NIHR Global Health Research Group
on Stillbirth Prevention and Management in Sub-Saharan Africa
at The University of Manchester

**PROTOCOL**

# Feasibility and acceptability of an antenatal care package to improve birth outcomes in subsequent pregnancies following stillbirth: Study protocol

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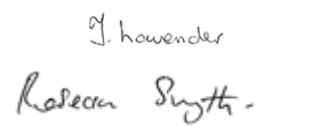

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**GLOSSARY OF TERMS**

1. Feasibility
   To determine whether a project or system is desirable or practicable by examining the time and money commitment, the researcher's expertise, availability of subjects, facility and equipment, cooperation of others and the ethical considerations (Burns and Grove, 2009:701; Chambers Concise dictionary,2010).
2. Acceptability
   In the context of clinical trials, this means that participants agree to participate in the study and remain involved in the study until completion.
3. Stillbirth
   A baby born dead at 28 weeks gestation or more, with a birth weight of 1000grams or more or a body length of 35cm or more (WHO, 2019)
4. Standard Antenatal Care
   The care provided by skilled health care professionals to pregnant women in order to ensure the best health conditions for both mother and baby during pregnancy; to reduce maternal and perinatal morbidity and mortality both directly through detection and treatment of pregnancy related complications, and indirectly through the identification of women and girls at increased risk of developing complications during labour and delivery (WHO, 2016). The WHO guideline recommends a minimum of 8 visits, first visit being at 12weeks.
5. Specialised Antenatal Care
   Elements of prenatal care given to specific groups of women over and above that given as standard antenatal care, designed to improve the quality of antenatal care provision and thereby reduce the risk of pregnancy complications, including stillbirth and neonatal death and give women a positive pregnancy experience.
6. Psychosocial support
   Support which helps individuals and communities to heal the psychological wounds and rebuild social structures after an emergency or a critical event. It can help change people into active survivors rather than passive victims (http://www.unicef.org).
   This is an approach to victims of disaster, catastrophe or violence to foster resilience of communities and individuals. It aims at easing resumption of normal life, facilitate affected people participation to their convalescence and preventing pathological consequences of potentially traumatic situations (www.definitions.net/definition).
7. Adverse Event
   Any untoward medical occurrence in a participant recruited to a research study, including occurrences which are not necessarily caused by or related to the intervention.
8. Community Engagement and Involvement/ Public Patient Involvement
   Research being carried out 'with' or 'by' members of the public rather than 'to', 'about' or 'for' them. This includes, for example, working with research funders to prioritize research, offering advice as members of a project steering group, commenting on and developing research materials and undertaking interviews with research participants (INVOLVE, 2012).

## 2) INTRODUCTION

Annually, there are at least 2.6 million stillbirths worldwide, 98% of which occur in low and middle- income countries of which a vast majority are preventable. The cause of stillbirth can often be complex as there are many contributing and interacting factors. One such factor is the increased risk of stillbirth in subsequent pregnancies after a previous pregnancy ended in stillbirth. However, there is no currently defined pathway for care in pregnancy following stillbirth in low and middle-income countries. Furthermore, little attention has been given to intervention studies in this population; in particular looking at ways women can be supported in a subsequent pregnancy to prevent future perinatal deaths.

This study will examine whether it is possible to conduct a large scale research study testing a specialised antenatal clinical service with psychosocial support and preparation for birth for women following stillbirth to improve birth outcomes. The specialised antenatal clinical service will be designed to improve the quality of antenatal care provision, reduce the risk of pregnancy complications, including stillbirth and give women a positive pregnancy experience. A psychosocial support and preparation for birth programme will be developed to enhance women's pregnancy experience and help women approach birth positively.

If this study demonstrates feasibility of the intervention and proposed trial, and acceptability of the intervention, with or without minor amendments we will seek funding for an intervention study to determine the effectiveness of a specialised antenatal clinical service for women who have experienced a previous stillbirth.

## 3) BACKGROUND

The World Health Organization (WHO) defines stillbirth as a baby born dead at 28 weeks gestation or more, with a birthweight of ≥1000 g, or a body length of ≥35 cm (WHO 2019). In 2015, globally the stillbirth rate was 18.4 per 1000 total births, compared with 24.7 stillbirths per 1,000 total births in 2000 (Lawn et al 2016). Most of the world's annual 2.6 million stillbirths occur in low and middle-income countries (98%), with three quarters in

sub-Saharan Africa and south Asia (Lawn et al 2016). Although stillbirth rates have decreased, the average annual rate of reduction of stillbirths (2.0%) has not matched that for either maternal (3.0%) or post-neonatal mortality of children younger than 5 years (4.5%). Importantly, reduction rates have not been uniform across the world, if reduction continues at the present rate; it will take more than 160 years before a pregnant woman in Africa has the same chance of her baby being born alive as a woman in a high-income country today (Lawn et al 2016). Stillbirth rates are presently ten-fold higher in low-income countries than in high-income countries.

