Group Antenatal Care to Promote a Healthy Pregnancy and Optimize Maternal and Newborn Outcomes: A Cluster Randomized Controlled Trial

Principal Investigators: Jody Lori, PhD, University of Michigan and Dr. John Williams, Dodowa Health Research Centre

Co-investigators: Cheryl Moyer, PhD, University of Michigan

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1.0 Background and Rationale

We are at a critical time to examine new, innovative strategies to promote healthy pregnancy and optimize maternal and newborn outcomes. Generating successful strategies will require careful examination of existing service delivery models, challenging the current structure of care provision. One aspect of care, recently identified by the World Health Organization, which merits further research, is group antenatal care (GANC).

Antenatal care has the potential to play a pivotal role in ensuring positive pregnancy outcomes for both mothers and their newborns. Since ANC is widely available and attended by the majority of pregnant women in Ghana without the expected impact on birth outcomes, it is vital to examine the way antenatal health messages are delivered. Pregnant women must receive health information that is accurate and easy to understand for them to make informed choices to improve their health and the health of their baby. A critical component of all ANC is teaching women to recognize the major complications that account for the majority of preventable maternal and newborn deaths. Antenatal care provides an opportunity to promote a healthy lifestyle, to integrate positive health behaviors, and to develop a trusting relationship with a provider and the health system. Interactions during ANC provide the opportunity to identify and treat numerous problems, as well as providing a setting to improve women's health literacy. Patients must receive health messages in a manner that allows them to process and evaluate the information and ultimately use it to impact their own health.

The effectiveness of ANC depends on the multidimensional concept of health literacy. Initially considered only as a patient's ability to read and understand written information, it is now more broadly defined as a person's ability to acquire or access information, understand it, and use the information in ways that promote and maintain good health. Despite a burgeoning emphasis on health literacy in high resource countries, there are a dearth of studies examining interventions to improve health literacy in low-resource settings. Even fewer studies have examined maternal health literacy, defined as the "cognitive and social skills which determine the motivation and ability of women to gain access to, understand, and use information in ways that promote and maintain their health and that of their children''. New approaches to improve health literacy are sorely needed in countries where women and newborns continue to die from preventable causes.

Antenatal care has been delivered the same way for decades. Clinics and hospitals in low-resource countries are notorious for providing ethnocentric care, privileging northern medical values at the expense of traditional and community values. Yet health literacy is affected by the cultural context in which learning takes place, including, but not limited to, belief systems, traditions, understanding, and communication styles. Transmitting health information in a clinical setting often fails to take into account the social and economic circumstances of patients, therefore not achieving the expected impact on health behaviors. This divide has contributed to a lack of progress in reaching the most vulnerable populations. If pregnant women do not receive health messages in a comprehensible way, they cannot effectively maximize the benefits of the health system. Substantially improving women's ability to understand and utilize health information is

of utmost importance if we are to reach the global targets of 70 maternal deaths per 100,000 live births by 2030 and a neonatal mortality rate of 12 per 1000 live births set by WHO/USAID.

1.1 Ghanaian Context

In 2015, the maternal mortality ratio in Ghana was estimated at 319 per 100,000 live births – placing a woman's lifetime risk of maternal death at 1 in 74, compared to 1 in 3,800 in the United States. In 2014, while 87.3% of women in Ghana surveyed had attended the minimum standard of 4 antenatal care (ANC) visits, 27% gave birth alone or with a non-skilled attendant. Sixty-eight percent of all deaths among children under age 5 in Ghana happen before a child's first birthday, with 48% of deaths occurring in the first month of life - making the first 28 days in an infant's life crucial for survival. Only 22.8% of newborns received the recommended postnatal check-up within the first two days of life between 2012-2014 in Ghana. It should be noted that since 2008 there has been only a marginal decline (3%) in neonatal mortality within Ghana. Ghana is now one of 24 priority countries targeted by the United States Agency for International Development (USAID) to improve maternal and child health and end preventable deaths.

