South African National Essential Medicine List
Primary Health Care Level Medication Review Process
Component: Obstetrics and Gynaecology

PHC/Adult Hospital Expert Review Committee Review of KZN Appeal: Tranexamic acid (TXA), IV, for PHC Level

Date:16 May 2023
Reviewer(s): Prof S Gebhardt
Affiliation: Stellenbosch University and Tygerberg Hospital

QUESTION: Use of tranexamic acid, IV, for the management of postpartum haemorrhage (PPH) at primary health care level.

1. Background

The updated primary health care (PHC) obstetrics and gynaecology National Essential Medicines List Committee (NEMLC) approved chapter was published on the 16 January 2023 as part of the 2022-23 PHC Standard Treatment Guideline (STG) review cycle.

Tranexamic acid (TXA), IV, was reviewed for inclusion in the PHC chapter for the 2020 review cycle for the management of PPH. NEMLC did not accept the adult hospital level expert review committee recommendation for tranexamic acid, IV, to be included in the 2020 edition of the PHC STG or in the 2022-23 PHC review cycle. However, NEMLC did recommend Tranexamic acid (TXA), IV, for the Adult Hospital Level STG and Essential Medicines List (EML).[i]

Following publication of the updated chapter (2022-23), on the 22 February 2023, the KwaZulu Natal Pharmaceutical and Therapeutics Committee through the KZN Pharmaceutical services office submitted a motivation, through electronic mail, to reconsider the NEMLC decision not to include TXA, IV at PHC level. The request from the KZN PTC included a motivation for including tranexamic acid (TXA) 1g IV (by slow injection or infusion in 200mls of N Saline over 10 minutes) in the PHC EML for the management of Post Partum Haemorrhage (PPH) (within three hours of the detection of PPH).

2. NEMLC Recommendation: 11 October 2017[i]

NEMLC Recommendation: The NEMLC did not accept the Adult Hospital Level Committee recommendation to include TXA IV on the primary health care EML. (However, inclusion on the Adult Hospital Level EML was accepted).

Rationale:

- **"The composite primary endpoint of death from all causes or hysterectomy was not reduced with tranexamic acid (534 [5·3%] deaths or hysterectomies in the tranexamic acid group vs 546 [5·5%] in the placebo group, RR 0·97, 95% CI 0·87-1·09; p=0·65)"; statistically not significant. Death due to bleeding where tranexamic acid was administered within 3 hours of birth was a secondary endpoint. The effect size was small: ARR of 0.5% with NNT of 200 (1.2% in the tranexamic acid group vs 1.7% in the placebo group).**
- **Generalisability of the results of the WOMANS Trial to the local primary health care setting was not possible, as the trial was done in an emergency hospital setting.**
- **Referral to higher level of care for appropriate management from primary level may be delayed.**

Level of Evidence: I RCT

Review indicator: Evidence of efficacy and safety in the primary care setting.

3. KwaZulu Natal (KZN) Pharmaceutical Therapeutics Committee (PTC) Motivation/Appeal Against the NEMLC Recommendation

The KZN Pharmaceutical services motivation was shared as follows and also raised that the price of TXA was incorrectly reported in the October 2017 adult hospital level ERC review.

- *The review accepts the evidence from the WOMAN trial that the use of TXA within 3 hours of a PPH diagnosis reduces death from PPH by about 30%. The effect is not there if started after 3 hours*
- *Whilst this is a significant finding, the absolute risk reduction with the use of TXA is only 0.5%, meaning you would have to give TXA to 200 women with PPH (in addition to all other standard measures) to save one further life. This is a large NNT, but PPH is a common complication (about 4% of childbirths, occurring on a daily basis at any busy delivery unit. With 1 000 000 deliveries in ZA, that is a yearly number of 40 000 women*
- *The recommendation decided against making TXA available at PHC level, because the trial was only conducted at hospital level, and there was unwillingness to extrapolate the results to the PHC setting. Thus TXA is currently listed in the hospital level EML for management of PPH, but not in the PHC EML.*
- *The review made a major error in stating that the cost of treatment for 1 woman with PPH (1g iv of TXA), was R752. The actual cost is R75 (i.e., ten times cheaper).*

The KZN PTC argued that it is reasonable to extrapolate the WOMAN trial findings to the PHC level. The pathology of PPH after vaginal delivery is the same irrespective of where the woman delivers. In hospital, surgical options for management of PPH are available whereas they are not at PHC level. Therefore, the PHC is more reliant on drugs to stop the bleeding. It could well be that the benefits of TXA would be greater at PHC level.

