

RESEARCH PROTOCOL

TITLE: Group Antenatal Care: Effectiveness for Maternal/Infant and HIV Prevention Outcomes and Contextual Factors Linked to Implementation Success in Malawi

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LIST OF ABBREVIATIONS

ANC	Antenatal care (known as prenatal care in the US)
CFIR	Consolidated Framework for Implementation Research
Co-I	Co-investigator
DMC	Data Monitoring Committee
DSMP	Data and Safety Monitoring Plan
GCP	Good Clinical Practice
HIV	Human immunodeficiency virus
Hb	Hemoglobin
ICD	Informed Consent Document
IRB	Institutional Review Board
OHRP	Office of Human Research Protections
OPRS	Office for the Protection of Research Subjects
PHI	Protected Health Information
PI	Principal Investigator
QA/QI	Quality Assurance/Quality Improvement
RCT	Randomized clinical trial
SAE	Serious Adverse Event
WHO	World Health Organization

1.0 Project Summary/Abstract

Sub-Saharan Africa has the world's highest rates of maternal and perinatal mortality and accounts for 2/3 of new HIV infections and 1/4 of preterm births. Antenatal (prenatal) care is the entry point into the health system for many women and offers a unique opportunity to provide life-saving monitoring. However, provider shortages, low quality of care and failure to attend all recommended visits mean that the potential benefits of antenatal care are not realized. There is an urgent need to test novel interventions to reduce health risks for mother and child.

Group antenatal care is a transformative model of care that provides a positive pregnancy experience, uses provider time efficiently, and improves perinatal and HIV-related outcomes. Women in group antenatal care have 2-hour visits with the same provider in a group of 8-12 women at a similar stage of pregnancy. Women conduct self-assessments, briefly consult the midwife, and meet for 80-90 minutes of interactive health promotion enlivened by games and role-plays. Women form relationships with midwives and each other.

Our randomized pilot in Malawi and Tanzania had promising results. More women in group care than in usual care completed ≥ 4 antenatal visits (94% vs 58%). Their partners were more likely to be tested for HIV during pregnancy (51% vs. 27%). We established that group antenatal care can be offered in a rigorous RCT with high fidelity despite provider shortages. The next step is an adequately powered effectiveness trial. Malawi is an appropriate site because it has the world's highest prematurity rate (18%) and high HIV prevalence (10% nationally, 16% at the study site).

For this study, we use a hybrid design to simultaneously conduct an effectiveness RCT with individual-level randomization and examine implementation processes at 6 clinics in Blantyre District, Malawi.

Aim 1 is to evaluate the effectiveness of group antenatal care through 6 months postpartum. We hypothesize that compared to usual care, women in group care and their infants will have less morbidity and mortality and more positive HIV prevention outcomes. We test Aim 1 hypotheses using multi-level hierarchical models using data from repeated surveys and health records.

Aim 2 is to identify clinic-level degree of implementation success and contextual factors associated with success for each clinic and across clinics. Analyses use within and across-case matrices.

This high-impact study addresses three global health priorities, maternal and infant mortality and HIV prevention, that affect all women of childbearing age in Malawi. The Ministry of Health strongly supports our project; results will help them decide whether to scale-up this innovative model of group care. Negative results will avoid spending on ineffective care. Positive results will provide evidence needed to adopt group antenatal care nationally and in other low-resource countries.

2.0 Background/Scientific Rationale

Sub-Saharan Africa has the world's highest rates of maternal and perinatal mortality and accounts for 2/3 of new HIV infections, and 1/4 of all preterm births.¹⁻³ Antenatal (prenatal) care is the entry point to the health system for many women and offers a unique, often missed, opportunity to provide life-saving monitoring, health promotion, and links across the continuum of care.^{4,5} In sub-Saharan Africa, more than 90% of women attend antenatal care at least once, but only half of women complete all visits. Leveraging high intake rates, many countries integrate the first visit with HIV testing and the initiation of lifelong treatment (Option B+ policy), which has reduced transmission to children by 47% since 2010.⁶ However, in Africa severe provider shortages and burnout mean that women have long waits for very short visits (10-12 minutes).⁷ Essential services are inconsistently provided, and care is often disrespectful.⁸⁻¹² Opportunities to save lives are missed when complications such as preeclampsia, anemia, or HIV go untreated. Gaps persist in the continuum of HIV care for HIV-infected women and their infants during and after pregnancy.¹³⁻¹⁵ Health promotion is minimal, especially for HIV prevention, so women continue to be exposed to HIV from untested partners. To address antenatal care quality gaps, WHO now recommends doubling the number of antenatal visits from 4 to 8 and adopting a patient-centered approach to ensure a positive pregnancy experience.⁵ However, it will be difficult to do so without a major paradigm change in the individual antenatal care model (usual care).

Group antenatal care is a transformative model of care that provides a positive pregnancy experience and improves perinatal and HIV-related outcomes despite provider shortages. In a US randomized clinical trial (RCT), group care improved prematurity rates, antenatal care attendance, satisfaction with care, breastfeeding practices, safer sex behaviors, and uptake of family planning.¹⁶⁻²⁰ Women in group care bypass the waiting room and have a 2-hour visit with the same provider in a group of 8-12 women at a similar stage of pregnancy. Women assess their blood pressure and weight, briefly consult the midwife in a corner of the room, and meet for 80-90 minutes of interactive health promotion, enlivened by games and role-plays. Women form relationships with providers and each other and collaboratively generate strategies to improve health.

Our randomized pilot (n = 218) in Malawi and Tanzania had promising outcomes and established that group antenatal care can be offered in a rigorous RCT with high fidelity despite provider shortages. More women in group care than in usual care completed ≥ 4 antenatal care visits (94% vs 58%). Their partners were more likely to be tested for HIV during pregnancy (51% vs. 27%).²¹⁻²³ A midwife can serve 12 women in 2 hours, a time that equates to 10 minutes/client and is similar to observed visit length in African countries. Several non-randomized studies of group care in low-resource settings also showed promising results,^{19,24-28} but no effectiveness trial has been conducted in Africa.

3.0 Objectives/Aims

In this 5-year study, we use a Hybrid Type 1 design to simultaneously conduct an RTC with individual level randomization while we closely examine implementation processes at seven clinics in Blantyre District, Malawi.²⁹ Our two specific aims are:

Aim 1. Evaluate the effectiveness of group antenatal care through 6 months postpartum. We hypothesize that compared to usual care, women in group care and their infants will have less morbidity and mortality and more positive HIV prevention outcomes, including:

- 1a.** Fewer preterm births (*primary outcome*), stillbirths, low birthweight infants and neonatal and maternal mortality.
- 1b.** Higher rates of HIV testing for partners (*primary outcome*) and women at first visit and in late pregnancy if HIV negative, and more HIV prevention knowledge and behaviors.
- 1c.** More optimal secondary outcomes: healthcare utilization, satisfaction with care, pregnancy-related knowledge, healthy behaviors, mental distress, anemia, hypertension, postpartum bleeding (>500ml), exclusive breastfeeding, uptake of family planning and early repeat pregnancy.
- 1d. Exploratory:** For the subset of ~130 HIV-infected women: received antiretroviral therapy from intake through 6 months postpartum and infant tested by 6 months and results received.

Aim 2. Identify clinic-level degree of implementation success and contextual factors associated with success for each clinic and across clinics.

4.0 Eligibility

The **subject population** includes 5 sub-populations (each group will only participate in one study role, that is, aim 1 participants cannot participate in aim 2, or cognitive interview subjects cannot participate as effectiveness subjects):

Aim 1: Effectiveness of group antenatal care participants – both sub-populations are pregnant women attending one of the participating clinics for antenatal care:

1. Cognitive interview participants: will be recruited from one of the six participating clinics and eligibility will be determined by a member of the research team in a private space at the clinic using the Eligibility Screening Tool for Cognitive Interviews.
2. Effectiveness evaluation participants: will be recruited from one of the seven participating clinics and eligibility will be determined by a member of the research team in a private space at the clinic using the Eligibility Screening Tool Group Antenatal Care Effectiveness.

Aim 2: Implementation evaluation participants – both sub-populations are part of the health care system:

3. Co-facilitators: midwives, clinic staff, or community health volunteers trained to deliver and co-facilitate group antenatal care at one of the 6 study clinics.

