TRACTION

Embedded Trials in a Learning Health System:

A hospital policy of tranexamic acid to reduce transfusion in major noncardiac surgery

NIH Collaboratory Grand Rounds
September 11, 2026



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The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Hospital Policy of Tranexamic Acid to Reduce Transfusion in Major Noncardiac Surgery

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Two minute video summary of results



TRADITIONAL TERRITORIES ACKNOWLEDGEMENT

The University of Manitoba campuses are located on original lands of Anishinaabeg, Cree, Ojibwe-Cree, Dakota, and Dene peoples, and on the National Homeland of the Red River Métis. We respect the Treaties that were made on these territories, we acknowledge the harms and mistakes of the past, and we dedicate ourselves to move forward in partnership with Indigenous communities in a spirit of reconciliation and collaboration.

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THE TRIBULATIONS OF TRIALS

SLOW

~decade to plan/conduct
Can't keep pace with discovery or urgent health priorities

EXPENSIVE

New infrastructure built for every trial
Parallel infrastructure

SEPARATED FROM CLINICAL CARE

Duplication
Well-intentioned, but counter-productive barriers to participation

LIMITED BY FREQUENTIST PARADIGM

Systematically underpowered trials
…over & over & over again

INACCESSIBLE TO MAJORITY OF PATIENTS

Trials largely available at academic centres
Processes not accessible to minorities

TRIALS ARE POWERED FOR AVERAGE TREATMENT EFFECT BUT RESULTS ARE APPLIED TO INDIVIDUAL PATIENTS

Consequences

- <5% of patients are enrolled in clinical trials
- Unable to respond to health priorities
- Lack of comparative effectiveness trials to establish policy

- …Spending more; learning less

TRANEXAMIC ACID (TXA)

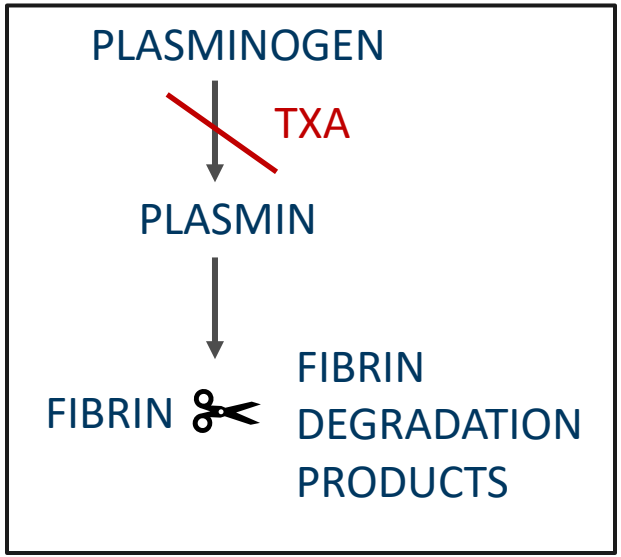


BLOOD

Expensive
Limited resource

TXA

Inexpensive · Widely available
Established safety profile



TXA reduces RBC transfusion in:

- Cardiac surgery
- Hip / knee arthroplasty
- Trauma
- Postpartum hemorrhage

WOMAN, Lancet, 2017
CRASH-2, Lancet, 2010
ATACAS, NEJM, 2017

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PREPARATORY STUDIES

1 RETROSPECTIVE STUDY

Procedures at high risk for transfusion

2 RETROSPECTIVE STUDY

TXA use in 'at risk' procedures

3 RETROSPECTIVE STUDY

TXA effectiveness

4 DATA VALIDATION

DAD & TraceLine variable validation

5 SYSTEMATIC REVIEW & META-ANALYSIS

Transfusion risk & baseline VTE event rates

6 PATIENT ENGAGEMENT

Patient engagement initiative

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TXA in non-cardiac surgery

Multicentre RCT

Co-primary outcomes:
Transfusions & VTE

Each preparatory study addressed a specific knowledge gap, characterized the target population, and informed the methodology, sample size, and outcome definitions of the definitive Phase III trial.