1.2 Scientific Premise

Research has shown community-based women's groups in low-resource settings catalyze action, provide supportive networks, educate and empower, and lead to substantial increases in neonatal survival. Women's groups at the community level have been found to devise their own culturally appropriate strategies for prevention of newborn problems, home care support, consultation and referral. Women participating in community groups in Guinea showed an increase in maternal health care-seeking behaviors; with women in community groups more than twice as likely to attend four ANC visits, seek care for signs of complications, and given birth in a health facility. A rigorous systematic review and meta-analysis of seven randomised control trials (119,428 births) found women's groups at the community level were associated with a 37% reduction in maternal mortality, a 23% reduction in neonatal mortality, and a 9% reduction in sitllbirths. [22]

While group ANC has been delivered and studied in high-resource settings for over a decade, it has only recently been introduced as an alternative to individual care in sub-Saharan Africa. Two randomized controlled trials of group ANC using a U.S group-based model verses routine care found women assigned to group care had significantly better antenatal knowledge, greater satisfaction with care, and were less likely to have a preterm birth than those in standard care. In addition, the trials showed more favorable birth, neonatal, and reproductive outcomes in the intervention groups. Although the experimental design of the studies from high-resource countries were scientifically rigorous, findings cannot be generalized to low-resource countries with low literacy rates and high rates of maternal and newborn morbidity and mortality. In sub-Saharan Africa, data from two small studies found ANC delivered in groups to be acceptable and feasible to both women and providers in Ghana, Tanzania, and Malawi. In the U.S., Australia, and the Netherlands, group ANC has improved outcomes in birth weight, preterm birth rates, satisfaction with care, and breastfeeding initiation.

2.0 Aims and Objectives

Aim 1: To quantify differences in BPCR, knowledge of pregnancy and newborn danger signs and recommended action steps.

Primary Outcomes

- Ability to identify danger signs in pregnancy (e.g. bleeding, severe headache, blurred vision, fever)
- Birth preparedness and complication readiness (e.g. saved money, identified birth facility and emergency transportation to facility, blood donor)
- Ability to identify newborn danger signs (e.g. poor suck, jaundice, difficulty/fast breathing, and convulsions)

Secondary Outcomes

- Ability to identify postpartum danger signs (e.g. increased bleeding or large clots; weakness/fainting; fever; pain in abdomen or breasts; painful urination)
- Ability to identify the recommended action steps when a problem is identified (e.g. call for help, have a plan for transportation, identify someone to accompany you to facility, identify someone to care for the family, go straight to the facility, supportive care along the way to the facility)
- Self-efficacy operationalized care-seeking history and health information knowledge

Aim 2: To assess behavioral differences in care-seeking patterns (e.g. facility birth rates, postnatal and postpartum care)

Primary Outcomes

- Attendance at 4+ ANC visits
- Facility birth
- Four postnatal/postpartum check-ups for both mother and newborn in the first 6 weeks after birth

Secondary Outcomes

- Uptake of modern family planning methods at 6 months postpartum
- Infant immunized per EPI scheduled at 1 year
- Completion of IPTp2 malaria prophylaxis during pregnancy

Aim 3: To evaluate the clinical outcomes of mothers and their newborns (e.g. decrease in maternal morbidities and perinatal and neonatal mortality)

Primary Outcomes

- Maternal pregnancy-related morbidities (puerperal sepsis, delayed postpartum hemorrhage)
- Birth outcome (stillbirth, live birth, early neonatal mortality)

Secondary Outcomes

- At least two tetanus toxoid vaccines during ANC

- Infant protected against neonatal tetanus
- Hemoglobin level upon hospital admission (dichotomized as normal or anemic (<9.5 g/dL)
- Infant birth weight (normal vs. low (<2500g)
- Repeat pregnancy within one year
- Exclusive breastfeeding at 6 months

We hypothesize that pregnant women randomized into group ANC will exhibit increased health literacy through: 1) increased BPCR, including recognition of danger signs and knowledge of how to respond to such signs; 2) higher rates of care-seeking behaviors, including seeking care for problems identified during pregnancy, higher facility delivery rates, and increased attendance at postnatal and postpartum care; and 3) better clinical outcomes for themselves and their newborns than women who received the routine, individual ANC.

