Pilot Study to Test Outcome Questions for the WOMAN-2 trial of tranexamic acid for the prevention of postpartum haemorrhage

Protocol

STUDY OVERVIEW

This protocol describes a pilot study to test a draft questionnaire for a subset of secondary outcomes in the future WOMAN-2 Trial. The WOMAN-2 Trial is a randomised, double blind, placebo-controlled phase III clinical trial testing the effects of giving Tranexamic acid (TXA) to women with anaemia who have just given birth vaginally in Africa and Asia. The primary outcome of the WOMAN-2 trial is postpartum haemorrhage. Secondary outcomes will include a clinical outcomes as well as a series of participant reported outcomes related to maternal health and wellbeing. To ensure the suitability of the questions used to measure the participant reported outcomes, it is necessary to pilot test them in advance of their use in the WOMAN-2 Trial.

The value of conducting this pilot study is to ensure that the questions included in the participant reported outcomes questionnaire will be effective at answering the relevant trial research questions. This pilot study intends to verify that each question is clear, understood by participants in the same way the trial team understands them, culturally appropriate, translated correctly, and is able to measure what it intends to measure.

This pilot study will be conducted in a selection of hospitals which will be conducting the WOMAN-2 Trial in Nigeria, Pakistan, and Uganda. The pilot study population will include participants similar to those to be included in the WOMAN-2 Trial: women who are anaemic, and having given birth. Participantswill take part in one interview which includes answering questions from the draft participant reported outcomes questionnaire. A small subset of participants enrolled in this pilot study will also take part in a cognitive interview directly following the questionnaire to learn how they understood the questions.

Overall aim of project

To pilot test the suitability of the draft participant reported outcomes questionnaire intended to be used within the WOMAN-2 Trial.

Specific objectives of project

- Assess whether items would address the relevant aspects of outcomes and experiences
- How is each question understood by participants?
- Does the research team understand each question in the same manner?
- Are the translations of each question accurate and appropriate?
- Are the questions, answer choices, and directions clear to respondents?
- How differently do participants with different birth outcomes answer the questions?

METHODOLOGY

The draft questionnaire will be developed and “outcomes” questions will be informed by a literature review focusing on the impact of anaemia on physical, emotional and mental well-being. The draft questionnaire will be refined through discussions with obstetricians and women with different birthing experiences. The final draft questionnaire will then be translated in collaboration with partnering sites in Nigeria, Pakistan, and Uganda. A selection of WOMAN-2 Trial sites will be used to pilot the questionnaire. Anaemic women at the selected sites who plan to give vaginal birth or who

have recently given birth with be approached and asked to participate in this pilot study to help test these draft questions, which will take place as one interview. The interview will be conducted just before women are discharged from the hospital or anytime up to 42 days after giving birth. Administration of the pilot questionnaire is expected to take about 15-30 minutes. A short demographics form will be completed to document key health and birth information about each woman. A range of women with different birth outcomes will be included to understand how women with different birth experiences, in the various settings, react to and answer questions.

A small subset of respondents will also be asked to participate in a cognitive interview directly following administration of the questionnaire. This will include asking participants how they understood the questions, their thoughts as they listened to and answered the questions, their opinions about questions and the answer response choices, and any other thoughts they would like to share about the questionnaire. Cognitive interviews are expected to take about 30 minutes. Voice recording for a selection of the interviews will be done where participants have given consent for this.

All potential participants will be provided with both written and verbal information about the study. They will be reassured that participation is totally voluntary and non-participation will not impact their care in anyway. Also, they will be informed that they can withdraw at any time. Those women who are willing to participate will be asked to provide written informed consent. In the event a woman cannot read or write, her consent will be independently witnessed.

Much of the information gathered from the pilot study will be analysed in real time as this pilot is intended to be a dynamic study, changing as results are understood. For example, if after the first several interviews it is evident that one question is not understood well by participants, it will be revised and the new question will be included.