There are many maternal and fetal conditions associated with stillbirth (Wojcieszek et al 2018). These conditions often co-exist and include maternal infections, non-communicable diseases, nutrition and lifestyle factors, fetal growth restriction and advanced maternal age (Lawn et al 2016), preterm labour, post-term pregnancy and suboptimal care (Flenady et al 2016). Notably, there are many studies demonstrating an increased risk of stillbirth in subsequent pregnancies following stillbirth (Samueloff et al 1993, Sharma et al 2006, Reddy 2007, Lawn et al 2009, Bhattacharya et al 2010, Abiola et al 2016, Malacova et al 2018).

Lamont and colleagues (2015) performed a systematic review of case-control and cohort studies of stillbirth reoccurrence in high-income countries. The review included over three million women, and reported a four-fold increase in the odds of stillbirth in a subsequent pregnancy. Even after adjusting for potential confounding factors, the increased risk remains. A more recent systematic review meta-analysed data from 17 cohort studies and reported that pregnancies following stillbirth are also at higher risk of additional adverse pregnancy outcomes, such as preterm birth, low birth weight and placental abruption (Malcova et al 2018). However, evidence for the reasons underpinning the recurrence risk of stillbirth remains debateable (Lamont et al 2015), particularly given that for most pregnancies the cause remains unknown (Malcova et al 2018). Critically, in high-income settings, having a previous stillbirth is the strongest risk factor for stillbirth known in early pregnancy.

Significantly, associated risk factors vary across the globe, making it important for each country to understand their local causes so that appropriate screening and treatment strategies can be implemented (Goldenberg et al 2009). To this end, we recently carried out a cross-sectional study in Bulawayo, Zimbabwe (UREC Ref 2018-4429-6165). Data were collected by reviewing finished episodes of health records for 1807 women birthing at the study site, Mpilo Central Hospital including 64 stillbirths. Maternal age (OR 1.03, 95% CI 1.00 to 1.07), history of stillbirth (OR 224.8, 95% CI 113.7 to 74.9), ambulance travel (vs non-ambulance travel) (OR 2.10, 95% CI 1.13 to 3.72), reduced fetal movements (OR 109.8, 95% CI 51.03 to 254.0) and 'other' method of birth vs spontaneous vaginal birth (OR 22.72, 95% CI 7.87 to 62.55) all gave an increased odds of stillbirth. Any antenatal care (OR 0.16, 95% CI 0.09 to 0.30), ≥ 4 ANC visits (OR 0.19, 95% CI 0.08 to 0.37), syphilis positive (OR 0.36, 95% CI 0.15 to 1.06), tetanus vaccination (OR 0.12, 95% CI 0.06 to 0.28) and gestational age (OR 0.66, 95% 0.60 to 0.71) a decreased odds of stillbirth.

Current recommendations for care in subsequent pregnancies have focused primarily on data from high-income countries (ACOG 2009, Robson et al 2006, Siassakos 2010). Heightened antenatal surveillance has been recommended for women with a previous stillbirth (RCOG 2011, Heazell and Clewlow 2015, Stillbirth Priority Setting Partnership 2015, Silver et al 2018). Priority conditions to address include pregnancy-induced hypertension; antepartum haemorrhage; maternal infections such as syphilis, malaria and HIV; and obstetric risk conditions such as multiple pregnancy and abnormal lie (Lawn et al 2009, Menezes et al 2009, Page and Silver 2017). Women often want increased antepartum surveillance and early birth in these pregnancies (Robson et al 2009) but in many cases the medical benefits of such practices remain uncertain (Wojcieszek et al 2016).

The need for specialist care should also take into account the additional psychological needs of parents during pregnancies that follow a stillbirth (Mills et al 2014, Heazell and Clewlow 2015, Burden et al 2016, Ellis et al 2016, Wojcieszek et al 2016, Shakespeare et al 2018). Notably, subsequent pregnancies are associated with high stress and anxiety for parents

(Huberty et al 2017). The potential for the long-term detrimental impact of depression, general anxiety disorder, social phobia, financial costs of additional care that stillbirth may have on the mother and her family may extend into subsequent pregnancies and parenthood (Ogwulu et al 2015, Burden et al 2016, Heazell et al 2016). Additional support from health professionals has been shown to be valued highly by parents (Mills et al 2014), as well as more opportunities to participate actively in decisions about care (Wojcieszek et al 2016).

However, we do not know whether the potential benefits of increased surveillance and preparedness outweigh the potential harm to mothers and babies (Reddy 2007, Monari and Facchinetti 2010, Robson and Leader 2010, Wojcieszek et al 2016). Wojcieszek et al (2018) in their Cochrane Review assessing the effects of different medical interventions or models of care during subsequent pregnancies found there to be insufficient evidence to inform clinical practice. Therefore, there is little guidance regarding care such women should receive in their subsequent pregnancy. The authors recommending the urgent need for well-designed trials addressing this question. Importantly, interventions need to be provided within a trial setting, as any intervention needs to be monitored to ensure the approaches used reduce stillbirth and improve birth outcomes in the next pregnancy without increasing morbidity from unnecessary interventions (Lamont 2015).

## 4) STUDY OBJECTIVES

### 4.1 Aim:

To assess the feasibility of a full-scale evaluation trial to assess the effectiveness of specialised antenatal clinical service for women with subsequent pregnancies following stillbirth to improve birth outcomes for women in Zimbabwe.

