STUDY PROTOCOL

Official Study Title

Behavioral Interventions for Multiple Micronutrient Supplement Adherence in Cambodian Pregnancy: A Mixed-Methods Study

Study Information

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Mai A. Hoang
mhoang@hki.org

Research Protocol: Trial of Improved Practices (TIPs) to Improve Adherence to Multiple Micronutrient Supplementation (MMS) During Pregnancy in Cambodia and Formative Research for MMS Product Packaging Design

PI: Mai-Anh Hoang

Co-PI: Cassandra Sauer and Meng Sokchea

Other Investigators: Hou Kroeun, Sambo Sreang, Aman Sen Gupta, Rem Ngik, Ashutosh Mishra, Crystal Karakochuk, Rolf Klemm

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1. Background and rationale

Guidelines in Cambodia recommend iron and folic acid (IFA) supplementation during pregnancy (National Nutrition Program, MOH, 2012). However, recent research has proven the superiority of multiple micronutrient supplementation (MMS) over IFA in reducing the risk of maternal anemia and adverse birth outcomes (Keats et al, 2019; WHO 2020). MMS has been shown to confer additional benefits over IFA, including a reduced risk of preterm birth, low birth weight, and small for gestational age births (Keats et al 2019; Sudfeld & Smith, 2019; WHO 2020). The internationally recognized standard for MMS is the United Nations International Multiple Micronutrient Antenatal Preparation (UNIMMAP), a formulation containing iron, folic acid, and 13 other micronutrients, including thiamine, vitamin C, vitamin D, calcium, zinc, and iodine The broad range of vitamins and minerals offered in UNIMMAP MMS, referred to hereafter solely as MMS, serve to address the wide spectrum of micronutrient deficiencies commonly faced by women of reproductive age and pregnant women. Based on this evidence, in 2020 the World Health Organization (WHO) updated their antenatal care guidelines to recommend MMS in the context of 'rigorous research' including acceptability and feasibility trials (WHO 2020). In 2021, MMS was included in the WHO Essential Medicines List (EML) as an antenatal supplement for pregnant women. The Cambodian Ministry of Health has expressed strong interest to transition from IFA to MMS during pregnancy but sought evidence in the Cambodian context to rigorously inform this policy change.

In 2023, a cluster randomized non-inferiority trial was completed in Kampong Thom province Cambodia (n=1546) to assess pregnant women's adherence to MMS compared to IFA supplementation during pregnancy (Hoang et al, 2024). In-depth interviews were completed with study participants who were high adherers (>80%), low adherers (<80%), and those who did not complete the trial. Thematic analysis revealed a range of factors influencing adherence. At the individual level, forgetfulness and negative pregnancy-related experiences (e.g., nausea, fatigue) emerged as barriers for low adherence. Conversely, high adherers highlighted establishing routines, using visual cues (cue to action) in the house as a stimulus or trigger to take the prenatal, and positive beliefs in MMS benefits as facilitators.

Interpersonal factors significantly influenced adherence. Strong existing norms around IFA and discouragement from family/friends during pregnancy-related symptoms were barriers for some. On the other hand, support from family (husbands, mothers-in-law) and healthcare providers, including reminders and endorsement of MMS, were enablers for high adherence. No institutional barriers were identified. However, institutional enablers included endorsement by government health providers and counseling from healthcare professionals. In conclusion, it was found that factors that influenced adherence to MMS included pregnant women's knowledge about the importance of supplementation during pregnancy, the use of visual cues in the house, the strength of ANC counseling, and family and community influence. Based on these findings, strategies must involve pregnant women, family members, and midwives to effectively scale up and promote MMS adherence.

The Trial of Improved Practices Study (TIPS) is a participatory formative research technique used to test and refine potential health interventions, focusing on behavior change on a small scale before introducing them on a large scale (The Manoff Group, 2005). TIPS are used to gauge the acceptability of proposed new practices by engaging with potential participants in the design of the intervention. This study will use TIP principles to explore and design culturally

appropriate cues tot action or stimulus/triggers to action and motivational strategies to improve MMS adherence during pregnancy.

