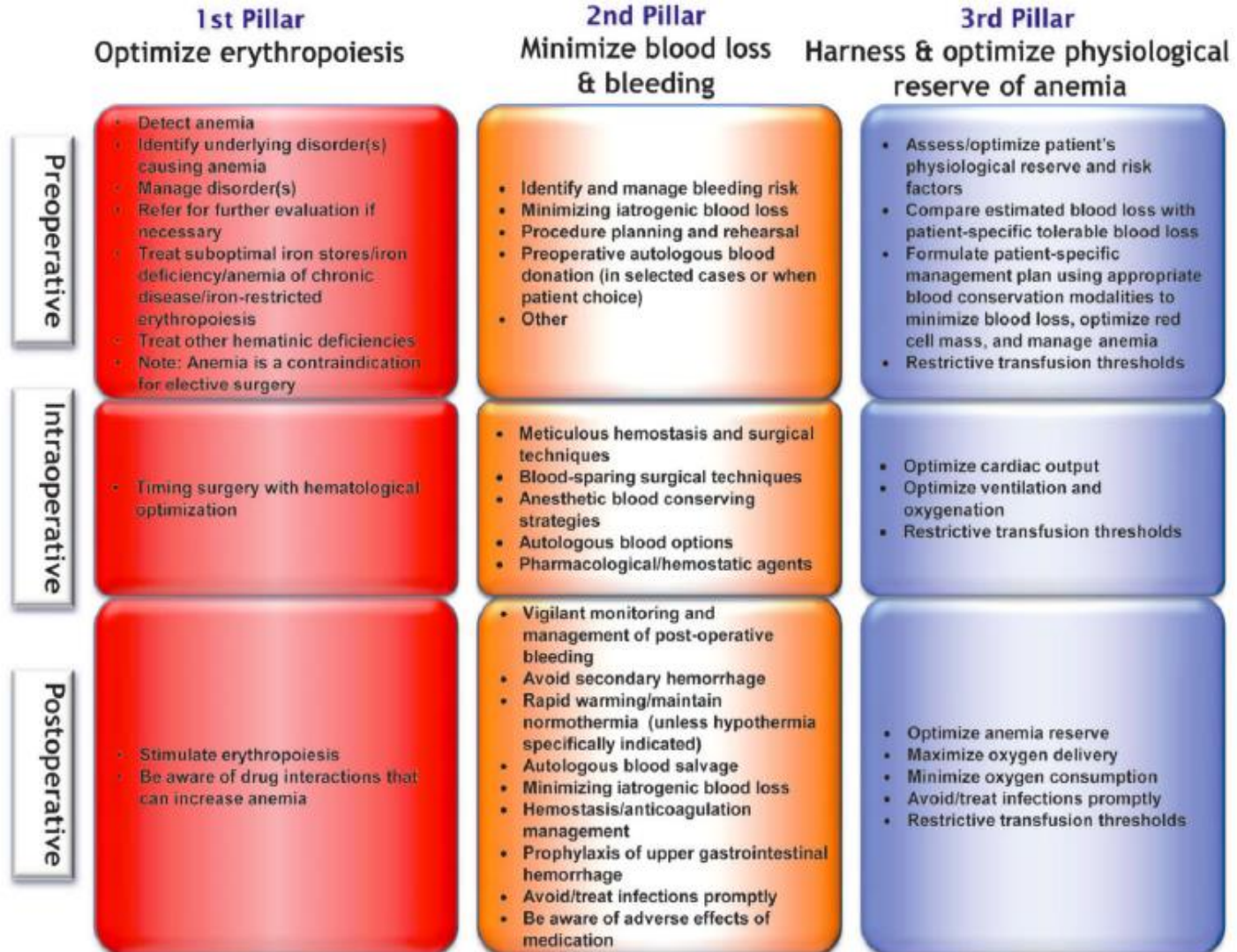
*Patient Blood Management* (PBM) is an evidence-based, multidisciplinary approach to optimising the care of patients who might or do need blood transfusion.