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TXA IN NON-CARDIAC SURGERY

EFFICACY

POISE-3 · 9,535-patient RCT

Major bleeding
9.2% vs 11.7%

RBC transfusion at 30 days (tertiary)
9.4% vs 12.0%

Most other prior RCTs small/moderate with unclear or high risk of bias

SAFETY

✓ **No thrombosis signal at day-30**
Consistent across pooled analyses

! **Generalizability, especially in oncologic surgery is uncertain**
Thrombotic risk less well characterized

Houston et al, Transfus Med Rev, 2020
Tsan et al, Anaesthesia, 2023
POISE-3, NEJM, 2022

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TXA IN NON-CARDIAC SURGERY

? KNOWLEDGE GAPS

- Impact of hospital-wide policy of TXA use
- Effectiveness in high-risk surgeries, rather than high-risk patients
- Thrombotic outcomes beyond 30 days
- Safety in oncology patients

🎯 HYPOTHESIS

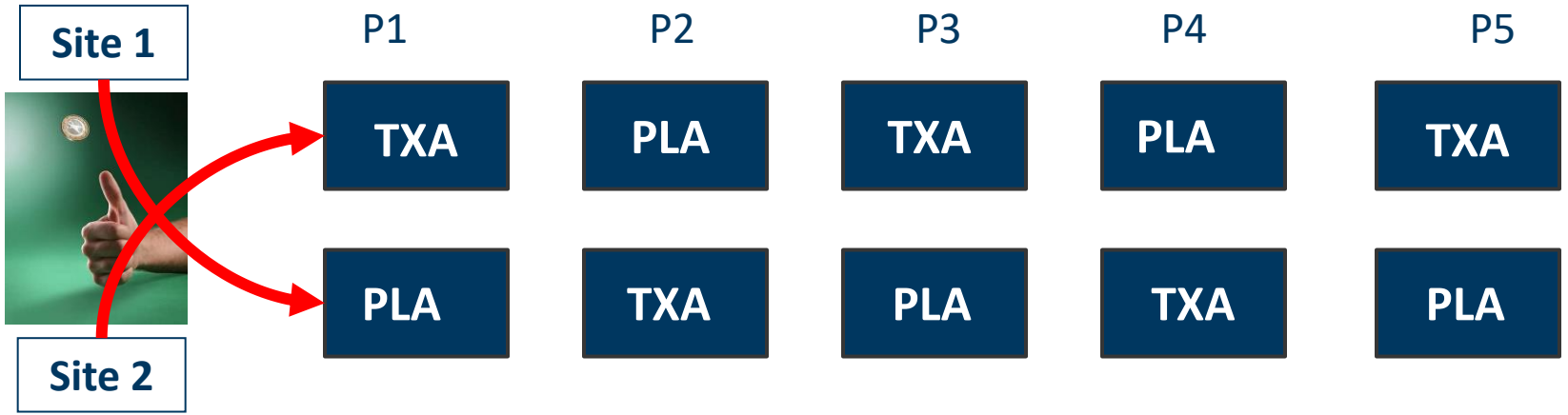
Does hospital-level implementation of TXA in patients having major non-cardiac surgery safely reduce RBC transfusion without increasing thrombotic risk?

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TRIAL DESIGN

- Multicenter (n = 10) cluster cross-over trial
- Each **site** was randomized every 4 weeks
- Sample size estimation 8300 patients





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POPULATION

HOSPITAL-LEVEL
Cluster inclusion

Leadership commitment

Anesthesia, surgery, hospital leaders agree to implement trial policy

≥ 100 major non-cardiac surgeries/month

Sufficient case volume

PATIENT-LEVEL
Individual inclusion

Adults ≥ 18 years

Undergoing major non-cardiac surgery

Inpatient surgery

Open or laparoscopic ≥ 3 hours

≥ 5% transfusion risk

Estimated risk of in-hospital RBC transfusion

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ELIGIBLE SURGERY EXAMPLES



General	*GI resections, hepatobiliary surgeries*
Orthopedics	*hip fracture, femur repair/fixation, lower extremity amputation*
Spine	*vertebrectomy, ≥3-level surgery, tumor resection*
Otolaryngology	*glossectomy, mandibulectomy, radical laryngectomy*
Thoracic	*lung resection, decortication, esophagectomy*
Vascular	*aortic / proximal arterial bypass, endarterectomy or aneurysmorrhaphy*
Gynecology	*hysterectomy, TAH BSO, pelvic exenteration*
Urology	*nephrectomy, cystectomy, prostatectomy, pelvic exenteration*
Plastics	*neoplasm resection, burns or debridement*
Other	*any with ≥5% transfusion risk*

Inclusion: surgeries with ≥ 5% anticipated risk of in-hospital RBC transfusion

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EXCLUSION CRITERIA



Active thromboembolic disease	*Anticoagulated for venous or arterial event within prior 3 months*
Standard-of-care indications	*Cardiac surgery, hip / knee arthroplasty*
Free-flap reconstruction	*Microvascular surgery*
Recent TXA in trauma	*TXA administered within prior 3 hours*
Pregnancy	

INTERVENTION / CONTROL

INTERVENTION



Tranexamic acid (TXA)