All women with PPH at PHC level are routinely transferred to hospital. That is why there are few PPH deaths at PHC level in South Africa, and many at hospital. In many cases there are delays of over 3 hours in referring such patients to the hospital, so that they arrive in critical condition. By the time they have arrived at hospital, TXA will no longer be of value because of the delay. But such patients could have benefitted from receiving the TXA earlier while they were still at PHC. There is no reason for concern that giving TXA at PHC level could lead to harm.

The KZN PTC suggest that the availability of TXA for the management of PPH at PHC level should be re-looked at by the NEMLC. It does not seem to make sense that women are deprived of a potentially life-saving drug, because they deliver at a PHC, rather than a hospital. The treatment guideline for use of TXA in the management of PPH would be the same as in the hospital level EML

Admittedly, the occurrence of PPH would be relatively less frequent at PHC clinics that conduct small numbers of deliveries each month. A minimal stock of TXA could be allocated to such clinics (e.g. 4 ampoules = 2 g; this could be kept in the PPH box in the labour ward) and could be carefully controlled and rotated as required by the mother hospital, to ensure that there is no wastage.

4. NEMLC Review of the KZN Appeal and Recommendation for a Way Forward

At the 30 March 2023 NEMLC meeting NEMLC deliberated the request from the KZN PTC. NEMLC recommended that the previous discussion by the Committee be revisited, as the discord between the ERC and NEMLC recommendations would justify a review of previous deliberations in response to the appeal from the KZN PTC.

NEMLC recommended that the PHC/Adult Hospital Level ERC review through a very quick search (using content experts if necessary) data available (specifically safety and efficacy on use of TXA IV outside of hospitals i.e., for PHC use even if observational).

5. PHC/Adult Summary of Recent (since the WOMAN trial) Publications with Safety Evidence on Tranexamic acid (TXA) IV for Postpartum Hemorrhage