# Three pillars of Patient Blood Management

(<http://www.health.wa.gov.au/bloodmanagement/>)

1. optimising the patient's own blood
2. minimising surgical blood loss and bleeding
3. harnessing and optimising the patient-specific physiological reserve of anaemia (including restrictive transfusion thresholds)





# Practical implementation of PBM in the Netherlands

# National Guideline “Blood Transfusion”

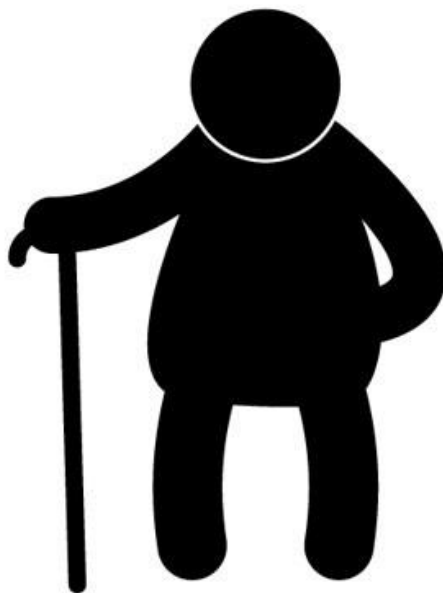
- Effective use of blood products
  - **so-called 4-5-6 rule**  
(depending on the presence of co-morbidity, the threshold for RBC transfusion varies between 4.0 mmol/L (6.4 g/dL) and 6.0 mmol/L (9,7 g/dL))
  - **alternatives for red blood cell transfusion**  
pharmaceuticals, cell savers
  - **improvement of operation techniques**

Colofon: *Richtlijn Bloedtransfusie*





4.0 mmol/l = 6.4 g/dl



5.0 mmol/l = 8.0g/dl



6.0 mmol/l = 9.7 g/dl

# Alternatives for blood cell transfusion

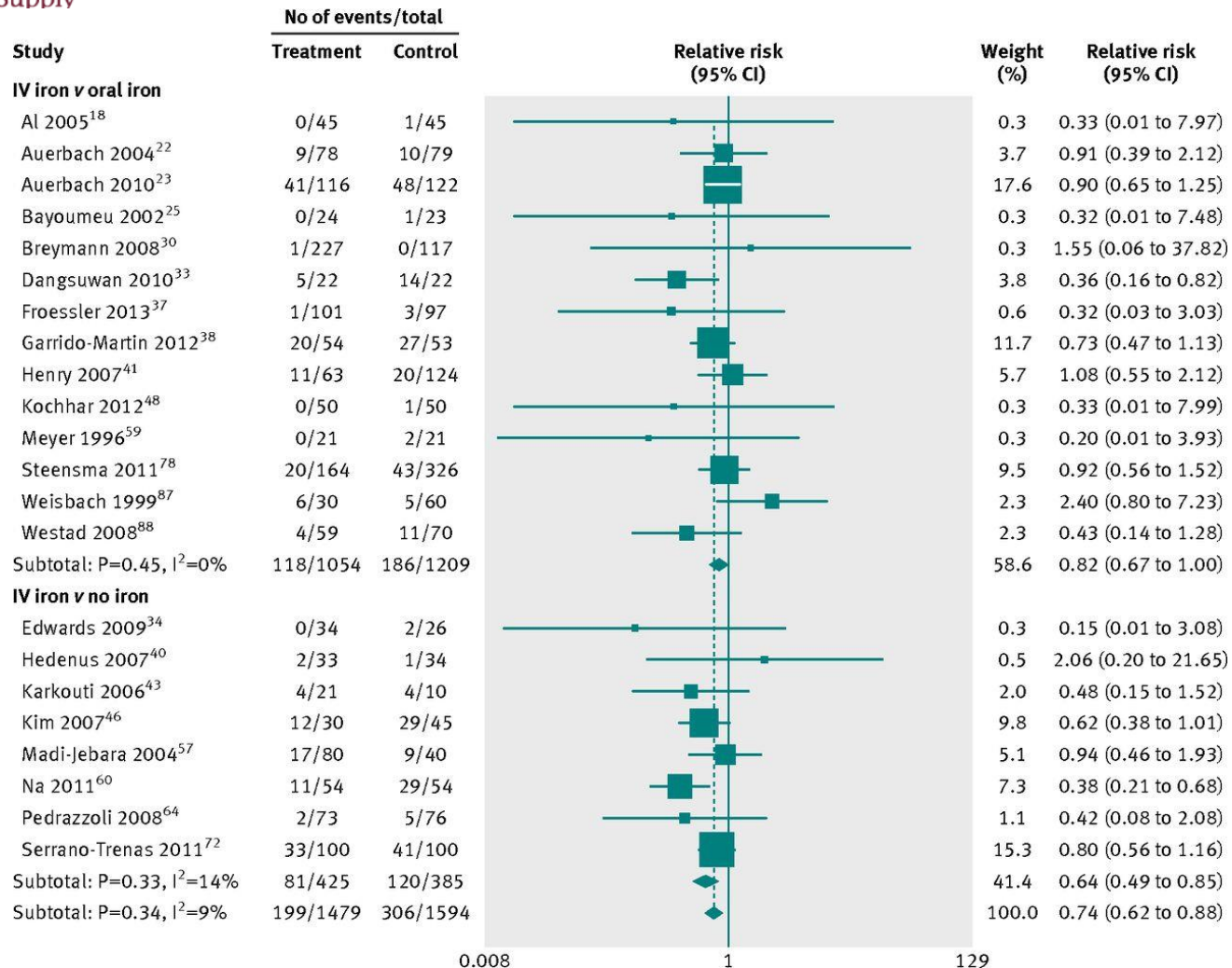
- Iron (oral or IV) -> pre-operative anaemia
- Erythropoietin -> pre-operative anaemia
- Cell savers -> intra-operative/ post-operative
- Tranexamic acid (cheap)-> pre- and during operation, IV and topical



