Anemia in Hospitalized Patients

Vampirism and Other Tales

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Disclosures

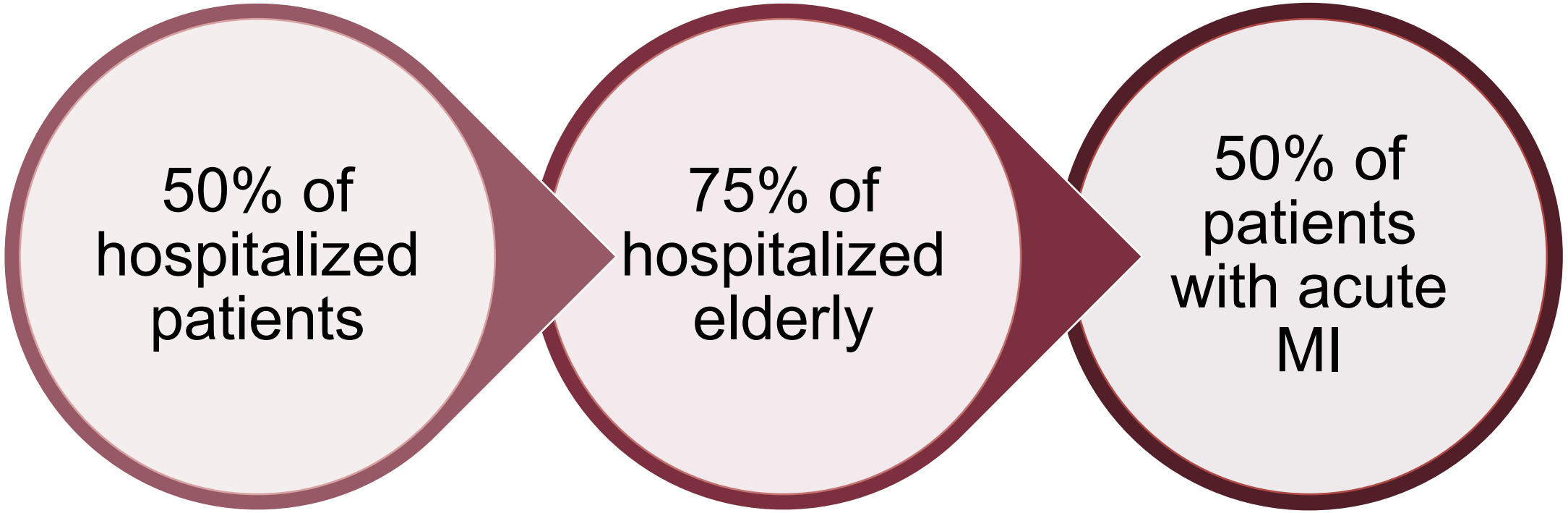
I have received honoraria paid indirectly to my research institute from AstraZeneca, BMS-Pfizer, Roche, Servier for educational presentations (my own content) UNRELATED to this presentation.

Objectives

After this presentation attendees will be able to:

- Describe the burden of anemia in hospitalized patients
- Discuss laboratory testing as a modifiable cause of blood loss and anemia
- Discuss the effect of switching to tubes that collect less blood for lab testing on RBC transfusion in ICU

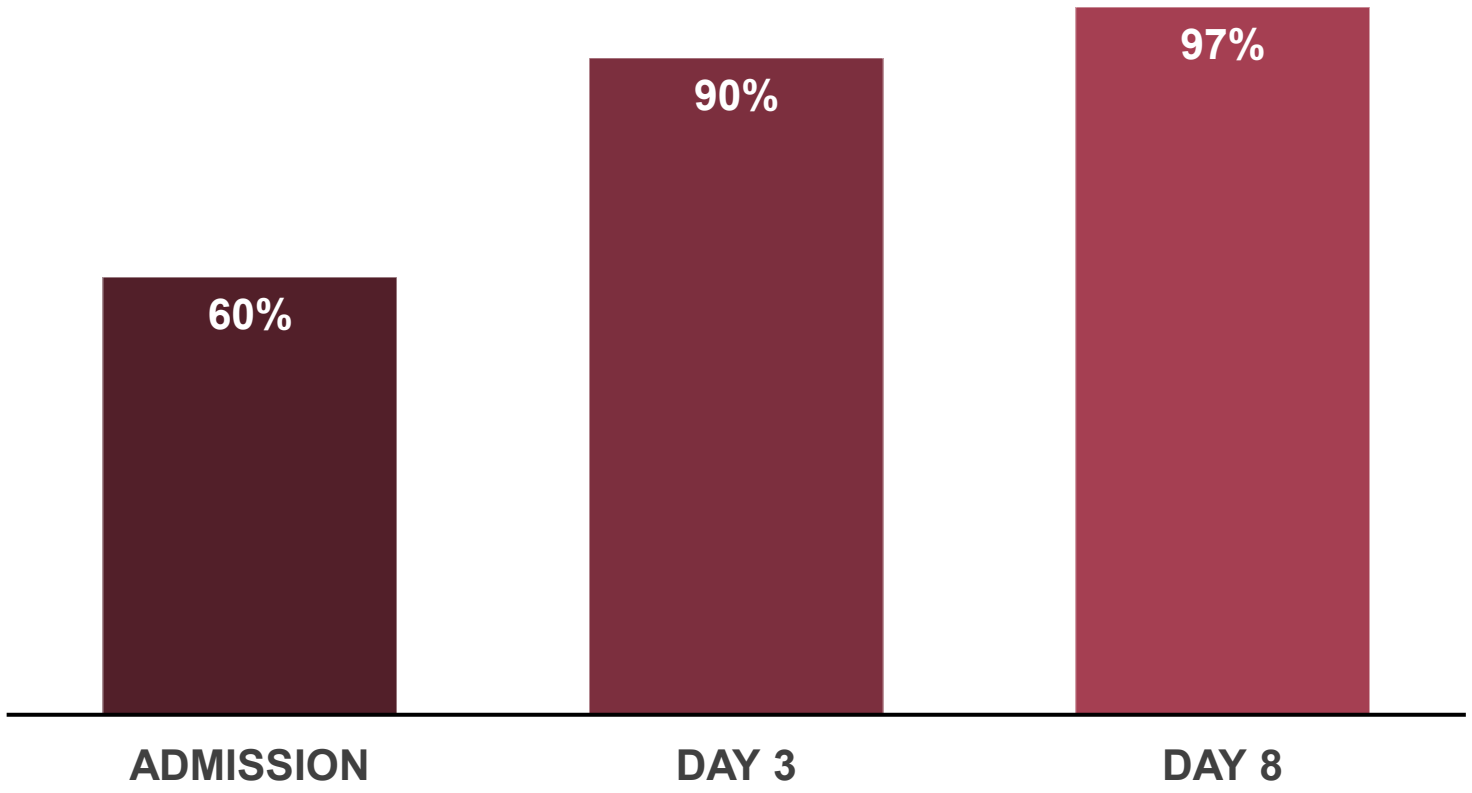
Anemia is a common problem in hospital



Vincent et al. JAMA 2002. Corwin et al. Crit Care Med 2004. Thomas et al. Heart Lung 2010. Ania et al. J Am Geriatr Soc 1997.

Patients in ICU are at high risk for anemia

Proportion of patients with anemia during ICU admission



Vincent et al. JAMA 2002. Corwin et al. Crit Care Med 2004.

Anemia is associated with adverse outcomes

Higher 30-day mortality

Hb<80 g/L OR 1.49 (1.13-1.95)

Hb80-90 g/L OR 1.54 (1.12-2.12)