### 4.2 Objectives

4.2.1. The objectives for the feasibility study are to:

- Develop a specialist antenatal clinical service for the management of pregnancy subsequent to stillbirth for women

- Assess the acceptability, implementation and uptake of the proposed antenatal clinical service. Components of which include: (i) specialised antenatal clinical care and (ii) psychosocial support and preparation for birth.
- Explore impacts of the research on practice / services and delivery of the intervention
- Assess recruitment, retention, compliance of women in the study

4.2.2. To prepare for a full-scale evaluation, we will also:

- Define the most appropriate research design for a full-scale evaluation trial
- Choose the most appropriate primary and secondary outcomes to assess the effect of the intervention in a full-scale trial
- Assess the acceptability and burden associated with data collection for participants.
- Use data to assess the sample size required for a full-scale trial
- Determine the feasibility of an economic evaluation, through an exploration of key resources associated with implementing the intervention and how these may be reliably captured.

4.2.3. To synthesise all feasibility, acceptability and uptake data, to develop a full trial protocol at the end of the study.

## 5) STUDY DESIGN & PROTOCOL

### 5.1 Methodology and methods

A mixed methods approach will be used throughout this hospital-based feasibility study designed in accordance with MRC framework for Developing and evaluating complex interventions (MRC 2008). The pragmatic paradigm, which has gained increasing popularity amongst healthcare researchers in recent years, will inform research design for this study. This approach, often termed the 'third way' emerged in response to the inherent limitations of traditional paradigms, including post-positivism and constructivism, in fully addressing multifaceted research questions (Tashakkaori and Teddlie 1998). The pragmatic approach has intuitive appeal for health-care research as rigid adherence to any particular

philosophical stance is rejected and the emphasis is placed on the research question and how best to address it (Armitage 2007). Methods of data collection and analysis are selected according to the likelihood of providing insight into the question (Creswell 2003). Pragmatism underpins the use of mixed methods research, accepting qualitative and quantitative methods either in parallel or sequential stages (Tashakkaori and Teddlie 1998, Creswell 2003). Advocates of mixed-methods research argue that this integration of approaches enhances the quality of many studies, increasing the breadth and depth of enquiry into complex social phenomena (Tashakkaori and Teddlie 1998).

For a full-scale evaluation, individual randomisation would be undesirable due to the risk of contamination between the trial arms and the organisational-level changes required by the intervention. A stepped-wedge (one-way crossover) design in which the intervention is rolled out in phases, the order determined at random but all clusters receiving the intervention by the end of the trial, is currently considered as the most appropriate design. For feasibility, a pre and post-cohort design, over 12 months, will be conducted to allow implementation of the intervention in the study site and assessment of the feasibility of a stepped wedge approach.

**5.2 Setting**

The study will take place in a health facility in the metropolitan province of Bulawayo in Zimbabwe. MPilo Central Hospital is the largest hospital in Bulawayo, and second largest in Zimbabwe after Parirenyatwa Hospital in Harare. Mpilo is a public hospital and referral centre for the Matabeleland North, Matabeleland South and Midlands provinces of Zimbabwe. Births per year exceed 9,000. The hospital is a teaching hospital for obstetric care providers and centres for research and specialised care. Data from our recently performed cross-sectional study (UREC Ref 2018-4429-6165), confirms women in a subsequent pregnancy following stillbirth book for antenatal care between 18-35 weeks gestation (median 26 weeks).

**5.3 Participants**

During the recruitment periods, we will approach as many eligible women meeting the inclusion criteria as possible who are currently pregnant and who have experienced a stillbirth previously to explore (i) their experiences of the current antenatal care provided at the study site, (ii) the proposed antenatal clinical service and (iii) pilot data collection tools.

We estimate over a two-month period 25-30 women will be eligible to join the study. Given a refusal rate of 25% we envisage approximately 20 women per study recruitment phase (2 month period) will be recruited, giving a total of 40-50 women maximum (approximately).

Phase 1 (Pre-implementation/control phase): we will recruit for a two month period, we estimate approximately 20 pregnant women who have experienced a stillbirth previously having the current pattern of antenatal care at the study site in the time period prior to the introduction of the proposed antenatal clinical service will be recruited.

Phase 2 (implementation/ intervention phase): we will recruit for a two month period, giving an additional 20 pregnant women (maximum) experiencing the proposed antenatal clinical service for their pregnancy care (study intervention) will be recruited.

A maximum of 30 health workers (midwives, nurses, obstetricians, and support staff), and other hospital staff, including administrators, involved in the care of pregnant women with a history of stillbirth will be recruited in Phases 1 and 2 to contribute to all aspects of the research including refinement, implementation and evaluation of the intervention.

**5.4 Study Phases:**

**5.4.1 Phase 1: (Pre-implementation - control phase; months 1-7)**

Women recruited during the control phase will have existing care provided for women with subsequent pregnancies following stillbirth. There is no current defined pathway for care in pregnancy following stillbirth. The control phase of the study will provide clearer

understanding of usual care in the study site; refine content and delivery of the intervention and pilot data collection tools for the subsequent trial.