4. Training video participants: will be recruited from participating clinics. Eligibility will be determined by a member of the research team in a private space at the clinic.
5. Health officials (clinic, district, national): employees that oversee healthcare at the six participating clinics (administrators), within Blantyre District Health Office, or the Malawi Ministry of Health

4.1 Inclusion Criteria

Aim 1: Effectiveness participants

1. Cognitive interview participants
 - a. Pregnant
 - b. Aged 18 or older
 - c. No marked cognitive impairment that would prevent the providing informed consent
 - d. Speaks and understands Chichewa (the national language)
2. Effectiveness evaluation participants
 - a. Pregnant
 - b. 24 weeks gestation or less
 - c. Aged 18 or older
 - d. No marked cognitive impairment that would prevent the providing informed consent
 - e. Speaks and understands Chichewa (the national language)

Aim 2: Implementation participants

3. Co-facilitators
 - a. Trained as a co-facilitator of group antenatal care and working at one of the seven participating clinics
 - b. Speaks and understands Chichewa (the national language)
4. Training video participants
 - a. Pregnant
 - b. Aged 18 or older
 - c. No marked cognitive impairment that would prevent the providing informed consent
 - d. Speaks and understands Chichewa (the national language)
5. Health officials (clinic, district, national)
 - a. Holds this position at the respective institution
 - b. Speaks and understands Chichewa (the national language)

4.2 Exclusion Criteria

Aim 1: Effectiveness participants

1. Cognitive interview participants
 - a. Has a marked cognitive impairment that would prevent the providing informed consent
 - b. Is not pregnant
 - c. Is younger than aged 18
 - d. Does not speak and understand Chichewa (the national language)
2. Effectiveness evaluation participants

- a. Has a marked cognitive impairment that would prevent the providing informed consent
- b. Is not pregnant
- c. Is younger than aged 18
- d. Over 24 weeks gestation
- e. Does not speak and understand Chichewa (the national language)

Aim 2: Implementation participants

- 3. Co-facilitators
 - Does not speak and understand Chichewa (the national language)
 - Does not hold one of these positions at respective institutions
- 4. Training video participants
 - a. Has a marked cognitive impairment that would prevent the providing informed consent
 - b. Is not pregnant
 - c. Is younger than aged 18
 - d. Does not speak and understand Chichewa (the national language)
- 5. Health officials (clinic, district, national)
 - Does not speak and understand Chichewa (the national language)
 - Does not hold one of these positions at respective institutions

4.3 Excluded or Vulnerable Populations

Vulnerable population include disadvantaged and pregnant women from Malawi, some of which will be HIV positive.

Malawi is a low-resource country, and a significant proportion of the population is economically and educationally disadvantaged. Justice is an important ethical value in research and the patients/population who can most benefit from the research should be included. Safeguards are in place for all potential participants to avoid coercion. The women will receive remuneration for their time and transportation. All participants are native Malawian Africans living in the Blantyre District in Malawi's Southern Region. Convenience sampling is used to recruit all generally healthy research participants. Ages will be 18 years or older for all participants. A total of 1,972 participants are projected to be enrolled.

Pregnant women: Because this is a study to test a group model of antenatal care, pregnant women will be included. Other individuals who volunteer to be in the study are generally healthy adults, and some women may be pregnant, but their pregnancy is not a focus of the study. Participants are generally healthy individuals who are able to decide for themselves whether they want to participate. The study poses no special risks to pregnant women. Indeed, the group model of antenatal care may offer advantages in terms of better health outcomes, as compared with usual care. Since women who are pregnant have obviously been sexually active, study participants may benefit from participating in the intervention by learning how to protect themselves from HIV infection and other sexually transmitted infections. It would not be possible to conduct this study if we exclude women are pregnant.

HIV positive women: Malawi has a high prevalence of people living with HIV (PLHIV). HIV positive women will not be asked to disclose their status and will not be excluded from this study because they get the same antenatal care as HIV negative women. We consider them a vulnerable population because of the stigma surrounding this disease.

5.0 Subject Enrollment

Aim 1: Effectiveness Participants

1. Cognitive interview participants (n=60)

Cognitive interviews will be conducted for development purposes to verify comprehensibility of survey items before the start of data collection for Aim 1. Midwives at the clinic will direct women attending antenatal care to our research station so that they can learn more about this part of the study. A member of our research team and the woman will move to a private space. If the woman meets the inclusion criteria and is willing to participate, she will be enrolled. No screening data will be collected. If the woman is ineligible, she will be thanked and informed that she cannot participate. We will track the number of ineligible participants using the Eligibility Screening Tool for Cognitive Interviews. To minimize coercion, the description of the study and obtaining signed informed consent will occur privately, so that others are not aware of whether the woman is a research participant. Those who consent will move right into the 60-minute cognitive interview.

2. Effectiveness evaluation participants (n=2064 or ~296/clinic)

When a woman goes to clinic for her intake antenatal care visit, her midwife will direct her to our research station so that she can learn about the study. The researcher and woman will move to a private space to describe the study and assess eligibility. If eligible, they will move to informed consent. If ineligible, the woman will be thanked and informed that she cannot participate in the study. We will track eligibility using an eligibility screening form which will be developed for this study. To minimize coercion, the consent process provides full information about the research: purpose, procedure, risks, benefits, the right to discontinue participation at any time, to not answer any questions, who and where to obtain information about the project at any time, that participation is strictly voluntary, and safeguards against potential risks. We will ask the woman a series of questions to ascertain understanding before she signs the consent form (signature or thumb print if she is not literate).

Aim 2: Implementation evaluation participants

3. Co-facilitators (n=90; ~66 midwives/nurses and ~24 community volunteers)

Midwives, staff, and community volunteers at each clinic are approached privately by a research team member, who explains the study, risks, and protection from risk and answer any questions. The team member discusses whether the potential participant wants to take part in facilitating group antenatal care and then obtains signed informed consent. To minimize coercion, we discuss how they can decline to participate unobtrusively. Consent is verbally reconfirmed before observations and interviews occur. Regardless of type of care model, all are expected to provide care to meet national guidelines. These expectations are not altered and do not change clinical responsibilities.

4. Training video participants (n=96)

At the beginning of the study, we will develop a training video to be used in training of the co-facilitators who will run the group care sessions. A convenience sample of groups of 8-12 pregnant women will be asked to participate in a group antenatal care practice session and allow us to video record it. Midwives at the clinic will direct women attending antenatal care to our research station so that they can learn more about this part of the study. A member of our research team and the woman will move to a private space. If the woman meets the inclusion criteria and is willing to participate, she will be enrolled. No screening data will be collected. If the woman is ineligible, she will be thanked and informed that she cannot participate. To

minimize coercion, the description of the study and obtaining signed informed consent will occur privately. Those who consent will be provided with details about the day and time for the practice session and video recording and asked to return then to participate. Practice sessions will last ~2 hours.

5. Health Officials (n=46)

At the first health officials individual meeting, a researcher will explain the research/evaluation aspect of the project, the health official's participation in it, potential risks, and protection from risks; officials have an opportunity to ask questions. To minimize coercion, we also discuss how they can decline to participate unobtrusively. Then they give signed consent. Consent is verbally reconfirmed before observations and interviews occur. Participation in this study does not alter the health official's role or responsibilities. We estimate that ~30 clinic administrators, ~6 from Blantyre District and ~10 from Ministry of Health will participate.

6.0 Study Design and Procedures

Collaborating Sites:

University of Illinois at Chicago and the University of Malawi, Kamuzu College of Nursing.

Study Design: Hybrid Type 1 design²⁹

The **Figure** below provides an overview of the project. In Year 1, we hire and train staff, finalize measures, and contract to build the Audio Computer-Assisted Self-Interview (ACASI) program. We then begin implementation and evaluation at 6 clinics, following the 3-Step Implementation Model (**P**repare, **R**ollout, **S**ustain).

	YEAR 1			YEAR 2			YEAR 3			YEAR 4			YEAR 5		
	3	6	9	12	15	18	21	24	27	30	33	36	39	42	45
Prepare															
Team, Instruments & Toolkit	X	X	X												
Video Production				X	X			X	X						
Group ANC Trainings				X	X			X							
3-Step Implementation (P = Prepare; R = Rollout; S = Sustain)															
Clinics 1 & 2				P	R	S	S	S	S						
Clinic 3					P	R	R	S	S	S					
Clinic 4						P	R	R	R	S	S	S			
Clinics 5 & 6							P	R	R	S	S	S	S		
Evaluation															
Aim 1: Data Collection				X	X	X	X	X	X	X	X	X	X		
Aim 1: Effectiveness Analysis				X	X	X	X	X	X	X	X	X	X	X	
Study Notes															
Ongoing															
Aim 2: Staff Survey & Interviews						X	X	X	X	X	X	X	X		
Aim 2: Mixed-Methods Analyses				X	X	X	X	X	X	X	X	X	X	X	X
Dissemination															
Safe Motherhood Task Force Meetings	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Group ANC Dissemination Workshops														X	X
Manuscripts & Conferences				X			X			X				X	X

Figure 1. Project Overview and Timeline

We work with each clinic and will stagger implementation of group antenatal care across year 2.

1. In Months 11-12, Clinics 1 & 2 **prepare (P)**. Prepare ends after group antenatal care training of co-facilitators
2. **Rollout (R)** begins when eligible and consented women (Aim 1, effectiveness participants) are randomly assigned either of these two study conditions, the individual (usual) care or the group care. Women in both conditions participate in the study for ~10 - 14 months, from early pregnancy to 6 months post-partum, depending on the women's weeks of gestation when they join the study.

- Individual care (usual): Women are provided antenatal care services on a first come, first serve basis and listen to a health lecture. They meet individually with a midwife for a physical assessment. Women complete laboratory tests (including HIV testing) at their first visit. Congruent with the new WHO recommendations, usual individual antenatal care consists of 8 antenatal care visits and 2 postnatal visits at 1 week and 6 weeks.
 - Group care: Women have the same number of visits as those in usual care, 8 antenatal care visits and 2 postnatal visits at 1 week and 6 weeks. Their first antenatal care (intake) and first postnatal visit is done individually. Both are identical to usual care. It is not feasible to have a group visit at 1 week postpartum because the 1-week date corresponds with a woman's delivery date. The intake visit ends with assignment to group care and each woman is given her group appointment schedule.
- All participants will complete the study procedures described under **Aim 1, Effectiveness Subject Activities**
 - After the RCT recruitment is completed, clinics will enter into the **sustain (S)** step if they decide to offer group care as part of regular practice.
 - These three steps (**P**, **R**, and **S**) take place at Clinics 3 & 4 in Months 19-42 and Clinics 5 & 6 in Months 29-48.