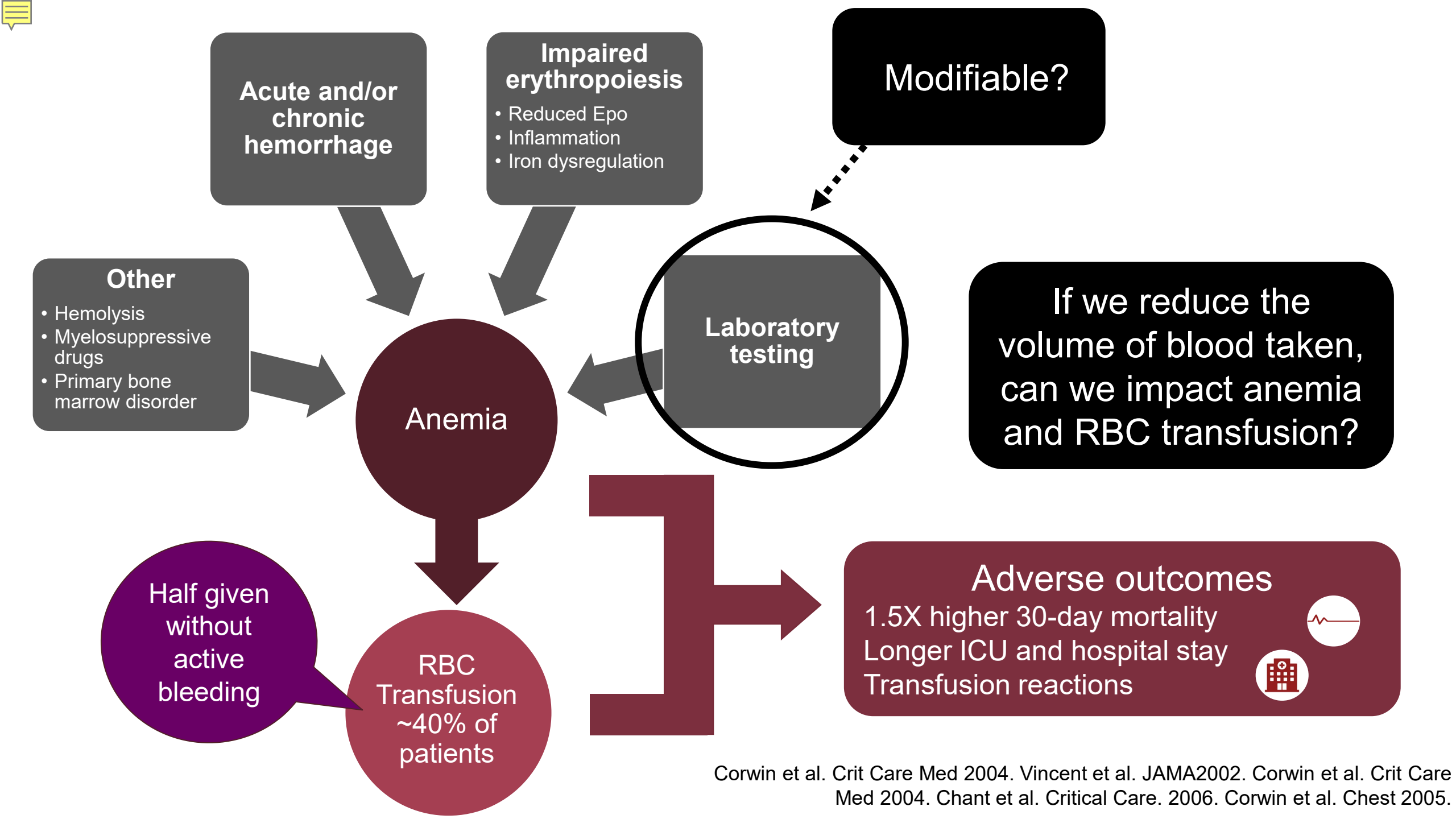
Longer ICU stay

40% to 57%

Longer hospital stay

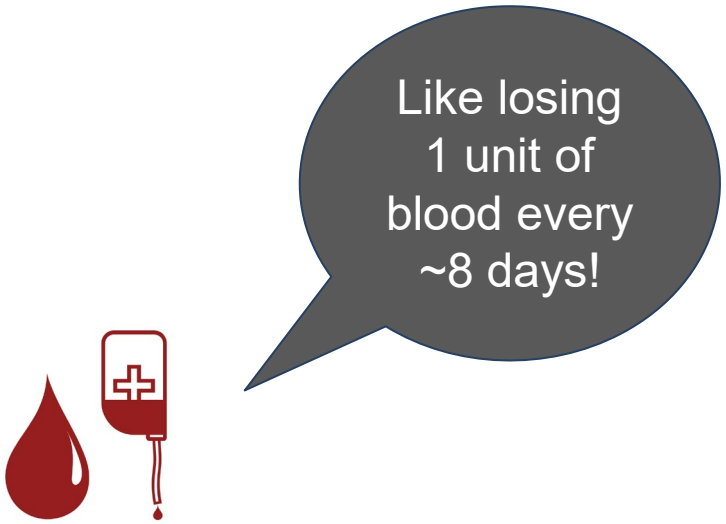
20% to 30%

Corwin et al. Crit Care Med 2004.



Corwin et al. Crit Care Med 2004. Vincent et al. JAMA2002. Corwin et al. Crit Care Med 2004. Chant et al. Critical Care. 2006. Corwin et al. Chest 2005.

Blood loss for lab testing is substantial

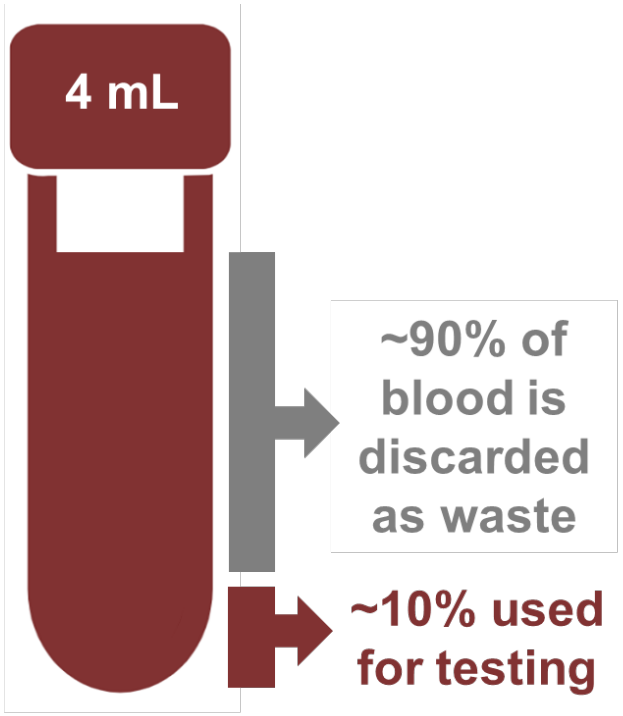


Daily during ICU stay

Up to 41 mL/day

During ICU stay

214 mL (IQR 133-382)



Chornenki, Siegal et al, Transfusion 2019. Vincent et al. JAMA 2002. Chant et al. Critical Care 2006. Salisbury et al. Arch Int Med 2011. Dale et al. Arch Pathol Lab Med 2003.

Proof of principle: blood loss reduces hematocrit

TABLE II Initial and final Hct values

Subject	*Hct_i (%)*	*Hct_f (%)*	*Observed (% points)*	*Predicted (% points)*
1	44.4	37.3	7.2	2.3
2	46.6	45.0	1.6	3.1
3	43.6	40.3	3.4	2.2
4	47.0	39.3	7.8	3.3
5	42.4	38.8	3.7	2.2
6	45.0	42.0	3.0	2.2
7	40.2	38.3	2.0	2.1
8	44.0	38.3	5.8	2.4
Mean	44.2	39.9*	4.3	2.5
SD	2.2	2.5	2.3	0.5

Cortinez et al. Can J Anesth 2004.

Diagnostic blood loss worsens anemia

Patients with MI

Every 50 mL increases risk of Hb ≤ 110 g/L by 15%

Hospitalized medical patients

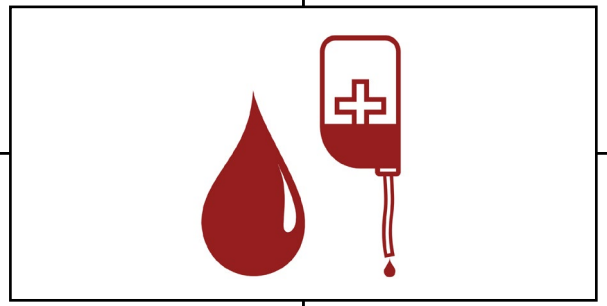
Every 100 mL associated with ↓Hb of 7 g/L

Salisbury et al. Arch Intern Med 2011. Thavendiranathan et al. J Gen Intern Med 2005.