3.0 Research Methods and Study Design

To accomplish our aims we propose a cluster randomized controlled trial (cRCT) in the Eastern District of Ghana. The study is designed in collaboration with the Dodowa Health Research Center under the direction of John Williams (Co-PI). Health facilities were selected based the number of deliveries and average gestational age of women in each facility and matched so that each pair of facilities are similar to each other with regard to these matching factors. For each pair of facilities, one will randomly be assigned to group ANC (intervention) and the other to routine, individual ANC (control). The locations of the chosen facilities ensure that participating facilities will be far enough apart to minimize the likelihood of cross-group contamination. The unit of randomization is the health facility stratified by site and gestational age. Cluster randomization will be produced through nbpMatching package from R software. During the study, 1680 participants will be randomized into 120 groups of 12 to 14 women of the same gestational age at the cluster site. This will result in approximately 8-10 groups per site during the study period.

3.1 Recruitment and Informed Consent

Recruitment of women will occur at individual health facilities. The research staff will work with clinic staff to identify women who meet the eligibility criteria and are healthy enough to discuss enrolling in an ANC intervention. The RA will inform health facility staff when they will be at the clinic and available to women interested in learning more about the study. Midwives will identify women who are: 1) less than 20 weeks gestation; 2) speak Dangme, Ga, Aka, Ewe, or English; 3) over the age of 15; and 4) are not considered high risk. Thus, the midwife (as a medical professional) will make the assessment that a woman is healthy enough to participate in the study.

The midwife will instruct women who qualify to should talk to the RA if they are interested in learning more about the study. Women who approach the RA will be read an approved

recruitment script. Those who are willing to participate will be taken through an informed consent procedure and will then complete baseline data collection.

Due to the high rates of illiteracy in Ghana, we will ask for a waiver of the standard written informed consent procedure. Instead, oral consent will be obtained individually from all participants and witnessed. The procedures for informed consent will include: 1) We will prepare an informed consent document in English that will be translated into Dangme, Ga, Akan, and Ewe; 2) The informed consent document will be read aloud individually to all potential participants in private; 3) The Ghanaian RA will ask the potential participant questions to ensure understanding of the research process and informed consent document and will invite questions until the information is clear; and 4) as we anticipate that many participants will not be able to read the form themselves, a witness (health facility staff) will sign that he/she was present while the benefits, risks, and procedures were read to the participant, that all questions were answered, and that women voluntarily agreed to take part in the research. A teach-back method will be used to confirm participant comprehension of the study requirements and methodology. The RA will ask potential participants to describe their understanding of the study's purpose, procedure, risks, and benefits using open-ended prompts and repeating the material until understanding is achieved.

The participant will sign, or mark with a thumbprint, the informed consent and the RA will use the camera on the encrypted tablet to take a shot of the signed/ thumbprint page. The image will be stored similar to all study data; that is, when internet connection is not available, data will be collected off-line and stored in a password protected file on the encrypted tablet. Once a connection is available, these data will be uploaded, managed, and stored on a secure server.

Participants will be given their signed/thumbprint informed consent that contains the following elements: title of project, name, credentials and institution of researcher, invitation to participate, statement that the study involves research, description of the research, description and length of participant involvement, benefits and risks, compensation, confidentiality, voluntary participation, and contact information.

3.2 Inclusion/Exclusion Criteria

Inclusion criteria are as follows: 1) willingness to participate in the study; 2) less than 20 weeks' gestation 3) able to speak Dangme, Ga, Akan, Ewe, or English; 4) over the age of 15 years; and 5) no history of medical problems that would indicate the participant might be considered "high risk" (e.g., hypertension, insulin-dependent diabetes mellitus) and thus requiring a more individualized approach to care.

In the eastern region, 10.4% of females age 15-49 have never attended school and only 15.7% percent have completed secondary school or higher. Thus, we will not limit participation based on literacy, however we will control for years of education and literacy status in the analysis. This is a study of an intervention for pregnant women to improve maternal and newborn outcomes; thus no males will be included.

3.3 Data Collection and Measures

All quantitative data will be collected by trained RAs using encrypted and password protected tablets and the REDCap secure web application for data collection database management. Redcap, a secure web application, is geared to support online or offline data capture for research studies. When internet connection is not available, data will be collected off-line and stored on the encrypted tablet. Once a connection is available, these data will be uploaded, managed, and stored on a secure server.