All of the antenatal care procedures, regardless of study condition, meet Malawi's standard of care expectations. Our evaluation reflects the procedure related to the research. Data collection for both of our aims occurs simultaneously.

The research team working on the effectiveness evaluation of group care is blinded to study condition and is charged with collecting the Aim 1 effectiveness data from the individuals (n=2064).

The Aim 2 implementation process data collection begins with orientation in Month 3. Data include periodic interviews with stakeholders and clinic staff, repeated brief staff surveys, and our Study Notes. Aim 2 data collection ends in month 57 with the national conference to disseminate study results. Implementation participants will be part of the study for nearly the duration of the project (~57 months).

Coded data transfers from Malawi to UIC (where [the associated master list linking the participant's name to the ID code will not be transferred to UIC](#)) will be done through a PIH secure Box.com folder hosted and supported by UIC. The coded research data will be directly uploaded from the password-protected computer in Malawi to the UIC Box.com folder.

1. **Aim 1 Cognitive interviews (up to 60 women)**

Subject Activities

- a. Screening: Pregnant women attending antenatal care will be directed to our research station to be screened for eligibility in a private room by a trained researcher.
- b. Consent: If interested and eligible, they move to the informed consent process.
 - i. If the woman declines, she will be thanked and can leave
 - ii. If the woman participates, the researcher will move into the cognitive interviewing
- c. Procedures:
 - i. To verify comprehensibility of new and/or revised healthy pregnancy knowledge and behavior survey items, a researcher reads the question and records the woman's answer

- ii. Researcher then asks the woman to explain her understanding of what it is being asked.
- iii. If the item's meaning is unclear, respondent is asked to provide alternate wording to improve comprehensibility of the question
- iv. Cognitive interviews will take about 60 minutes, and each woman will participate in only one interview. If the researcher notices the woman is fatigued, they will end the interview.

2. Aim 1 Effectiveness participants (n=2064)

At each clinic, clusters of 24 women are recruited until the clinic's enrollment goals are met. Dr. Li will generate 86 sets of randomization cards with each set containing randomized group assignment for 24 women (12 to each study condition). A new packet of cards is used with each new cluster of 24 women.

As part of usual care, every woman first completes her individual intake visit where her overall health, gestational age, and medical test results will be recorded in the Health Passport that she carries with her throughout her pregnancy, and it is updated with each visit.

After intake, the midwife, who is part of the research team, will direct the woman to our research station so the woman can learn about our study. If she is interested, eligibility will be determined from data in her Health Passport.

Eligible women will be asked to join the study. Refusals and reasons given will be documented as indicators of self-selection bias. Women then give informed consent.

Before randomization, with guidance from an effectiveness team member each woman completes the baseline survey administered using ACASI.⁹¹ The interviewer reads questions and shows the participants the responses and how to select one. The interviewer then looks away to maintain the woman's answers private while the participant touches the screen to select her response and the screen then automatically moves to the next question. Because a response selection is required before the next question (with one option always being to skip the question), using this ACASI system minimizes the potential for missing data.

To manage data collection for the remaining three time points, a spreadsheet will be generated with a name, ID code, contact information, enrollment date, and weeks of gestation. A team member will call (or visit her home if no phone is available) to schedule and remind participants about each of the four data collection appointments (1) at intake visit, 2) late pregnancy, 3) 6 weeks postpartum, and 4) 6 months postpartum).

At the data collection appointment, a team member will greet the woman and verbally reconfirm consent. Following standard procedures, each woman's hemoglobin (Hb) will be assessed using a simple point-of-care blood droplet test. At the 4th survey, the woman will be asked to take a pregnancy urine test kit in the clinic restroom. Her results will be reviewed with her and recorded. All materials will be discarded in our trash container which will be disposed of in the clinic incinerator.

Pregnancy and birth outcomes data will be verified using clinic medical records. For women who were identified as HIV+ at intake or during pregnancy, maternal and infant HIV clinic attendance and infant HIV status at 6 months will be verified from medical records. Coordinators will help our team locate these in clinic records.

Aim 1, Effectiveness Subject Activities

1. Screening: After completing her intake visit, the woman will be screened for eligibility in a private space at the antenatal care clinic. Eligibility is determined by looking at data

entered into the woman's Health Passport based on the inclusion/exclusion criteria (~5 minutes)

2. Consent: If eligible, researcher will immediately move to the informed consent process (~25 minutes)
3. Survey (T1): Next, all women enrolled in the study will complete a baseline survey (T1) and the fingerprick to measure Hb (~60 minutes)
4. Study condition assignment: Women will then select a card at random to select her study condition (group or usual care) and attend her antenatal and postnatal care according to this assignment
5. T2 Survey: In late pregnancy, all participants will be called or contacted to schedule an appointment for the survey and fingerprick. Participants will complete the survey and fingerprick for Hb (~45 minutes)
6. T3 Survey: At approximately 6 weeks postpartum, all participants will be called or contacted to schedule an appointment for completing the survey and fingerprick (time point 3). Participants will complete the time point 3 survey and fingerprick for Hb (~45 minutes)
7. T4 (final) Survey: At approximately 6 months postpartum, all participants will be called or contacted to schedule an appointment for completing the survey, fingerprick, and pregnancy test. Participants will complete the survey, fingerprick for Hb, and pregnancy test (~30 minutes).

Aim 2, Training Video Subject Activities

1. Screening: Pregnant women attending antenatal care will be directed to our research station to be screened for eligibility in a private room by a trained researcher.
2. Consent: If interested and eligible, they will proceed with informed consent.
 - a. If the woman declines, she will be thanked and will leave the clinic
 - b. If the woman decides to participate, the researcher will provide the woman with information about the day and time of the practice group session.
3. Procedures:
 - a. ~8-12 women will return to the clinic on the specified date and day to participate in the 2-hour practice session led by trained co-facilitators
 - b. Consent for voluntary participation will be reaffirmed verbally (observation by the research team and video recording)
 - c. The group session will take ~2 hours

Data Sources

Language considerations: The national language in Malawi is Chichewa. The study participants, the researchers in the Malawian team who will be recruiting, consenting, and completing the study procedures with the participants, as well as the midwives, clinic staff and volunteers, will speak Chichewa. The study surveys were developed in English, translated to Chichewa by native speakers, and tested in our randomized pilot study. We made minor modifications to the surveys and will confirm comprehensibility as part of this study's cognitive interviews. The English consent forms will be translated by our Malawian co-investigators.

Cognitive interview subjects: This one-time interview will help to improve comprehensibility of survey items. No identifying information will be collected. Only researcher notes are collected.

Effectiveness (see table pasted summarizing measure, time points, and data sources):

- List: Contact information for effectiveness evaluation participants is stored in a password-protected computer and accessible only to research staff. When needed to schedule data collection appointments, the participant's information will be provided to the community health worker with instructions about safeguarding the information and to return the contact sheets after scheduling the appointment. We will retain the master list until the first set of publications are completed. It will then be destroyed.
- Survey: antenatal care participants complete an audio-assisted computer survey assessing HIV-prevention knowledge and behaviors, pregnancy knowledge, health behaviors, satisfaction with antenatal care and mental health. Two point-of-care standard medical tests are used: Hb level and pregnancy status (at time point 4 only). Health data (birth outcome and adherence to care) are extracted from women's Health Passports and clinic medical records and directly entered onto encrypted and password-protected computer by ID code. The data will be saved in a coded database.

Effectiveness outcomes (Aim 1)

Construct	Operational Measure	Time				Source*
		1	2	3	4	
H1. Less prematurity and mortality						
Preterm Birth (Primary)	<37 weeks gestational age			•		H, S
Spontaneous abortion	Pregnancy loss <20 weeks			•		H, S
Stillbirth	Baby born with no signs of life at or after 28 weeks gestation ⁸¹	•	•			H, S
Low birthweight	<2500 grams, measured within 24 hours of birth			•		H, S
Neonatal death	Newborn dies with 28 days after birth	•	•	•	•	H, S
Maternal mortality	Death in pregnancy or within 42 days of end of pregnancy	•	•	•		H, S
H2. More positive HIV prevention outcomes						
Partner HIV Test (Primary)	Proportion whose partners were tested during pregnancy	•	•			S
Women, HIV Test	Initial HIV test; If seronegative, repeated in 3 rd trimester	•	•			
HIV Knowledge	General knowledge (5 items); Mother-to-child transmission (4 items)	•	•			
Sexual Health Behaviors	Consistent condom use; Partner communication (5 yes/no items)	•	•	•	•	S
H3. Optimal secondary outcomes						
Healthcare Utilization	Pre- and postnatal care attendance; birth in a health facility (yes/no)			•		H, S
	Services received (21 items); Content covered (18 items) (<i>modified for this study</i>)		•			
Satisfaction with Care	10-item index; 5 point Likert scale; Range 10-50, $\alpha = 0.980$		•			S
Pregnancy Knowledge	20 item; 2-3 per visit based on content (<i>modified for this study</i>)	•	•			S
Healthy Behaviors	14 recommended behaviors (<i>modified for this study</i>)	•	•			S
Mental Distress	Self Reporting Questionnaire; ^{82–85} 20 Yes/No Items; $\alpha = 0.789$	•	•	•	•	S
Anemia	Hemoglobin (Hb), Point-of care bloodspot, HemoCue® (Hb <11//dL) ⁸⁶	•	•	•	•	T
Hypertension	Blood pressure changes and symptoms	•	•	•		H, S
Postpartum bleeding	Postpartum bleeding (>500 ml); postpartum hemorrhage (>1,000 ml)			•		H, S
Exclusive Breastfeeding	Exclusive breastfeeding duration, # days				•	S
Family Planning	Using a family planning method				•	S
Early repeat pregnancy	Negative pregnancy test and no reported pregnancy loss				•	S, T
H4. Exploratory: Successful transition in continuum of HIV care (subset of HIV-infected women)						
Women	Received ART medication from intake through 6 months postpartum	•	•	•	•	S
Infant	Infant HIV test, results received			•	•	H, S
*Source: H = Health record; S = Self-report survey; T = medical test						

*Source: H = Health record; S = Self-report survey; T = medical test

Aim 2: Implementation Evaluation Data

Measures and data sources to document degree and variation of implementation success are summarized in the table below.

