Guidelines, the evidence to practice gap, and OBS UK study

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Disclosures

I am an investigator on research relevant to this presentation

I have no direct financial disclosures

NHS
Blood and Transplant

Aims

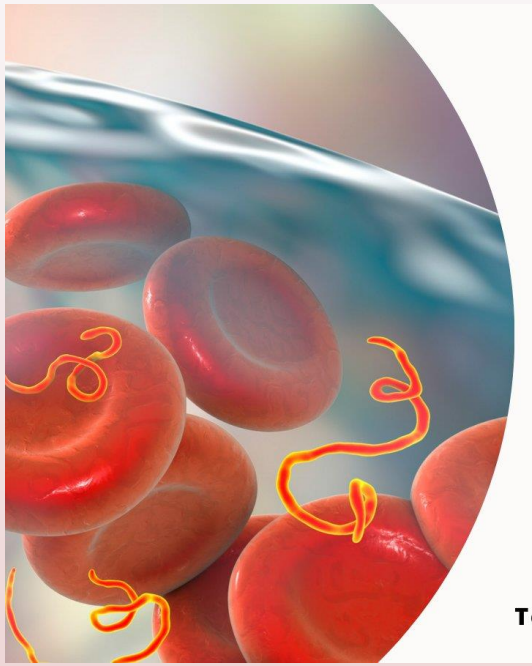
Guidelines

Changing practice

Implementation research studies

A guideline for the haematological management of major haemorrhage: a British Society for Haematology Guideline

Simon J. Stanworth[1,2,3] | Kerry Dowling[4] | Nikki Curry[2,3] | Heidi Doughty[5,6] | Beverley J. Hunt[7] | Laura Fraser[8,9] | Shruthi Narayan[10] | Juliet Smith[11] | Ian Sullivan[12] | Laura Green[13,14,15] | The Transfusion Task Force of the British Society



British Society for Haematology
Listening • Learning • Leading

NEW GUIDELINE

Guideline for the Haematological management of major haemorrhage

To view our guidelines please visit our website: www.b-s-h.org.uk/guidelines

https://b-s-h.org.uk/guidelines/guidelines/haematological-management-of-major-haemorrhage-2022

BJHaem
BRITISH JOURNAL OF HAEMATOLOGY

Overview of Guideline: structure

Use of Blood Components

Major haemorrhage protocols and blood banking

Tranexamic acid

Other haemostatic agents

Coagulation testing and Cell Salvage

Specific Clinical Settings and mass casualty

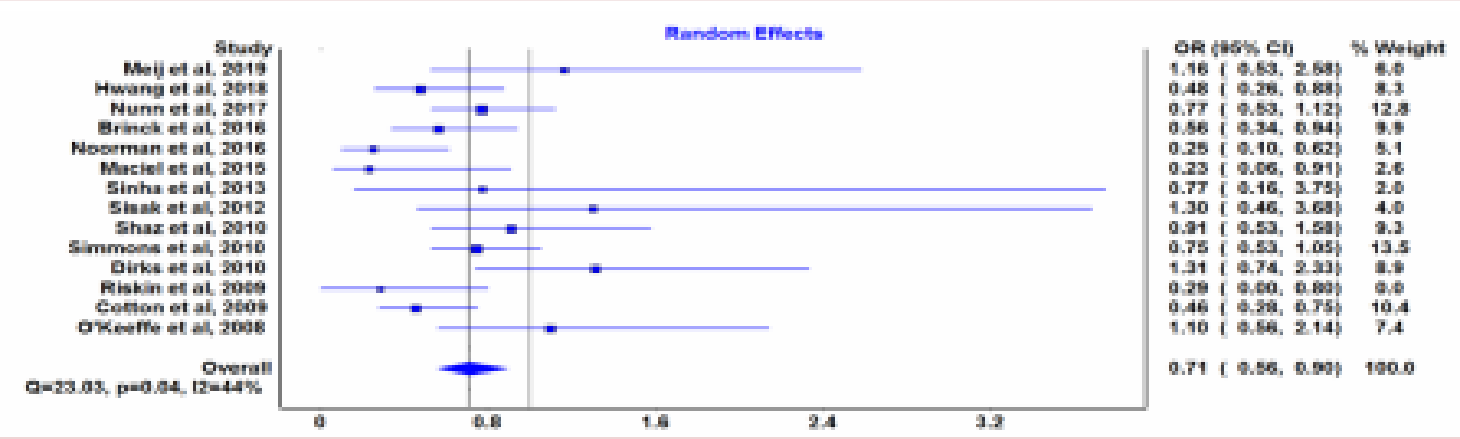
Audit, education and Quality management

The effect of massive transfusion protocol implementation on the survival of trauma patients: a systematic review and meta-analysis

Rafael Consunji[1], Alaa Elseed[1], Ayman El-Menyar[1,2,3], Brijesh Sathian[1], Sandro Rizoli[1], Hassan Al-Thani[1], Ruben Peralta[1,4]

since 1956 BLOOD TRANSFUSION

Results - Fourteen studies met inclusion criteria, analysing outcomes from 3,201 trauma patients. There was a wide range of outcomes, patient populations, and process indicators utilised by the different authors. MTP significantly reduced the overall mortality for trauma patients (OR 0.71 [0.56-0.90]). No significant reduction was seen in either the 24-hour mortality (OR 0.81 [0.57-1.14]) or the 30-day mortality (OR 0.73 [0.46-1.16]). However, when mortality timing was unspecified, mortality was statistically reduced (OR 0.69 [0.55-0.86]).