- A group comprising of women having the current standard of antenatal care at the study site will be recruited as controls to explore experiences of standard antenatal care, worries in pregnancy and perceptions of preparation for childbirth by completing questionnaires at the beginning and towards the end of their pregnancy (study months 1-7 of Phase 1).
- A sub-sample of women will also be invited to attend focus group interviews or individual interviews, whichever they prefer, at the end of their pregnancy to capture pregnancy experiences, including impacts of the intervention (study months 1-7 of Phase 1).
- Health workers (midwives, nurses, obstetricians, and support staff), and other hospital staff, including managers and administrators, will be invited to attend focus group interviews to contribute to refinement of the intervention and identify areas requiring a change of practice in the existing antenatal clinic area. The focus group interviews will identify the needs for education and training of staff and establishing care pathways for women attending the study site in a subsequent pregnancy following stillbirth (study month 1).
- Specialist antenatal clinical care staff will be identified to run the specialist clinic and provide psychosocial support and delivery of birth preparation information needs to the women in Phase 2 an obstetrician and two midwives and one support worker with an interest in this topic will be required (study month 2).
- Specialist antenatal clinical care staff will attend a training workshop (content based on existing educational resources, to be refined during Phase 1) to introduce the intervention, raise awareness of women's needs and identify areas requiring a change of practice in the existing antenatal clinic area (study month 2).
- Health workers (midwives, nurses, obstetricians, and support staff), and other hospital staff, including managers and administrators, directly involved in the

intervention will be asked to compete a staff experience questionnaire at the end of Phase 1 (study month 12).

- The proposed intervention has been informed by exploratory work from NIHR Global Health Research Group on Stillbirth Prevention and Management in Sub-Saharan Africa, and the Lugina Africa Midwives' Research Network (lamrn.org). The local Zimbabwe stillbirth Community Involvement and Engagement group, local women who have experienced a stillbirth, will be asked to contribute to the refinement and implementation of the proposed antenatal clinical service (July/August 2019).

**5.4.2 Phase 2: (Specialised antenatal clinical care with psychosocial support and preparation for birth – intervention phase); months 4-12)**

The proposed specialised antenatal clinical service will be designed to improve the quality of antenatal care provision, reduce the risk of pregnancy complications, including stillbirth and give women a positive pregnancy experience. The clinic will comprise two major components: specialised antenatal clinical care and psychosocial support and preparation for birth. Women will be considered high risk, have continuity of carer, an individualised structured care plan and regular antenatal appointments. The clinic will adhere to guidelines set out by WHO Recommendations on antenatal care for a positive pregnancy experience (WHO 2016). A psychosocial support and preparation for birth programme will be developed to enhance women's pregnancy experience and help women approach birth positively. The programme will comprise specialist antenatal classes for women including preparation for birth, and recognising and managing worry. Women will be offered the opportunity to build relationships with other women to enhance social support during pregnancy. The precise content and delivery of the programme will be finalised during this phase.

The intervention will be implemented in the study site in month 4.

- The specialised antenatal clinic will be launched at the study site. The specialist antenatal clinical care staff will initiate this with support from a research team facilitator, research assistants/midwives, and hospital staff including managers and administrators (study month 4).
- Specialist antenatal care, including psychosocial support and a preparation for birth programme will be delivered by the specialist antenatal clinical care staff, with support from the research team facilitator (study months 4-12).
- Women booking at the study site will be recruited during months 4 and 5 to explore experiences of attending the specialised antenatal clinic, worries in pregnancy and preparation for pregnancy and asked to complete questionnaires, at the beginning and towards the end of their pregnancy. A sub-sample of women will also be invited to attend focus group interviews or individual interviews, whichever they prefer, towards the end of their pregnancy to capture pregnancy experiences, including impacts of the intervention (study months 4-12).
- Monthly meetings (attended by the specialist antenatal clinical care staff, research team facilitator, hospital staff including managers and administrators) to share experiences and develop further strategies to improve clinical care practice and outcomes for women will be planned (study months 4-12).
- Health workers (midwives, nurses, obstetricians, and support staff), and other hospital staff, including managers and administrators, directly involved in the intervention will be asked to compete a staff experience questionnaire and offered the opportunity to attend a focus group interviews at the end of Phase 2 (study month 12).

## 6) STUDY PARTICIPANTS

### 6.1 Inclusion Criteria:

- Pregnant women booking at the study site for antenatal care (during Phases 1 and 2) with subsequent pregnancy following stillbirth (baby born dead at 28 weeks

gestation or more, with a birth weight of 1000grams or more or a body length of 35cm or more (WHO, 2019))

**OR**

Health workers (midwives, nurses, obstetricians, and support staff), and other hospital staff, including managers and administrators directly involved in the study intervention or who provide care of services to pregnant women at the study site.

- 18 years or over, at the time of recruitment (women).

**6.2 Exclusion Criteria:**

- Unable to give consent (women)

**6.3 Recruitment:**

Individual consent will not be sought for attendance at either the current antenatal clinic (control phase 1) or the proposed specialised antenatal clinic (intervention phase 2), as both are considered standard practice. The current antenatal clinic running throughout Phase 1 will be superseded with the specialised antenatal clinic in Phase 2 of the study period. Both will be provided for all women attending antenatal services at the study site who have experienced a previous stillbirth, irrespective of their participation in the study / questionnaire completion / focus group / individual interview participation.