In addition, attractive and informative packaging plays a crucial role in building a brand name (Keller KL, 2005). Studies have shown that recognized and reputable brand names are associated with increased consumer acceptance and adherence compared to generic drugs (Rafael GB et al, 2019; Faasse K, et al, 2013; Faasse K, et al, 2016). Thus, understanding women's and their partners' preferences regarding packaging design can help create a brand for antenatal MMS that is delivered through the national health system that promotes optimal use throughout pregnancy.

2. Study aims and objectives

This study aims to assess the relevance, acceptability, and utility of three interventions in supporting adherence to the MMS regimen of one tablet per day. The overall aims of the study are to:

1. Learn what pregnant women prefer regarding visual reminders and motivational messages to help them remember to take their MMS.

2. Identify challenges and supports that affect whether women can take their MMS daily throughout their pregnancy.

3. Work with end users (pregnant women) to design motivational messages and visual reminders that are culturally appropriate and relevant for the local community. These will be designed to help women consistently take one MMS tablet each day for the entire 180 days of their pregnancy.

4. To collect feedback from pregnant women and their partners regarding the packaging design for antenatal MMS delivered through the national health system. This feedback will be used to help finalize the MMS packaging design, including the color scheme, logo, brand name, and packaging features.

3. Study design

This is a longitudinal mixed-method study that uses a cross-over TIPS design. All enrolled pregnant women will be asked to take MMS for the duration of their pregnancy and will experience all three interventions in a specific order. In this way, everyone gets to experience each approach. The women will receive exposure to each intervention for 3-4 weeks. On approximately the fourth week, eight week, and twelfth week of the study, the pregnant women will be asked to participate in a focus group discussion (FGD) with other women in the province who also received the same intervention the previous weeks. This process will be iterated in the same way for Intervention A, Intervention B, and Intervention C.

At the end of the study, in week 13 or 14, after having experienced all three adherence interventions, women in the TIPS study and their husbands/partners will be invited to a participatory workshop to discuss their preferences for the MMS product packaging.

The interventions are described below.

Intervention A: MMS + Family Support

- This intervention focuses on leveraging the power of a pregnant woman's social support network.
- Participants will receive 180 tablets of MMS and be asked to take MMS for the duration of her pregnancy.
- Additionally, study team members will work with participants to enlist the support of family members (spouse, mother-in-law, sister-in-law, etc.).
- Family members will be invited to a 1-hour orientation meeting to discuss the benefits of MMS for pregnant women and babies. They will be encouraged to provide daily encouragement and reminders to help the pregnant woman stay on track with her MMS regimen.
- Family members will be provided with an illustrative list of messages that could help encourage and motivate the women to take the MMS daily.
- This approach aims to harness the family's positive influence in promoting medication adherence.

Intervention B: MMS + Visual Reminders

- This intervention emphasizes the use of visual cues to support medication adherence.
- Participants will receive 180 tablets of MMS and be asked to take MMS for the duration of her pregnancy.
- They will also be provided with wall calendars specifically designed for the TIPS program.
- These calendars will likely include:
    - Designated spaces to mark MMS intake days.
    - Educational information about MMS and its benefits for maternal health.
    - Motivational messages to encourage consistent medication use.
    - Additional health information relevant to each trimester of pregnancy.
- By having a visual reminder readily available, participants can easily track their MMS intake and stay motivated throughout the program.

Intervention C: MMS + Social Media Posts and Videos

- This intervention utilizes a social media approach to encourage adherence.
- Participants will receive 180 tablets of MMS.
- They will also be exposed to educational and motivational messages delivered by healthcare providers through social media videos and social media posts.
- These social media posts and videos will be posted on various social media platforms (Facebook, Tik Tok) and participants will be sent links to their emails and phones and asked to watch them.
- Approximately 3 social media videos and posts will be developed.
- The videos and posts might cover topics like:
    - The importance of MMS for maternal health and growing baby’s health.
    - Benefits of consistent medication adherence.
    - Benefits of healthy eating.
    - General pregnancy care information and warning signs.
    - Reminders to attend prenatal checkups.