1 g IV bolus within 10 min of incision

+ 1g IV before skin closure

Timing of second dose at anesthesiologist's discretion

CONTROL



Normal saline (0.9%)

Volume-matched placebo

Administered on identical schedule

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CO-PRIMARY OUTCOMES

1

TRANSFUSION

Proportion of patients transfused red blood cells in hospital

SUPERIORITY

2

SAFETY

Venous thromboembolism (VTE) within 90 days of surgery

NON-INFERIORITY

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SECONDARY OUTCOMES

TRANSFUSION

Number of RBC units transfused, at cluster and patient level

SAFETY

In-hospital MI, stroke, DVT/PE, perioperative anaphylaxis and seizure

CLINICAL

Hospital length of stay, ICU admission, hospital and 90-day survival

COMPLIANCE

Eligible patients receiving the policy intervention; compliance in enrolled patients

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SAMPLE SIZE ESTIMATION

DESIGN ASSUMPTIONS

Hypothesis

Non-inferiority on safety

Margin

≤ 1% increase in 90-day VTE

Baseline VTE

2.2%

Upper 95% CI of the relative risk

1.46

TARGET SAMPLE

8,300

patients

83% POWER

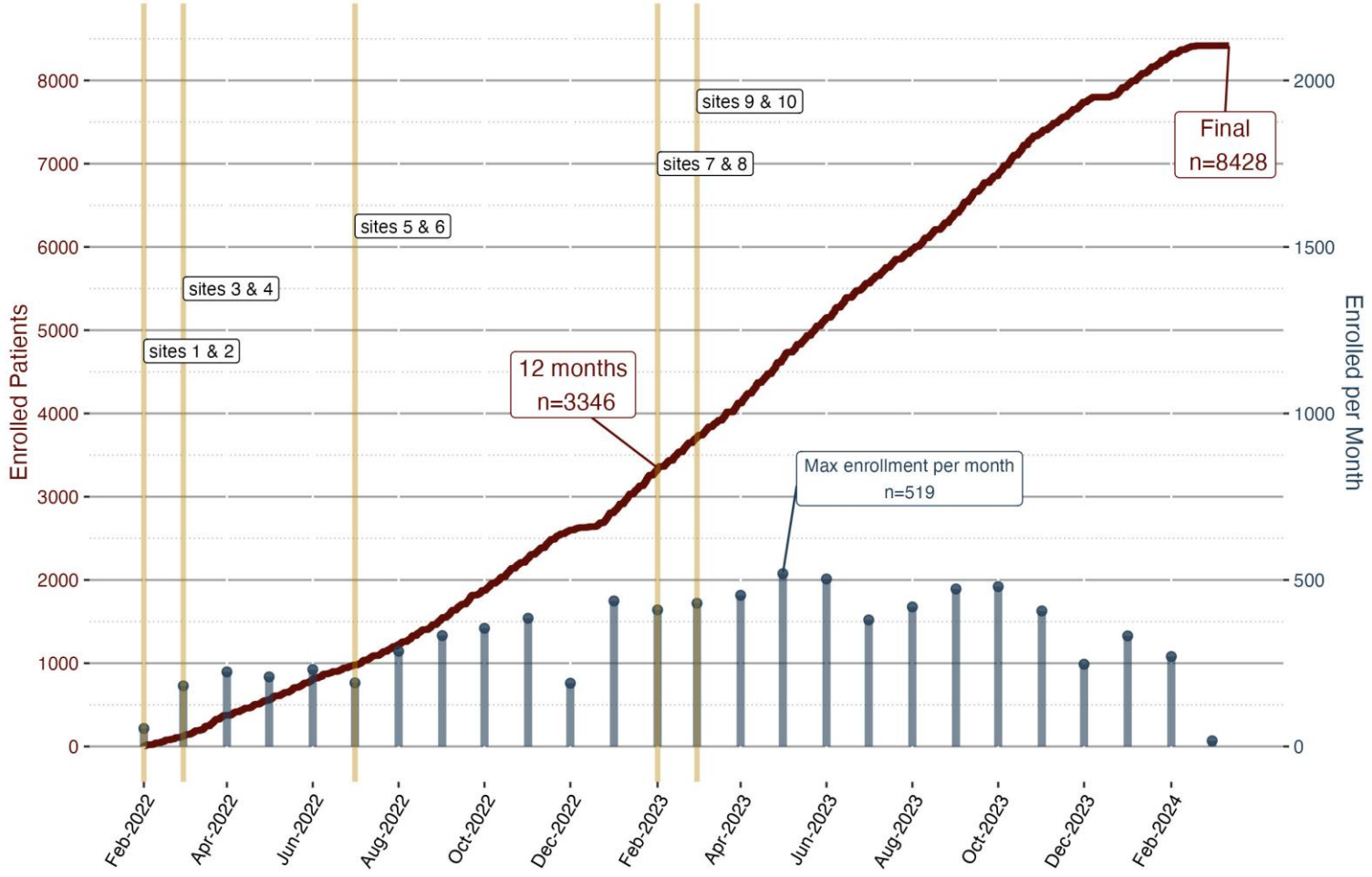
Effectiveness and safety jointly assessed — sample size driven by the safety co-primary outcome