Blood Transfus. 2020;18(6):434–45

OR 0.71 [0.56-0.90]

Draw on expanding number of randomised trials

Trial name	Number of patients	Trial design	Key findings
WOMAN[2]	20060	Randomised, placebo-controlled	Tranexamic acid reduces death due to bleeding in women with postpartum haemorrhage
CRASH-3[3]	12737	Randomised, placebo-controlled	Tranexamic acid reduces head injury-related death in patients with mild-to-moderate head injury
PAMPer[4]	501	Cluster randomised trial	Prehospital plasma reduces 30-day mortality compared to standard-care resuscitation
COMBAT[5]	144	Randomised trial	Prehospital plasma did not reduce mortality at 28-days when compared to normal saline
FIBRES[6]	827	Randomised trial	Fibrinogen concentrate is non-inferior to cryoprecipitate for the management of bleeding after cardiac surgery
HALT-IT[7]	12009	Randomised, placebo-controlled	Tranexamic acid does not reduce the risk of death due to bleeding in patients with gastrointestinal haemorrhage and is associated with higher rates of thromboembolic complications
iTACTIC[8]	396	Randomised, placebo-controlled	Viscoelastic testing in the setting of traumatic injury does not improve patient outcomes and results in higher rates of component transfusion
RePHILL[9]	432	Randomised trial	Prehospital red blood cells and lyophilised plasma does not improve patient outcomes, when compared to normal saline
POISE-3[10]	9535	Randomized, placebo-controlled	Tranexamic acid decreases the risk of major bleeding after non-cardiac surgery

Callum et al, Brit J Haem2022

Role of education: algorithms for different populations

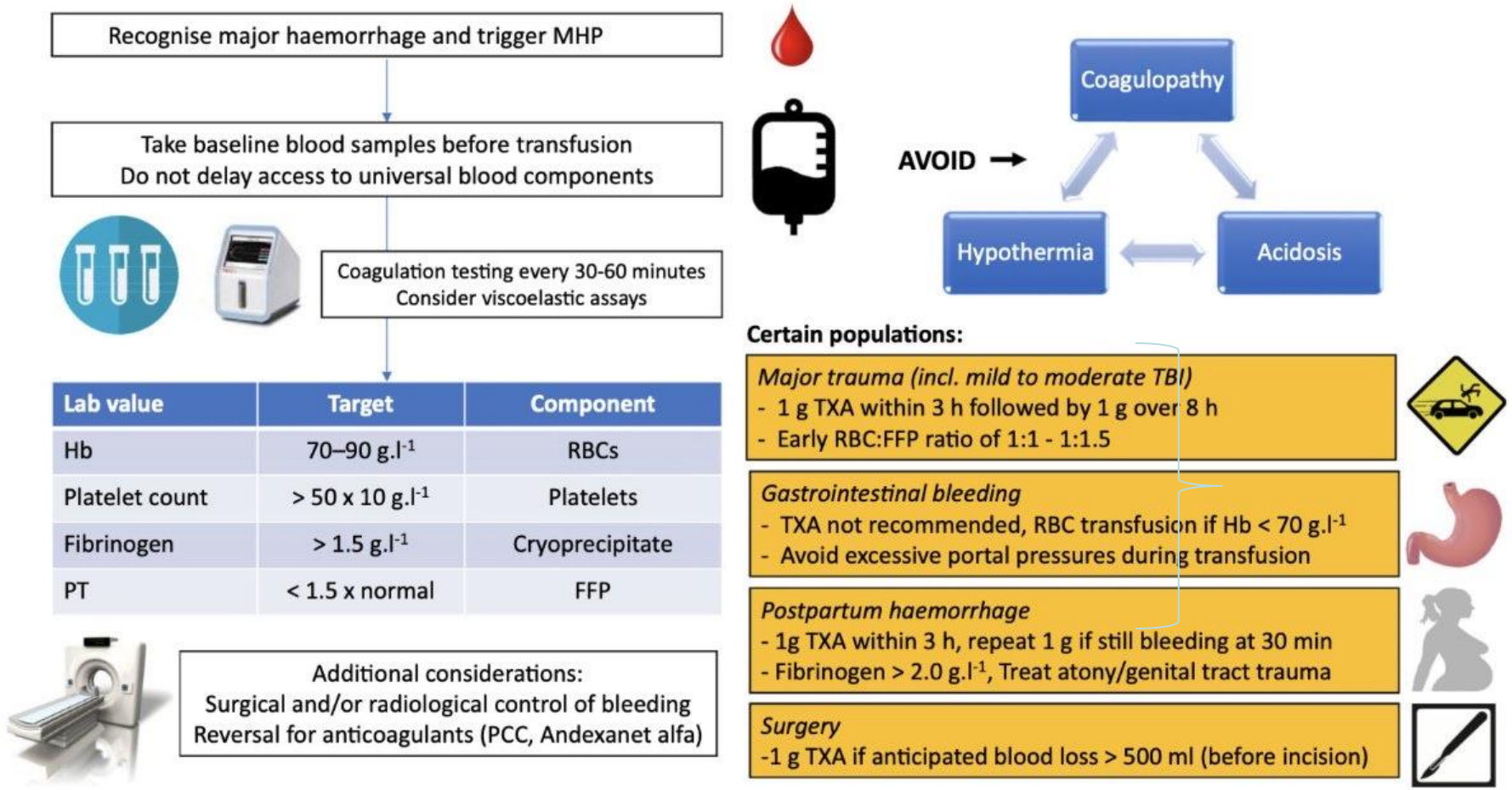


Figure 1 Key principles for the management of major haemorrhage in general, and across different clinical situations. MHP, major haemorrhage protocol; Hb, haemoglobin; RBC, red blood cell; PT, prothrombin time; FFP, fresh frozen plasma; PCC, prothrombin complex concentrate; TBI, traumatic brain injury; TXA, tranexamic acid.

Cases are different

- 25 year man admitted to emergency department following motorcycle accident
  - Injuries: open pelvic fracture, active bleeding
- 35 year pregnant woman admitted to maternity unit with major PV blood loss
- 75 year old presents with large volume frank haematemesis
  - HR 98, BP 125/85, RR 28
  - PMH: TIA, Hypertension
  - Takes Clopidogrel, Statin, CCB

Can we support better practice - Getting the basics right

What is your major haemorrhage protocol, MHP?

How do ED clinical staff communicate with Blood Bank?

What education is provided to clinical and lab staff?
Is the use of your MHP audited and are ‘lessons learnt’?