Randomised Controlled Trials

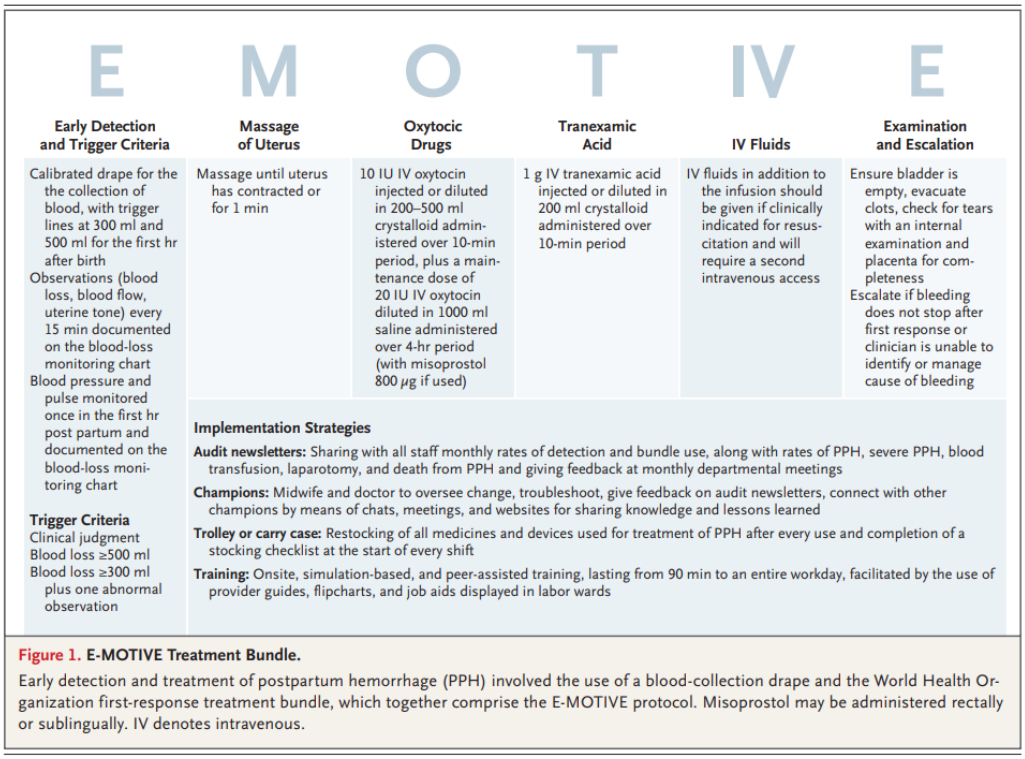
The evidence for the use of TXA in management of PPH was reviewed by the Adult Hospital ERC. The following summary is a brief description of the trial methods and quality appraisal.
E-MOTIVE (WHO) trial[ii] was an international, cluster-randomised trial to assess a multicomponent clinical intervention for postpartum haemorrhage in patients having vaginal delivery. A total of 80 secondary-level hospitals across Kenya, Nigeria, South Africa, and Tanzania, in which 210,132 patients underwent vaginal delivery, were randomly assigned to the intervention group or the usual-care group. Data for analysis were available from 78 hospitals (from 14 in Kenya, 38 in Nigeria, 14 in South Africa, and 12 in Tanzania), with a total of 210,132 patients (110,473 in the baseline phase and 99,659 in the implementation phase). Analyses were done by modified intention to treat including all randomised facilities where data were available. A Blinded Endpoint Review Committee assessed incoming data relevant to the primary outcome. The sample size calculation expected to have over 90% power to detect a 25% relative reduction in the primary outcome from 2% to 1.5% after allowing for clustering. Results were presented with Risk ratios or Risk reductions with 95% confidence intervals and was statistically significant with $p<0.001$. Compliance to the bundle was 92% in the E-MOTIVE group and 19% in the usual care group.

The intervention was the early detection of postpartum haemorrhage and treatment using the WHO MOTIVE 'first response' bundle. The bundle includes the following:

Early detection with a calibrated blood collection drape. When 500mls was noted in the drape and/or clinical assessment of PPH, which when identified was immediately given with the additional components as close together as possible:

- Uterine **M**assage,
- **O**xytocin and
- **T**ranexamic acid and
- IV fluids,
- **E**xamination of the genital tract & **E**scalation of care when needed.

The control hospitals used an uncalibrated drape and usual care.



E	M	O	T	IV	E
Early Detection and Trigger Criteria	**Massage of Uterus**	**Oxytocic Drugs**	**Tranexamic Acid**	**IV Fluids**	**Examination and Escalation**
Calibrated drape for the the collection of blood, with trigger lines at 300 ml and 500 ml for the first hr after birth Observations (blood loss, blood flow, uterine tone) every 15 min documented on the blood-loss monitoring chart Blood pressure and pulse monitored once in the first hr post partum and documented on the blood-loss monitoring chart **Trigger Criteria** Clinical judgment Blood loss ≥500 ml Blood loss ≥300 ml plus one abnormal observation	Massage until uterus has contracted or for 1 min	10 IU IV oxytocin injected or diluted in 200–500 ml crystalloid administered over 10-min period, plus a maintenance dose of 20 IU IV oxytocin diluted in 1000 ml saline administered over 4-hr period (with misoprostol 800 μg if used)	1 g IV tranexamic acid injected or diluted in 200 ml crystalloid administered over 10-min period	IV fluids in addition to the infusion should be given if clinically indicated for resuscitation and will require a second intravenous access	Ensure bladder is empty, evacuate clots, check for tears with an internal examination and placenta for completeness Escalate if bleeding does not stop after first response or clinician is unable to identify or manage cause of bleeding

Implementation Strategies

Audit newsletters: Sharing with all staff monthly rates of detection and bundle use, along with rates of PPH, severe PPH, blood transfusion, laparotomy, and death from PPH and giving feedback at monthly departmental meetings

Champions: Midwife and doctor to oversee change, troubleshoot, give feedback on audit newsletters, connect with other champions by means of chats, meetings, and websites for sharing knowledge and lessons learned

Trolley or carry case: Restocking of all medicines and devices used for treatment of PPH after every use and completion of a stocking checklist at the start of every shift

Training: Onsite, simulation-based, and peer-assisted training, lasting from 90 min to an entire workday, facilitated by the use of provider guides, flipcharts, and job aids displayed in labor wards

Figure 1. E-MOTIVE Treatment Bundle.