Study notes from observed planning meetings, selected trainings and group antenatal care visits: Names of participants and other identifying information will not be recorded.

Video clips: selected trainings and practice sessions will be recorded to produce the Training Video for use in future trainings. Unused clips will be destroyed after the training video is finalized.

Audio-recorded interviews (individual or focus group): stored recordings will be accessible only to the research team and will be erased after transcriptions and translations are completed and verified for accuracy.

Transcripts and translated transcripts of recorded individual and focus group interviews: The stored data will be accessible only to the research team and kept until all publications are completed for the project.

Fidelity: an observer will take detailed notes on the semi-structured fidelity form to monitor fidelity to the original group prenatal care model. Coded and stored data will only be accessible to the research team and kept until all publications are completed for the project.

Self-evaluations of group care visits by co-facilitators: Coded and stored data will only be accessible to the research team kept until all publications are completed for the project.

Benchmark scores are compiled from project records and data routinely reported by the clinic sites. Aggregate data from the clinic does not involve human subjects. These data will be kept until all publications are completed for the project.

NOTE: Since funding for this study is still pending, the survey and interview questions for the co-facilitators and health officials are being developed. They will be finalized and submitted for IRB approval once funding is obtained.

Measures and data sources for degree and variation of implementation success (Aim 2)

Indicators of Degree of Implementation Success based on data from the last quarter of sustain independently		Source
Continuation	Yes/No indicating ceased or continued to offer group antenatal care	Benchmarks
Reach	Percentage in group care based on the total number of antenatal care clients	Benchmarks
Fidelity	Quarterly clinic mean scores; High fidelity is indicated by high group engagement, high session management and interpersonal facilitation skills (e.g., controlling negativity, drawing out participants), and overall rating as more like a discussion than a classroom.	Observations
Contextual Factors by CFIR Domain ⁷¹ (ongoing)		
Intervention	- Time: Group vs. usual time required to deliver antenatal care - Additional expenses: associated with group care (training, equipment and supplies) - Other: factors affecting implementation (space, scheduling)	Interviews Study Notes
Outer Setting	Ministry of Health (annually); District Health Office (annually); Safe Motherhood Task Force (Quarterly); Other stakeholders, as needed	Meetings Interviews
Inner Setting	- Clinic characteristics and events reported (staff transfers, leadership, interactions) - Successes, challenges, solutions, decisions, interpersonal interactions, and evaluation of evidence; coded as positive, negative or mixed	Benchmarks Interviews Observation
Individual (Staff)	- Basic demographics, including education level and professional experience - Maslach Burnout Inventory (9 items; $\alpha > .79$);⁸⁷⁻⁸⁹ - Health Worker Motivation (10-item; range 10-50);^{75,90}	Survey

	Perspectives on group care (5 items) at baseline and beginning and end of sustain	
Process	Quarterly Benchmark Scores: 25 yes/no items (1 point for each yes). Integrates co-facilitators' self-evaluation of fidelity and time records. Patterns over time: Fail; Interrupted; Sporadic; Continuous	Benchmarks Self-evaluations
	Fidelity: Quarterly ratings	Observations

7.0 Expected Risks/Benefits

Cognitive interview participants: These participants answer pregnancy knowledge and healthy behavior questions and explain their interpretation of each question's meaning. Their names are not associated with their data. There is a relatively low risk of loss of confidentiality due to participation, but if information about their participation or responses were to become publicly known, no appreciable harm should result to the participant.

Training video participants: Because the recordings will clearly indicate the identities of the participants, who will provide consent to be video-recorded, these participants have unique confidentiality concerns. These are not confidential, as they are intended to be viewed in future trainings. To alleviate concerns, at the end of each recorded session, participants will be asked if they want to exclude any portion of the session (for example, if they are embarrassed or it felt too personal). This video clip will not be included.

Participants in effectiveness evaluation: Antenatal care participants complete a survey 4 times over the study period. The survey asks about a few sensitive topics (sexual behavior and partners) that may make some participants feel uncomfortable. They have a fingerprick to screen for anemia at all 4 survey times. At the 4th survey, women will use the clinic's toilets so that they can take a pregnancy test. They have a low risk of loss of confidentiality as data are collected privately and their names are not attached to their data. Only the ID code is attached to the survey and other data. For participants randomized to group antenatal care, there is also a relatively low risk of loss of confidentiality due to participation in the group discussions, as other members of the group might talk about what was said in the groups.

- Psychological discomfort may be experienced related to being asked to discuss or think about sensitive issues in the effectiveness evaluation survey. Some participants taking the survey may also become mildly distressed by being asked questions about their sexual behaviors and relationships. The ACASI format for the survey offers nearly complete privacy, which somewhat reduces distress. Our evaluation team will be alert for anyone who seems distressed and will offer to talk with them about it. In our experience, this event is extremely rare.
- Some participants in the group antenatal care intervention, especially adolescents, may feel uncomfortable openly discussing certain information related to sexual health, HIV prevention or family planning. Our team will be trained to explain why these discussions are important and to respond to nonverbal and verbal discomfort cues. Group antenatal care takes place in a room apart from the public waiting areas, to provide privacy for these discussions.

Co-facilitators: They participate in a 3-day training. Parts of sessions will be videotaped to create the Training Video for future trainings. They have a moderate risk of loss of confidentiality from this. Participants also agree to allow observations of planning meetings. Names will not be written in meeting notes. They take part in 3-4 focus group interviews. Midwives and other clinic staff also complete a survey 3 times over the study period that assesses motivation, burnout, self-efficacy, knowledge and attitudes about group care. Although names will not be associated

with their data, they have a low-moderate risk of loss of confidentiality, because there are a limited number of clinic staff clinic at each selected clinic. If information about their participation or responses were to become publicly known, no harm greater than what might occur in everyday living should result to the participant. Staff may also feel moderate pressure-to-participate because the health facility where they work is supporting the project, and their clinic administrator is supportive of the project.

Health officials (clinic administrators, district and national): They allow the research team to observe and take notes at selected planning meetings and will participate in an interview annually in years 1-5. Because there are only a few health officials at these institutions, they have a moderate-to-high risk of loss of confidentiality. They may also feel low-to-moderate pressure to participate because they have agreed to support the program. Although names will not be used in meeting transcripts, their identities may not be able to be concealed due to their role at their institution.

Benefits

There may be no benefit to participating in this study. However, women in group antenatal care often experience more positive, respectful interactions with their health providers and complete more of their recommended antenatal care visits than do those receiving usual care. This increases the opportunity that any problems with their pregnancy will be identified and treated, with better health outcomes and decreased morbidity and mortality for mothers and their infants. Women spend less time at antenatal care appointments and spend more time on health promotion. Women interact with other women who become a source of social support and collective problem-solving. Group antenatal care is social, fun and engaging, in contrast to usual care which is prolonged, rushed, and often disrespectful and boring. Increased HIV testing may lead to more optimal treatment and health promotion behaviors, and thus to longer lives for participants who are found to be HIV positive or already HIV positive.

If clinics successfully implement group care model and this increases attendance and quality of antenatal care visits, we will see reduction in pregnancy-related maternal and infant morbidities and deaths. The risks of participation are minimal and reasonable given the high prevalence of HIV and extraordinarily high rates of maternal and infant mortality in Malawi, these larger benefits are important to the science of healthcare delivery from a local to the national levels.

8.0 Data Collection and Management Procedures

Cognitive interviews (Aim 1)

Data are procured from researcher notes about each question, response, explanations and alternate wording of each question using paper and pencil. This is an iterative process of change until the comprehensibility of new and/or revised healthy pregnancy knowledge and behavior survey are clear. We will document the changes over time, but no data are stored.

Effectiveness participants (Aim 1)

Coded survey data collected via ACASI that includes self-report responses, data from health records and the medical tests (Hb and pregnancy). These data are stored on encrypted and password protected computers. The data will be transferred from the computer to PHI protected and UIC-supported box.com folder for collaborator sharing.

Training Video (Aim 2)

After the video is completed and all clips illustrating important aspects of offering group care are identified, remaining video clips will be deleted.