No data will be collected by clinical providers. Data collection will occur at five time points in both intervention and control arms:

1. Time 0: at ENROLLMENT (in person)
2. Time 1: at THIRD TRIMESTER (in person)
3. Time 2: POST BIRTH up to 6 weeks after delivery (in person)
4. Time 3: SIX MONTHS POSTPARTUM (by phone)
5. Time 4: ONE YEAR POSTPARTUM (by phone)

1) T0: The baseline session occurs immediately following the consent process and will be held for approximately 1 hour. Data will be collected by trained RAs using a structured survey; medial information will be self-reported, and thus, are not protected health information (PHI).
2) T1: This session will occur at the third trimester of pregnancy and will last 45 – 60 minutes. Data will be collected by trained RAs using a structured interview and retrieving data from the ANC card. Data collected from the ANC card are PHI and will be protected.
3) T2: This session will occur in the period immediately to 6 week after delivery and will last 45 – 60 minutes. Data will be collected by trained RAs using a structured interview and information from ANC cards on maternal and newborn clinical outcomes using a pre-determined set of indicators.
4) T3: This session will occur 6-months postpartum; data will be collected via phone by a trained RAs using a structured interview. This session will take approximately 20 - 30 minutes.
5) T4: This session will occur 1-year postpartum; data will be collected via phone by a trained RAs using a structured interview. This session will take approximately 20 - 30minutes.

During all visits midwives will record Clinical Health Related Outcomes (Place of birth, hemoglobin levels, newborn birth weight, maternal & newborn morbidities, stillbirth, postpartum visit within 2 days post birth) on the women's ANC card. These data will be collected by the RA during all study visits except baseline.

Measures

Time Point	Domain	Data collection
T0 – Baseline	**Demographic Characteristics** (Age, gravida, living children, marital status, age at marriage, pregnancy history, medical history)	Face-to-face Survey
	Self-efficacy	
	Recognize problems and understands health information	Face-to-face Survey
	Care-seeking history	Face-to-face Survey
	Educational Background	
	Level of Education	Face-to-face Survey
	Prior Knowledge	
	Ability to identify danger signs/BPCR	Face-to-face Survey
	Health Literacy Skills (understanding, engagement with health system)	Face-to-face Survey
	Ecological Influences (social support, community and family resources)	Face-to-face Survey
T1 – Third trimester	**Comprehension of Stimuli** (identification of danger signs, BPCR)	Face-to-face Survey
	Self-determination	
	Intent to use family planning / preparation for birth	Face-to-face Survey
	Two or more tetanus toxoid vaccines / Completion of ITP_2 malaria prophylaxis	ANC Card
T2 – Post birth	**Clinical Health Related Outcomes** (Place of birth, hemoglobin levels, newborn birth weight, maternal & newborn morbidities, stillbirth, postpartum visit within 2 days post birth)	ANC Card
	Self-determination	
	Attendance at 4 or more ANC visits	ANC Card
	Adherence to care - Number of ANC Visits	ANC Card
	Health Related Behavior (Maternal and newborn postpartum visits)	Survey
	Clinical Health Related Outcomes (Perinatal mortality (<7 days), maternal morbidities)	ANC Card
T3 – Six months postpartum	**Health Related Behavior** (Uptake of modern family planning, exclusive breastfeeding, 4 postnatal check-ups completed on both mother and newborn in first 6 weeks)	Survey via phone
	Clinical Health Related Outcomes (Neonatal mortality(<28 days), maternal morbidities)	Survey via phone
T4 – One year postpartum	**Health Related Behavior** (Repeat pregnancy)	Survey via phone
	Clinical Health Related Outcomes (Infant immunized per EPI schedule; maternal morbidities)	Self-report Survey via phone

During all visits midwives will record Clinical Health Related Outcomes (Place of birth, hemoglobin levels, newborn birth weight, maternal & newborn morbidities, stillbirth, postpartum visit within 2 days post birth) on the women's ANC card. These data will be collected by the RA during all study visits except baseline.