How often is your MHP updated to reflect new evidence?

Delays to activation is important to avoid

Every 1 minute delay from activation to first RBC is associated with a 5% increase in mortality

Multivariate regression predicting 30-day mortality

	Odds ratio	95% C.I.	p-value
Time to receipt of first cooler (min)	1.05	1.01–1.09	0.016
Anatomic injury severity (ISS)	1.05	1.03–1.06	<0.001
Disturbed arrival physiology (w-RTS)	0.61	0.53–0.69	<0.001
Randomization group (1:1:2)	1.46	0.92–2.29	0.102
Resuscitation Intensity (units)	1.03	0.60–1.44	0.184

680 patients from PROPPR study

Meyer DE, et al. Every minute counts: Time to delivery of initial massive transfusion cooler and its impact on mortality. J Trauma Acute Care Surg. 2017 Jul;83(1):19-24

Preventable delays in transfusion

- The UK Serious Hazards of Transfusion program put out an alert regarding delays in transfusion leading to preventable deaths:
  - 2010-2020: 809 reports to the haemovigilance system
  - There were 54 preventable deaths reported; accounting for 25% of all transfusion-related deaths

SHOT Serious Hazards of Transfusion

Preventing transfusion delays in bleeding and critically anaemic patients.

Date of Issue:	17-Jan-22	Reference No:	SHOT/2022/001
This alert is for action by: **NHS and independent (acute and specialist) sector where transfusions are carried out.**			
Access to blood components and products is a complex safety critical issue that is relevant across many departments and professions. Implementation of this alert should be coordinated by an executive leader (or equivalent role in organisations without executive boards) and supported by their designated senior leads for medical, nursing and pathology teams.			

Must have:

Protocols
Policies
Conduct drills
Investigate failures

https://www.cas.mhra.gov.uk/ViewandAcknowledgment/ViewAlert.aspx?AlertID=103190

Early and Empirical High-Dose Cryoprecipitate for Hemorrhage After Traumatic Injury: The CRYOSTAT-2 Randomized Clinical Trial

JAMA

JAMA. 2023;330(19):1882-1891. doi:10.1001/jama.2023.21019

QUESTION Does early transfusion of high-dose cryoprecipitate in addition to standard care improve survival in patients with trauma and bleeding who require activation of a major hemorrhage protocol (MHP)?

CONCLUSION The addition of early and empirical high-dose cryoprecipitate to usual care did not improve clinical outcomes in patients with trauma and bleeding.

POPULATION

1251 Men 330 Women

Patients 16 years or older with major trauma hemorrhage in the emergency department

Median age: 39 years

LOCATIONS

26 Major trauma centers in the UK and the US

INTERVENTION

1604 Participants randomized
1531 Participants analyzed

799
Cryoprecipitate
Standard treatment with an additional 3 pools of cryoprecipitate (6-g fibrinogen) as early as possible

805
Standard care
Standard treatment according to the local MHP with a balanced ratio of red blood cells and fresh frozen plasma

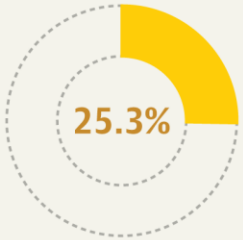
PRIMARY OUTCOME

All-cause mortality at 28 days

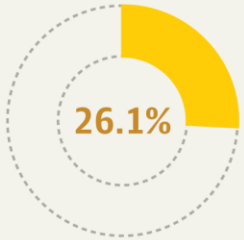
FINDINGS

All-cause mortality at 28 days

Cryoprecipitate
192 of 760 participants



Standard care
201 of 771 participants



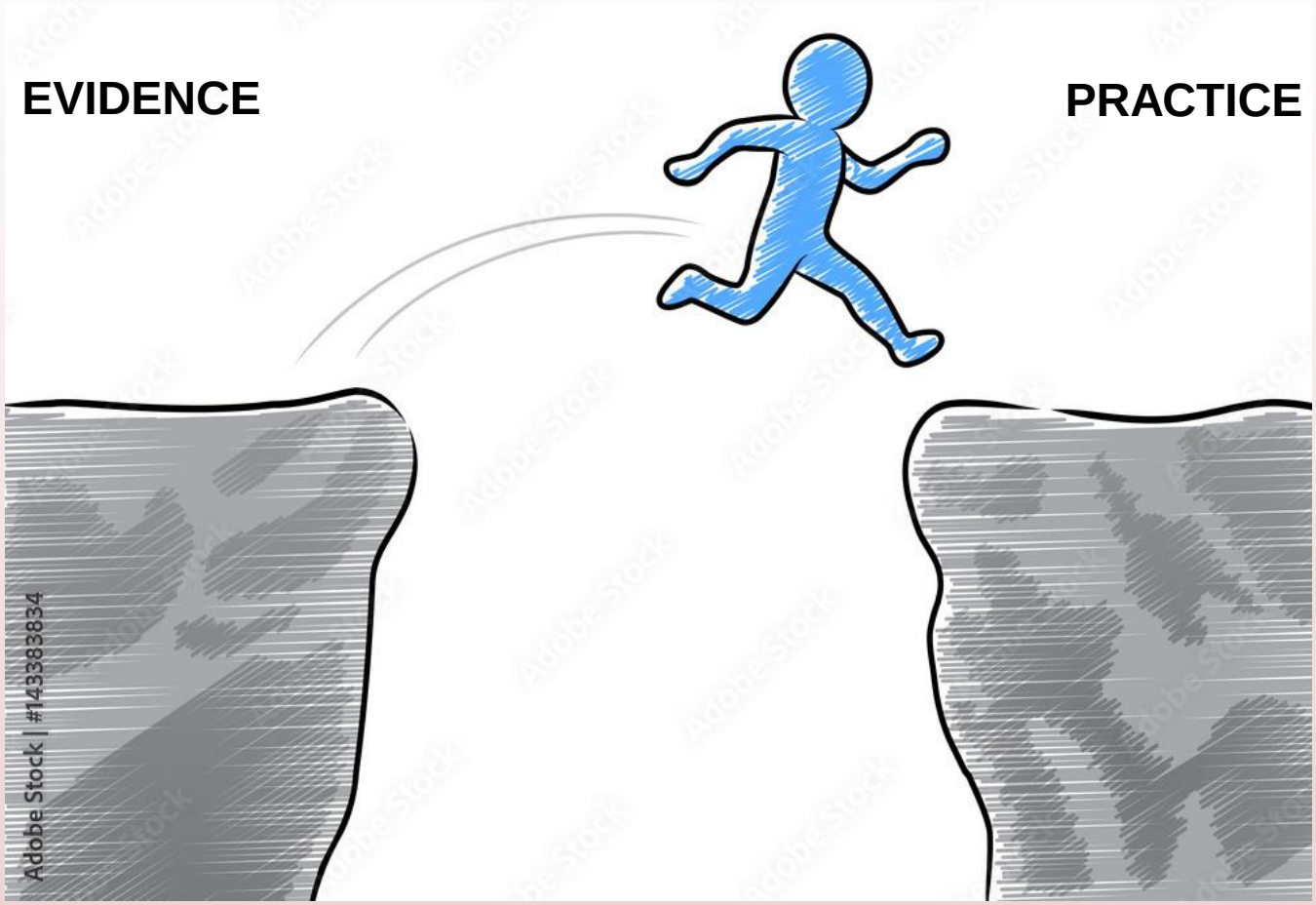
There was no improvement in mortality:
Odds ratio, **0.96** (95% CI, 0.75-1.23); *P* = .74