Anemia leads to frequent transfusion in ICU

Up to 50% of patients receive ≥1 RBC transfusion

75% of patients in ICU >7 days are transfused

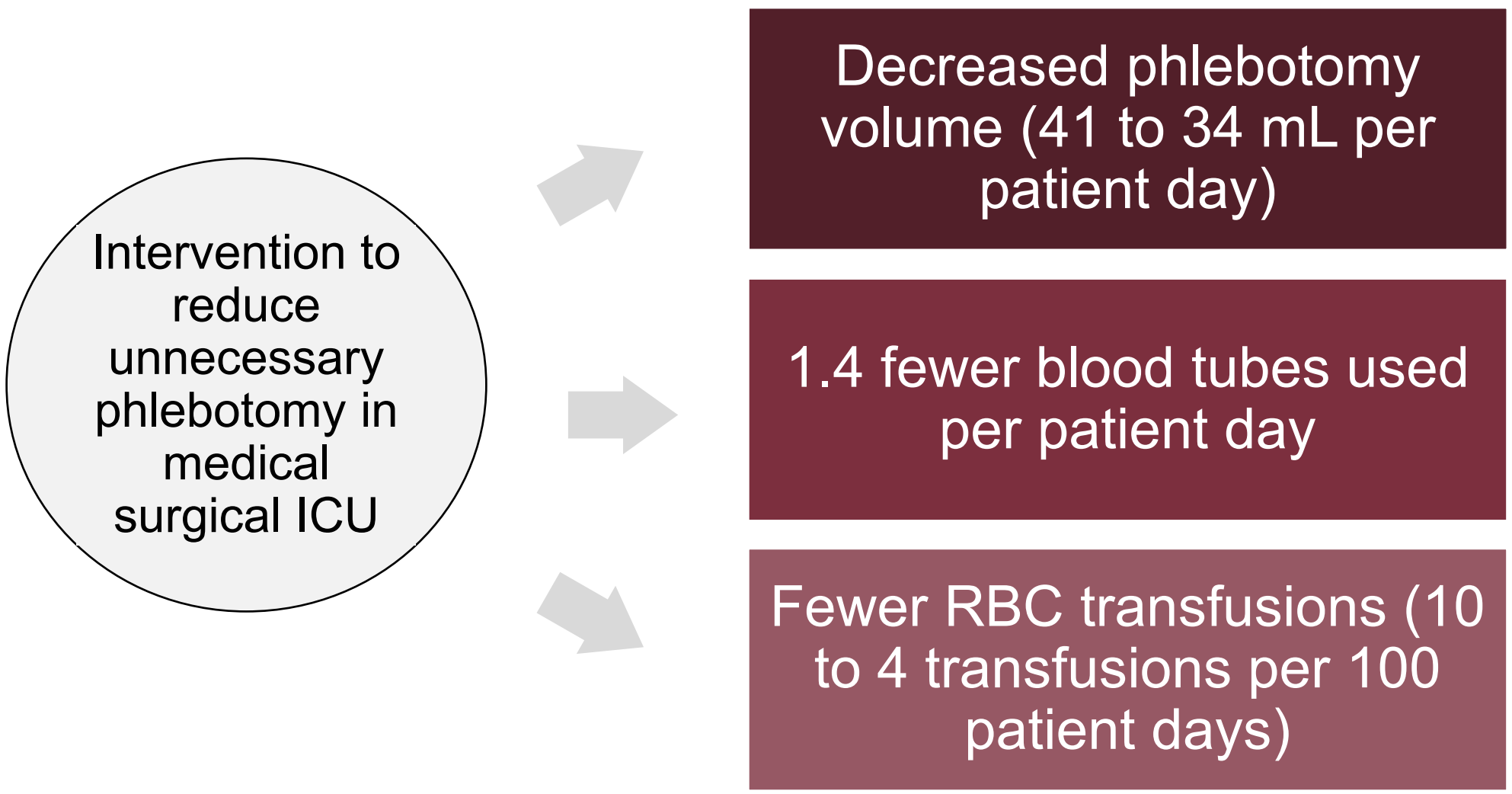


Every 150 mL increases the risk of RBC transfusion by 2-fold

>50% of RBC transfusions given without active bleeding

Vincent et al. JAMA2002. Corwin et al. Crit Care Med 2004. Chant et al. Critical Care. 2006. Corwin et al. Chest 2005. Chornenki et al. Transfusion 2019.

Lower phlebotomy volume = fewer transfusions

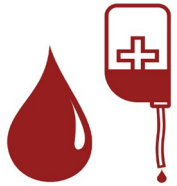


Bodley et al. BMJ Qual Saf. 2023 Jan 19;bmjqs-2022-015358

RBC transfusion is associated with harms

Resource Implications

Limited availability
Direct cost ~$500 per unit
Indirect costs (testing, preparation, storage, administration, reactions)



Transfusion Harms

Reactions
Volume overload
Lung injury (TRALI)
Infection
Allosensitization
Allergy

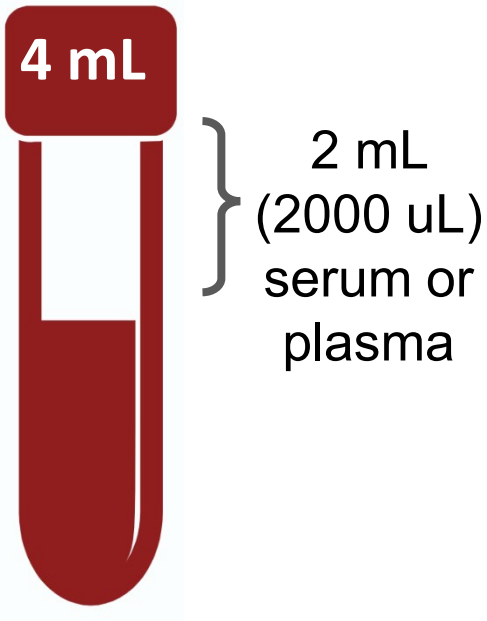
Adverse Clinical Outcomes

Death
Longer admissions
Infection
Prolonged mechanical ventilation
Organ dysfunction

Vincent et al. JAMA2002. Corwin et al. Crit Care Med 2004.

How much blood is actually used for testing?

Test	Volume of Plasma Required		
	Minimum	Maximum	Average
Chemistry	2 uL	35 uL	5 – 15 uL
Immunoassays	10 uL	200 uL	25 – 50 uL



Courtesy of Dr. S. Hill, Department of Pathology and Molecular Medicine, McMaster University

Tubes that *automatically* collect less blood

a.k.a short-draw or soft-draw or low vacuum

- Less vacuum = fill to lower volume
- Same cost
- Same physical dimensions
- Same analyzers

Not used routinely in adults!

Why are lower volume tubes *NOT* used?

Evidence gap

- No randomized trials
- Benefits?
- Harms?

Barriers to implementation

- Concerns: problems for sampling, testing and results
- Laboratory processes (e.g. validation of tests)
- Lack of awareness and/or complacency

Rationale for a randomized trial

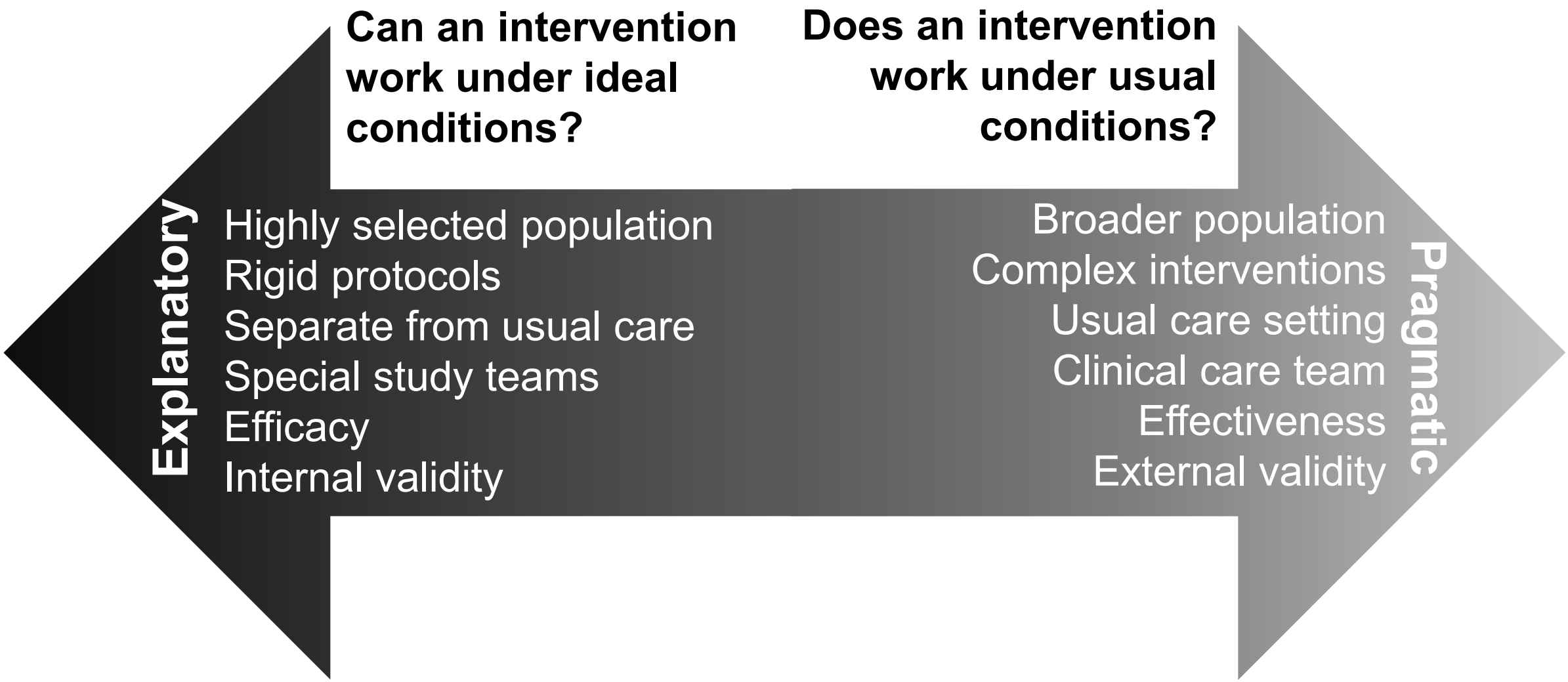
Blood sampling contributes to anemia and RBC transfusion