3.4 Process Evaluation

We will concurrently conduct a process evaluation to identify and document patient, provider, and system barriers and facilitators to program implementation**.** Using both quantitative and qualitative methods, we will identify potential and actual influences on the quality and conduct of the program's operations, implementation, and service delivery.

Data Collection (Process Evaluation): Process evaluation data will be collected via audiotaped semi-structured interviews with facility staff and women participating in GANC. Process evaluation data will include an assessment of both providers' and women's perceptions.

All midwives (providers) involved in the intervention arm (GANC) will be asked to participate in the process evaluation. Midwives will be approached by the RA at the end of the 7th group meeting and asked if they are interested in providing feedback about group care. Those willing to participate will be taken through a consent process before the first interview begins. Each midwife will be interviewed at two random times and each interview will last approximately 40 minutes. A structured interview using open-ended questions will be conducted to explore the midwife's perceptions of group versus standard ANC, barriers to implementation, challenges to integrating it into the existing clinic workflow, and strategies that have helped with implementation. Interviews will be audiotaped (with permission from the participant) to ensure accuracy of responses; midwives can refuse to be audiotaped yet continue with the interview. The RA will write short answer responses on a data collection form. Audio tapes will be transcribed and will be de-identified; tapes will be destroyed immediately after transcription. We have 7 health facilities randomized to the intervention arm and 2 to 4 midwives at each facility; As each midwife may be interviewed twice, we expect approximately 56 midwives may participate in the process evaluation.

Groups of women in the intervention arm will be randomly selected to participate in focus groups for process evaluation. We anticipate 10 random groups of 10 women through the course of the study for a total of 100 women in focus groups. Women will be asked to describe their perceptions of group versus standard ANC, their perceptions of the value of group ANC, and how they could envision the process being improved. Each focus group discussion will last about 1 hour. Women will be given a small baby gift for their participation.

We will employ structured observations of group sessions, interviews with providers, focus groups

of women, and tracking logs to record how the intervention is delivered and received, document program fidelity, and identify opportunities to enhance the delivery of the intervention, while maximizing consistency in intervention delivery across sites. This process evaluation will add value to the analysis of the group ANC intervention by identifying barriers and facilitators at multiple levels throughout the study. For this process evaluation we will focus on both fidelity of the intervention and dose (or frequency).

We will not conduct focus groups with women in the control arm or interviews with midwives at facilities in the control arm as the intent of the focus group is to glean information about women's experience in GANC.

Structured Observations: A sample of 2 of 7 group ANC visits will be observed for each provider to monitor fidelity to the model (e.g. if content is delivered as intended, women are engaged to actively participate in group discussions and activities, picture cards are used as written in the Facilitators Guide, feedback is provided to participants during demonstrations).

Focus Groups: Focus group discussions will be led by the RA or study coordinator with randomly selected groups of women completing GANC throughout the study. Focus groups participants will be consented individually before they enter the focus group room so they may choose whether they want to participate. The group will be conducted in a private setting, and names will not be used during the discussion. Participants will be reminded that the discussion is private and they should avoid discussing the focus with others outside the group. Focus groups will be audiotaped to ensure accuracy of responses. Women who do not want to be audiotaped will not be included in the focus group. Audio tapes will be transcribed and will be de-identified; tapes will be destroyed immediately after transcription.

Tracking logs: A brief form completed by the provider each time an ANC visit is held to track the date of the session and the number of participants from the group in attendance (to track dose).

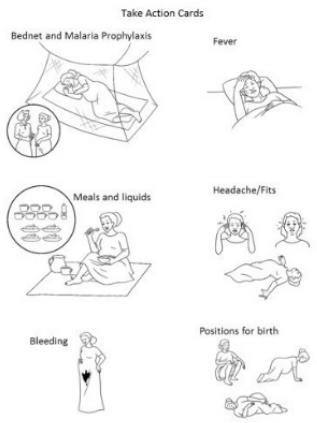
3.5 Intervention - Description of the Model for Group Antenatal Care