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PATIENT & PUBLIC ENGAGEMENT

- Trial Design
- Method of Consent
- Study Materials
- Trial Outcomes

ENROLMENT

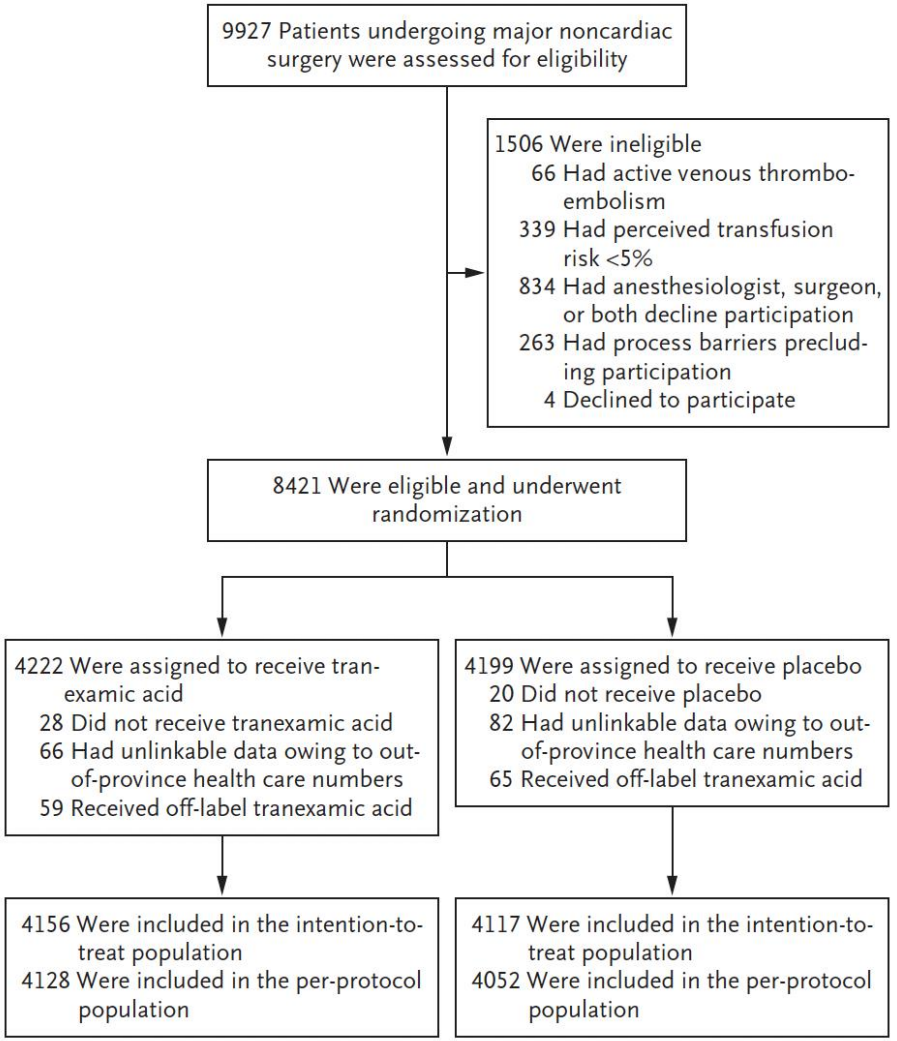

sites 1 & 2
sites 3 & 4
sites 5 & 6
sites 7 & 8
sites 9 & 10
12 months
n=3346
Final
n=8428
Max enrollment per month
n=519
Enrolled Patients
Enrolled per Month
0
1000
2000
3000
4000
5000
6000
7000
8000
0
500
1000
1500
2000
Feb-2022
Apr-2022
Jun-2022
Aug-2022
Oct-2022
Dec-2022
Feb-2023
Apr-2023
Jun-2023
Aug-2023
Oct-2023
Dec-2023
Feb-2024

