TRACTION

# A Phase IV trial of a hospital policy of Tranexamic acid to reduce transfusion in major non-cardiac surgery (TRACTION)

TRACTION

# TXA in NON-CARDIAC SURGERY

- **Efficacy**
  - Many supportive, small/moderate size RCTs; many at unclear or high risk of bias
  - POISE-3 - highest quality data is trial
    - Reduced Bleeding (9.2% vs. 11.7%)
    - *Tertiary outcome: Reduced RBC transfusion at 30 days (9.4% vs. 12%)*

- **Safety**
  - No suggestion of thrombosis
  - Seizures are likely restricted to cardiac surgery
  - Unclear thrombotic risk in cancer patients

Montroy J. *Transfus Med Rev* 2017; **31**(3): 141-8

Houston BL, 2019 (Manuscript Accepted. Transfusion Medicine Reviews)

# TRANEXAMIC ACID USE TO REDUCE TRANSFUSION IN MAJOR NON-CARDIAC SURGERY

- **Hypothesis:**
  - Does the hospital-level implementation of TXA in patients undergoing major non-cardiac surgery safely reduce RBC transfusion without increasing thrombotic risk

- **Population:**
  - Hospital level: hospitals performing major non-cardiac surgery
  - Patient level: patients undergoing major non-cardiac surgery with an estimated transfusion risk of ≥5%

# TRIAL DESIGN

- Multicentre (n = 10) cluster cross-over trial
- Each **site** will be randomized every 4 weeks
- Overall estimated enrollment ~ 8300 patients / 10-12 months

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# INCLUSION CRITERIA

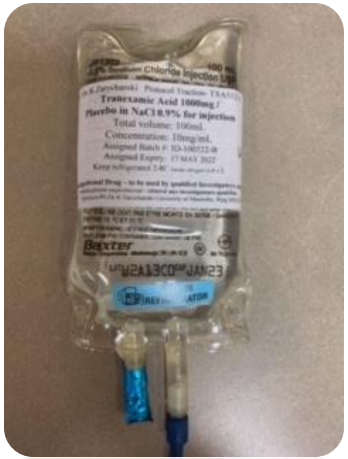
Cluster-level inclusion criteria:

Hospital sites where anesthesia and hospital leadership agree to manage patients as per the policy being implemented and evaluated in the trial

Patient-level inclusion criteria:

- Patients ≥ 18 years of age undergoing **major non-cardiac surgery**
  - **Inpatient** surgeries, with:
  - Estimated **≥ 5% risk of RBC transfusion**
  - **Open or laparoscopic** (if ≥ 3 hours)

# INTERVENTION / CONTROL




Intervention group

- Tranexamic acid (TXA) 1 gram bolus IV administered within 10 min of surgical incision followed by:
- 1 additional gram given intravenously prior to skin closure - timing at the discretion of the anesthesiologist

Control group

- Normal saline placebo

# Co-PRIMARY OUTCOMES

1. Transfusion: Proportion of patients transfused red blood cells (RBCs) in hospital
2. Safety: Incidence of venous thromboembolism (VTE) within 3 months of surgery

*Outcome justification:*

- Primary outcomes inform a patient's, surgeon's and anesthestist's decision to use TXA, by placing the expected benefits in the context of potential harm.
- Reflect the specific views and input of clinician knowledge users and the TRACTION patient committee.

# Patient and Public Involvement and Engagement CONSENT MODEL

- **Informed by focus-group discussions with reference to ethical principles and regulatory requirements**
  - Current practice
  - Objectives
  - Risk & benefit
  - Privacy & disclosure
  - System practicalities

# TRACTION CONSENT MODEL

**Waived/altered consent:**

- Both interventions (TXA / no TXA) fall within usual care
- Minimal risk
- Impracticable to test a hospital policy
- Informed through extensive discussions with patients and caregivers
- Study information provided to enrolled patients post-operatively with ability to opt-out of data collection (Manitoba)

## What are the potential risks associated with this study?

The only protocolized intervention in this study is whether or not you will receive tranexamic acid during your surgery. All other aspects of your care will not be affected.