Implementation (Aim 2)

Study notes and transcriptions will be coded by replacing any identifying information with pseudonyms or code numbers. These data are also stored on encrypted and password protected computers. The data will be transferred from the computer to PHI protected and UIC-supported box.com folder for collaborator sharing. Once the audio-recordings are verified for accuracy, we will discard those files.

9.0 Data Analysis

Aim 1. Cognitive interviews analysis

The researcher takes notes about each question, response, explanations and alternate wording of each question. This is an iterative process of change until the comprehensibility of new and/or revised healthy pregnancy knowledge and behavior survey are clear.

Aim 1. Effectiveness analyses

Dr. Liu will supervise data analysis procedures. She will produce a codebook with variable names, descriptions, and value codes. Missing data will be minimized through our retention efforts but are inevitable, to some degree, in any longitudinal study.

In preliminary analyses, we will complete a CONSORT diagram of recruitment, retention and loss to follow-up from initial recruitment through final data collection. We will determine retention rates and examine attrition bias, e.g., significant demographic differences between those retained and those lost to follow-up using Cox proportional hazards regression for time-to-dropout. Randomization success will be evaluated by comparing group differences in baseline demographics and measures of interest such as HIV testing, pregnancy knowledge and behaviors, etc. Any significant differences in sites' demographic characteristics at baseline and attrition biases will be controlled in later analyses.

Bivariate analyses between the outcome variables and study group will first be conducted using t-tests (continuous variables) or Chi-squared tests. Potential clinical site differences will be identified using Analysis of Variance (ANOVA) models for continuous variables or Chi-squared tests for categorical variables. All multivariate analyses will be conducted using multi-level hierarchical models, with clinical site entered into the models as both fixed effects (to adjust for mean site differences) and random effects (to account for within-site correlations). For outcomes that are measured only once, mixed-effects linear regression (continuous), Poisson regression (count data), or logistic regression (dichotomous or ordinal) models will be employed. Intra-class (site) correlation coefficient (ICC) will be estimated. Group assignment, sites, women's demographics, and obstetric characteristics will be included as fixed effects. Potential effect modifiers will be identified (based on theoretical reasons) by testing the interaction between group and the potential modifier. For continuous outcomes that are measured more than once such as mental distress or partner communication, mixed-effect regression models will be employed to examine group effect over time with both random site and individual (nested within site) effects. Generalized Estimating Equation (GEE) models will be employed to analyze dichotomous repeated outcomes (such as consistent condom use in the last 2 months). In all repeated measures models, the interaction between group and time will be the parameter of interest, and time-point specific group difference will be estimated from the model. In all multivariate models, backward selection methods will be employed to select significant factors that are associated with the outcome. All statistical tests will be two-sided tests, controlling for probability of Type I error of 0.05.

Aim 2: Degree of Implementation Success and Contextual Factors Analyses

This is an iterative process that begins in Month 3 and continues throughout the study. We extract contextual factors (events or statements) from Study Notes, interviews, observations. We focus on reported successes, challenges, solutions tried and whether successful, as well as champions and naysayers. We then categorize events or statements according to CFIR domains and constructs using the on-line codebook and in consultation with Damschroder.

Using well-established mixed methods analyses,^{94,97} we then compare across cases to identify constructs most strongly related to degree of implementation success (variable-oriented approach).⁹² Our mixed method analysis to construct the final across case matrix is also guided by the procedures used by Damschroder and Lowery to identify contextual factors associated with greater or less implementation success for an obesity program in the US.⁷³ At the conclusion of Aim 2 analyses, we will identify the contextual factors that consistently relate to degree of implementation success (or failure) across all 6 clinics.

10.0 Quality Control and Quality Assurance

Aim 1 Effectiveness: Dr. Liu will supervise data analysis procedures. She will produce a codebook with variable names, descriptions, and value codes. Missing data will be minimized through our retention efforts but are inevitable, to some degree, in any longitudinal study. The 6 clinics rollout at different time points and require their own clinic data so they can assess the impact of group antenatal care for their own clients. Every 6 months, we generate a descriptive report summarizing outcomes for group and usual care by each clinic and totals for all clinics, using the cumulative data available. Reports will be shared with the Ministry of Health's Safe Motherhood Task Force.

Aim 2 Implementation: Our data are coded separately by 2 coders who will consult with the team to review discrepancies, refine code definitions and recode until intercoder reliability exceeds 85%. Thereafter, 10% of randomly selected transcripts will be double-coded.

11.0 Data and Safety Monitoring

This research study meets the definition of a clinical trial and will be registered as such if funded. We use a hybrid design to test the effectiveness of the group antenatal care and its implementation in real-world conditions.

Our data and safety monitoring plan (DSMP) includes maintaining data in secured locations at University of Malawi and UIC that are accessible only to the research team. Coded data will be transferred electronically from Kamuzu College of Nursing to University of Illinois at Chicago using UIC-supported PHI cloud-based storage: box.com.

Here we describe the oversight and monitoring by our research team to ensure the safety of participants and the integrity of the data. As part of the data and safety review process, data will be analyzed on an ongoing basis by Patil and Chirwa. We will comply with responsibilities as outlined by the NIH and specifically, NINR.

The probability and magnitude of harm or discomfort anticipated in the research are not greater than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. However, we describe what we will do to monitor the foreseeable adverse events.

We will hold regular in-person or skype meeting to monitor the protocol for effectiveness and safety so that participants are not exposed to unreasonable or unnecessary research risks. We will monitor our study progress and conduct. The integrity of the study design will be protected and monitored through a) initial training for research members, b) regular meetings with research staff, c) review of qualitative and quantitative data collection.

Because the level of complexity and associated risks are minimal, the PI and in-country investigators will review all protocols regularly (in-person when the PI is there and via skype when the PI is the USA). The initial training of research staff will help to make sure staff are aware of their own and others' roles and responsibilities. Training will include: 1) an overview of research objectives, the basic theoretical framework, and research design and rationale, 2) conduct of the informed consent process; 3) background and training on collecting data free of bias, 4) basic information on evaluation items; 5) protection of human subjects and confidentiality issues; 6) detailed demonstration of group antenatal care; and 7) data and intervention monitoring and quality assurance procedures. Activities for training will consist of brief lectures, discussion, role-play and evaluation. Thereafter, regular research staff meetings and/or skype conferences will be used to review the protocol, identify protocol issues and make decisions about changes to the protocol based on this monitoring.

We will monitor oversight of the study as well as consider factors external to the study when interpreting data, including new scientific or therapeutic developments that may impact the safety of the participants or the ethics of the study. We will also review any changes needed to the consent form or study protocol, and conflict of interest issues that might arise during the study. We will assess how enrollment is proceeding, how the providers and women are working together in their groups, as well as all adverse events (Adverse events and procedures are described below).

Quality assurance will also involve engaging in good data management activities. Project meetings with data collection staff will take place quarterly or as needed. To ensure reliability of the Excel data entry it will be double entered and checked for 100% accuracy. Procedures that include such things as checking the integrity of data storage and examining frequency distributions to look for anomalies will be in place.

On a quarterly basis or as needed, the PI together with Li, our team biostatistician, will oversee preparation of reports that will include summaries of: cumulative accrual and by clinic, randomization, cumulative attrition, attrition by clinic, study condition, gender, and ethnicity, adverse events and serious adverse events, data completeness and quality. The PI will report changes to study procedures deemed necessary to the appropriate IRB offices and NIH as the funding agency if needed.

Risk and Adverse Events

Pregnant women participants in the pilot will be assigned to either group antenatal care or individual care. While there are certainly risks surrounding pregnancy, there is no reason to believe that participation in group care will significantly alter or increases the normal medical risks associated with pregnancy. There are no medically significant or identified reasons to believe that participation in group healthcare delivery of antenatal care would increase risks. The standard of care is the same for both study conditions and meets expectations required by the Ministry of Health. It is only the delivery format that differs by study condition.

Foreseeable risks

The probability and magnitude of harm or discomfort anticipated is likely no greater than that of a typical antenatal care visit for both women and health professionals. Therefore, the foreseeable risks are minimal.

Foreseeable risks may include a negative psychological experience for participants should they feel embarrassment or discomfort about some aspect of their personal life that they choose to reveal in the interviews or to the group. Associated with this is risk of breach of confidentiality. Special efforts are planned to ensure that this risk is minimized. For example, at the first group session, women discuss the importance of confidentiality and will be asked to sign a confidentiality agreement form.

Adverse Events

The study is minimal risk; however adverse events are defined here and will be monitored throughout the study by the effectiveness study team, who will promptly inform the co-Is and PI, to be sure that they are not associated with participation in group care.

Although we do not anticipate any serious adverse events (SAEs) associated with antenatal care, we are tracking the following as SAEs: maternal death, pregnancy loss, stillbirth and newborn/infant death, attempted suicide and major depression

All adverse events, serious or otherwise, will be reported by the study team to the PI within 24 hours. The PI and in-country co-investigators will evaluate all unexpected AEs and if deemed serious, the PI will report SAEs immediately to UIC's IRB and the NIH (NINR) project officer within 24-48 hours. UIC also has an established protocol (UIC OPRS Adverse Event/Unanticipated Problem Review/Reporting Policy and Instructions) for reporting and addressing adverse events which we will adhere to (published at <http://research.uic.edu/node/1835>).

All participants will be provided with a toll-free number to contact the investigators directly should they have other issues or concerns. All classifications of adverse events will be entered into the study database and tracked on quarterly reports.