Early detection and treatment of postpartum hemorrhage (PPH) involved the use of a blood-collection drape and the World Health Organization first-response treatment bundle, which together comprise the E-MOTIVE protocol. Misoprostol may be administered rectally or sublingually. IV denotes intravenous.

The intervention was administered by midwives who were authorised to diagnose and treat PPH (including IV fluids and TXA, and oxytocin)

Results of the trial

The primary-outcome was a composite of severe postpartum haemorrhage (blood loss, ≥1000 ml), laparotomy for bleeding, or maternal death from bleeding. Secondary outcomes included detection of PPH and implementation outcomes, i.e., adherence to the intervention. Further outcomes were postpartum hemorrhage (defined as blood loss of ≥500 ml), death from any cause, blood transfusion for any cause, blood transfusion for postpartum hemorrhage, blood loss as a continuous variable, uterine tamponade use, intensive care unit (ICU) admission or higher-level hospital transfer, newborn death.

Composite outcome:

The composite outcome occurred in 794 of 48,678 patients (1.6%) in the intervention group and in 2139 of 50,044 (4.3%) in the usual-care group (risk ratio, 0.40; 95% confidence interval [CI], 0.32 to 0.50). This is a risk difference of 26 fewer per 1000 (2.6%), ranging from 55 to 40 fewer per 1000 for severe outcomes. For numbers needed to treat, you need to treat 37 cases of PPH using the EMOTIVE bundle to prevent one event of a severe outcome (a composite of death, laparotomy, or severe blood loss). Noting that those 37 women will require treatment for PPH regardless. The authors did not report on thrombotic events in the puerperium (not included in the trial design).

Detection of PPH:

Detection of PPH was less frequent in the Intervention group compared to standard of care. PPH (defined as blood loss of ≥500 ml) was diagnosed in 8.5% of the patients in the intervention group and in 16.7% of those in the usual care group (risk ratio, 0.51; 95% CI, 0.44 to 0.60) (NNT 12 women would need to be treated with the EMOTIVE bundle to prevent one case of PPH >500ml). Severe PPH (defined as blood loss of ≥1000 ml) in 1.6% and 4.3%, respectively (risk ratio, 0.39; 95% CI, 0.31 to 0.49) (NNT 37 women would need to be treated with the intervention rather than the control to prevention 1 case of severe PPH).

Transfusion requirements:

Relatedly, requirements for transfusion were lower in the intervention group - 1.2% in the intervention group and 1.9% of usual-care group (risk ratio, 0.71; 95% CI, 0.55 to 0.90). NNT 146 women need to be treated with the intervention to prevent a transfusion event.

Maternal deaths:

Maternal deaths are a rare event, there were 17 maternal deaths in the intervention group and 28 deaths in the usual-care group (risk ratio, 0.73; 95% CI, 0.40 to 1.31). A total of 12 and 18 of these deaths, respectively, were attributed to postpartum bleeding. NNT 4817 women need to be treated with the interception to reduce one death. Said another way the intervention results in 1 fewer death/ 10,000 women treated with the bundle of care.

The trial reported important clinical endpoints, and did not report any adverse events related to the study medication. The trialists stated "…the independent data monitoring committee monitored maternal deaths and ICU admissions as markers of serious adverse events".

As the scalability of the trial intervention is supported by the use of components that can be administered by a midwife and are accessible in facilities with fewer resources and by the local procurement of oxytocin and tranexamic acid. Risk for bias were addressed in the protocol. In summary, the scientific methods used are sound enough to recommend that improved detection of PPH AND implementing treatments using readily available and recommended medicines and intervention strategies can substantially reduce the risk of severe outcomes.