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>80%

of patients screened were enrolled

8,421 of 9,927



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BASELINE CHARACTERISTICS

Characteristic	Tranexamic acid (N=4156)	Placebo (N=4117)
Age – year	64 (54-72)	64 (54-73)
Male sex – no. (%)	1985 (47.8)	1908 (46.3)
Weight – kg	80 (68-95)	80 (68-94)
Charlson comorbidity score	2 (0-2)	2 (0-2)
Surgical specialty – no. (%)		
General surgery	1358 (33.1)	1384 (34.1)
Orthopedic	87 (2.1)	78 (1.9)
Spine	244 (5.9)	217 (5.3)
Otolaryngology	16 (0.4)	21 (0.5)
Thoracic	451 (11.0)	466 (11.5)
Vascular	286 (7.0)	296 (7.3)
Gynecologic	799 (19.5)	741 (18.3)
Urology	735 (18.3)	699 (17.2)
Neurosurgery	126 (3.1)	140 (3.4)



Arms were well balanced across demographics and surgical specialty

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BASELINE CHARACTERISTICS

Characteristic	Tranexamic acid (N=4156)	Placebo (N=4117)
Surgical urgency – no. (%)		
Elective	3806 (93.0)	3753 (92.6)
Urgent/emergent	287 (7.0)	299 (7.4)
Surgical indication – no. (%)		
Oncologic	2536 (62.3)	2466 (61.2)
Non-oncologic	1536 (37.7)	1561 (38.8)
Surgical modality – no. (%)		
Open	1969 (55.0)	1848 (54.3)
Laparoscopic/endoscopic	1614 (45.0)	1554 (45.7)
Preoperative RBC transfusion – no. (%)	56 (1.3)	64 (1.6)

⚖ *Majority elective and oncologic — arms balanced across urgency, indication, and modality*

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CO-PRIMARY OUTCOMES

TRANSFUSION

7.4% vs 9.8%

RR 0.73 (95% CI 0.61–0.86)

Reduced proportion of patients transfused red blood cells

SAFETY (VTE)

2.1% vs 2.1%

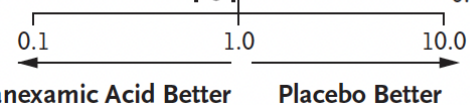
RR 0.96 (95% CI 0.65–1.38)

No increase in venous thromboembolism at 90 days

TXA reduced transfusion without increasing thrombotic risk

Red blood cell transfusion during hospitalization

Subgroup	Tranexamic Acid	Placebo	Relative Risk (95% CI)
	no. of patients with event/total no. (%)		
Overall	306/4156 (7.4)	403/4117 (9.8)	0.73 (0.61–0.86)
Age			
<40 yr	15/287 (5.2)	21/289 (7.3)	0.73 (0.31–1.39)
40–64 yr	111/1821 (6.1)	153/1814 (8.4)	0.69 (0.50–0.88)
65–74 yr	87/1282 (6.8)	125/1226 (10.2)	0.64 (0.47–0.83)
≥75 yr	93/766 (12.1)	104/788 (13.2)	0.86 (0.63–1.12)
Surgical specialty			
General surgery	102/1358 (7.5)	155/1384 (11.2)	0.65 (0.48–0.81)
Orthopedic surgery	10/87 (11.5)	9/78 (11.5)	0.85 (0.35–1.91)
Spine surgery	22/244 (9.0)	27/217 (12.4)	0.74 (0.34–1.49)
Neurosurgery	<6/126	11/140 (7.9)	0.47 (0.09–1.31)
Thoracic surgery	14/451 (3.1)	20/466 (4.3)	0.71 (0.30–1.47)
Vascular surgery	68/286 (23.8)	53/296 (17.9)	1.28 (0.83–1.95)
Gynecologic surgery	31/799 (3.9)	55/741 (7.4)	0.50 (0.25–0.84)
Urologic surgery	51/735 (6.9)	64/699 (9.2)	0.73 (0.48–1.09)
Surgical urgency			
Elective	243/3806 (6.4)	329/3763 (8.7)	0.70 (0.55–0.83)
Urgent or emergency	63/350 (18.0)	74/364 (20.3)	0.84 (0.61–1.11)
Surgical indication			
Oncologic	161/2536 (6.3)	241/2466 (9.8)	0.63 (0.49–0.77)
Nononcologic	139/1536 (9.0)	154/1561 (9.9)	0.87 (0.64–1.13)
Risk of red-cell transfusion			
<10%	98/2583 (3.8)	144/2523 (5.7)	0.64 (0.48–0.84)
≥10%	208/1573 (13.2)	259/1594 (16.2)	0.78 (0.62–0.95)



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TXA IN SURGICAL ONCOLOGY

TXA use in surgical oncology has been variable due to thrombosis concerns

5,002

patients undergoing surgery for cancer

TXA	Placebo
2.4%	2.8%

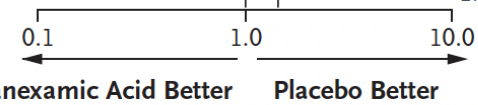
VTE within 90 days of surgery

0.88

relative risk
(95% CI 0.63 – 1.36)