Consent will be sought for data collection associated with the assessment of the feasibility of a full-scale trial, acceptability and uptake of the intervention for women and facility staff. Identification of women with a history of stillbirth will be undertaken by appropriately trained and experienced members of the clinical team and confirmation of eligibility and consenting of participants undertaken by research assistants/midwives.

**6.3.1. Women:**

Eligible women will be initially identified and approached via a member of the clinical care team at the woman's hospital booking appointment who will introduce the study. If

permission to consider the study has been granted, they will notify the research assistant/midwife to discuss the study further. Written and verbal information (available in local languages) will be supplied and potential participants will be given time to consider participation. The woman will be encouraged to discuss with family/others (if accompanying her) and provided additional opportunities to ask questions. She will be informed that her participation is voluntary and a decision not to take part in the research will have no impact on her current or future healthcare provision. Women will be given the opportunity to confirm participation at the booking visit should they wish and provided with the consent form to sign. Others will be given the opportunity to confirm participation at their next antenatal clinic appointment, where consent form completion will take place. Women will be able to withdraw up until 1 week after taking part in the interviews.

### 6.3.2. Health workers (midwives, nurses, obstetricians, and support staff) and other hospital staff, including managers and administrators:

Staff and others directly involved in the delivery of the intervention will be informed about the research during workshops facilitated by the research team at the beginning of the study. They will be invited to contact the research team directly if they are interested in participating and given a written and verbal explanation. Potential participants will be reassured that they are under no obligation to participate and can withdraw at any time up to 1 week after the focus group interview. They will be asked for permission to re-contact by their preferred method, once they have had time to consider participation and not less than 24 hours later. If the health worker or other agrees to participate, they will be provided with the planned date of the focus group interview (Phase 1 & 2). On the agreed focus group date, the research assistant/midwife will bring the study information and consent form, and will take approximately 10 minutes to discuss the study and read through the consent form with the potential participants in order to ensure that the content is well understood. A further opportunity will be provided for questions to be asked of the researchers. If the potential participant agrees to take part, they will be asked to sign the consent form.

In addition, at the end of phase 2, the health workers in the facility will be invited in writing to complete a short, anonymous paper questionnaire to assess awareness of the research, experiences of either routine antenatal care or the intervention and to capture any wider impacts on practice. The questionnaire will be accompanied by participant information, return will be taken as confirmation of consent.

### 6.4 Participants who withdraw consent:

At the point of recruitment, all participants will be informed that participation in the research is voluntary and that they can withdraw consent at any time up to the point of 1 week after the focus group discussion / individual interview without giving any reason, without their current or future care or legal rights being affected. Data collected up to the time participant leaves the study or is lost to follow up will continue to be included in the findings. Participants will be informed that no data can be removed once the findings are anonymised and sent for publication.

## 7) OUTCOME MEASURES

The key feasibility outcomes will be recruitment and retention of women in the study.

Other outcomes will include:

- Acceptability and uptake of the intervention and experiences of study processes which will be explored through questionnaires and interviews with women (Flenady et al 2016, Wojcieszek et al 2016) and healthcare staff (midwives, nurses, obstetricians, and support staff), involved with the delivery of antenatal care.
- Psychological measures:
    - **Cambridge Worry Scale** (Green et al 2003), a 16-item content-based measure specifically designed to assess the extent and content of worries in pregnancy (women).

    - **Birth Preparedness and Complications Readiness Tool** (JHPIEGO 2004), a atructured questionnaire to assess knowledge, attitudes and perceptions of preparation for childbirth (women).
- Questionnaire to assess awareness of the research, experiences of either routine antenatal care or the intervention and to capture any wider impacts on practice (women & staff).
- Clinical measures:
    - Investigator-designed case report forms will be used to collect data for women participants via patient health records (including hospital, patient-held and electronic records) and self-report (where no secondary source available): Demographic (age, ethnicity, socioeconomic status [highest level of education, occupation]) medical (history, body mass index, smoking status, medication use), obstetric history (previous pregnancies, mode of birth, outcomes), current pregnancy and outcome. Previous stillbirth data including the onset of labour, mode of birth, maternal and infant outcomes, cause of death (if known) length of hospital stay, and postnatal complications/all healthcare utilisation (for example; antenatal visits to the hospital, ultrasound scans) and access to external support will be collected. Data will be collected at recruitment and birth (study completion).
- Basic demographic data (age, job title, year qualified, area of work) will also be collected via self-report for participating health workers and support staff at recruitment (staff).
- Human and healthcare resources associated with delivering the intervention.

## 8) DATA COLLECTION, SOURCE DATA AND CONFIDENTIALITY

### 8.1. Recruitment and retention:

A participant log of women who are eligible but not invited to participate, invited to participate in the study, those recruited and any participants who leave the study before completion will be kept. Reasons for non-recruitment (e.g. refusal to participate, language

barrier) will also be recorded. Permission will be sought to collect data on reasons for non-participation from women, and health workers who have been offered participation but decline to take part. During the course of the study, reasons for withdrawal and loss to follow-up will be documented.