Davenport R, Curry N, Fox EE, et al; for the CRYOSTAT-2 Principal Investigators. Early and empirical high-dose cryoprecipitate for hemorrhage after traumatic injury: the CRYOSTAT-2 randomized clinical trial. *JAMA*. Published online October 12, 2023. doi:10.1001/jama.2023.21019

Guidelines are strategies for quality improvement

- Guidelines
  - International/national
  - Local
- Education
  - Group
  - Individual
- Audit / Feedback
- Audit / Approval
- Reminders & prompts
  - Computerized
  - Paper

Bridge the gap & improve uptake of evidence



What strategy works best for me and is most cost-effective?

All of transfusion practice is characterised by variation e.g. despite restrictive transfusion strategies recommended by evidence-based guidelines

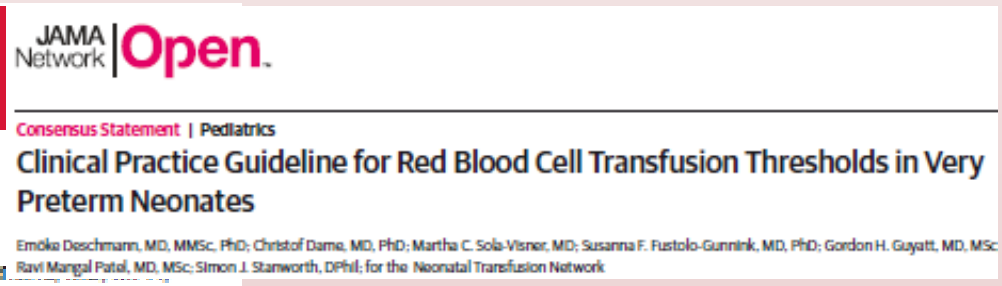
Red cells: 49 randomized trials enrolled 20,599 participants at baseline (now 70 trials!)

Platelets: 19 randomized trials enrolled 4,715 patients


JAMA | Special Communication

Red Blood Cell Transfusion
2023 AABB International Guidelines

Jeffrey L. Carson, MD; Simon J. Stanworth, MD, DPhil; Gordon Guyatt, MD; Stacey Vale
Jane Dennis, PhD; Sara Bakhtary, MD; Claudia S. Cohn, MD, PhD; Allan Dubon, MLS;
Brenda J. Grossman, MD, MPH; Gaurav K. Gupta, MD, PhD; Aaron S. Hess, MD, PhD; Jessica L. Jacobson, MD;
Lewis J. Kaplan, MD; Yulia Lin, MD; Ryan A. Metcalf, MD; Colin H. Murphy, MD; Katerina Pavenski, MD;
Micah T. Prochaska, MD; Jay S. Raval, MD; Eric Salazar, MD, PhD; Nabiha H. Saifee, MD, PhD;
Aaron A. R. Tobian, MD, PhD; Cynthia So-Osman, MD, PhD; Jonathan Waters, MD; Erica M. Wood, MD;
Nicole D. Zantek, MD, PhD; Monica B. Pagano, MD