90% of blood collected is discarded as waste

Lower volume tubes are available, compatible, same cost

RCT + clinical outcomes needed to change practice

Explanatory vs. pragmatic trials



Examples of pragmatic trial designs

Registry Based Trials

Parallel Cluster Trials

Cluster Cross-Over Trials

Stepped Wedge Trials

Examples of pragmatic trial designs

Registry Based Trials

Parallel Cluster Trials

Cluster Cross-Over Trials

Stepped Wedge Trials

Stepped wedge cluster randomized trial

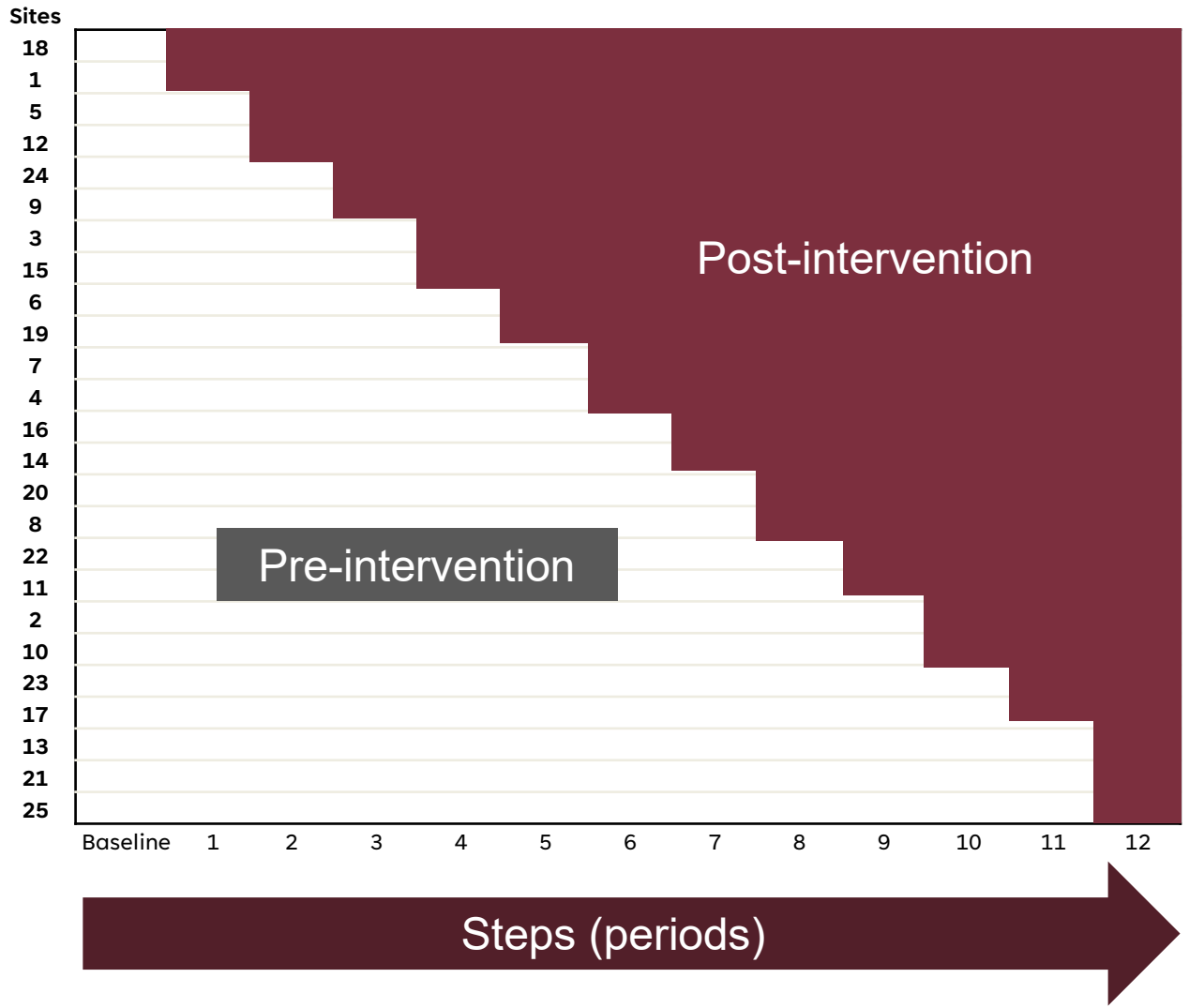
Introduction of new policy or treatment

Intervention introduced in timed “steps”

≥1 sites receive intervention at each step

Timing of switch is randomized

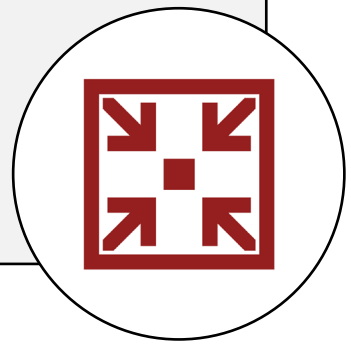
Eventually all sites have intervention



Effectiveness + implementation

- **TEST** effects of a clinical intervention on relevant outcomes
- **IMPLEMENT** a likely effective therapy in clinical practice

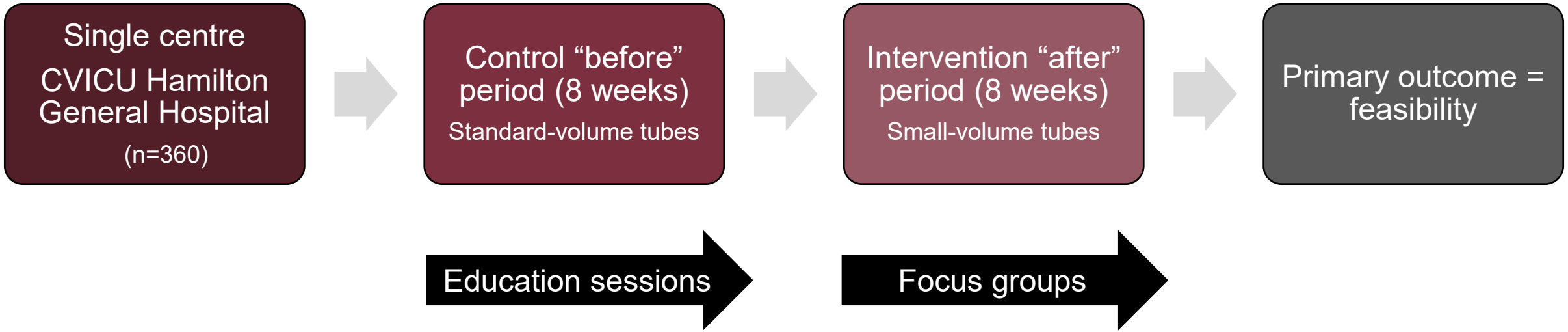
Dual focus



- Randomized
- Each cluster exposed to control and intervention
- Information for research and policy-makers
- Improved speed of translation into practice