## Iron in pre-operative anaemia

- No randomized controlled studies yet
- PREVENTT: preoperative intravenous iron to treat anaemia in major surgery: study protocol for a randomised controlled trial (Trials 2015, 16; 254)
- Litton et al: Safety and efficacy of intravenous iron therapy in reducing requirement for allogeneic blood transfusion: systematic review and meta-analysis of randomised clinical trials (BMJ 2013; 347: f4822)
- Recommendations: A Kotze et al.: British Committee for Standards in Haematology Guidelines on the Identification and Management of Pre-Operative Anaemia. BJM 2015, September epub

**Fig 3 Risk of red blood cell transfusion in patients who received intravenous iron compared with oral iron and no iron.**



Edward Litton et al. BMJ 2013;347:bmj.f4822

# Evidence of erythropoietin and cellsavers – Dutch study in orthopaedic patients

Dr Cynthia So-Osman





# Rationale

- Hip- and knee-replacement surgery result in large blood losses
- Ageing population will result in 3 fold increase of joint replacements in 2030 (> 100.000 per year)
- Blood sparing modalities are very popular and much investigated
- However:
  1. NO evidence on combined effect of several modalities
  2. NO evidence on effect of restrictive transfusion trigger
  3. Most studies lack power, are methodologically poor



## Patients characteristics

Parameter	Numbers (%) or mean (SD)
Evaluated patients	2442
Females	1699 (70%)
Mean age (years)	69 ( $\pm 11$ )
THR Of which revision	1462 (60%) 130 (5%)
TKR Of which revision	980 (40%) 54 (2%)
Mean pre-operative Hb (mmol/L) Hb (g/dL)	8.6 ( $\pm 0.8$ ) 13.9 ( $\pm 1.3$ )
Epo eligible patients	683 (28%)

# General results

- RBC transfusions in 11.6% of 2442 (n=284)
- If transfused: median of 2 RBC (range 1- 27)
  - Intra-operatively n= 37 (range 1-12)
  - 0-14 days n= 246 (range 1-11)
  - 14 days-3 months n= 43 (range 1-27)
- Due to heterogeneity of revision patients, primary surgery group is separately reported in case of RBC use
- In case of cost analysis all patients were evaluated

## Epo effect

- Significant reduction in % patients transfused:  
2 times less
- Non-significant mean RBC reduction:  
29%

## Autologous blood re-infusion effect

No reduction in mean RBC use AND in proportion transfused (with or without epo)

No difference between cell saver and drain

# Cost analysis Epo and autologous re-infusion devices

Costs ( in Euro' s) N=683	Total costs (in Euro)	Difference (95% CI)
Low Hb (stratum I) with epo (n=339) no epo (n=344)	5615 4829	785 (262-1309)