The number of participants to be enrolled for this studywill be dynamic and will depend on how women answer draft questions and what types of issues are identified during the pilot. Enrolment is expected to be between around 30-300 women.

Results from the pilot will be analysed quantitatively and qualitatively. Quantitative analysis will examine which answer choices are selected or not selected, ceiling or floor effects, and if different birth experiences result in different answer choices selection. Qualitative analysis will include examining how respondents understood the questions, and suggestions for improvement in questions, answer choices, wording, and translations. Results of the analysis will inform the design of the final questionnaire to be included in the WOMAN-2 Trial.

Participant responses to the draft questionnaire will be captured on the draft questionnaire form. Information about each participant's health and birth status will be documented on a demographics form. For those women participating in cognitive interviews, results will be documented on a cognitive interview capture formand voice recordings made for a selection of interviews. Voice recordings may be transcribed and translated. Data will be entered into a database in London at the Clinical Trials Unit (CTU). Data will be analysed in real time, and also after the study is completed.

Questionnaire Topics

Physical State& Symptoms of Anaemia

- Ability to perform activities
- Pain
- Fatigue
- Energy level
- Dizziness
- Headache
- Strange or fast beating heart
- Shortness of breath

Feeling state

- Sad
- Confused/forgetful
- Frustration
- Difficulty concentrating

Exercise ability

- Pre & Post breathlessness test
- 6 minute exercise test

Opinions on how questions were asked

- Visual analogue scales – different methods
- Understanding of questions
- Suggestions for improving questions

CONFIDENTIALITY AND DATA STORAGE

Each woman will be given an identification number for her study participation. The study identification number will be written on the study forms (demographics, pilot questionnaire, and cognitive interview capture form). The consent form will contain the participant's full name. A link log will be used to link each participant's name to her participant identification number.

Data captured on forms and audio recordings will be stored securely in locked cabinets at the participating hospitals. Data will also be stored at the CTU in London in locked cabinets and in a password-protected database. Once the pilot study is completed, the data will become a part of the WOMAN-2 Trial documentation, and will be subject to the data storageprocedures for the WOMAN-2 Trial.

RISKS

Women who agree to enrol in this pilot study will be agreeing to answer a questionnaire soon after giving birth. Women who have recently given birth will be tired and recovering. Answering a questionnaire might be uncomfortable. This questionnaire will also be asking women about their mood, feelings, and physical abilities in light of just having given birth. This might highlight feelings of sadness or concern for some women. The physical process of answering the questions might also contribute to a woman's physical or mental tiredness.

If a woman is feeling too tired or uncomfortable to answer the questions in the pilot study, she can stop at any time. She will be told this at consent and before starting the questionnaire. Staff administering the questionnaire will be trained to be sensitive to each woman's needs, look for signs of discomfort, and how to respond in those situations. Written into the pilot questionnaire are check points to ask if the respondent is willing to continue. If a woman is particularly upset, triggered, or would like psychological support, with her permission, her doctor will be asked to arrange appropriate care or referral.

BENEFITS

There may not be a direct benefit to women who participate in this study. Women may be pleased that they are able to contribute to improving the quality of a future study which will look at whether tranexamic acid prevents postpartum haemorrhage and improves maternal health and wellbeing outcomes.

PROJECT TIMELINE

Pilot testingwill begin in Pakistan once LSHTM and the local Pakistan site Ethics Committees give a favourable opinion. Nigeria will be the second country to begin pilot testing, followed by Uganda. Exact timelines depend on the local ethics committee review cycles. The pilot is expected to start as early as the end of March or April 2018. The pilot is expected to last from one to several months, and this will depend on how women respond to questions. This pilot study will be conducted while other preparations from the WOMAN-2 Trial are ongoing.

Investigators

Overall Study Principal Investigator	Haleema Shakur-Still
LSHTM Co-investigators	
	Lori Miller
	Ian Roberts
	Phil Edwards
	Katherine Ker
	Danielle Beaumont
Local Pakistan Principal Investigator	Rizwana Chaudhri
Local Nigeria Principal Investigator	Bukola Fawole