**8.2. Experiences of standard antenatal care (Phase 1):**

- The survey questions will be translated into the women's preferred language (Shona, Ndebele, and English). Assistance by bilingual research assistant/midwife will be provided to participants unable to read or write.
- A sub-sample of women will also be invited to attend focus group interviews or individual interviews, whichever they prefer, towards the end of their pregnancy. Discussions will be presented in the women's preferred language (Shona, Ndebele, and English) by bilingual research assistant/midwife.
- Staff experience questionnaire survey of health workers involved in the delivery of antenatal care at the end of Phase 2. Questions will be presented in English.
- Focus group interviews with health workers (midwives, nurses, obstetricians, and support staff), and other hospital staff, including managers and administrators to contribute to refinement of the intervention, establish areas requiring a change of practice in the existing antenatal clinic area, and identify the needs for education and training of staff.

**8.3 Acceptability of the intervention (Phase 2):**

- The survey questions will be presented in the women's preferred language (Shona, Ndebele, and English). Assistance by bilingual research assistant/midwife will be provided to participants unable to read or write.
- A sub-sample of women will also be invited to attend focus group interviews or individual interviews, whichever they prefer, towards the end of their pregnancy. Discussions will be presented in the women's preferred language (Shona, Ndebele, and English) by bilingual research assistant/midwife.
- Staff experience questionnaire survey of health workers involved in the delivery of the intervention at the end of Phase 2. Questions will be presented in English.
- Focus group interviews with health workers (midwives, nurses, obstetricians, and support staff), and other hospital staff, including managers and administrators to contribute to refinement of the intervention, establish areas requiring a change of practice in the existing antenatal clinic area, and identify the needs for education and training of staff.

**8.3.1. Uptake and additional impacts of the intervention on the practice and environment of care will be captured by:**

An intervention log completed by specialist antenatal clinical care staff will summarise study related activities, to determine what was done, when and by whom. This will include training, meetings, adminstration, data for additional contacts including number of contacts, time spent, mode of support (additional clinic apointment or telephone call) with women to determine uptake of the support component of the intervention.

**8.4. Psychological assessments**

Women participants will complete the psychological assessment questionnaires at the time of booking and towards the end of their pregnancy:

**8.5. Health economics**

Data will be captured to identify the key resources associated with the intervention, including:

Human resources (direct) – the intervention log as described above will be used to identify person (antenatal clinical care staff) time spent performing all aspects of the intervention, including attending training and meetings.

Indirect resources – as part of the staff experience questionnaire, clinic staff will be asked about their perceived impact of the intervention on human and other resources and any additional equipment purchased in order to deliver the intervention.

Antenatal visits and out of pocket expenses – women will be asked in the questionnaire survey to report all antenatal visits and any interventions (e.g. scans) and about any out of pocket expenses incurred related to the intervention e.g. travel costs for attending additional specialist antenatal classes.

## 9) DATA ANALYSIS AND STATISTICAL CONSIDERATIONS

### 9.1 Statistical Analysis

**9.1.1. Recruitment and retention:** Participant log data will be used to assess recruitment to targets and retention rates. A full-scale trial would be considered feasible if recruitment targets were met and a rate of 75% retention achieved. If retention is below 75% but at least 60%, we will consider whether any identified barriers could be addressed to improve recruitment and/or retention to acceptable levels and hence make a full-scale evaluation trial potentially feasible; in this situation, the success of strategies to overcome these barriers would be expected to be assessed during an internal pilot phase. Questionnaire and interview data will clarify possible barriers to recruitment and retention, in addition to assessing whether the intervention was delivered consistently and according to the clinical protocol, which will be addressed, where possible, in preparation for a definitive trial.

**9.1.2. Acceptabilty of a participation, usual care and the intervention and quality of implementation** will be explored through analysis of the intervention log, questionnaires and interviews.

Thematic analysis conducted in six recursive phases (Braun and Clarke 2006), using multiple analysts to ensure credibility; will establish participants' views and experiences of recruitment, usual care in the control phase (Phase 1), components of the intervention including psychosocial support, preparation for birth and psychological measures used. Data will also help determine appropriateness of proposed outcomes measures. Participants' views and experiences of completing questionnaires and attending interviews will contribute to evaluating the burden of trial assessments and inform data collection methods for the main trial. The views and experiences of healthcare staff delivering the intervention and others involved in care will be used to determine acceptability of the intervention and fidelity of the components as delivered in practice compared with those planned, including any impacts on wider services. This data will also identify any areas where further refinement of the intervention is needed.

**9.1.3. Psychological assessments, and clinical data**: Quantitative data will be inputted into an electronic system (REDCap). REDCap (Research Electronic Data Capture) is a secure web application used to build and manage the on-line Case Report Form (https://www.project-redcap.org/). The University of Manchester is a member of the REDCap Consortium. Outcome measures will be compared descriptively, using frequencies and percentages for categorical variables and descriptive statistics including means, standard deviations, medians and ranges for numerical variables. Data from psychological tools will be compared to determine whether characteristics, including rates of missing items/scale totals are comparable across different measures. Analysis will focus on the estimation of confidence intervals for differences between the control and intervention cohorts and the estimation of variances to inform the design of the full scale trial.

**9.2 Sample Size:**

A formal power calculation is not appropriate for a feasibility study, therefore an approximate sample size of 50 women and 30 healthcare workers has been determined pragmatically according to the accepted criteria for feasibility studies (Whitehead et al

2016). These numbers will allow implementation of the intervention in the study site and estimation of recruitment/ retention rates and uptake.