12.0 Statistical Considerations

Aim 1 Effectiveness. To evaluate the overall effectiveness of group antenatal care compared to usual care.

Sample calculations:

Our two primary outcomes are preterm birth and HIV testing for women and partners (hypotheses H1 & H2). A national preterm birth rate of 18%³ was used. Because a US-based RCT found a 30% reduction in the preterm birth rate for women in group antenatal care, we expect that the preterm birth rate for women in group antenatal care in Malawi will be 12%, a 30% reduction from the national rate.

Our pilot data showed an attrition rate of 19% through 6 weeks postpartum; therefore, we assumed a 30% attrition rate for a longer duration of 6 months follow-up. Recruitment and randomization will be done in clusters of 24 women, and we assume a within-cluster correlation of 0.1. Therefore, a sample size of 2064 (86 clusters of 24 women) ensures 80% statistical

power (two-sided alpha = 0.05) for detecting group preterm birth rate difference after attrition (Final N at 6 months = 1244).

For H2, our pilot results from Malawi showed that 51% of group antenatal care partners were tested during pregnancy versus 27% for usual care. The proposed sample size of 2064 will ensure a statistical power of > 99% for detecting similar difference. Power analyses for Aim 1 were performed via simulations in SAS for dichotomous outcomes in a multi-level design.

A sample of 2064 women (1244 after attrition) ensures > 80% statistical power for testing all of our Aim 1 secondary outcomes. The primary outcome of preterm birth is a dichotomous variable with relatively low prevalence rate (12% for group antenatal care, 18% for Individual antenatal care). Testing this hypothesis with adequate power requires a large sample. Our secondary outcomes in Aim 1 are either dichotomous variables with relatively high prevalence compared to preterm birth rates (e.g., family planning, safer sex practices) or they use more efficient measurements, (e.g. continuous measurements such as birthweight or satisfaction scores; count data (e.g., visit adherence), or ordinal measures (e.g., service and content coverage, partner communication). Thus, these outcomes are less power costly.

For our exploratory hypothesis (H4), we used 6-month 2017 data from participating clinics to calculate an average HIV infection rate of 10.7% at these clinics. From the proposed N=2064 (1244 after attrition), we estimate that there will be a subsample of 133 HIV-infected women at 6 months postpartum. Only 78.8% of women diagnosed at their first antenatal care visit are retained in care 12 months later; 60% of those get their infant tested do not return for the infant's results.⁴⁹ Although our small sample will not provide adequate power, descriptive information will provide clinically important information about group antenatal care's effect on continuation of care for HIV-infected women and infant follow-up through 6 months postpartum.

Statistical Analyses:

See our analytical plan in section 9.0.

13.0 Regulatory Requirements

All investigators are compliant with the education in the protection of human research participants. Additions to our team will be trained prior to working on the project.

UIC

Crystal Patil	05/12/2010	CITI
Kylea Liese	02/04/2020	Investigator Training 101
Li Liu	02/08/2001	CITI
Kathleen Norr	09/12/2000	Investigator Training 101
Rohan Jeremiah	08/02/2021	Investigator Training 101

University of Malawi

Diana Jere	07/04/2002	Investigator Training 101
Ursula Kafulafula	05/20/2018	CITI
Elizabeth Chodzaza	05/15/2018	CITI
Ellen Chirwa (was Mbweza)	12/16/2015	CITI

Genesis Chorwe-Sungani completed the Research Ethics Course as part of his PhD program at the University of KwaZulu-Natal, South Africa on 12/10/2009 as well as the NIH online training 05/19/2018.

Please note that the Malawi team does not need the HIPAA training, Information Privacy and Security IPS for Researchers, since this training is specific to the US. However, the team will be trained by the investigators on privacy, confidentiality, and the protection of subjects' health information.

13.1 Informed Consent

All research team members who obtain informed consent will have received IRB investigator training and will have been trained by one of the investigators on the informed consent process specific to this study.

Aim 1 Cognitive Interviews: These participants are recruited from among women waiting to be seen for antenatal care at one or more of the selected clinics. A research team member approaches a woman individually and asks permission to speak with her privately for a few minutes about this project. Description of the study and obtaining signed informed consent will occur privately, so that others are not aware of whether she is a research participant. Those who consent will meet the researcher during her antenatal care visit and complete the cognitive interview in a private space within the clinic.

Aim 1 Effectiveness participants: Potential participants are recruited at the time of their initial antenatal care appointment. They meet with a member of the research team, who will provide full information about the research: purpose, procedure, risks, benefits, the right to discontinue participation at any time, to not answer any questions, who and where to obtain information about the project at any time, participation is strictly voluntary, and safeguards against potential risks. Potential participants will be asked a series of questions to ascertain that they understand the research before the signed consent process is completed.

Aim 2 Training video participants: Those who express interest will have this portion of the study and their role explained; they will be given an opportunity to ask questions. Participants will give informed consent to participate in a practice session, including permission to be videotaped and observed as they take part in the practice session. They know that they can request that a portion of the video not be used in the final Training Video (for any reason, for example, it's too personal, embarrassing, etc.).

Aim 2 Implementation participants: All clinic administrators, midwives, nursing staff, and volunteers at each selected clinic are approached privately by a research team member, who explains the study, risks, and protection from risk and answer any questions. The team member discusses whether the potential participant wants to take part in facilitating group antenatal care and then obtains signed informed consent. If the potential trainee doesn't want to participate, the researcher discusses what the person can say to the clinic administrator or supervisor to avoid coercion. Health officials have already agreed to support the project, but they have not yet been asked to take part in the evaluation of the project. At one of the first individual's meetings with the researchers after initiation of the project, the research team explains the research/evaluation aspect of the project, the official's participation in it, potential risks, and protection from risks; officials have an opportunity to ask questions. We also discuss how they can decline to participate unobtrusively (see below, protection from risks). Then they give signed consent. Subsequently they are reminded of the research and their verbal consent is reconfirmed before they are observed at meetings, participate in a focus group or have an individual interview.

13.2 Subject Confidentiality

Loss of confidentiality:

This risk is relatively low for cognitive interview participants and effectiveness evaluation survey participants (Aim 1), in that their identifying information is not associated with their data, and their names do not appear with their data at any time.

For the co-facilitators and training video participants (Aim 2) there are unique confidentiality concerns regarding the videorecording of selected training and group antenatal care visits to make video clips that illustrate key points. These cannot be not confidential, as they are intended to be viewed. To alleviate concerns, participants will have an opportunity to decide that certain clips cannot be included in the final Training Video. Because the recordings clearly indicate the identities, we cannot make assurances about confidentiality. However, the videos will only be used for training of other co-facilitators, who are healthcare workers, and thus will be viewed by a limited number of people.

Risk of loss of confidentiality is moderate to high for administrators and health officials (Aim 2) because there are only a few of them and they have readily identifiable jobs. For them, we make every effort to make sure that they understand that we cannot assure them that what they say will remain confidential, and therefore they should not say anything they would not want known publicly. We also make every effort to protect identity. Since these persons are political and public health leaders, they are accustomed to considering what they say in public. Moreover, the topics discussed are not likely to be highly controversial or sensitive. However, to ensure protections, in addition to the safeguards already described, these individuals are given an opportunity to review their statements and request that some not be included in published documents.

Access to Identifying information

Patil, Chirwa and members research team who will schedule appointments with the women in the effectiveness study (Aim 1) will have access to participants' identifying information (name, phone number and ID code). Only the individual interviews and effectiveness evaluation surveys have names with a matching ID. For effectiveness evaluation participants we also have cell phone numbers to contact them regarding scheduling surveys. Names are not obtained for the other data. All data are stored separately from documents containing names, including the survey data, which are coded with participants' unique project identification number. Data are stored on password-protected computers that are stored in a locked project office.

Protection of Data

Aim 1 Cognitive interview: Names of participants and other identifying information will not be recorded in the data (all is de-identified).

Aim 1 Effectiveness evaluation surveys: antenatal care clients complete an audio-assisted computer survey (ACASI) of HIV-prevention knowledge and behaviors, pregnancy knowledge, health behaviors, satisfaction with antenatal care and mental distress, with data entered directly on encrypted and password-protected laptop computers. Participants' data are labeled with their unique project identification number; this is the only identifier linking the data to the participant. The survey data are transferred from Malawi to UIC using the Box.com secure system supported by UIC. We have experience using ACASI, which has the major advantage that the privacy ACASI allows enhanced reporting of sensitive sexual behaviors. ACASI has been well-received in our current study with community adults and adolescents. However, we conduct the survey by face-to-face interview for any participant who is not comfortable using the computer. In those cases, participants will complete the questionnaires in private locations, with the questions read aloud by a research team member in Chichewa, the local language. Responses will be entered by the researcher on the computer for all questions except for the questions on

sexual activity and condom use. The interviewer shows the participant each of those questions on the computer screen and shows them where to touch to provide their response, and then allows them to touch their answer, following which the screen will move to the next question. Names of participants are not recorded in the database.

Contact information (names, cell phone numbers) of effectiveness evaluation participants are stored in a password-protected computer and accessible only to research staff. When contact information is needed to make appointments for the next data collection survey, a copy of the names and cell-phone numbers are provided to the community health worker with the instructions to safeguard the information and to return the contact sheets after scheduling the next data collection has been completed.