We are not collecting additional information beyond what is routinely collected while patients are admitted to hospital. While we do plan to share the results of this study with patients and the medical community, the results will not and cannot identify individual patients.

CIHR IRSC
Canadian Institutes of Health Research / Instituts de recherche en santé du Canada

Health Sciences Centre FOUNDATION

The Ottawa Hospital | L'Hôpital d'Ottawa
RESEARCH INSTITUTE / INSTITUT DE RECHERCHE

Hôpital St-Boniface Hospital

University of Manitoba

Shared health Soins communs Manitoba

Version 4, dated October 1, 2021

## WHO CAN YOU CONTACT IF YOU HAVE QUESTIONS?

If you have any questions about your participation in the research study please contact the Study Coordinator at **(204) 430-9815.**

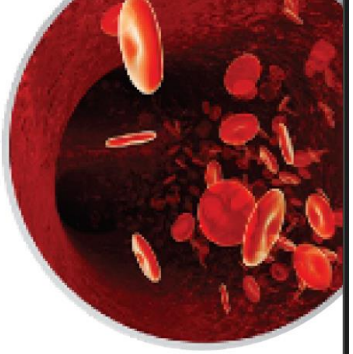
If you have any questions regarding your rights as a research participant, you may contact the University of Manitoba Research Ethics Board at **(204) 789-3389.**

## CAN YOU REQUEST TO HAVE YOUR INFORMATION REMOVED FROM THE STUDY?

You can request to have your information removed from the study. This request can be made to the Study Coordinator listed above. Requesting your information to be removed will not affect your care.

A complete description of the research study and research team can be found online at the following internet address:

**www.tractiontrials.org**



# TRACTION

## A Phase IV trial of a hospital policy of Tranexamic acid use to reduce transfusion in major non-cardiac surgery

You have participated in a research study, led by Dr. Brett Houston, Dr. Thomas Mutter, and Dr. Ryan Zarychanski at the University of Manitoba, This study is currently underway at this Hospital to assess the ability of tranexamic acid to reduce blood transfusion in major non-cardiac/heart surgery where the risk of blood transfusion is more than 5%.

The purpose of this study is to evaluate whether the hospital-level policy of routinely administering tranexamic acid to patients undergoing major non-cardiac surgery will reduce red blood cell transfusion without increasing thrombotic risk (blood clots).

# WHEN CAN CONSENT BE ALTERED: What says TCPS-2?

**Waived/altered consent:**

- ☑ Involves no more than minimal risk to participants
- ☑ Alteration to consent is unlikely to adversely affect the welfare of participants;
- ☑ it is impossible or impracticable otherwise
- ☑ The precise nature of the proposed alteration is defined
- ☑ the plan to provide a debriefing is in accordance with Article 3.7B.

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# ADAPTED CONSENT
## Ethical principles require context

- Risk and benefit need be to contemplated together
- Requires knowledge of current practice
- Patients should be part of the conversation
- Practicability is complicated - contextual & proportional

- In Health Canada regulated trials…none of this is considered

# ADAPTED CONSENT
# When will Health Canada consider?

If the trial is not Health Canada regulated

Depends on the product monograph indication

- Little incentive to update once a product is approved
- No incentive once generic

Represents a profound challenge to the conduct of pragmatic and comparative efficacy trials and trials repurposed drugs with known minimal risk

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- ☑ The precise nature of the proposed alteration is defined
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- ✗ Not if the trial is Health Canada regulated

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# COULD OUR ANCHOR BE WEIGHING US DOWN?

- Does ‘research’ we perform to today resemble experiments of the past?
- Were embedded pragmatic comparative efficacy trials or cluster trials on the minds those who drafted the declarations that anchor our default and accept positions regarding consent?
- Is all knowledge generated from clinical care best characterized as research?
  - When is it the responsible functioning of learning health system?