The group ANC model was modified from a curriculum initially developed by the American College of Nurse Midwives to mobilize communities in low-resource countries for early problem identification of pregnancy related problems and referral. Using an iterative process with Ghanaian providers, pregnant women, and stakeholders as well as content experts from the U.S. to ensure local and cultural relevance and the WHO Standards for Maternal and Neonatal Care, the group ANC model was developed and tested for acceptability and feasibility by Dr. Lori and her Ghanaian team for the first time in a clinical setting in Ghana. At the core of the model is a negotiation process that acknowledges some health messaging may be in conflict with cultural beliefs. The model allows participants to incorporate safe, feasible, and culturally acceptable health beliefs into self-care actions by being inclusive of traditional practices that are not

harmful. Participants and the facilitator 'agree' on safe and acceptable actions within the context of the setting that are then practiced by the group.

The intervention consists of nine meetings; one individual meeting and eight group meetings. At the initial ANC visit, women are assigned to a small groups with 12-14 women of similar gestational age. Women meet individually with the midwife and the standard complete history and physical exam as well as lab tests are completed; group visits start at the second ANC visit. Prior to the start of each group, blood pressure, weight, and a urinalysis are measured for each woman. The midwife, health facility staff member, and patients then sit in circle facing one another for a 60-90 minute facilitated discussion. The health facility staff member will assist the midwife with group activities. The model uses strategies such as story-telling, peer support, and demonstration and teach-back to enhance its effectiveness. Health literacy is incorporated as an integral part of clinical practice within the model – not as an add-on to care.

Evidence-based information is presented in a non-hierarchical, patient centered, participatory way. Picture cards are used to enhance communication and learning in the group setting. They provide a mechanism to envision new concepts and ideas. The picture cards provide a valuable group discussion and learning aid to stimulate thinking and reflection, dialogue, and learning among participants. A Take Action Card booklet comprised of pictures corresponding to each topic covered in the group sessions, is provided for each pregnant woman to take home and use as a reminder of problems and actions to take if problems arise. Women are encouraged to discuss and share the information with family members and friends - reinforcing what was learned during ANC visits. Content is repeated multiple times in a variety of ways to enhance retention, including: 1) auditory (listening to stories and signs of problems); 2) visual (through use of demonstration and picture cards); 3) kinesthetically (practicing actions and "handling" picture cards); and 4) the Take Action Card Booklet for home use.



A Facilitator's Guide for Antenatal Care developed during the Fogarty-funded study in Ghana, provides a step-by-step guide that details how to conduct each of the group ANC visits care, becoming a facilitator, enhancing adult learning, respectful maternity care, and monitoring for program quality, performance, and fidelity.

3.6 Control - Antenatal Care as Usual.

The control arm is standard antenatal care delivered at health facilities in Ghana. During these visits women meet individually with a midwife who conducts a brief history and physical exam including weight and blood pressure. Following the standard ANC visit, women enrolled in the study at a control site will complete the same survey as the women in the intervention arm. Follow-up visits are the same across conditions.

3.7 Randomization

There are 14 sites in the study. We randomized these 14 sites into the control group and the intervention group. To improve the balance between the two groups and improve the efficiency of estimating intervention effect, we used the facility type, district of site, and ANC registrant numbers in 2018 to conduct matched randomization. The randomization process were carried out using nbpMatching package from R software.

Control Sites				Intervention Sites			
Facility	**Facility Type**	**District**	**ANC 2018**	**Facility**	**Facility Type**	**District**	**ANC 2018**
Adawso	Health Center	Akuapim North	403	Akuse	Hospital	Lower Manya Krobo	378
Abiriw	Clinic	Akuapim North	322	Adkukrom	Health Center	Akuapim North	299
Tetteh Quarshie	Hospital	Akuapim North	654	Atua	Hospital	Lower Manya Krobo	715
St Martin's	Hospital	Lower Manya Krobo	1081	Nsawam	Hospital	Nsawam	4930
Nsawam	Health Center	Nsawam	901	Adoagyiri	Health Center	Nsawam	817
Djankrom	Health Center	Nsawam	295	Klo Agogo	Polyclinic	Yilo Krobo	237
Nkurakan	Health Center	Yilo Krobo	469	Somanya	Polyclinic	Yilo Krobo	616