Advantages

STRATUS mixed-methods pilot study

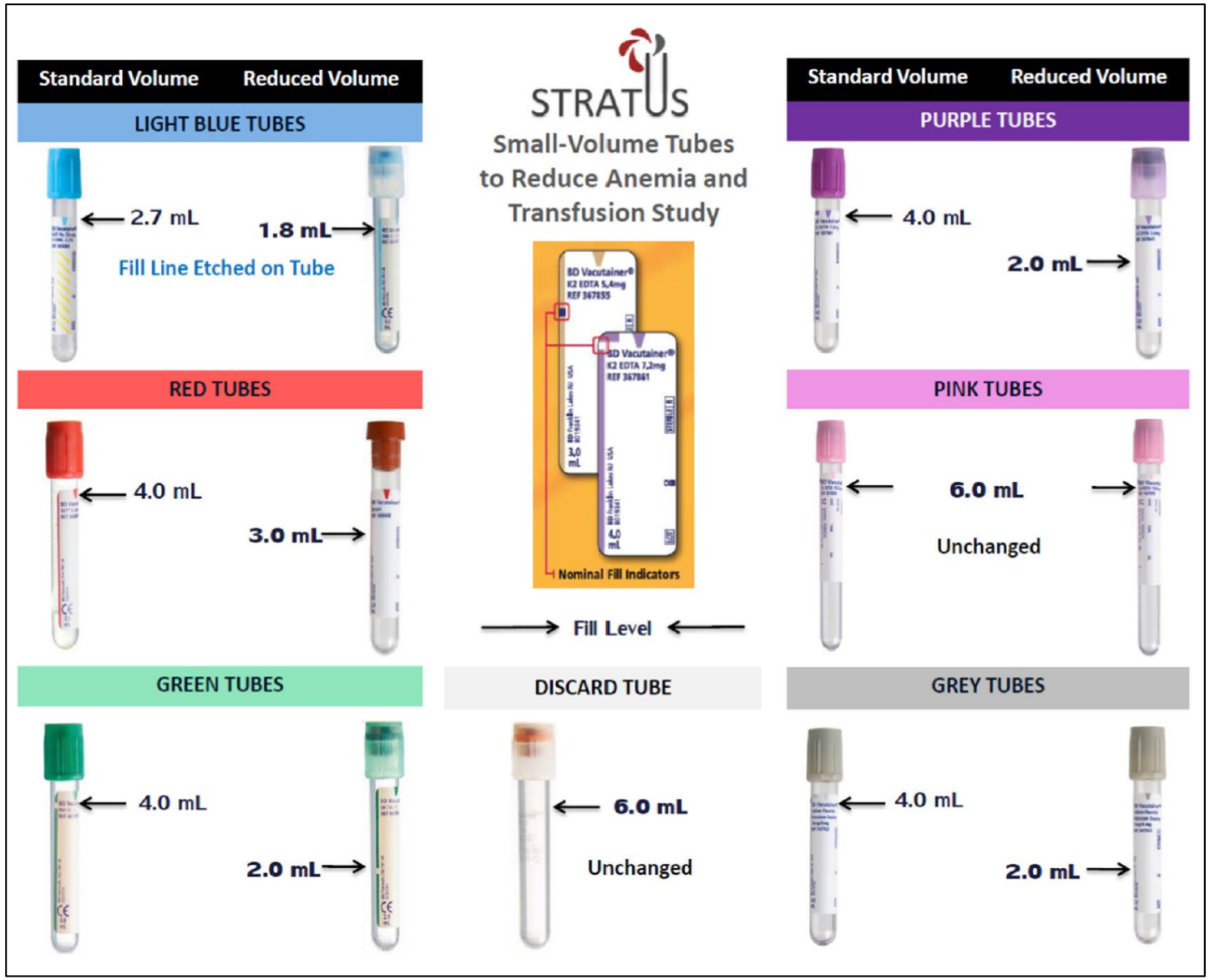


Primary outcome = feasibility

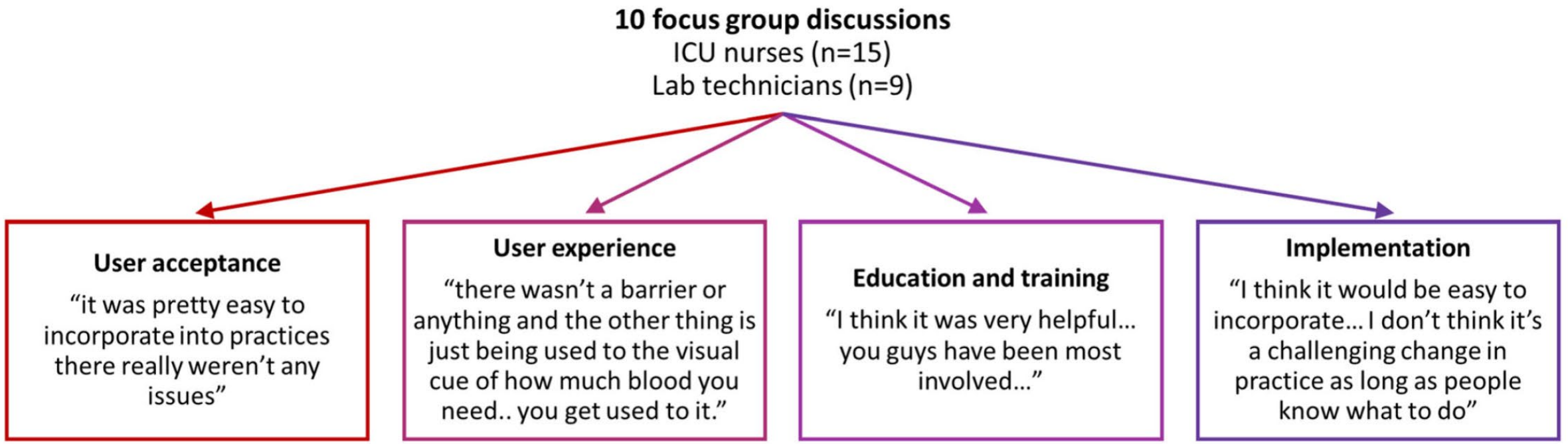
successful switch, adherence, insufficient samples, user acceptance, barriers/facilitators, data collection

Siegal et al. Can J Anaesth. 2023 Jul 28.

Example poster



Acceptable to end users



Siegal et al. Can J Anaesth. 2023 Jul 28.

Summary of STRATUS Pilot Study results

- Successfully implemented with 100% adherence
- Acceptable to end-users
- No increased insufficient samples
- 45% reduction in blood collected
- Full-scale trial feasible

Siegal et al. Can J Anaesth. 2023 Jul 28.

Small-Volume Tubes to Reduce Anemia and Transfusion (STRATUS) Trial

Deborah M. Siegal on behalf of the STRATUS Trial Investigators

Siegal et al. JAMA. Published online October 12, 2023. doi:10.1001/jama.2023.20820

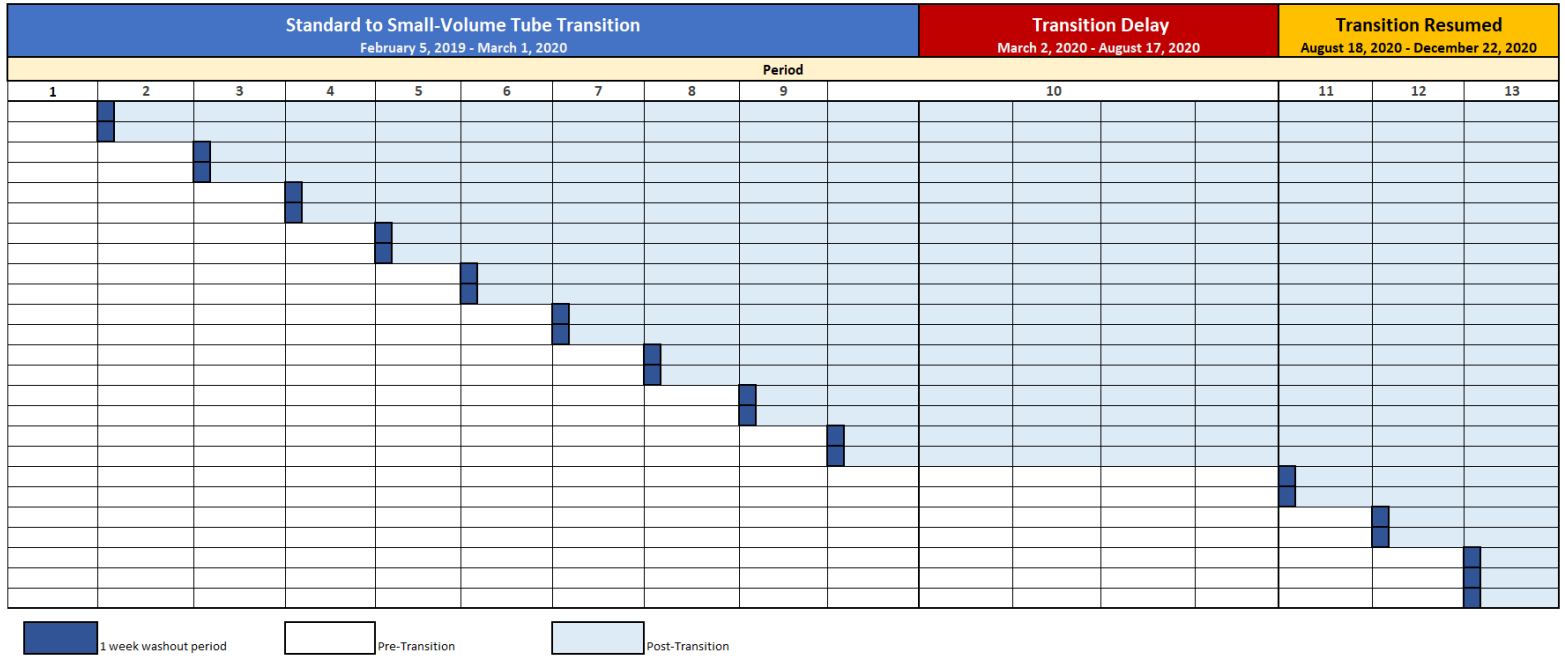
McMaster University
Population Health Research Institute
HEALTH THROUGH KNOWLEDGE
uOttawa
The Ottawa Hospital Research Institute
L'Hôpital d'Ottawa Institut de recherche