JAMA Network Open

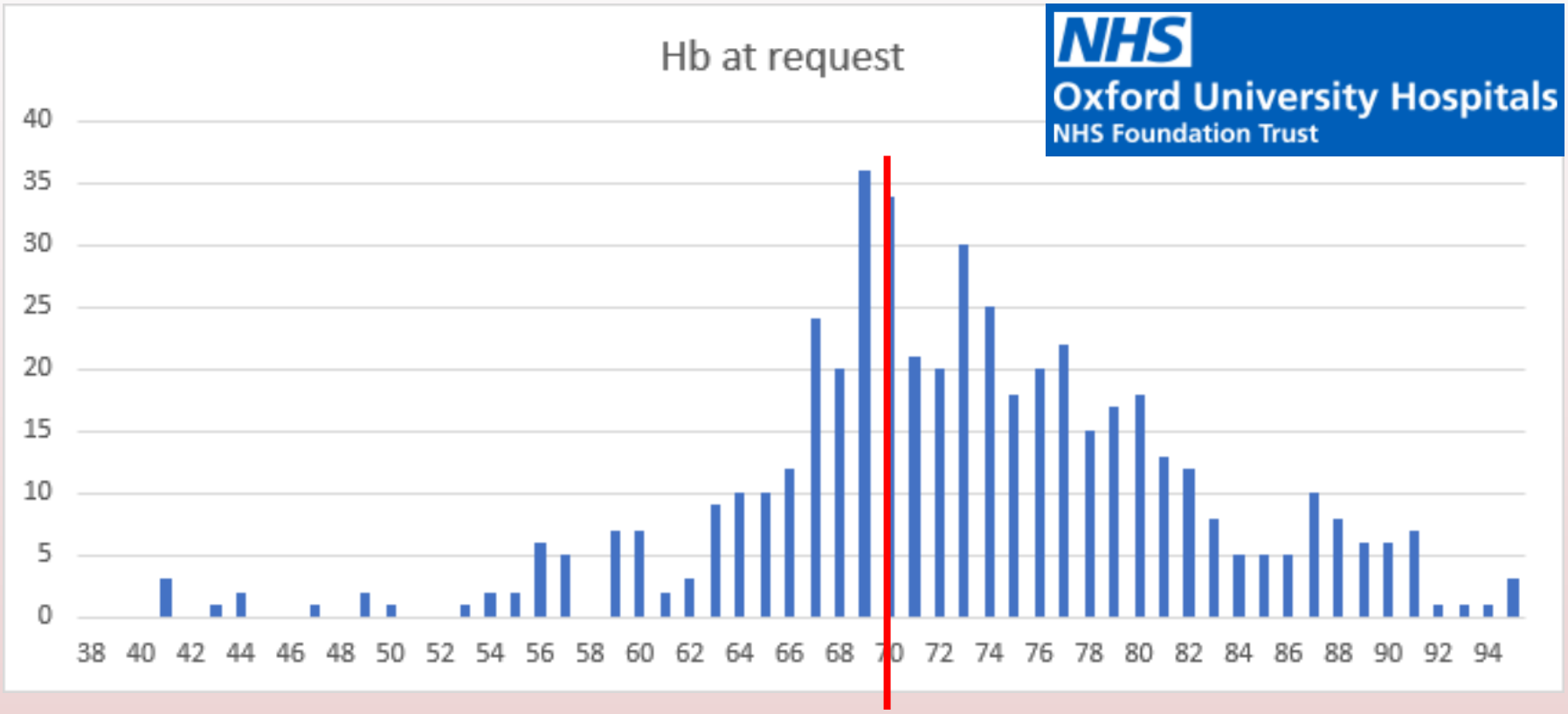
Consensus Statement | Pediatrics

Clinical Practice Guideline for Red Blood Cell Transfusion Thresholds in Very Preterm Neonates

Emöke Deschmann, MD, MMSc, PhD; Christof Dame, MD, PhD; Martha C. Sola-Visner, MD; Susanna F. Fustolo-Gunnink, MD, PhD; Gordon H. Guyatt, MD, MSc
Ravi Mangal Patel, MD, MSc; Simon J. Stanworth, DPhil; for the Neonatal Transfusion Network

Stanworth & Shah, 2021

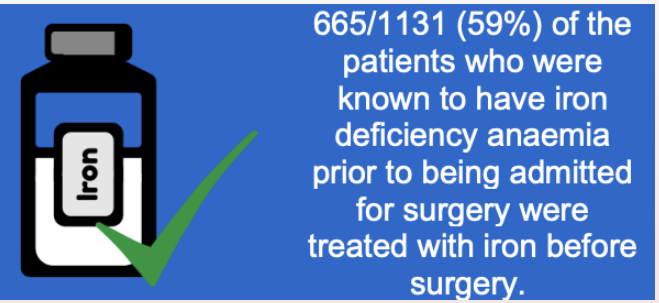
Example of variation in practice: Real world data for ICU:



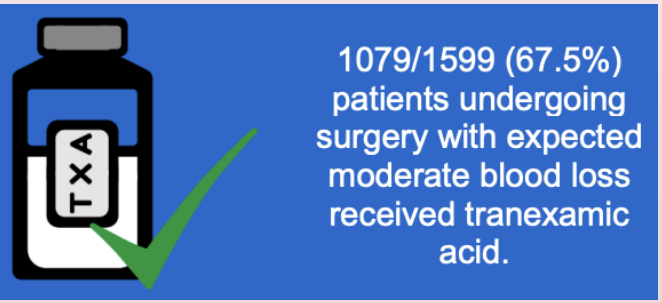
J Staves

Other common practices

Preventing bleeding



665/1131 (59%) of the patients who were known to have iron deficiency anaemia prior to being admitted for surgery were treated with iron before surgery.



1079/1599 (67.5%) patients undergoing surgery with expected moderate blood loss received tranexamic acid.

Transfusion Practice

893/1534 (58%) patients receiving elective red blood cell transfusions had both their Hb checked and a clinical re-assessment after a unit of red cells was transfused.

Information & consent

1032/1622 (64%) of transfused patients had evidence of receiving written or verbal information about the risks, benefits and alternatives to transfusion.

Only 422/1622 (26%) received both written and verbal information

Infected Blood Inquiry

2021 National Comparative Audit of NICE Quality Standard QS138

NHS Blood and Transplant

This problem is widespread in health care

Le Mythe de Sisyphe par Serge Mazel
https://www.serge-mazet.fr/mythe

Grimshaw *et al. Implementation Science* 2012, 7:50
http://www.implementationscience.com/content/7/1/50

IMPLEMENTATION SCIENCE

DEBATE Open Access

Knowledge translation of research findings

Jeremy M Grimshaw[1*], Martin P Eccles[2], John N Lavis[3], Sophie J Hill[4] and Janet E Squires[5]

A consistent findings from clinical and health services research is the failure to translate research into practice and policy

Implications

30-40%

of people do not receive care according to current scientific evidence[1,3]

14-25%

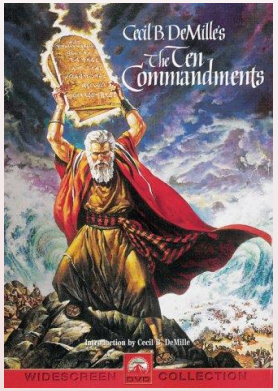
of healthcare provided is not needed[3]