After using each intervention for 3-4 weeks, women will be invited to a FGD to share their experiences. The discussion will focus on whether they liked the intervention, how well it helped them remember to take their MMS and any pros and cons they saw. It will also ask the women to compare the current intervention with other intervention (i.e. family support, wall calendars, and public service announcements). Adherence data will be collected by asking women to bring their MMS pill bottle to the FGD for counting. Acceptability data will be collected through a Likert survey and will be administered by a member of the study team.

By using this TIPS crossover design, researchers can see which approach works best and use the women's feedback to improve the program throughout the study. This collaborative process, where participants try different interventions and share their experiences, allows researchers to refine the program iteratively (meaning in steps) based on the feedback, resulting in a more effective program by the end of the study.

4. Study setting

The research will be conducted in Kampong Chhnang, Rattanakiri, Takeo, and Kampot, representing the four regions in Cambodia: Coastal, Upland (Northeast), Lowland, and Tonle Sap.

5. Sample size calculation and sampling process

For the TIPS, the sample size of 48-60 women (around 12-15 women per province) is purposive but has been selected for two reasons. First, the sample size of 12-15 women per province allows enough women to participate in a FGD. Considering that an ideal number for FGD is 8-10 people if 20% of the participants are expected not to show, there would still be enough participants to conduct an FGD. Second, based on previous formative research with pregnant women in Kampong Thom, there was not much variation in the experiences of women regarding MMS acceptability and their perceptions of the benefits of various strategies to improve adherence. Thus, one FGD per province is believed to be sufficient to capture the range of perspectives on the different interventions and achieve saturation, or the point at which no new significant themes or insights emerge from the data.

For the participatory workshops to design the MMS product package, approximately 100 participants will be recruited across four provinces in Cambodia (25 participants per workshop, 4 workshops total). Participants will be pregnant women who have previously participated in the TIPS program and their husbands/partners. The sample size is a convenience sample and chosen for the following reasons. First, it is anticipated that with a focused group like pregnant women and their partners who have a shared experience with the TIPS program, 25 per province is likely enough to reach saturation. Second, the study must consider logistical manageability and group dynamics. With 25 participants, workshops can maintain a manageable size for group discussions and activities. This allows for active participation, ensures everyone has a chance to be heard, and facilitates effective interaction. Thirdly, smaller workshops require fewer facilitators, materials, and space, making them more cost-effective and easier to organize across four different provinces.

6. Participant recruitment and selection

The research team will aim to recruit 12-15 pregnant women attending their first ANC per province. Ideally, from 8-10 of these women will then join the FGD to discuss their experiences with that specific intervention (see Table 1).

Figure 1. TIPS sample size per province

Week	Interventions	Kampong Chhnang	Rattanakiri	Takeo	Kampot	Total
1-3	A	12-15	12-15	12-15	12-15	**48-60**
4	**Focus Group Discussions**					
5-7	B	Same women	Same women	Same women	Same women	
8	**Focus Group Discussions**					
9-11	C	Same women	Same women	Same women	Same women	
12	**Focus Group Discussions**					
Total		**12-15**	**12-15**	**12-15**	**12-15**	**48-60**

The study participants will include approximately 48-60 pregnant women attending their first ANC in their first trimester at a public health center. Approximately 48-60 pregnant women will be recruited across 4 health centers in Kampong Chhnang, Rattanakiri, Takeo, and Kampot. It is estimated that approximately 12-15 pregnant women will be enrolled per province. Pregnant women will be purposively recruited at their **first antenatal care visit** (~8-14 weeks gestation). An attempt will be made to select women of diverse sociodemographic characteristics.