Hypothesis

Transition to small-volume blood collection tubes will reduce RBC transfusion in ICU patients

Study design and population

Stepped wedge cluster randomized trial

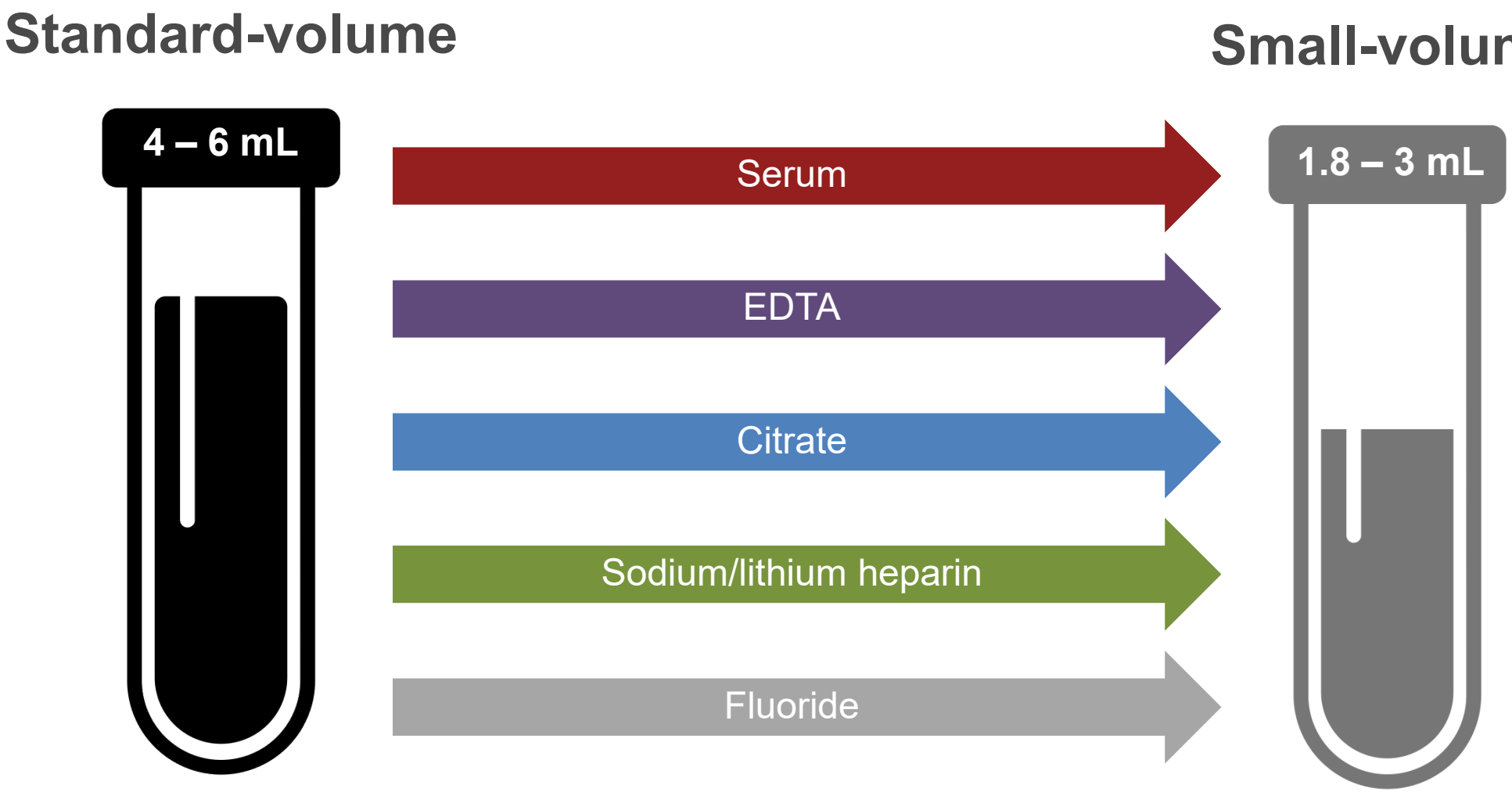


ICU eligibility

Adults
Medical-surgical ICU
≥14 beds
Invasive mechanical ventilation
Standard-volume tubes
Electronic data available

All patients admitted to ICU during study period
Waiver of individual participant consent
Electronic data (administrative, transfusion, lab) up to 30 days, hospital discharge, or death

Intervention: transition to small-volume tubes



Outcomes

Primary Outcome

RBC units transfused per patient during ICU admission

Key Secondary Outcomes

Proportion of insufficient specimens

Proportion of patients who received RBC transfusion

ΔHb from admission to discharge (adjusted for RBC)

ICU and hospital length

Mortality in ICU and hospital

Analysis

Primary analysis

- Patients admitted to ICU ≥48 hours
  - Excluded patients admitted during COVID hiatus
- Negative binomial mixed model
- Study periods (steps) modelled as fixed effect, ICUs modelled as random effect, duration of ICU stay as an offset, adjusted for age and sex

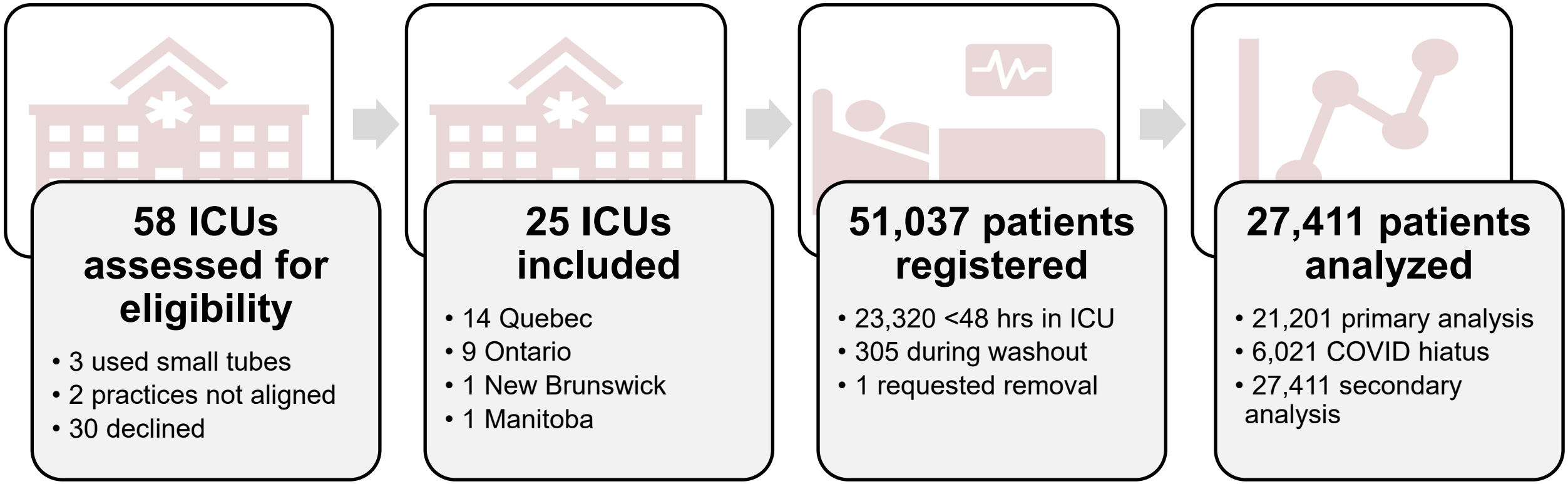
Key secondary analyses

- All patients admitted to ICU ≥48 hours (+ hiatus)
- Proportion of specimens insufficient for testing
- Mortality in ICU and hospital
- Change in hemoglobin (adjusted for RBC transfusion)
- Temporal trends and effect of COVID pandemic

Sensitivity analyses

- Adjustment for imbalanced baseline characteristics

Results


58 ICUs assessed for eligibility
• 3 used small tubes
• 2 practices not aligned
• 30 declined
25 ICUs included
• 14 Quebec
• 9 Ontario
• 1 New Brunswick
• 1 Manitoba
51,037 patients registered
• 23,320 <48 hrs in ICU
• 305 during washout
• 1 requested removal
27,411 patients analyzed
• 21,201 primary analysis
• 6,021 COVID hiatus
• 27,411 secondary analysis