Venous thromboembolism within 90 days

Subgroup	Tranexamic Acid	Placebo	Relative Risk (95% CI)
	no. of patients with event/total no. (%)		
Overall	86/4128 (2.08)	85/4052 (2.10)	0.96 (0.65–1.38)
Age			
<40 yr	<6/286	<6/286	5.08 (0.44–8.37)
40–64 yr	41/1808 (2.3)	34/1792 (1.9)	1.21 (0.73–2.05)
65–74 yr	22/1271 (1.7)	27/1204 (2.2)	0.77 (0.45–1.58)
≥75 yr	18/763 (2.4)	23/770 (3.0)	0.79 (0.47–1.59)
Surgical specialty			
General surgery	32/1351 (2.4)	26/1367 (1.9)	1.24 (0.77–1.86)
Orthopedic surgery	<6/86	<6/77	2.76 (0.33–4.95)
Spine surgery	<6/242	<6/217	0.92 (0.21–3.67)
Neurosurgery	<6/126	6/135 (4.4)	0.84 (0.16–2.25)
Thoracic surgery	8/449 (1.8)	16/455 (3.5)	0.52 (0.28–2.04)
Vascular surgery	<6/284	<6/286	1.83 (0.50–10.75)
Gynecologic surgery	12/789 (1.5)	12/729 (1.6)	0.84 (0.42–1.83)
Urologic surgery	14/731 (1.9)	15/691 (2.2)	0.90 (0.39–1.92)
Surgical urgency			
Elective	70/3782 (1.9)	74/3692 (2.0)	0.93 (0.68–1.42)
Urgent or emergency	16/346 (4.6)	11/360 (3.1)	1.40 (0.73–2.79)
Surgical indication			
Oncologic	60/2526 (2.4)	64/2421 (2.6)	0.92 (0.68–1.48)
Nononcologic	25/1527 (1.6)	20/1541 (1.3)	1.26 (0.71–2.07)
Risk of red-cell transfusion			
<10%	45/2564 (1.8)	49/2482 (2.0)	0.89 (0.61–1.37)
≥10%	41/1564 (2.6)	36/1570 (2.3)	1.15 (0.73–1.95)



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SECONDARY OUTCOMES

Outcome	Tranexamic acid (N=4156)	Placebo (N=4117)	Effect Estimate (95% CI)
RBC units transfused Patient level per 100 patients (mean, SD)	24.7 (3.6)	34.2 (2.6)	mean difference -9.5 (-19.2 to -0.2)
RBC units transfused Hospital level per 100 patients (mean, SD)	23.5 (27.2)	39.6 (80.6)	mean difference -16.2 (-33.5 to 1.1)
Myocardial infarction – no. (%)	29 (0.7)	34 (0.8)	NA
Stroke – no. (%)	9 (0.2)	9 (0.2)	NA
Deep vein thrombosis – no. (%)	<6	<6	NA
Pulmonary embolism – no. (%)	8 (0.2)	6 (0.2)	NA



Reduced volume of red cells transfused

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SECONDARY OUTCOMES

Outcome	Tranexamic acid (N=4156)	Placebo (N=4117)	Effect Estimate (95% CI)
Hospital LOS (days) – (mean, SD)	6.20 (8.89)	6.26 (9.42)	mean difference -0.15 (-0.69 to 0.77)
ICU admission – no. (%)	693 (16.7)	721 (17.5)	mean difference -0.01 (-0.03 to 0.02)
Hospital survival – no. (%)	4112 (98.9)	4076 (99.0)	NA
Survival at 90 days – no. (%)	4066 (97.8)	4017 (97.6)	hazard ratio 0.95 (0.71 to 1.28)
Days alive and out of hospital to day 30 – median (IQR)	26 (22 to 27)	26 (22 to 27)	mean difference 0.03 (-0.33 to 0.39)



No differences in hospital course or survival — TXA effect was specific to transfusion