Choosing Wisely Canada™

[1]Schuster, McGlynn, & Brook (1998); [2]Grol (2001); [3]Squires et al (2022)

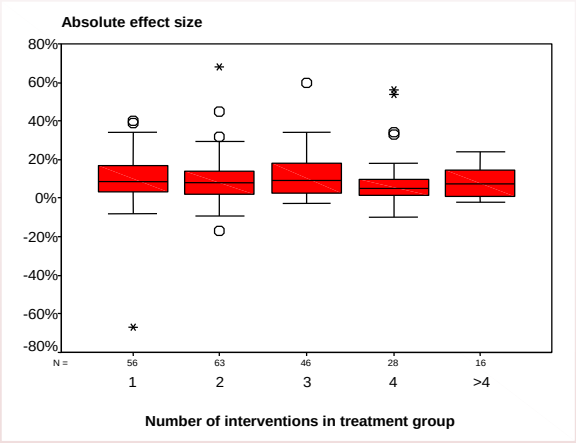
Our current approaches to implementation?

Develop & issue local guidelines



They do not self-implement

Throw everything at the issue and see what sticks



Grimshaw et al (2004) *Health Technology Assessment*

More ≠ better

Choose a favorite solution (eg A&F)

May not be fit for purpose

Deliver training/CPD

Is content including strategies to address barriers to change?

Develop an app

What about change techniques ? What about use?

F Lorencatto

Developing own (internal) solutions

Most frequently used approach to implementation in the literature:

ISLAGIATT

It Seemed Like A Good Idea At The Time!

Problems: trial and error

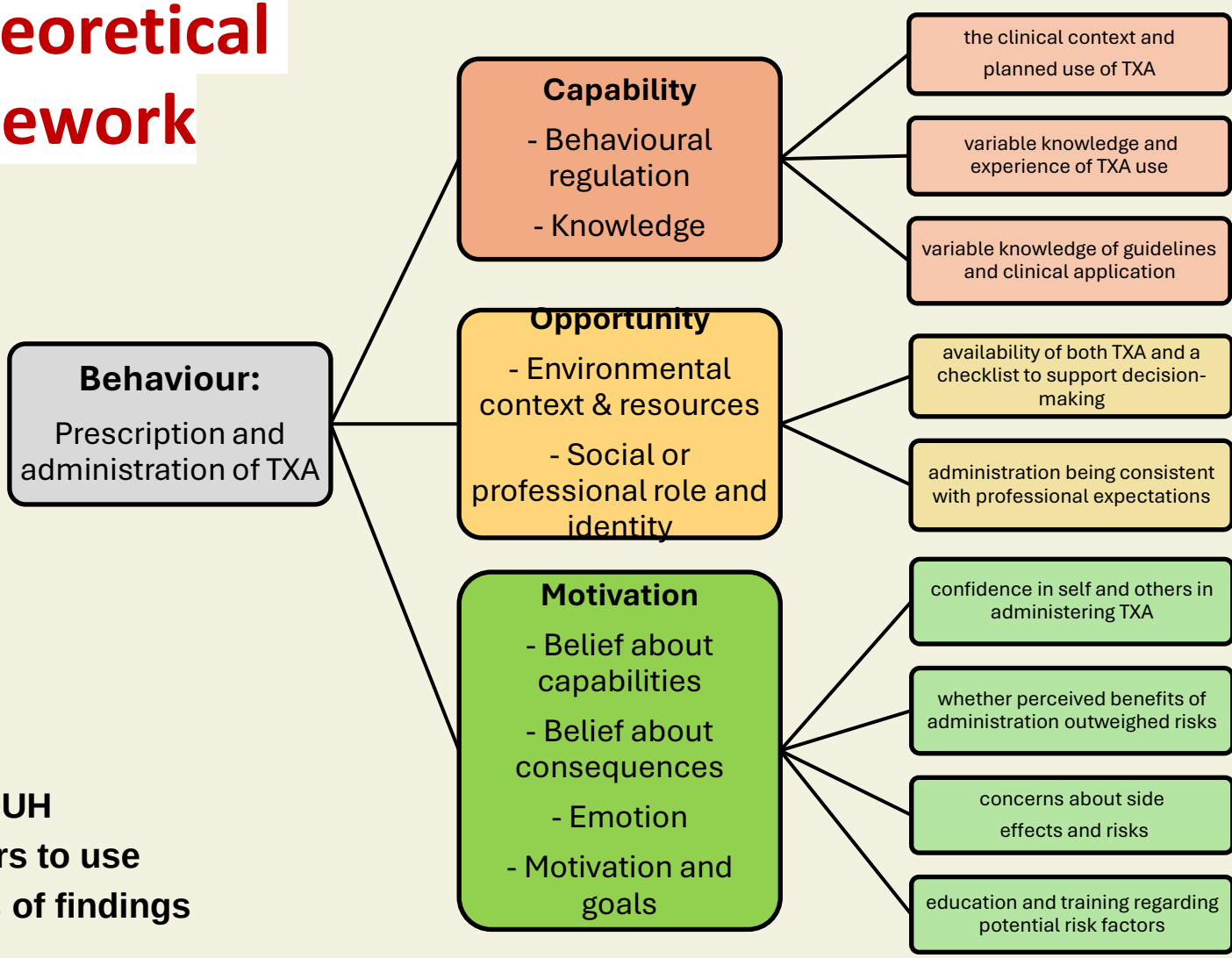
- **Inefficient:** Does not build on what we already know
- **Insufficient:** May miss important underlying factors or barriers
- **Unscientific:** Based on implicit ideas of what drives change in practice, undermining scale, spread, and evidence accumulation

J Francis

More interest in trying to ‘change practice’ in a more ‘scientific’ way - Two examples in bleeding

Influences on the use of tranexamic acid in surgery (to prevent bleeding): a qualitative study using Theoretical Domains Framework