Selected baseline characteristics

Characteristic	Primary analysis population		Secondary analysis population	
	Small-volume (n=10,261)	Standard-volume (n=10,940)	Small-volume (n=12,703)	Standard-volume (n=14,708)
Age, y, mean (SD)	63 (16)	63 (16)	63 (16)	63 (16)
Female, n (%)	4090 (40)	4178 (38)	4832 (38)	5804 (40)
Diagnosis (ICD codes)				
Cardiovascular	2245 (25)	1762 (21)	1813 (19)^	3329 (25)^
Nervous system	1156 (13)	1155 (14)	1365 (14)	1586 (12)
Respiratory	1047 (12)	881 (10)	996 (10)	1461 (11)
Injury	965 (11)^	1577 (18)^	1932 (20)^	1363 (10)^
Infection	807 (9)	676 (8)	743 (8)	1134 (9)
Cancer	779 (9)	801 (9)	890 (9)	1152 (9)
Digestive	787 (9)	728 (8)	814 (8)	1106 (8)
Genitourinary	216 (2)	191 (2)	209 (2)	299 (2)
Endocrine	113 (1)	239 (2)	113 (1)	239 (2)
Other	912 (10)	641 (8)	784 (8)^	1469 (11)^

RBC units per patient per ICU stay

30% of patients admitted ≥48 hours received RBC transfusion

RBC units per pt per ICU stay	Primary analysis population (COVID hiatus excluded n=21,201)			
	Small Volume	Standard Volume	Mean Difference (95% CI)	P
Least squares mean (95% CI)	0.72 (0.52, 0.98)	0.79 (0.58, 1.07)	-0.07 (-0.19, 0.03)	0.19

Absolute mean difference
7.24 RBC units/100 patients
(95%CI -3.28, 19.44)

Mean difference results were adjusted for age and sex and accounted for the stepped wedge design with periods modelled as fixed effects and ICUs as a random effect.

RBC units per patient per ICU stay

30% of patients admitted ≥48 hours received RBC transfusion

RBC units per pt per ICU stay	Primary analysis population (COVID hiatus excluded n=21,201)				Secondary analysis population (all patients n=27,411)			
	Small Volume	Standard Volume	Mean Difference (95% CI)	P	Small Volume	Standard Volume	Mean Difference (95% CI)	P
Least squares mean (95% CI)	0.72 (0.52, 0.98)	0.79 (0.58, 1.07)	-0.07 (-0.19, 0.03)	0.19	0.71 (0.53, 0.93)	0.80 (0.61, 1.06)	**-0.10 (-0.21, -0.002)**	**0.04**
	Absolute mean difference 7.24 RBC units/100 patients (95%CI -3.28, 19.44)				Absolute mean difference 9.84 RBC units/100 patients (95%CI 0.24, 20.76)			

Mean difference results were adjusted for age and sex and accounted for the stepped wedge design with periods modelled as fixed effects and ICUs as a random effect.

Specimens with insufficient quantity

EDTA, sodium/lithium heparin tubes

Specimens with insufficient quantity for testing	Primary analysis population (COVID hiatus excluded)		Secondary analysis population (all patients)	
	Small Volume (n=193,695)	Standard Volume (n=195,383)	Small Volume (n=285,273)	Standard Volume (n=224,868)
N (%)	42 (0.022)	60 (0.031)	65 (0.023)	64 (0.028)

Change in hemoglobin

From ICU admission to ICU discharge

Outcome	Primary analysis population (COVID hiatus excluded n=21,201)			Secondary analysis population (all patients n=27,411)		
	Small Volume	Standard Volume	Mean difference (95% CI)	Small Volume	Standard Volume	Mean difference (95% CI)
ΔHb adjusted for RBC transfusions, g/L, median (IQR)	-14.0 (-30.0, -2.0)	-15.0 (-32.0, -4.0)	1.0 (-0.4, 2.3)	-14.0 (-31.0, -03.0)	-15.0 (-32.0, -4.0)	**1.7 (0.5, 2.9)**
ΔHb, g/L, median (IQR)	-8.0 (-19.0, 2.0)	-9.0 (-21.0, 1.0)	**1.0 (0.2, 1.8)**	-8.0 (-20.0, 2.2)	-9.0 (-21.0, 1.0)	**1.2 (0.5, 1.9)**
ΔHb in patients without RBC transfusions, g/L, median (IQR)	-8.0 (-19.0, 1.0)	-10.0 (-21.0, 0.0)	**1.0 (0.1, 1.9)**	-9.0 (-20.0, 0.0)	-10.0 (-21.0, 0.0)	**1.0 (0.2, 1.8)**

Analyses were adjusted for baseline admission hemoglobin. Mean difference was adjusted for age and sex and accounted for stepped wedge design with periods modelled as fixed effects and ICUs as random effect. Hemoglobin adjusted for RBC transfusion 1 transfusion = Hb – 1 g/dL.

Conclusions

Transition from standard- to small-volume tubes in ICU

May reduce RBC transfusion in patients admitted ≥ 48 hrs

- No difference primary analysis (6210 patients excluded)
- Decrease of ~10 RBC units per 100 patients in secondary analysis

Lessens ICU-related reduction in hemoglobin

Does not negatively impact lab testing (specimen sufficiency)

Discussion

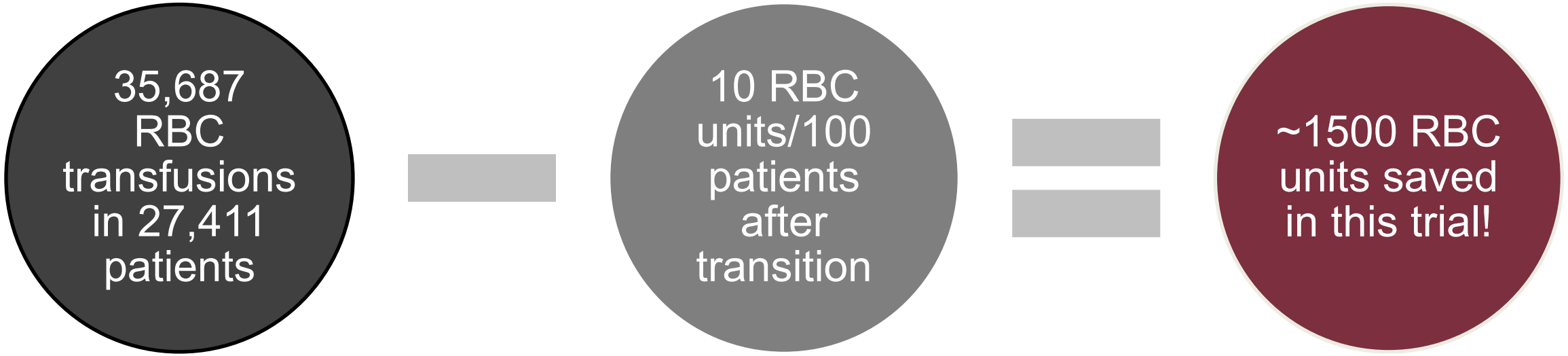
- Implemented easily into routine practice with brief targeted education (scalable)
- Pragmatic data collection (cost effective)
- Community and academic sites
- Small effect at individual level but potential for impact at health system level

Strengths

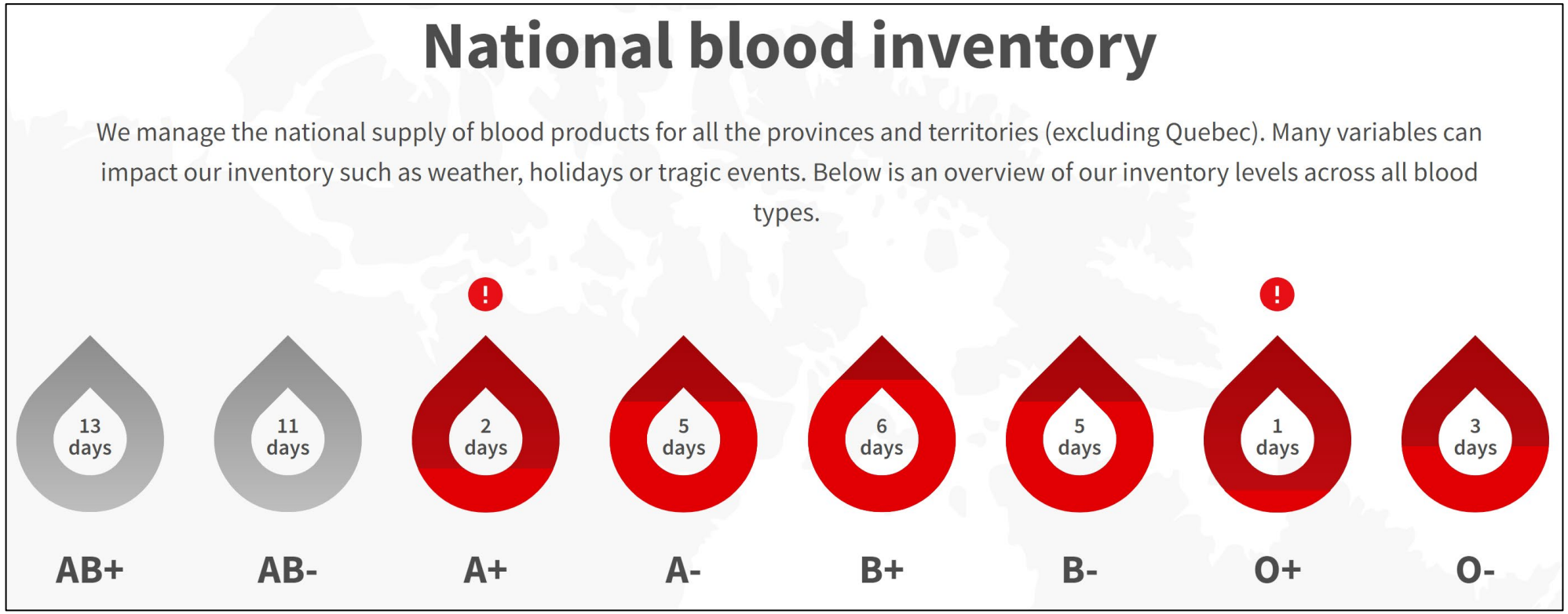
- Changes in study conduct and primary analysis due to COVID
- Limited availability on baseline characteristics and co-interventions
- Transfusion and waste practices not protocolized
- One aspect of lab testing (deemed most important)