## 10) DATA MONITORING AND QUALITY ASSURANCE

### 10.1 Trial management

This study will be subject to the audit and monitoring regime of the sponsor, The University of Manchester. Formal monitoring via a data monitoring committee will not be undertaken during this feasibility study as the anticipated risk of harm is low. The existing NIHR Global Health Research Group for Stillbirth Prevention and Management in Sub-Saharan Africa at The University of Manchester Advisory Board chaired by Professor Matthews Mathai (Liverpool School Hygiene and Tropical Medicine) will provide technical support and advice on the conduct of the feasibility study and full trial. The independent Advisory Board will review the study protocol prior to commencment of the research and any amendments, receive progress updates, advise on issues arising with the study conduct and dissemination of the findings in preparation for a full trial.

The study will be managed by Professor Lavender with support from the research team and country principal investigators. A start up meeting with UK and local research teams will be held in-country (Bulawayo, Zimbabwe in Month 1) The Zimbabwe Study leads will be responsible for day to day co-ordination of trial activity from month 1-month 12, supported by research assistants/midwives, Meetings between the CI/UK research team and Country leads will be conducted via Zoom 2 weekly initially and at least monthly for the duration of the research. The wider research team, including all co-applicants and the Africa research leads, research assistants/midwives will meet bi-monthly to review progress and compliance with research governance.

### 10.2 Research Team and roles

**Professor Dame Tina Lavender**: Chief Investigator responsible for overall study management, research governance, supervision of the research. Supervise training and

supervision for delivery of the intervention, qualitative and clinical analysis, interpretation, reporting and dissemination.

**Dr Rebecca Smyth**: Chief Investigator responsible for supervising the training and supervision for delivery of the intervention, qualitative and clinical analysis, interpretation, reporting and dissemination.

**Prof Alexander Heazell:** Co investigator, advise on obstretric aspects of the research, quantitative and clinical analysis, interpretation, reporting and dissemination.

**Dr Christopher Sutton**: Co investigator, supervise analysis of the quantitative data, provide statistical advice and guidance for the design of the full trial.

**Dr Elizabeth Camacho**: Co investigator, supervise health economics and cost-effectiveness components, advice on design of economic evaluation for main trial .

**Kushupika Dube**: Principal Investigator Zimbabwe, responsible for overall study management, research governance, supervision of the research in Zimbabwe. Supervise training and supervision for delivery of the intervention, qualitative and clinical analysis, interpretation, and dissemination.

**Dr Solwayo Ngwenya**: Co investigator Zimbabwe, advise on obstretric aspects of the research, quantitative and clinical analysis, interpretation, reporting and dissemination. Responsible for supervision of training and delivery of the intervention.

**Ms Valentina Actis Danna:** Co applicant; trial manager in Manchester responsible for day to day management of the study under sthe supervision of the CI. Adminstration of REDCap, management and analysis of quantitiaitve data.

### 10.3. Safety Reporting: Adverse Event definitions and reporting

For the purposes of this study the following definitions will apply:

#### 10.3.1. Adverse events (AE)

***Definition:***

*Any untoward medical occurrence in a participant recruited to the study, including occurrences which are not necessarily caused by or related to the intervention.*

For this study the following is a list of expected maternal and neonatal adverse events which will be recorded but not reported:

**Common pregnancy related complications:**

Anaemia defined as haemoglobin level <110 g/L at booking, <105 g/L in 2$^{nd}$ and 3$^{rd}$ trimesters, <100 g/L postpartum

Hypertension

New onset/gestational diabetes

Small for gestational age fetus (Estimated fetal weight <10$^{th}$ centile by ultrasound)

Fetal malpresentation

Vaginal bleeding/APH/ placenta praevia identified on ultrasound scan

Premature rupture of membranes

Bacterial or viral infection

Labour related complications including: 3$^{rd}$ or 4$^{th}$ degree perineal tear, postpartum haemorrhage

**Common neonatal complications**

Jaundice

Feeding problems

Bacterial or viral infections

**Psychological instruments**

Any other abnormal or concerning findings arising from questionnaires will be reported by the research assistant/midwife to the CI directly and in accordance with the adverse event protocol as above.

**10.3.2. Serious adverse events (SAE)**

***Definition:***

*Any adverse event (see definition at 10.3.1) that:*

*a) results in death,*

*b) is life-threatening,*

*c) requires hospitalisation or prolongation of existing hospitalisation,*

*d) results in persistent or significant disability or incapacity*

*e)* ***Or*** *is otherwise considered medically significant by Professor Dame Tina Lavender or Dr Rebecca Smyth or Professor Alexander Heazell. (Health Research Authority, 2015)*

The following are expected serious maternal and neonatal adverse events which will be recorded but not reported for further investigation:

**Pregnancy related complications:**

Admission to hospital for anaemia.

Admission to hospital for hypertension.

Admission to hospital with new onset/ gestational diabetes

Admission to hospital for monitoring or care related to small for gestational age fetus (Estimated fetal weight <10$^{th}$ centile by ultrasound)

Admission to hospital with fetal malpresentation

Admission to hospital with vaginal bleeding/APH/ placenta praevia/premature rupture of membranes (identified clinically, or on ultrasound scan)

Admission to hospital for investigation or treatment of bacterial or viral infection

Admission to hospital for elective birth.

