PROTOCOL SUMMARY

FULL TITLE OF STUDY	Tranexamic acid by the intramuscular or intravenous route for the prevention of postpartum haemorrhage in women at increased risk: a randomised, placebo-controlled trial				
SHORT TITLE	Intramuscular tranexamic acid to prevent heavy bleeding after childbirth in women at higher risk				
TRIAL ACRONYM	I'M WOMAN				
SPONSOR ID NUMBER	2021-KEP-588	**LSHTM ETHICS REF**	28252	**CLINICALTRIALS.GOV**	NCT05562609

BACKGROUND: Postpartum haemorrhage (PPH) causes about 70,000 maternal deaths every year. Tranexamic acid (TXA) is a lifesaving treatment for women with PPH. Intravenous (IV) TXA reduces deaths due to PPH by one third when given within 3 hours of childbirth. Because TXA is more effective when given early and PPH usually occurs soon after childbirth, giving TXA just before childbirth might prevent PPH. Although several clinical trials have examined TXA for the prevention of PPH, the results are inconclusive. Because PPH only affects a small proportion of births, we need good evidence on the balance of benefits and harms in this population before using TXA to prevent PPH. The I'M WOMAN trial will evaluate the effects of TXA for PPH prevention in women with one or more risk factors for PPH giving birth vaginally or by caesarean section. The trial will also evaluate the effect of the route of TXA administration. TXA is usually given by slow IV injection. However, recent research shows that TXA is well tolerated and rapidly absorbed after intramuscular (IM) injection, achieving therapeutic blood levels within minutes of injection. There may be fewer side effects with IM TXA because peak blood concentrations are lower than with the IV route. IM TXA also has practical advantages as it is quicker and simpler to administer.

AIM: To assess the effects of IM and IV TXA in women at increased risk of PPH

OBJECTIVES:

1. Assess the effect of TXA on the risk of PPH and other bleeding-related outcomes;
2. Compare the effects of IM and IV TXA on the risk of PPH;
3. Compare the effects of IM and IV TXA on the risk of adverse events.

PRIMARY OUTCOME: A clinical diagnosis of primary PPH.

SECONDARY OUTCOMES: Surgical and postpartum blood loss, interventions for bleeding (drugs for PPH treatment, blood transfusion, non-surgical and surgical interventions), prespecified maternal adverse events (nausea, retching, vomiting, dizziness, skin reaction or pain at injection sites, thromboembolic events, seizure, sepsis, organ dysfunction), days in ICU/HDU, length of hospital stay, death by cause, neonatal outcomes (breastfeeding, congenital abnormality, death by cause, thromboembolic event, seizure, intracranial or pulmonary bleeding, bruising), other adverse events.

TRIAL DESIGN: A randomised, placebo-controlled, three arm trial.

POPULATION: Women having a vaginal or caesarean birth, who are at increased risk of PPH

INCLUSION/EXCLUSION CRITERIA: Women thought to be aged 18 years or older at increased risk (one or more risk factors) of PPH who are admitted to hospital to give birth vaginally or by caesarean section are eligible. Women who have a clear indication or contraindication for the trial treatment should not be recruited.

TRIAL TREATMENT, REFERENCE THERAPY, DOSE AND MODE OF ADMINISTRATION AND RESTRICTIONS:

a) 1 gram of tranexamic acid as two 5 ml IM injections (100 mg/ml) and IV placebo (10 ml 0.9% sodium chloride); b) 1 gram of tranexamic acid by IV injection and two 5 ml IM placebo injections; or c) matching placebo.

The trial treatment will be given just prior to skin incision (after draping) in caesarean births and at crowning in vaginal births. For IM administration, the 1 g dose (10 ml) is divided into two 5ml IM injections to reduce the injection volume, and given into the vastus lateralis (preferred), the ventro-gluteal region, or the deltoid. Women will receive all the usual care in labour and after birth. Participation will not result in any needed treatment being withheld. Women who develop PPH should be treated in the usual way.

SETTING: The trial will be conducted in hospitals in Africa and Asia where maternal mortality due to PPH is high.

DURATION OF PARTICIPATION: Trial participation ends at discharge, death or 42 days after randomisation, whichever occurs first.

CRITERIA FOR EVALUATION: Women who receive IM TXA will be compared with those who receive IV TXA in a per-protocol analysis. All those allocated to receive TXA will be compared to those allocated to receive placebo, whether they received the allocated treatment or not (intention-to-treat analysis).

CLINICAL PHASE	3	**PLANNED TRIAL START**	01/08/2023	**PLANNED TRIAL END**	14/09/2025