Limitations

Small change, big difference



Blood product shortage: Canada



https://www.blood.ca/en

Acknowledgements

"It Takes a Village"

STRATUS

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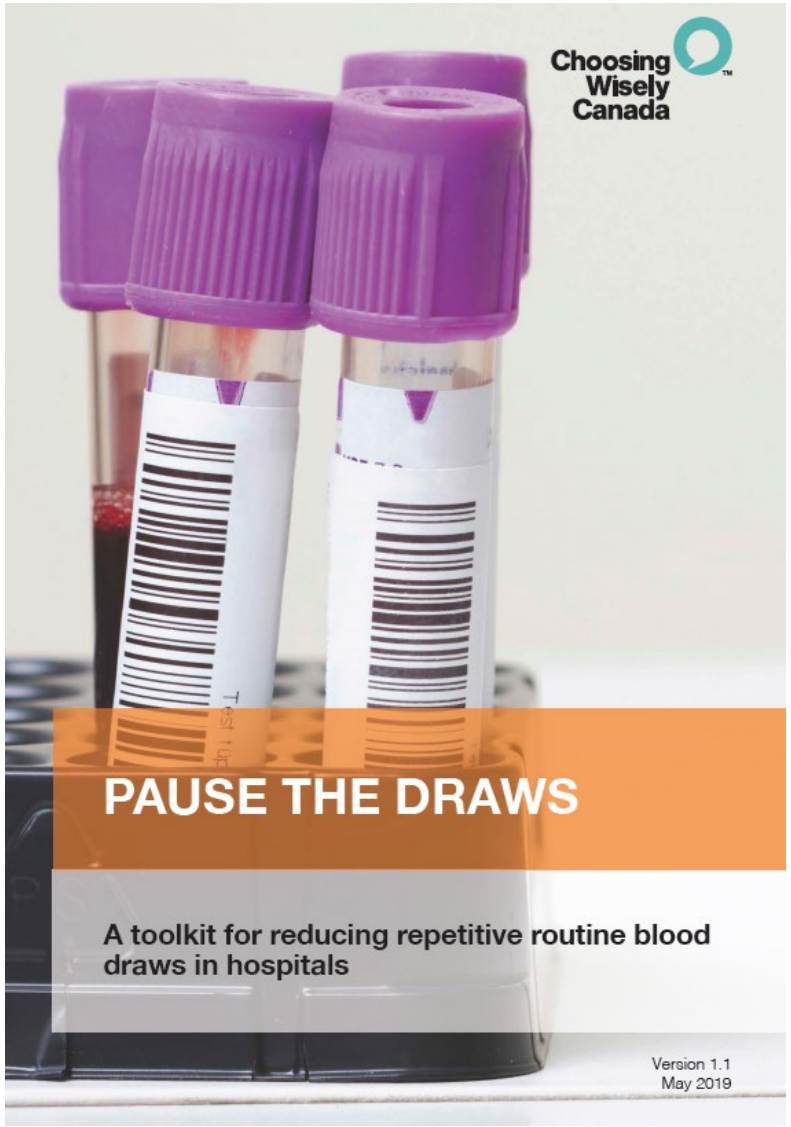
HEALTH THROUGH KNOWLEDGE

‘ICU vampirism’ – time for judicious blood draws in critically ill patients

Ranasinghe BJH 2013 doi:10.1111/bjh.12613



Journal of Thrombosis and Haemostasis, **12**: 1591

FORUM

Iatrogenic anemia (can it be prevented?)

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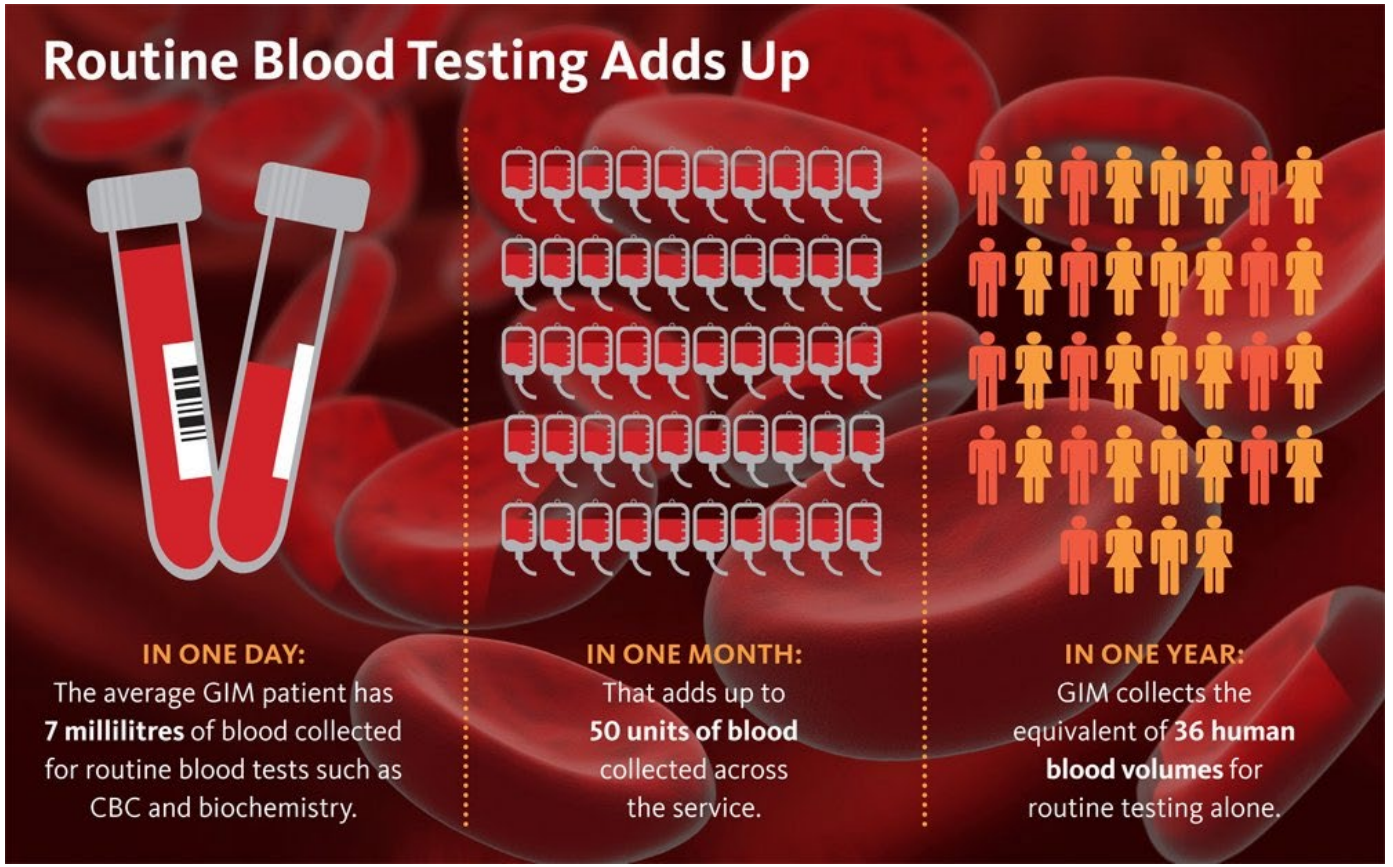
Department of Medicine, Clinch Valley Medical Center, Richlands, VA, USA



Key messages

- Anemia is a common complication during hospitalization (especially ICU admission) that leads to RBC transfusion
- Laboratory testing is a ***modifiable*** cause of blood loss that contributes to anemia and RBC transfusion
- Switching to tubes that collect less blood for lab testing may reduce RBC transfusion and reduce anemia in ICU

QUESTIONS?

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