Quality of Study

Overall, the trial was well reported. The analysis plan was pre-specified in a protocol. Randomisation was performed sequentially, using a minimisation algorithm to ensure a balance of the intervention and control/usual care hospitals. The researchers minimised identification and recruitment bias by utilising broad inclusion criteria to include all vaginal births in the trial hospitals. Due to the pragmatic design of the trial, information on some clinical outcomes (postnatal haemoglobin level, anaemia, and patients' experience of care) was not collected possibly impacting reporting bias. Lack of blinding to the uncalibrated drapes used in the usual care hospitals for the purpose of gathering trial-outcome data would have influenced midwives' actions and had an impact on detection or performance bias as the observed effect of the intervention would have been known.

Trial reporting was clear and followed CONSORT reporting requirements. Two independent reviewers (N Gloeck and S Ebrahim) applied the Risk of Bias 2.0 tool for cluster trials to appraise the trial internal validity. Appraisal is done for each outcome separately, as data informing those outcomes may be gathered differently (Table 1). For the primary composite outcome, the risk of bias is 'low', as data on blood loss in both groups was objectively verified by weighing the drapes. Research staff captured a photograph of the drape, with collected blood inside it, on a weighing scale, with the weight visible in the photograph. drapes. Risk of bias for the outcomes PPH, maternal death and other secondary outcomes had 'some concerns' mostly due to lack of information about allocation concealment.

With respect to generalisability, the intervention was a bundle of calibrated drapes for detection of blood loss volumes and first-response treatments (uterine massage, oxytocic drugs, TXA intravenous fluids, examination, and escalation), i.e. although TXA was usually reserved for refractory bleeding because TXA was part of a bundle of treatment understanding of the impact of the TXA alone on post-partum haemorrhage is limited.

Table 1. Risk of Bias per outcome (Cochrane Risk of Bias tool 2.0 for cluster trials[iii])

Outcome	D1a	D1b	D2	D3	D4	D5	Overall
Postpartum hemorrhage (defined as blood loss of ≥500 ml)	!	+	+	+	+	+	!
Maternal death (any cause)	!	+	+	+	+	+	!
Blood transfusion for any cause	!	+	+	+	+	+	!
Laparotomy post delivery	!	+	+	+	+	+	!
Uterine tamponade use	!	+	+	+	+	+	!
Intensive care unit admission or higher-level hospital transfer	!	+	+	+	+	+	!

D1a = Randomization Process
D1b = Timing of identification of recruitment of participants
D2 = Deviations from the intended interventions
D3 = Missing Outcome Data
D4 = Measurement of the outcome
D5 = Selection of the reported results

+ = Low Risk

! = Some concerns

- = High Risk

The following trials included cesarean delivery

2. Pacheco et al[iv]: Tranexamic Acid to Prevent Obstetrical Hemorrhage after Cesarean Delivery

- 11,000 (uncomplicated CS) participants underwent randomization (5529 to the tranexamic acid group and 5471 to the placebo group)
- Prophylactic use of tranexamic acid during cesarean delivery did not lead to a significantly lower risk of a composite outcome of maternal death or blood transfusion than placebo
- The frequencies of thromboembolic events and other adverse events were similar in the two groups.

3. Shalaby et al[v]: Safety and Efficacy of Preoperative Tranexamic Acid in Reducing Intraoperative and Postoperative Blood loss in High-risk Women Undergoing Cesarean Delivery: A Randomized Controlled Trial

- The estimated blood loss was significantly higher in the placebo group when compared to TXA group (896.81 ± 519.6 vs. 583.23 ± 379.62 ml, P < 0.001)
- Preoperative TXA is safe and effective in reducing blood loss during and after high-risk cesarean delivery.

4. Sentilhes et al[vi]: Tranexamic Acid for the Prevention of Blood Loss after Cesarean Delivery (Multicenter, Double-Blind, Randomized, Controlled trial)

- TXA treatment resulted in a significantly lower incidence of calculated estimated blood loss greater than 1000 ml or red-cell transfusion by day 2 than placebo
- Thromboembolic events in the 3 months after delivery occurred in 0.4% of women (8 of 2049) who received tranexamic acid and in 0.1% of women (2 of 2056) who received placebo (adjusted risk ratio, 4.01; 95% CI, 0.85 to 18.92; P = 0.08). [but only 58.8% (TXA) vs 59.1% (placebo) received anticoagulant prophylaxis after the surgery].