NHS
Oxford University Hospitals
NHS Foundation Trust

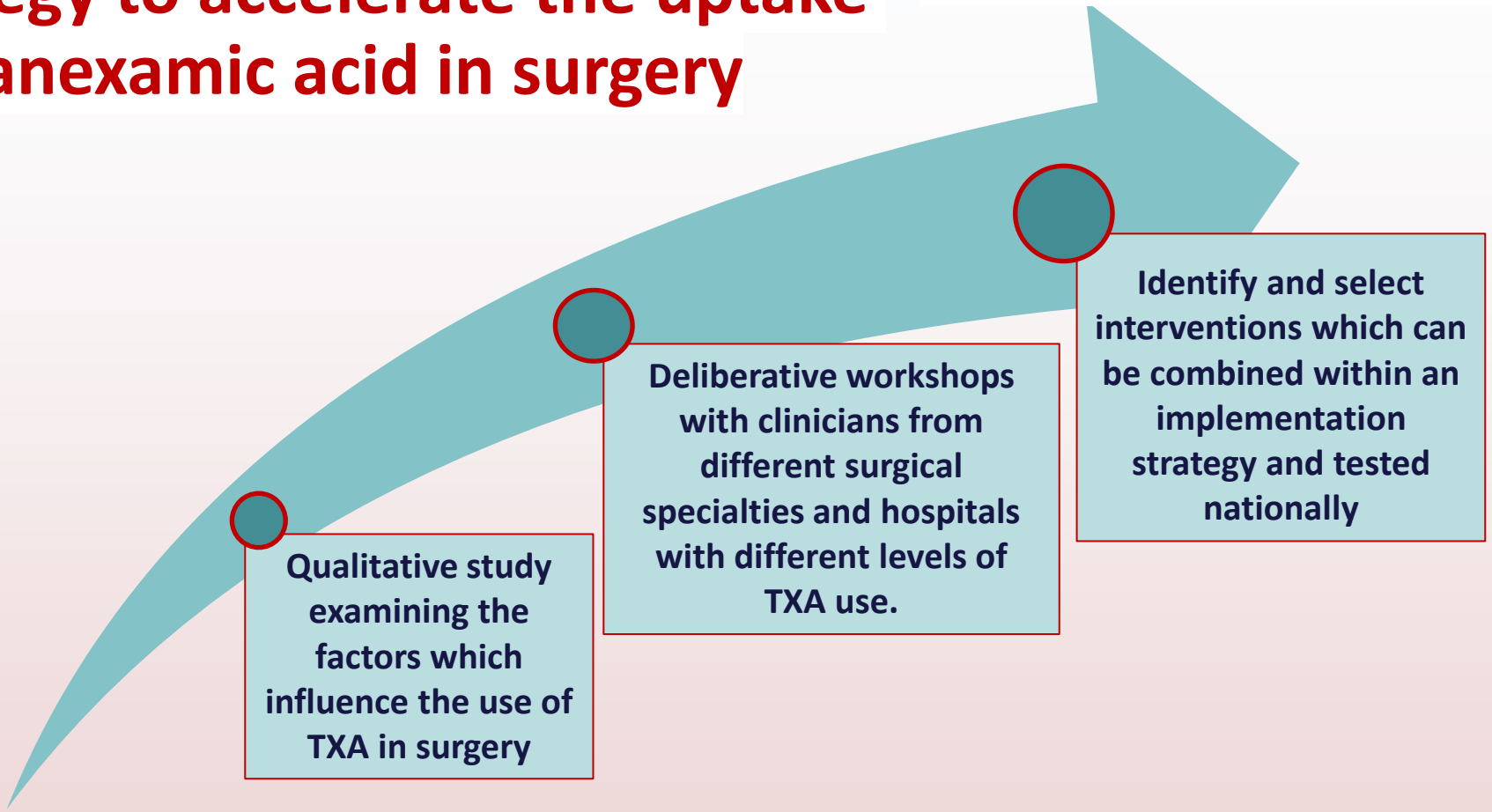


Qualitative Study

- **Surgical Teams at OUH**
- **Enablers and barriers to use**
- **Framework analysis of findings**

Developing an implementation strategy to accelerate the uptake of tranexamic acid in surgery

NIHR | NIHR Blood and Transplant Research Unit in Data Driven Transfusion Practice



Joint approach:

- **Data Driven BTRU**
- **PQIP Team**
- **NHSBT PBM Team**
- **Royal Colleges TXA Group**

- Single site study in write up
- Workshop ethics has been reviewed
- Recruitment to start in August
- Workshops in Autumn

OBS UK
Obstetric Bleeding Study UK

Clinical and cost-effectiveness of a maternity quality improvement programme to reduce excess bleeding and need for transfusion after childbirth: the Obstetric Bleeding Study UK (OBS UK)

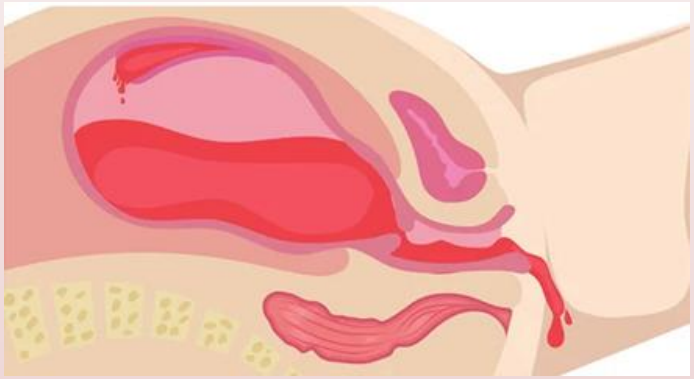
OBS UK Co-CI: Dr Sarah Bell, Prof Peter Collins
OBS UK Co-Investigators: Mairead Black, Rachel Collis, Haddy Fye, Ayse Gur-Geden, Philip Pallmann, William Parry-Smith, Stavros Petrou, Catherine Pope, Tanvi Rai, Julia Sanders, Pauline Slade, Simon Stanworth, Julia Townson

FUNDED BY
NIHR | National Institute for Health and Care Research

Why do women bleed during childbirth?