Aim 2: Implementation Evaluation study data:

Study notes from observed planning meetings, selected trainings, and Group antenatal care visits: Names of participants and other identifying information will not be recorded.

Videotapes of selected trainings and practice session: Video clips will be integrated into Training videos for use in future group antenatal care co-facilitator trainings. This is to promote fidelity to the group antenatal care model. Because the video will indicate the identities of the participants, who will provide consent to be video recorded, there is no way to ensure confidentiality. All participants will know this, and consent will indicate that they accept this as part of participation. The co-facilitators and pregnant women participants will have an opportunity request that any clip they identify as unsuitable not be used in the final Training Video.

Audio-recorded individual and focus group interviews: The stored data will be accessible only to the research team. Recordings will be erased after transcriptions and translations are completed.

Transcripts and translated transcripts of recorded individual and focus group interviews: The stored data will be accessible only to the research team.

Fidelity ratings of selected antenatal care visits observed by research staff: These discussions will not be audio recorded; observers will take detailed notes instead and will be instructed not to write peer group participants' names on the data forms. The data will be used by the research team to monitor fidelity to the original peer group model, and to provide corrective feedback to Group antenatal care co-facilitators about their performance.

Self-evaluations of group antenatal care visits by the co-facilitators: The stored data will be accessible only to the research team.

Benchmark scores are compiled from project records and antenatal care and HIV-related data routinely reported and provided by the clinic sites: Aggregate data from the clinic do not involve human subjects.

Health outcomes data on pregnant women and their infants taken from participants' medical records and Health Passports: The stored data will be accessible only to the research team.

13.3 Unanticipated Problems

Any unanticipated problems will be promptly communicated by the research team to the in-country investigators and PI. If the unanticipated problem is determined to be serious, the PI will report it to the IRB, and to the NIH if necessary. This report will include actions taken to resolve or ameliorate the problem, as possible, or avoid or minimize its re-occurrence.

14.0 References

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APPENDICES

Eligibility Checklist

- Eligibility Screening Tool for Cognitive Interviews

Eligibility Screening Tool for Cognitive Interviews

Inclusion & Exclusion Criteria		Yes	No
1	Cognitive limitations that will prevent participation?		
		exclude	
2	Currently pregnant?		
			exclude
3	Aged 18 or older?		
			exclude
4	Speaks and understands Chichewa		
			exclude

- Eligibility Screening Tool for Effectiveness Participants

Eligibility Screening Tool for Effectiveness

Inclusion & Exclusion Criteria		Yes	No
1	Cognitive limitations that will prevent participation?		
		exclude	
2	Currently pregnant?		
			exclude
3	Aged 18 or older?		
			exclude

4	Speaks and understands Chichewa		
			exclude
5	Gestational age of 24 weeks or less?		
			exclude

- Eligibility Screening Tool for Training Video Participants

Eligibility Screening Tool for Training Videos

Inclusion & Exclusion Criteria		Yes	No
1	Cognitive limitations that will prevent participation?		
		exclude	
2	Currently pregnant?		
			exclude
3	Aged 18 or older?		
			exclude
4	Speaks and understands Chichewa		
			exclude

Research Involvement:

1. Attend a 4-day training on group antenatal care and Benchmarks.
2. Allow training and practice sessions to be observed and some sessions to be videotaped to produce the Training Video to complete the Toolkit.
3. Allow observation and allow note-taking by research staff of select group session and from weekly phone calls intending to support fidelity and resolve problems.
4. Complete group antenatal care data forms, such as attendance and self-evaluation of fidelity.
5. Participate in 2 focus group interviews over the 1-year period with a possible 3rd interview during the Year 5 Clinic Dissemination Conference.
6. Complete 3 surveys over 12 months assessing motivation, burnout, self-efficacy, knowledge and attitudes about group antenatal care.
7. Selected antenatal care Staff become Trainers of Trainers for development of future cadres of Group antenatal care facilitators.

Data sources: Study notes from observations of meetings, training and group antenatal care visits, videotapes of trainings and group antenatal care visits to develop video-clips for Training Video, Audio-recorded interviews, transcripts and translated transcripts of interviews, fidelity rating forms, self-evaluations of group antenatal care visits completed by the co-facilitators, and benchmark scores

Study notes from observed planning meetings, selected trainings and group antenatal care visits: Names of participants and other identifying information will not be recorded.

Video clips: selected trainings and group antenatal care visits will be recorded to produce the Training video for use in future trainings, to promote fidelity to the model.

Audio-recorded interviews (individual and/or focus group): stored data will be accessible only to the research team. Recordings will be erased after transcriptions and translations are completed

Transcripts and translated transcripts of recorded individual and focus group interviews: The stored data will be accessible only to the research team

Fidelity: an observer will take detailed notes on the semi-structured fidelity form to monitor fidelity to the original group prenatal care model. Coded and stored data will only be accessible to the research team

Self-evaluations of group care visits by co-facilitators: Coded and stored data will only be accessible to the research team

Benchmark scores are compiled from project records and data routinely reported by the clinic sites. Aggregate data from the clinic does not involve human subjects.

Perceived pressure to participate

Pressure to participate may be moderate for all the participants except those in effectiveness evaluation. The Clinic Administrators, Malawi Ministry of Health Department Officials and Blantyre District Health Officials have already expressed public support for this study and might be embarrassed to not also participate in the evaluation.

The adults and adolescents in cognitive Interviews, group antenatal care and effectiveness evaluations may also feel some pressure to participate because its endorsed at the clinic. Again, we emphasize the right to not participate or to stop participating without penalty. We will also reassure the person that we will not tell anyone of their decision.

The co-facilitators are invited to participate by their employer and the research team. We cannot eliminate this pressure, but we will make every effort to emphasize the right to not participate or to stop participating without penalty. We will also offer tactful strategies to decline for those invited to become group antenatal care co-facilitators who do not wish to accept. Since in some clinics there will likely be more eligible co-facilitators than available slots, it will be less obvious whether someone declined or wasn't able to be assigned to facilitate Group antenatal care.



**University of Illinois at Chicago
Research Information and Consent for Participation in Research
Group Antenatal Care in Malawi
Effectiveness Evaluation**

You are being asked to participate in a research study. Researchers are required to provide a consent form such as this one to tell you about the research, to explain that taking part is voluntary, to describe the risks and benefits of participation, and to help you to make an informed decision. You should feel free to ask the researchers any questions you may have.

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Why am I being asked?

You are being asked to participate in a research study that compares two different types of antenatal care: usual antenatal care and group antenatal care.

You have been asked to participate in the research because you are a healthy pregnant woman who completed your first antenatal care visit and are 15 years old or over.

Your participation in this research is voluntary. Your decision whether or not to participate will not affect your current or future dealings with this clinic. **If you decide to participate, you are free to withdraw at any time without affecting relationships.**

Approximately 2,000 women from six antenatal care clinics in Blantyre District may participate in this research.

What is the purpose of this research?

We are doing this research to learn which type of antenatal care is better for pregnant women and their babies, antenatal care in a group of 8 to 12 women or antenatal care offered to women individually (as usual). A study in the United States showed that group antenatal care reduced the risk for preterm birth. We want to know if this will happen in Malawi.

What procedures are involved?

This research will take place in a private space in this clinic, like the room we are in now. You will be asked to answer some questions in a survey today and three more times: once in late pregnancy, once at six weeks after birth, and once at 6 months after birth. We will ask you to answer the questions a total of four times. Each survey will take between 30-60 minutes to complete.

If you agree to participate in this study, the following will happen:

1. You will be assigned by chance to receive antenatal care in a group with other women or individually.
2. If you are assigned to individual care, you will attend antenatal care as you regularly would, which typically includes a total of 8 visits, plus visits at 1 week after birth and 6 weeks after birth. Each individual care visit will be conducted as usual at your clinic, where you will have a one-on-one visit with your midwife. You may also receive education in the form of a lecture or with your midwife.
3. If you are assigned to group care, you will attend antenatal care appointments, which typically includes a total of 8 visits, in a group of 8 to 12 women, plus two visits after birth. The 1-week after birth visit will be an individual visit as usual. The 6-week postpartum visit will be a group visit.
 - Group care visits include the same midwife assessments that occur in individual care, but you will be taught to take some of your own health measures. You will have a brief one-on-one private visit with the midwife. You will also receive education in the form of a group discussion.
4. We will ask you to complete four individual surveys. We will arrange to meet you at the clinic at a convenient time each time a survey needs to be completed.
 - Each survey will take between 30-60 minutes to complete. The first survey will take the most time (~60 minutes). Surveys 2 and 3 will take about 45 minutes and the last survey ~30 minutes.
 - The surveys ask questions about your household; previous pregnancies; knowledge about pregnancy, HIV, and prevention of mother-to-child transmission; if you were tested for HIV during your pregnancy and if you received the treatments you needed. In the third survey, questions are added about your birth experience, the health of your newborn, and infant care.
 - We may ask you to refer to the information on your Health Passport to remind you about the health services you have received including your infant's birth date, weight, whether the baby had a well-child visit and appropriate treatments.
5. Every time we see you for a survey we will also do a fingerprick to measure your hemoglobin levels.
6. At the final interview, 6 months after birth, we will ask you for a sample of urine to do a pregnancy test to see if you are pregnant.

7. You will participate in the study for up to one year.
8. We will ask you for a phone number and/or address so that a team member can contact you between surveys. They will help schedule and remind you about the survey day and time.