5. The Impact of Early Outcome events on the Effect of Tranexamic Acid in Post-partum Haemorrhage: An Exploratory Subgroup Analysis of the WOMAN trial. (A Sub-group analysis of the WOMAN Trial[vii]**)**

- After excluding deaths from exsanguination at increasing time intervals following randomization, there was a significant reduction in the risk of death due to bleeding in the TXA acid group (RR = 0.41; 99% CI 0.19–0.89).

6. WOMAN II trial[viii]: Tranexamic acid for the Prevention of Postpartum Bleeding in Women with Anaemia: an International, Randomised, Double-blind, Placebo Controlled Trial.(6)

- Ongoing (started recruiting in 2018)
- Aim to recruit 10 000 women

New Trials

7. IM WOMAN trial[ix]: Tranexamic Acid by the Intramuscular or Intravenous route for the Prevention of Postpartum Haemorrhage in women at increased risk: a Randomised, Placebo-controlled trial.

- Recruitment has not begun

6. Cost and Economic Considerations

The current pricing for Tranexamic Acid; 500mg/5ml; injection; 5 ml is R37,60.[x] Therefore a 1-gram dose would cost R75,20 (2 x 500mg vials).

The price was incorrectly stated in the 2017 review as the Pack Size was not accounted for correctly (i.e., the price should have been divided by 5 as there were 5 vials in the box). At the time, the contract circular[xi] price was R376 for Tranexamic Acid, 100mg/mL, injection, 5ml (pack of 5). One injection at that time in State would have cost R75.20**.** The KZN motivation of an error in the price of tranexamic acid as included in the review has been affirmed.

Economic Considerations

An economic evaluation[xii] of the WOMAN trial in Nigeria and Pakistan concluded that early treatment of post-partum haemorrhage with tranexamic acid is highly cost-effective in Nigeria and Pakistan, and is likely to be cost-effective in countries in sub-Saharan Africa with similar incidence of PPH. It is a WHO essential medicine for PPH at all levels of care ('Early use of intravenous tranexamic acid (within 3 hours of birth) in addition to standard care is recommended for women with clinically diagnosed postpartum haemorrhage. Regardless of the level of health system resources, TXA should be recognized as a life-saving intervention and be made readily available for the management of PPH in settings where emergency obstetric care is provided'.

7. Summary & Conclusion

In summary the following should be noted:

- Obstetric haemorrhage kills more than 200 women annually in SA. [xiv]

- Postpartum haemorrhage (PPH) is a common birth complication that typically affects 2–4% of vaginal deliveries and 6% of caesarean deliveries.[xiii]

- As PPH remains a main cause of maternal death and morbidity it would be imperative to implement TXA IV at PHC level especially since late administration (after 3 hours) does not give any benefit and might be detrimental to outcomes for the patient.

- NEMLC indicated concerns regarding the generalisability of the hospital level WOMAN Trial reviewed in 2017 to PHC level. It can be argued that there is no fundamental difference in initial management or pathology between these two levels of care for the indication of TXA, IV for PPH.

- It was previously raised that availability of TXA IV at lower levels of care might delay referral to higher levels of care. It should be noted that clinics would refer all women with significant PPH and TXA IV could be part of the initial management while awaiting transfer. The current pricing is R37,60 for Tranexamic Acid; 500mg/5ml; injection; 5 ml. (May 2023 Master Health Products list) or R75,20 per 1gram dose. As a comparison the price for syntometrine and oxytocin combination is R27,85 and the price of 10U of oxytocin is R15,25.

- Emergency referrals from Community Health Centres (CHC)s or district hospitals are a concern. The saving mothers 2017-2019 executive summary shows that as 46.8% of women who died were managed at some point at a CHC with 2.9% dying at CHCs (referral problems 1%).[xiv]. However, individual case review of Obstetric haemorrhage cases suggest otherwise; as several patients waited a long time for an ambulance and died on the way or shortly after arrival at a hospital level. This raises concern regarding diagnosis and timely case management.