Prolongation of admission or readmission related to labour related complications eg perineal tears or PPH

**Neonatal complications**

Admitted to special care/neonatal unit after birth

Admission to hospital for jaundice

Admission to hospital with feeding problems

Admission to hospital with bacterial or viral infections

**10.3.3. Recording and reporting:**

**Adverse events** will be recorded in study documentation by the research co-ordinator, and collated for each participant on an Adverse Event Form at the end of the study. Adverse events will be reviewed at the end of the study by the NIHR Group Advisory Board and the Sponsor.

**Serious Adverse Events** (other than those listed above) will be recorded on a SAE report form and reported by the research assistant/midwife co-ordinator to the CI as soon as possible after becoming aware (normally within 24 hours).

**SAEs** will be reported to the to the Sponsor and Research Ethics Committee (REC) if in the opinion of Professor Dame Tina Lavender, Dr Rebecca Smyth, Professor Alexander Heazell they are:

**Related** - that is resulted from administration of any research procedures

AND

**Unexpected** –that is, the type of event is not listed in the protocol as an expected event

A **SAE** meeting these criteria with be reported in writing using the Serious Adverse Event Report as soon as possible and within 15 days of the CI becoming aware of the SAE. SAEs will be reviewed by the Sponsor using their standard criteria and a specific course of action will be recommended for the study and implemented by the Investigators.

## 11. ETHICAL CONSIDERATIONS

Ethical approval will be sought from the Research and Ethics Committee at Mpilo Central Hospital, Bulwayo, Zimbabwe in addition to administrative approval to carry out the study. The study will be reviewed by the Medical Research Council, Zimbabwe. Ethical approval will also be gained from The University of Manchester. The study will be conducted in full conformance with principles of the "Declaration of Helsinki", Good Clinical Practice (GCP) and within the laws and regulations of the country in which the research is conducted.

The death of a baby before or shortly after birth is an extremely sensitive area of maternity care with potential for women, partners, families and health workers participating in research to experience emotional distress when recalling difficult or traumatic events related to the death of their baby. However, accumulating evidence demonstrates that well-conducted research does not increase risk of harm to bereaved parents and might offer some benefits (Hynson et al 2006). Participants may become upset or distressed during contacts with the research assistant/midwife during completion of questionnaires, particularly in recalling their baby's death, care experiences, grief and current thoughts and feelings.

To ensure that study is conducted appropriately and sensitively all recruitment processes, participant information and consent forms will be produced with input from our established Community Involvement and Engagement group of local women with experience of perinatal bereavement. A study-specific distress policy will be available and followed at all times, research assistants will have a midwifery or nursing background and as experienced clinicians will have skills to deal with distressed participants.

## 12. STATEMENT OF INDEMNITY

The University of Manchester has insurance available in respect of research involving human subjects that provides cover for legal liabilities arising from its actions or those of its staff or supervised students. The University also has insurance available that provides compensation for non-negligent harm to research subjects occasioned in circumstances that are under the control of the University.

## 13. FUNDING

This study is funded through the NIHR Global Health Research Units and Groups stream, The NIHR Global Health Research Group in Stillbirth Prevention and Management at The University of Manchester

## 14. PUBLICATION POLICY

The findings of the study will be published in high-impact clinical journals (eg BJOG, BMC Pregnancy and Childbirth) with open-access where possible; costs are available to support this. The findings will also be presented at international multidisciplinary meetings including the LAMRN conference, GLOW conference and the International Stillbirth Alliance (ISA) meeting, International Confederation of Midwives triennial conference (ICM). The research team has established links with stakeholders. Using our combined experience in writing for service users and the public we will produce material for the websites and social media. Feedback to participants and local stakeholders is of key importance; therefore we will organise a local dissemination workshop in month 12. Participants, families, clinical staff, operational mangers and stakeholders including support groups will be invited to attend. A lay summary of findings will also be sent to all participants. Service-user members of the community engagement groups will be offered the opportunity and support to contribute to dissemination if they are willing.

These activities will ensure that potential beneficiaries can engage with the study progress and findings. The overall aim is to increase awareness of the topic, application of the

findings in clinical practice and reduction of the likelihood of duplication minimising future costs and burdens to funders and health systems.

Study members (those listed in this protocol and data collectors) will adhere to the following:

1. No raw data can be shared with anyone outside the core team prior to publication
2. Hard copy or electronic copies of any results cannot be disseminated beyond the immediate research team prior to publication
3. Results cannot be disseminated (written or oral) to external audiences without approval from the NIHR; this can be done through the Manchester team but requires 3 weeks' notice
4. Any press releases should be notified to the NIHR 14 days in advance of them happening
5. All publications should have a statement outlining how the data can be accessed
6. All publications should be submitted no later than 1 year after the project finishes and must contain the statement below:

   "This research was commissioned by the National Institute of Health Research using Official Development Assistance (ODA) funding. The view expressed in the publication are those of the author(s) and not necessarily those of the NHS, the National Institute of Health Research or the Department of Health".

Additionally, we will adhere to the International Guidelines: http://www.icmje.org/recommendations/browse/roles-and-responsibilities/defining-the-role-of-authors-and-contributors.html

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