- Uterine Atony - 65%
- Trauma; lacerations, inversions, rupture – 19%
- Retained tissue, invasive placentation – 10%
- Coagulopathy, hypofibrinogenaemia – 5%

Often multiple causes, requiring different strategies



Study overview

OBS UK
Obstetric Bleeding Study UK

Primary objective
Test the effectiveness of the Obstetric Bleeding Strategy (OBS) **‘care bundle’ intervention** vs standard care on clinical and psychological PPH outcomes after childbirth and to evaluate the cost-effectiveness

OBS UK intervention = OBS Cymru PPH care bundle rolled out as a quality improvement project

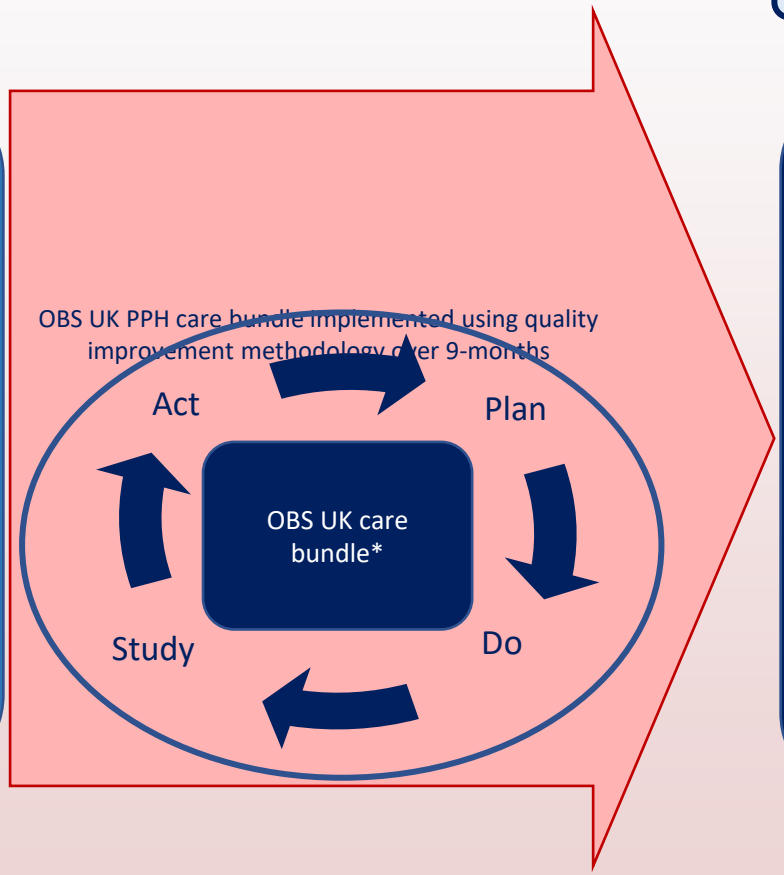
The intervention

OBS UK
Obstetric Bleeding Study UK

Comparator

Standard PPH care

- Risk assessment not always done
- Measured blood loss once abnormal bleeding identified
- Escalation to senior staff once abnormal bleeding identified
- Laboratory tests of clotting with empirical blood component transfusion



Intervention

OBS UK PPH care bundle*

- Universal risk assessment
- Real-time measurement of blood loss from birth
- Structured and consistent escalation of care to senior staff based on blood loss
- Bedside tests to identify and treat abnormal clotting with fibrinogen

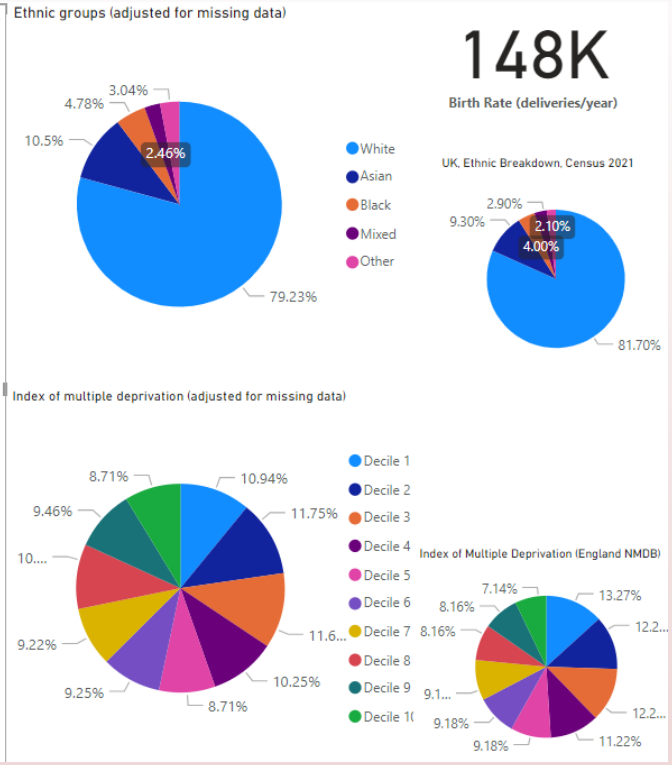
Maternity unit intervention

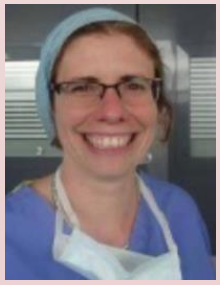
Population = everyone giving birth

Status

OBS UK
Obstetric Bleeding Study UK

Clinical and cost-effectiveness of a maternity quality improvement programme to reduce excess bleeding and the need for blood transfusion after childbirth





Dr Sarah Bell
OBS UK Chief Investigator
Consultant Obstetric Anaesthetist, CAVUHB

Professor Peter Collins
OBS UK Chief Investigator
Consultant Haematologist, CAVUHB

Summary – can we do better?

Guidelines on major haemorrhage

Background: need for more emphasis on implementation

Opportunities for research and sharing knowledge of what we are doing (what works/ what does not work?)

Any questions?