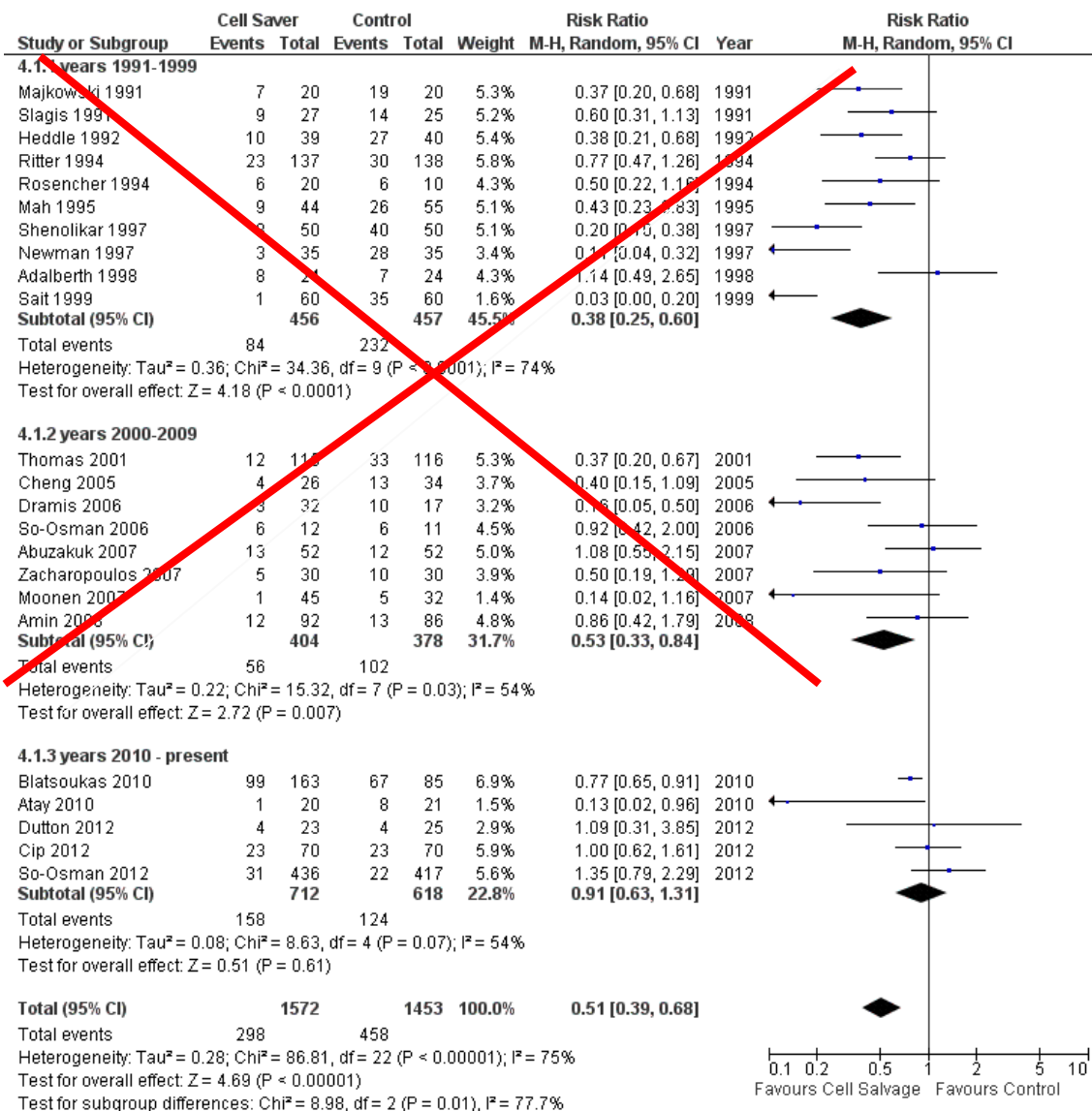
Costs ( in Euro' s) N=2442	Total costs (in Euro)	Difference (95% CI)
with autologous device (n=1481) without autologous device (n=691)	4399 4021	378 (161-595)

## Conclusions

- Significant red blood cell (RBC) reduction by Epo, however not cost-effective
- Neither red blood cell- nor cost-reduction by autologous blood reinfusion (i.e. cell saver or postoperative drain re-infusion)



# Meta-analysis cell savers



**Outcome:**  
Number of patients  
exposed to allogeneic  
RBC transfusion

## Conclusions meta-analysis cell saving

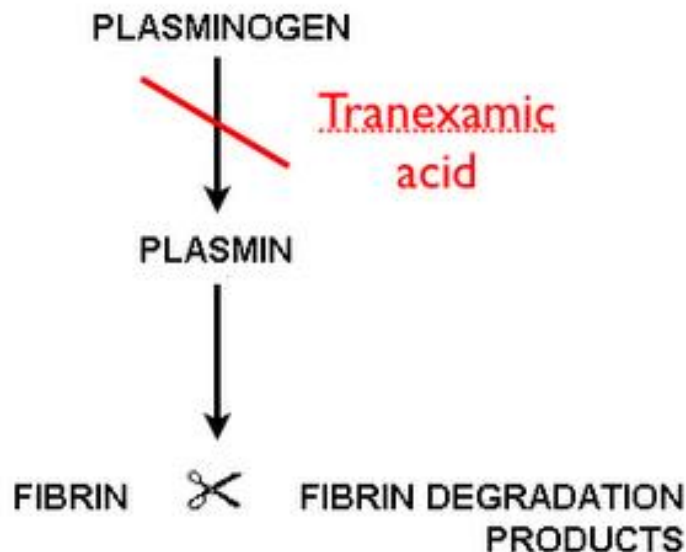
### Cell Saving significantly reduces

- the need for allogeneic RBC transfusion, and
- the volume of RBC transfused

However, in RCTs published more recently (2010-2012), Cell Saving does neither reduce the need for allogeneic RBC transfusion nor the volume of RBC transfused in both hip and knee surgery