4.0 Data Analysis (Aims 1-3)

Data on all patients randomly assigned to the intervention or control groups will be analyzed on an intention-to-treat basis. Deviations from randomized allocation will be reported. Summary statistics based on mean, standard deviation or frequency will be used to characterize the sample distribution of each arm. Proper transformations will be investigated and taken if the sample distributions of continuous variables violate the normality assumption. For Aims 1-3, generalized linear mixed models (GLMMs) will be used to test the differences between the two arms since cluster randomized control design is used. There are four components in GLMMs: outcome variable, fixed effects, random effect, and link function. The fixed effects include explanatory variable and covariates. In this study, all three aims have the same explanatory variable which is a binary variable indicating the arm to which women are assigned. The study sites, gestational age, and women's demographic variables such as education or literacy, marital status, pregnancy history, and medical history will be added to the GLMMs as covariates to increase the precision of estimates. The random effect is the 14 facilities. In this study, a random intercept model will be used to account for the cluster effect. The outcome variables and link functions in GLMMs depends on aims and are described below. The construct of GLMMs is to test if the explanatory variable is significant at 0.05 level using likelihood ratio test.

For **Aim 1** to quantify differences in the recognition of pregnancy and newborn danger signs and knowledge of recommended action steps, the BPCR Index will be measured at enrollment and third trimester. We will add baseline data as covariates. The logit link function will be used for each binary BPCR question to test the efficacy of the group-based ANC method. The identity link function will be used when the outcome variable is a summary statistic of the BPCR Index. When the p-value of the explanatory variable is less than 0.05, we will declare a significant difference between the two arms. Average changes in BPCR summary statistics or odds ratio in each question will be used to quantify the effect of the group-based ANC intervention.

For **Aim 2** of assessing behavioral differences in care-seeking patterns between the two arms, the outcome variables are number of attendances in ANC visits, facility birth, and postnatal/partum care. For the attendance outcome variable, identity function will be used. For facility birth or postnatal/partum care, the logit link function is used. When the p-value of the explanatory variable is less than 0.05, we will declare a significant difference between the two arms. The effect of group-based ANC on attendances is quantified by the average difference. The effects of group-based ANC on facility birth and postnatal/partum care are quantified by odds ratio. For the secondary outcomes in aim 2, the logit or identity links will be used in the way similar to the primary outcomes.

For **Aim 3** to evaluate the clinical outcomes of mothers and their newborns, the outcome variables are maternal pregnancy-related morbidities and newborn birth status. For maternal morbidities, the logit link function is used. Since the newborn birth status is classified into three categories (stillbirth, live birth, and early neonatal mortality), cumulative logit link function is used. When the explanatory variable is significant at 0.05, the effect of group-based ANC on maternal pregnancy-related morbidities and newborn birth status are interpreted using odds ratio. We will illustrate the difference between outcomes using odds ratios for each pair of newborn birth status. The secondary outcomes are analyzed similarly using identity or logit link functions.

For the multiple outcomes in the same family, we will conduct direct inference using the Holm's multiple testing procedure to control familywise error rate at 0.05 level. The GLMM analysis will be carried out using lme4 package from R software. All findings will be reported using the Consolidated Standards of Reporting Trials (CONSORT) statement as a guide. Full transparency will be provided when reporting experimental details so that others may reproduce and extend our findings. We will register the study with clinicaltrials.gov and disclose all demographic and baseline characteristics, as well as primary and secondary outcomes.

4.1 Data Analysis (Process Evaluation):

Steckler et al. will guide our analysis of our process evaluation data. Qualitative data will be obtained from semi-structured interviews. All qualitative data will be collected by trained RAs,

transcribed verbatim into English (leaving key phrases that are difficult to translate intact, with the closest approximate meaning put in parentheses in the transcription). No data will be collected by clinical providers. All transcripts will be stored on a password protected server. All data from semi-structured interviews will be entered into N-Vivo qualitative software to assist with the identification of key themes. Structured observations will be recorded and summarized for key points. The use of an audit trail composed of methodological and analytical documentation and validation with colleagues will be used to achieve validity.