- TXA, given within 3 hours of PPH, seems to be effective in reducing the blood loss. According to WHO recommendation, all interventions (oxytocin; uterine massage and TXA) should be given concurrently and not sequentially.[xv]

- The non-availability of TXA at primary care (where most deliveries in South Africa takes place) potentially reduces the impact of TXA when reserved for hospital level. One modelling article in sub-Saharan countries was identified with supporting results for availability of TXA treatment at lower levels of care: The study showed that with tranexamic acid availability at hospital level only, less than 2% of the PPH mortality would be reduced.[xii] However, if tranexamic acid were available in the home and clinic settings for PPH prophylaxis and treatment, a nearly 30% reduction (nearly 22,000 deaths per year) in PPH mortality is possible.[xvi]

- The WHO E-MOTIVE trial[ii] has shown that a bundle of care including detection of blood loss using specific drapes followed by TXA along with uterine massage, oxytocin, given by midwives at district hospital level reduces the risk of severe PPH by 61% (95 CI ranging from 69% to 51%) reduction, or a NNT of 37 women to benefit from the intervention. The results of this study can be extrapolated to CHC/Midwifery Obstetrics Unit (MOU) level, as all the interventions in the trial were given by midwives without intervention from a doctor,[ii] and all women with a significant bleed will be urgently transferred to the next level of care, so further management will be under doctor or specialist care.

- The E-MOTIVE bundle has been included in the updated version of the Maternity Care Guidelines for SA, which is under review for publication. Based on the evidence it is suggested the PHC STG is aligned in recommendation.

Author affiliation and conflict of interest details: SG has no interests pertaining to tranexamic acid.

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Secretariate Support: M Reddy

PHC/Adult ERC Recommendation: 8 June 2023

The PHC /AHL ERC supports the use of tranexamic acid (TXA) 1g IV (by slow injection or infusion in 200mls of N Saline over 10 minutes) for PPH for all levels of care as part of a bundle of care that includes early detection, uterine massage and oxytocin administration.

NEMLC Recommendation: 20 July 2023

NEMLC supports the use of tranexamic acid (TXA) 1g IV (by slow injection or infusion in 200mls of N Saline over 10 minutes) for PPH for all levels of care, which may be initiated by a nurse, but only with prior approval of a medical practitioner.

Version	Date	Reviewer(s)	Recommendation and Rationale
Initial	20 July 2023	SG, MM, TK, SE, TG, MR	NEMLC supported the use of tranexamic acid (TXA) 1g IV (by slow injection or infusion in 200mls of N Saline over 10 minutes) for PPH for all levels of care, which may be initiated by a nurse, but only with prior approval of a medical practitioner.
First Update	30 November 2023	SG, MM, TK, SE, TG, MR	In the initial version of the evidence summary two independent reviewers applied the Risk of Bias 2.0 tool for cluster trials to appraise the E-MOTIVE trial internal validity. For the primary composite outcome (PPH), the risk of bias was rated as 'high', for the way blood loss was measured because the article mentioned that uncalibrated drapes were used in the control hospitals to obtain data on blood loss versus calibrated drapes in the intervention group. Following publication of the initial version of the evidence summary a study investigator clarified that the way the blood loss was measured was identical in the intervention and control groups. The calibration on the drapes was irrelevant to this measurement for informing the primary outcome. In both groups the blood loss was objectively measured by research staff, by taking the drape, whether calibrated or not, and weighing it on a scale. It was the scale weight that determined the blood loss measurement for the purpose of determining the frequency of the primary outcome. In every case, for data verification, photographic evidence was provided of the labelled drape on the scale, with the scale reading visible in the photo. If there was no photographic verification, the case was not included in the data. The calibration of the drapes in the intervention sites was part of the intervention, enabling the health workers to diagnose PPH earlier. The calibration was not used for determining the frequency of the primary outcome. The risk of bias for measurement of the outcome of postpartum haemorrhage was therefore revised from high to low risk.

			Recommendation retained.

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