## Tranexamic acid to prevent/ diminish bleeding

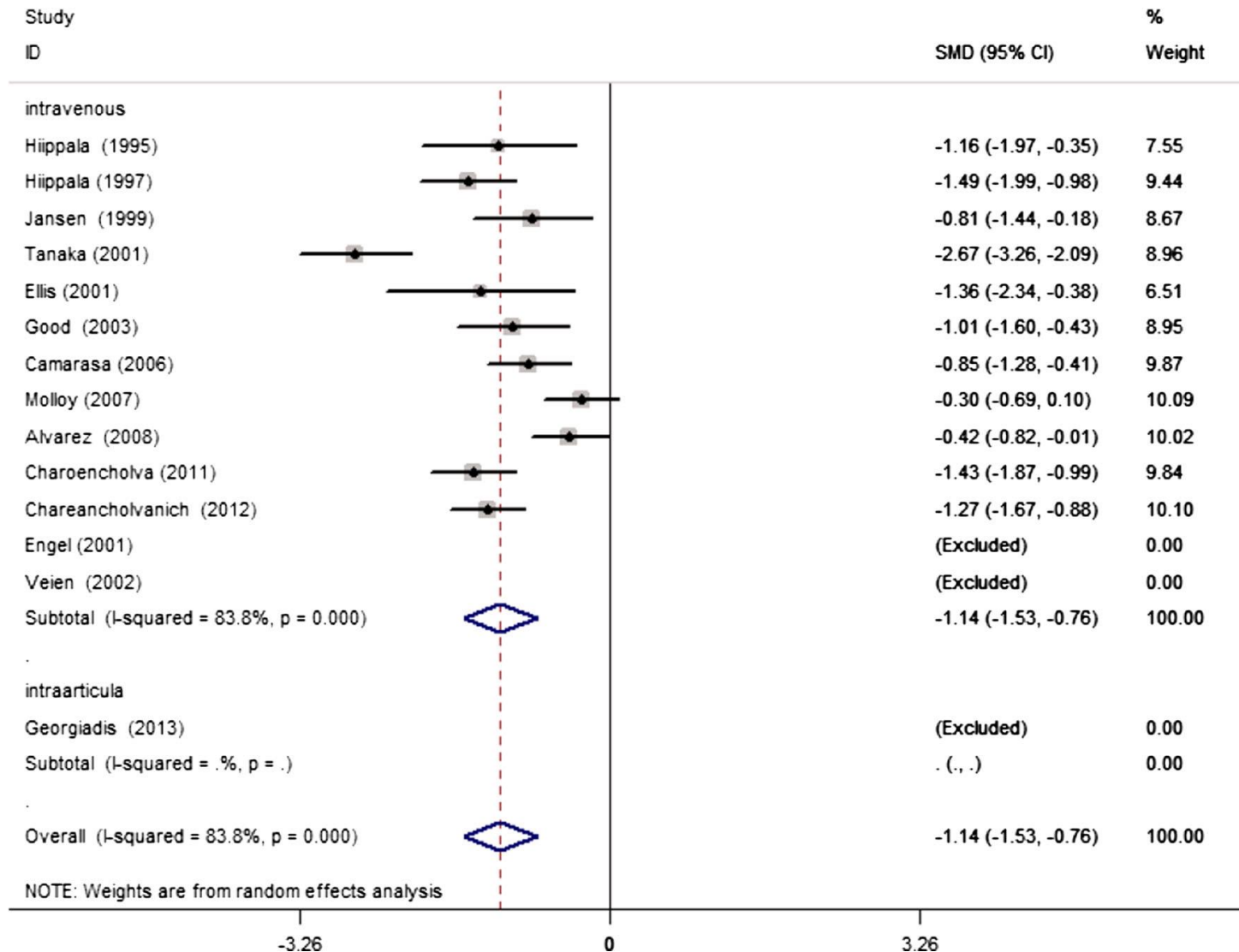
- TXA is a synthetic lysine analogue antifibrinolytic agent. It is an antifibrinolytic that competitively inhibits the activation of plasminogen to plasmin, by binding to specific sites of both plasminogen and plasmin, a molecule responsible for the degradation of fibrin.
- Oral, intravenous or topical administration



## Use of tranexamic acid

- in 2015 many randomized trials/ meta-analysis on tranexamic acid, i.e.:
  - Trauma
  - Postpartum haemorrhage
  - Orthopaedic surgery (total hip and knee, spine)
  - Upper gastro-intestinal bleeding
  - Open heart surgery

# Effect tranexamic acid in total knee arthroplasty in 34 randomized controlled trials



Effect on  
blood units  
transfused  
per patient

# More indications for PBM than surgery?

## Patient Blood Management in Europe (PaBloE)

Objectives of one of the working parties

- Data collection on current blood and blood component use and PBM practices
  - Survey of PBM practices among the PaBloE centres
  - Survey of top indications for red blood cell use

**Red Cell Issue Trace Audit Cycle 1, 2014**

Box a) No of units:

Box b) Patient's Year of birth

Box c) Male ☐ Female ☐

Audited Patient No.