4.2 Risks or Discomforts and Benefits

There are minimal risks to participants in this study. There is a rare risk of breach of confidentiality, emotional discomfort, and lack of privacy in the study that will be minimized as outlined below. For the survey portion of the study, participants will be informed in the informed consent as well as verbally in advance of the possibility of questions regarding sensitive subject matters that may make them feel uncomfortable. They will be told that they may skip any question that they find too distressing and/or withdraw from the survey at any time The Ghanaian RAs will be trained to monitor and to provide emotional support. If a participant experiences emotional discomfort while responding to the questions, the RAs will offer support, determine whether it is appropriate to continue and/or provide an appropriate local referral if needed. Local referrals sources will be determined in advance and supplied to the RAs at the time of the study. All forms will be retained by the Ghanaian RA in a locked office, transported to the US in a locked carry-on that is kept with the research team member at all times, and then will be stored in a secure location in a locked file cabinet in the locked office of the primary investigator at the University of Michigan after study completion to protect confidentiality.

4.3 Incentives

Incentives for participants will include baby layette items (e.g. baby hat, blanket, socks, tote bag) given at each time point.

4.4 Confidentiality of Data, Processes for Anonymizing Data

To maximize data confidentiality and participant protection in the proposed project, all project staff will be trained in these requirements and the importance of confidentiality emphasized on a regular basis. Participant confidentiality will be protected in that we are not recording names of participants on any paper study material or data collection tools. All study materials will be stored in a locked space every evening and all data will be encrypted. Data will be stored on an encrypted and password protected tablet in a locked space.

Focus groups participants will be consented individually before they enter the focus group room so they may choose whether they want to participate. The group will be conducted in a private setting, and names will not be used during the discussion. Participants will be reminded that the discussion is private and they should avoid discussing the focus with others outside the group. Audio tapes will be transcribed and will be de-identified; tapes will be immediately destroyed after transcription. Prior to transcription, all tapes will be stored in a locked file cabinet in a locked

office in the Dodowa Health Research Center. Access to the cabinet will be restricted to study investigators and the DHRC study team.

4.5 Data Storage and Management

Data will be considered strictly confidential and will be entered into an electronic record using a secure tablet with password-protected access. Prior to data collection, tablets will be encrypted to ensure all data is securely stored. Once a tablet is encrypted, a one-time process that is initiated from the tablet's settings page, users will be asked to enter a pin every time the device is turned on and data will only be available when the device is unlocked.

Data will be stored on a secure, cloud-based server, accessible only to trained members of the research team. No names will be included in any recorded data, instead using individual tracking numbers that will be kept in a separate encrypted data file for the purposes of long-term follow-up. There will be two contact lists: first, a full contact list that contains the participant's name, phone number, and study ID. This paper list will be kept in a locked file cabinet in a locked office. The second contact list (electronic list), for the purpose of study visits and data collection, will include only the participant's first name and study ID number. The RA will travel to the field for data collection carrying only a password protected file on the encrypted tablet to meet with participants.

Access will be available only to study members working directly with participants for follow-up data collection. We will destroy all links between respondents and survey data after project completion. Study material transported back to UM will be in a locked briefcase that will be carried onto the plane and remain with the research team at all times.

4.6 Long-term data storage and management; Clarity of data ownership

Upon completion of the project all data - stripped of any potential identifiers - will be kept in University of Michigan's Deep Blue, a permanent, publically available data repository.

5.0 Ethical considerations

This study will begin after approval from the University of Michigan Health Sciences Behavioral Sciences Institutional Review Board (IRB) and Ghana Health Service. An experienced, interdisciplinary and transnational team of researchers with a long-standing history of collaborations will carry out the proposed study. This innovative interdisciplinary group—nurse midwives, public health experts, and researchers from the United States and Ghana—bring a wealth of knowledge and skills to the proposed study. As required by the University of Michigan (regardless of the country of residence), all research staff, including principal investigators, coinvestigators, and research assistants on research projects that involve human study participants must complete the online Program for Education and Evaluation in Responsible Research and Scholarship (PEERRS) or equivalent, and must have their human subjects certification renewed every three years. The Ethics Boards at Ghana Health Services and DHRC are responsible to oversee the research activity of the DHRC study members.