☐ I agree to be randomly assigned to either individual or group ANC.

Initials or Thumbprint: _____

☐ I agree to allow a member of the research team to contact me at home or by phone to setup appointments to take the survey.

Initials or Thumbprint: _____

☐ I agree to take the four surveys and the fingerprick to measure my hemoglobin.

Initials or Thumbprint: _____

☐ I agree to take a pregnancy test at 6 months postpartum.

Initials or Thumbprint: _____

What are the potential risks and discomforts?

To the best of our knowledge, the things you will be doing as part of this study have no more risk of harm than you would experience in everyday life or during regular antenatal visits. Because this research involves a group of people, there is a risk that a breach of privacy (others will know that you are participating in this research) and confidentiality (accidental disclosure of information that has your name) may occur.

Because some topics discussed in the group and some questions on the survey are personal, you may experience some discomfort during the discussions. However, you are free to skip questions or sit quietly in the group. Also, if at any point you no longer want to participate, you may withdraw from the study at any time.

Will I be told about new information that may affect my decision to participate?

During the course of the study, you will be informed of any significant new research information (either good or bad), such as changes in the risks or benefits resulting from participation in the research or new alternatives to participation, that might cause you to change your mind about continuing in the research. If new information is provided to you, your consent to continue participating in this research may be obtained again.

Are there benefits to taking part in the research?

Taking part in this research study may not benefit you personally, but we may learn new things that will help other pregnant women by improving antenatal care.

What other options are there?

You do not have to be in this study to attend antenatal care at this clinic.

What about privacy and confidentiality?

Your privacy is important to the research team. For those in individual care, only members of the research team will know that you are in the study. For those in group care, other members of your group will know that you are in this study.

No information about you will be disclosed to others without your written permission, except if necessary to protect your rights or welfare (for example, if you are injured and need emergency care or when the UIC Office for the Protection of Research Subjects (OPRS) monitors the research or consent process) or if required by law.

Study information which identifies you and the consent form signed by you will be looked at and/or copied for checking up on the research by the National Institutes of Health (NIH) and/or the UIC OPRS.

A possible risk of the research is that your participation in the research or information about you might become known to individuals outside the research. We will make every effort to prevent this from happening by doing the following:

- Also, to ensure that others will not be able to connect you to your survey answers, we will assign you a special number, and all of your information will be identified by this number. We will keep the list of the participants' names, contact information and special numbers separate from other study materials.
- A copy of your signed consent form will be stored in a locked office in a locked cabinet at the Kamuzu College of Nursing.
- Your contact information will be destroyed when we finish all of the surveys.

Although we ask everyone in the group to respect each other's privacy and confidentiality, and not to identify anyone in the group or repeat what is said during the group discussion, please remember that other participants in the group may accidentally disclose what was said.

When the results of the research are published or discussed in conferences, no information will be included that would reveal your identity.

What are the costs for participating in this research?

There are no costs to you for participating in this research.

Will I be reimbursed for any of my expenses or paid for my participation in this research?

At the end of each of the four surveys you will receive \$12, for a total of \$48 at the end of the study.

Can I withdraw or be removed from the study?

If you decide to participate, you are free to stop participating at any time.

Who should I contact if I have questions?

Contact the researchers:

Ellen Chirwa, PhD

Professor, Kamuzu College of Nursing
Tel: 265 0 1 873623; Cell: 265 888940513
embweza@kcn.unima.mw

Crystal Patil, PhD

Associate Professor, UIC
Tel: 1 312 996-4327
cpatil@uic.edu

- if you have any questions about this study or your part in it,
- if you have questions, concerns or complaints about the research.

What are my rights as a research subject?

If you feel you have not been treated according to the descriptions in this form, or if you have any questions about your rights as a research subject, including questions, concerns, complaints, or to offer input, you may call the Office for the Protection of Research Subjects (OPRS) at 312-996-1711 or 1-866-789-6215 (toll-free) or e-mail OPRS at uicirb@uic.edu.

Remember:

Your participation in this research is voluntary. Your decision whether or not to participate will not affect your current or future relations with the University. If you decide to participate, you are free to withdraw at any time without affecting that relationship.

Signature of Subject

I have read (or someone has read to me) the above information. I have been given an opportunity to ask questions and my questions have been answered to my satisfaction. I agree to participate in this research. I will be given a copy of this signed and dated form.

Signature or Thumbprint

Date

Printed Name

Signature of Person Obtaining Consent

Date (must be same as subject's)

Printed Name of Person Obtaining Consent



**University of Illinois at Chicago
Research Information and Consent for Participation in Research
Group Antenatal Care in Malawi
Effectiveness Evaluation**

You are being asked to participate in a research study. Researchers are required to provide a consent form such as this one to tell you about the research, to explain that taking part is voluntary, to describe the risks and benefits of participation, and to help you to make an informed decision. You should feel free to ask the researchers any questions you may have.

Institution	Kamuzu College of Nursing	University of Illinois at Chicago (UIC)
Researchers	Ellen Chirwa, PhD	Crystal Patil, PhD
Address	P.O. Box 415 Blantyre, Malawi	845 S. Damen, M/C 802, Chicago, IL60612 USA
Phone	265 0 1 873623	1 312 996-4327
Fax	265 0 1 875 341	1 312 996-8871
Email	embweza@kcn.unima.mw	cpatil@uic.edu
Funding agency	National Institute of Nursing Research, Grant #R01 NR018115	

Why am I being asked?

You are being asked to participate in a research study that compares two different types of antenatal care: usual antenatal care and group antenatal care.

You have been asked to participate in the research because you are a healthy pregnant woman who completed your first antenatal care visit and are 15 years old or over.

Your participation in this research is voluntary. Your decision whether or not to participate will not affect your current or future dealings with this clinic. **If you decide to participate, you are free to withdraw at any time without affecting relationships.**

Approximately 2,100 women from seven antenatal care clinics in Blantyre District may participate in this research.

What is the purpose of this research?

We are doing this research to learn which type of antenatal care is better for pregnant women and their babies, antenatal care in a group of 8 to 12 women or antenatal care offered to women individually (as usual). A study in the United States showed that group antenatal care reduced the risk for preterm birth. We want to know if this will happen in Malawi.

What procedures are involved?

This research will take place in a private space in this clinic, like the room we are in now. You will be asked to answer some questions in a survey today and three more times: once in late pregnancy, once at six weeks after birth, and once at 6 months after birth. We will ask you to answer the questions a total of four times. Each survey will take between 30-60 minutes to complete.

If you agree to participate in this study, the following will happen:

1. You will be assigned by chance to receive antenatal care in a group with other women or individually.
2. If you are assigned to individual care, you will attend antenatal care as you regularly would, which typically includes a total of 8 visits, plus visits at 1 week after birth and 6 weeks after birth. Each individual care visit will be conducted as usual at your clinic, where you will have a one-on-one visit with your midwife. You may also receive education in the form of a lecture or with your midwife.
3. If you are assigned to group care, you will attend antenatal care appointments, which typically includes a total of 8 visits, in a group of 8 to 12 women, plus two visits after birth. The 1-week after birth visit will be an individual visit as usual. The 6-week postpartum visit will be a group visit.
 - Group care visits include the same midwife assessments that occur in individual care, but you will be taught to take some of your own health measures. You will have a brief one-on-one private visit with the midwife. You will also receive education in the form of a group discussion.
4. We will ask you to complete four individual surveys. We will arrange to meet you at the clinic at a convenient time each time a survey needs to be completed.
 - Each survey will take between 30-60 minutes to complete. The first survey will take the most time (~60 minutes). Surveys 2 and 3 will take about 45 minutes and the last survey ~30 minutes.
 - The surveys ask questions about your household; previous pregnancies; knowledge about pregnancy, HIV, and prevention of mother-to-child transmission; if you were tested for HIV during your pregnancy and if you received the treatments you needed. In the third survey, questions are added about your birth experience, the health of your newborn, and infant care.
 - We may ask you to refer to the information on your Health Passport to remind you about the health services you have received including your infant's birth date, weight, whether the baby had a well-child visit and appropriate treatments.
5. Every time we see you for a survey, we will also do a fingerprick to measure your hemoglobin levels.
6. At the final interview, 6 months after birth, we will ask you for a sample of urine to do a pregnancy test to see if you are pregnant.

7. You will participate in the study for up to one year.
8. We will ask you for a phone number and/or address so that a team member can contact you between surveys. They will help schedule and remind you about the survey day and time.

☐ I agree to be randomly assigned to either individual or group ANC.

Initials or Thumbprint: _____

☐ I agree to allow a member of the research team to contact me at home or by phone to setup appointments to take the survey.

Initials or Thumbprint: _____

☐ I agree to take the four surveys and the fingerprick to measure my hemoglobin.

Initials or Thumbprint: _____

☐ I agree to take a pregnancy test at 6 months postpartum.

Initials or Thumbprint: _____

What are the potential risks and discomforts?

To the best of our knowledge, the things you will be doing as part of this study have no more risk of harm than you would experience in everyday life or during regular antenatal visits. Because this research involves a group of people, there is a risk that a breach of privacy (others will know that you are participating in this research) and confidentiality (accidental disclosure of information that has your name) may occur.

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Signature or Thumbprint

Date

Printed Name

Signature of Person Obtaining Consent

Date (must be same as subject's)

Printed Name of Person Obtaining Consent