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INNOVATIVE METHODS

1



CLUSTER CROSSOVER DESIGN

Pragmatic trial design at the hospital level

2



WAIVED / ALTERED CONSENT

Enables population-level implementation

3



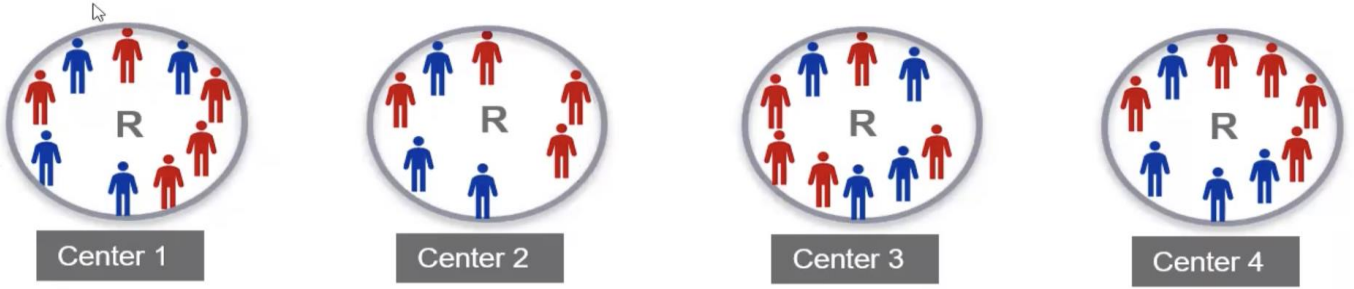
ELECTRONIC DATA CAPTURE

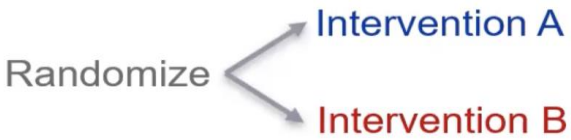
Routine clinical and administrative sources

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INDIVIDUAL PATIENT RANDOMIZATION

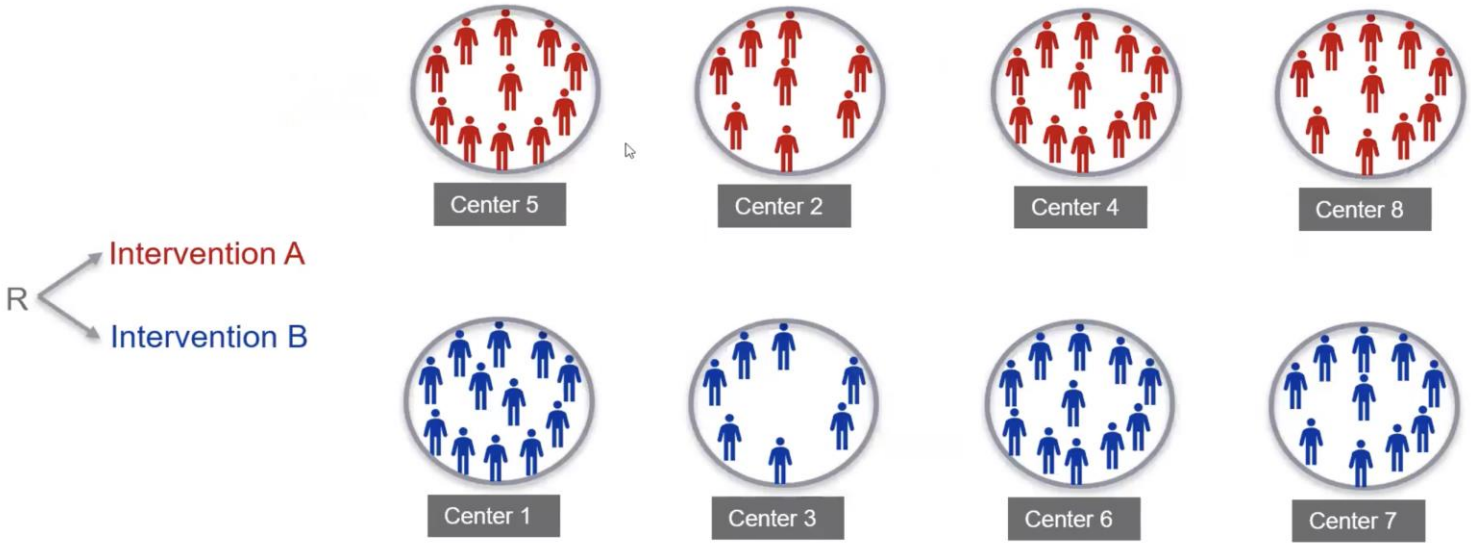
Roughly equal numbers of patients receive intervention or control at each center





CLUSTER RANDOMIZATION

Entire centers (clusters) receive different interventions



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INDIVIDUAL PATIENT vs CLUSTER RCTs