<b>Cardiothoracic Surgery</b> 1 CABG (first) <input type="checkbox"/> 2 CABG (redo) <input type="checkbox"/> 3 Valve replacement (+/- CABG) <input type="checkbox"/> 4 ECMO <input type="checkbox"/> 5 Congenital Heart Disease <input type="checkbox"/> 6 Other (please state) <input type="text"/> <b>ENT</b> 7 ENT <input type="checkbox"/> <b>Gastrointestinal Surgery</b> 8 Oesophageal <input type="checkbox"/> 9 Gastric <input type="checkbox"/> 10 Pancreatic <input type="checkbox"/>	<b>Vascular Surgery</b> 23 Emergency AAA repair <input type="checkbox"/> 24 Elective open AAA repair <input type="checkbox"/> 25 Other (please state) <input type="text"/> <b>Orthopaedics</b> 26 THR (first) <input type="checkbox"/> 27 THR (redo) <input type="checkbox"/> 28 TKR (first) <input type="checkbox"/> 29 TKR (redo) <input type="checkbox"/> 30 Other (please state) <input type="text"/> <b>Plastic surgery</b> <input type="checkbox"/>	<b>GI bleed</b> 43 Upper acute <input type="checkbox"/> 44 Lower acute <input type="checkbox"/> 45 Upper chronic <input type="checkbox"/> 46 Lower chronic <input type="checkbox"/> 47 Site of bleeding not known <input type="checkbox"/> <b>Anaemia due to:</b> 48 Renal failure <input type="checkbox"/> 49 Cancer (non haem) <input type="checkbox"/> 50 Iron deficiency <input type="checkbox"/> 51 B12/folate def <input type="checkbox"/> 52 Chronic disorders e.g. <input type="checkbox"/>
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## National Comparative Audit Program, NHS Blood & Transplant