INDIVIDUAL PATIENT RCT

UNIT OF RANDOMIZATION
Individual patient

CONSENT
Individual informed consent required

SAMPLE SIZE
Large — powered at the patient level

BEST SUITED FOR
Dose finding, novel therapies, uncertain adverse events

CLUSTER RANDOMIZED TRIAL

UNIT OF RANDOMIZATION
Hospital, site, or unit

CONSENT
Waived or altered consent enables population-level reach

SAMPLE SIZE
Larger — although within-cluster crossover boosts efficiency

BEST SUITED FOR
Pragmatic, system-level, policy interventions

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TYPICAL CLUSTER TRIAL CONSIDERATIONS

Policy-level interventions	*System-wide rules and protocols across centers*
Processes of care	*Workflow and care-delivery changes*
Low-risk interventions	*When consent can be waived or altered*
Complex provider training	*Extensive education or skill-build required*

When individual RCT doesn't make sense …

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PROS OF CLUSTER CROSSOVER DESIGN

Within-cluster comparisons	*Each cluster serves as its own control — reduces between-cluster variability*
Higher statistical efficiency	*Especially when clusters are small or heterogeneity is high*
Smaller sample size	*Compared to parallel cluster trials*
Better confounder balance	*Each cluster experiences both conditions*
Suits health-system trials	*Ideal for policy and system-level interventions*

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CLUSTER TRIALS IN TRANFUSION MEDICINE

Uncommon despite frequent policy-driven transfusion decisions

TACS	POC testing in cardiac surgery
STRATUS	Small-volume tubes in ICU
RESTRIC	Restrictive RBC transfusion in trauma · *enrolled 422 of 6,000 required*
FLUID	Normal saline vs Ringer's lactate · *43,000 patients across 7 centres*

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WAIVED / ALTERED CONSENT



Risk-adapted

Consent process scaled to the level of risk



Both arms within usual care

TXA and no-TXA fall within standard practice



Established safety profile

Decades of TXA use across surgical specialties



Hospital-level intervention

Impracticable to consent individual patients for a policy



Informed by stakeholders

Extensive discussion with patients and caregivers

DATA ACQUISITION

MANUAL CAPTURE

Targeted, low-burden

Limited and standardized

Only fields not available electronically

- Confirmation of eligibility
- TXA administration (at some sites)
- Limited to half page case report form

ELECTRONIC DATA

Routine clinical sources

Clinical + administrative

Drawn from existing hospital systems

- Electronic health records
- Hospital discharge data
- Provincial administrative databases

Pragmatic, low-cost data infrastructure

IMPACT OF TRIAL EFFICIENCIES

- Cluster-crossover
- Risk-adapted consent
- Electronic data capture

Category	Expense
Personnel	~$1,400,000
Pharmacy dispensing	$205,000
Drug/Placebo	$25,000
Data management	$30,000
Statistical analysis	~$30,000
Patient advisory	$15,000
Miscellaneous	$60,000
Site start up/close out	$20,000
TOTAL	**~$1,800,000 CDN**



~75% lower cost than conventional pragmatic trials of similar size

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SURGICAL IMPACT OF TRACTION



500,000 TRACTION eligible trials annually (CIHI data)



12,000 CDN patients would avoid blood transfusion/yr



50,000 to 80,000 units of RBC units saved/yr in Canada



>5 million RBC units saved annually globally

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SUMMARY

Reduces RBC transfusion

TXA reduced the proportion of patients transfused (7.4% vs 9.8%)

No increase in VTE

Thrombotic event rates were equivalent at 90 days (2.1% vs 2.1%)

Novel methods increased efficiency & reduced trial cost

Cluster-randomized embedded design substantially reduced trial cost

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FUNDING



CIHR



HSC FOUNDATION



THE OTTAWA HOSPITAL



MANITOBA & ONTARIO GOVERNMENTS

With sincere thanks to our funders for making this trial possible

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TRACTION TRIAL OPERATIONS

GEORGE & FAY YEE Centre for Healthcare Innovation

CHI

AURORA Clinical Research

AURORA CLINICAL RESEARCH

University of Manitoba

UNIVERSITY OF MANITOBA

LGI Research Chair in Hematology

The Ottawa Hospital Research Institute

OTTAWA HOSPITAL RESEARCH INSTITUTE

CancerCare Manitoba ActionCancerManitoba

CANCERCARE MANITOBA

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TRIAL TEAM

Trial Primary Investigators

Brett Houston
Dan McIsaac
Rodney Breau
Dean Fergusson
Ryan Zarychanski

Project Lead and Multicentre Coordinator

Dayna Solvason

Statisticians

Tim Ramsey
Rob Balshaw

Site Investigators

Marshall Tenenbein
Jayesh Daya
Hema Bagry
Sarah McIsaac
Kait Duncan
Tarit Saha
Chris Harle
Meghan Andrews
Sinziana Avramescu
Tina Kerelska

Patient/Caregiver Advisory Chair

Mac Horsburgh