<b>Neurosurgery</b> 14 Neurosurgery (including head injury) <input type="checkbox"/> <input type="text"/> <b>Trauma</b> 15 Blunt <input type="checkbox"/> 16 Penetrating <input type="checkbox"/> 17 Fractured femur <input type="checkbox"/> 18 Fractured pelvis <input type="checkbox"/> 19 Other fracture <input type="checkbox"/> 20 Other (please state) <input type="text"/> <b>Urology</b> 21 Urology <input type="checkbox"/> <b>Solid Organ Transplant</b> 22 Solid Organ Transplant (State organ) <input type="checkbox"/> <input type="text"/>	<b>Obs &amp; Gyn</b> 34 Gynae (non malignant) <input type="checkbox"/> 35 Gynae oncology <input type="checkbox"/> 36 Obstetric anaemia <input type="checkbox"/> 37 Obstetric haemorrhage <input type="checkbox"/> <b>Neonatal/fetal</b> 38 Neonatal top up <input type="checkbox"/> 39 Neonatal exchange <input type="checkbox"/> 40 Neonatal large volume transfusion <input type="checkbox"/> 41 Intrauterine transfusion <input type="checkbox"/> 42 Other (please state) <input type="text"/>	<b>Haematological</b> 55 MDS <input type="checkbox"/> 56 AML (including APML) <input type="checkbox"/> 57 ALL <input type="checkbox"/> 58 Myeloma <input type="checkbox"/> 59 Hodgkins/NHL/CLL <input type="checkbox"/> 60 Acquired Haemolytic Anaemia <input type="checkbox"/> 61 Thalassemia <input type="checkbox"/> 62 Sickle cell disease <input type="checkbox"/> 63 Other inherited anaemia <input type="checkbox"/> 64 Myeloproliferative disease <input type="checkbox"/> 65 CML <input type="checkbox"/> 66 Aplastic anaemia <input type="checkbox"/> 67 Other (please state) <input type="text"/>
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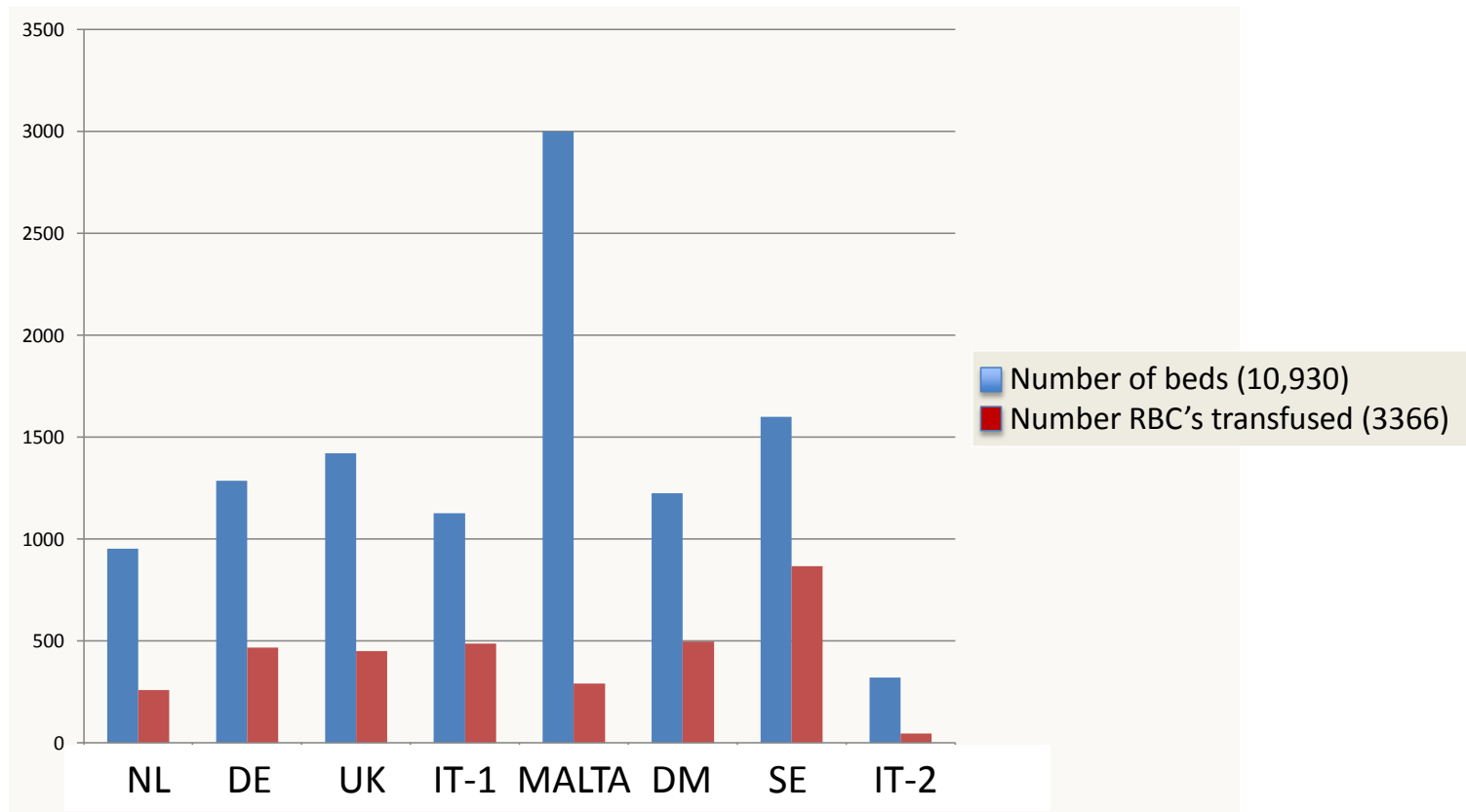
- Cardiothoracic Surgery
- ENT
- Gastrointestinal Surgery
- Neurosurgery
- Trauma
- Urology
- Solid Organ Transplant
- Vascular Surgery
- Orthopaedics
- Plastic Surgery
- Other Surgery

- Obstetrics & Gynaecology

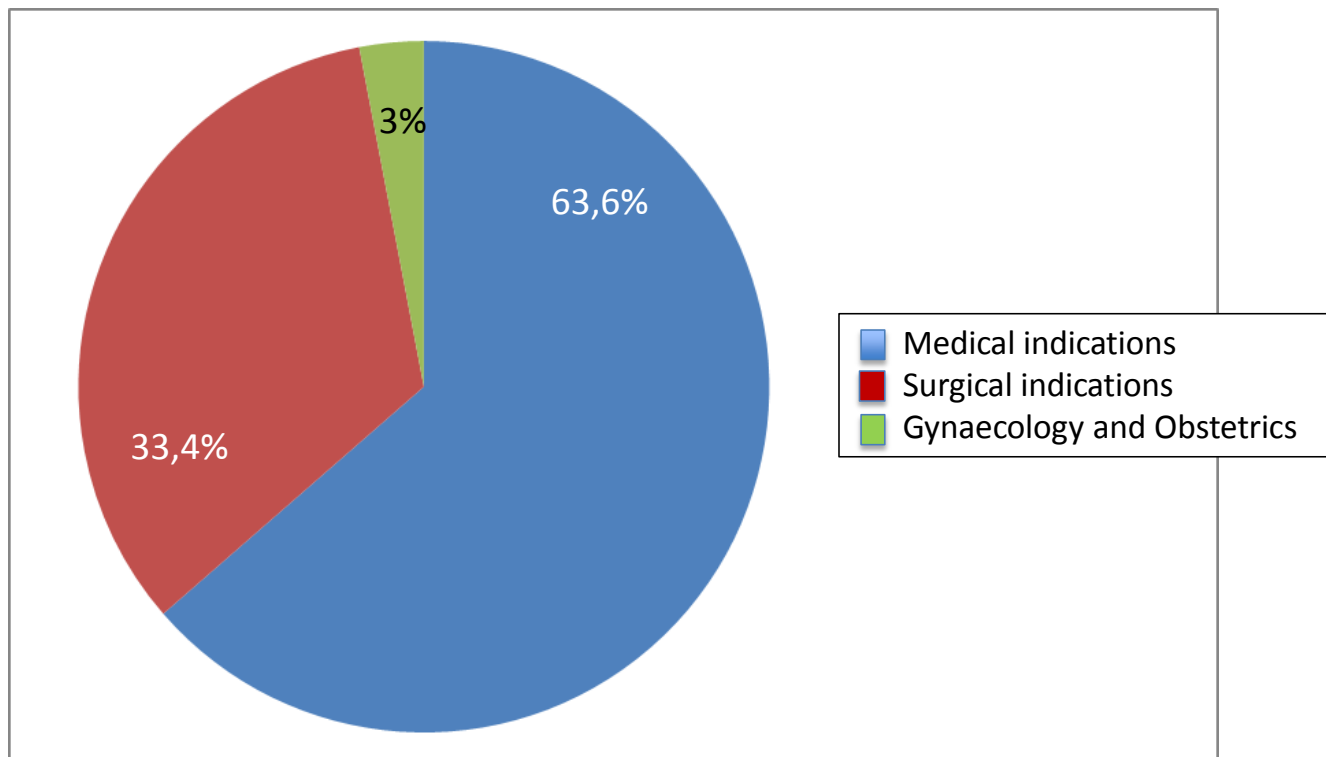
- Neonatal/fetal
- GI Bleed
- Haematological
- Anaemia due to other causes



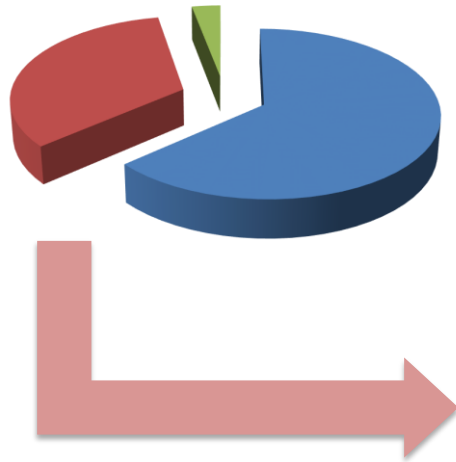
## 8 European Hospitals



## Where did red cells go to?

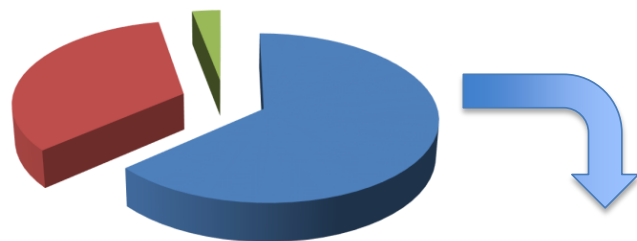


# Top Surgical Indications



Indication	Number of red cell units transfused	Percentage of total (3366)
Cardiothoracic	324	9.6%
Gastrointestinal	193	5.7%
Trauma	133	4%
Orthopaedics	118	3.5%
Vascular	101	3%

# Top Medical Indications



Indication	Number of red cell units transfused	Percentage of total (3366)
Haematological	1013	30.1%
Gastro-intestinal bleeding	239	7.1%
Critical Care	147	6.8%
Cancer non-haematological	144	6.7%
Neonatal	99	2.9%

# Conclusions

- Patient Blood Management = Good Clinical Practice
- A simple rule (4-5-6) may safe blood use
- Alternatives for blood transfusion may be useful, but
- Evidence is needed to implement PBM properly
- PBM had been investigated particularly in surgical patients, but
- Most red blood cells go to medical indications

More research is needed on the topic of PBM



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[www.sanquin.nl](http://www.sanquin.nl)