For the participatory workshops to co-design the MMS package, we plan to invite all women and their husbands enrolled in the TIPS study design. The first 25 from each province who agree to participate will be registered to attend the participatory workshop. We will aim to have a relatively equal proportion of men and women.

6a. Inclusion criteria for pregnant women

- Age 18-45 years
- Attending first ANC
- Low-risk pregnancy, which includes being pregnant with a single pregnancy and the absence of any other medical or surgical conditions
- Reside in Kampong Chhnang, Rattanakiri, Takeo, and Kampot and not planning to move away within four months
- Agree to try to take MMS as their prenatal supplement
- Agree to participate in three FGDs, one every three months
- Agree to bring MMS bottles to the FGD each month for tablet counting

6b. Exclusion criteria for pregnant women

- Pregnant women who do not fall into the age range of 18-45
- Came to the health facility after first ANC
- Midwives and/or doctors have classified pregnant women as having a high-risk pregnancy.

6c. Inclusion criteria for husbands

- Willingness to participate in the participatory workshop
- Confirmed availability for date and time of workshop

6d. Exclusion criteria for husbands

- Unwillingness to participate in the participatory workshop
- Did not confirm availability for the date and time of workshop

6e. Recruitment process and taking informed consent

Selected healthcare providers (e.g. midwives, doctors) from the primary health center will attend an orientation and training on the objectives and design of the study, the benefits of IFA or MMS supplementation during pregnancy, and any expected risks with participation. Healthcare providers will be trained on the protocol for enrollment (e.g., inclusion and exclusion criteria), obtaining verbal consent, and recording registration data. A primary healthcare worker in the health center (receiving an incentive payment from the study) will invite pregnant women to participate, give an overview of the study, including any risks, and ensure they meet all inclusion criteria. Healthcare workers will obtain verbal informed consent, provide the MMS-180, and explain that the study team will contact the participants within 72 hours and visit them in their homes to obtain written informed consent. If the woman agrees, she will provide her contact number, which the healthcare worker will submit to the study team by the end of the day. The women will then receive MMS-180 and be counseled on its use. A member of the study team will reach out to the new participant ideally within 72 hours to confirm participation, informed consent, and that the woman received the supplements. Up to two weeks will be allowed from the time of verbal informed consent at the health center until written consent is obtained at the participant's home. A record of all women screened but not enrolled will be maintained. The enrollment form is included in Annex A and the informed consent form for TIPS is included in Annex B. The informed consent from for the participatory workshop is in Annex C.

7. Study procedures

In each of the four health centers, a designated healthcare provider will enroll up to 15 pregnant women with first ANC visit. All women will receive all three interventions (family support, wall calendars, social media posts and videos) sequentially over 12 weeks. Women will be exposed to each intervention for 3-4 weeks, followed by a FGD to share their experiences and feedback. This iterative process helps researchers improve the interventions for better MMS adherence during pregnancy.

7a. Participant allocation

There is no allocation to any intervention group. Each enrolled woman receives all interventions in a specific sequence. Per province, in each health facility, the study team will purposively select pregnant women to ensure a diversity in sociodemographic characteristics. This helps ensure the interventions are appropriate for a broad range of women. After ensuring written informed consent, the eligible pregnant women will be asked to participate in taking MMS and arm experience all three interventions (A, B, and C) in a specific order. The sequence for each study arm and their exposure to the intervention is shown in Figure 2. This allows researchers to compare a participant's experience with each intervention.

7b. Enrollment data

Demographic and other enrollment data, such as gestational age at enrollment, maternal age, maternal BMI, maternal Hb, parity, as well as contact information and detailed directions to home of residence, will be collected from the health facility. This data will be included in the analysis for adherence, acceptability, and barriers and enablers.

7c. Intervention description

- **Intervention A (MMS + Family support)**: 180 tablets of MMS and daily encouragement and help from family members. Family members will receive an orientation on supporting pregnant women and encouraged them to provide daily motivational reminders until she finished 180 pills
- **Intervention B (MMS + Visual reminders)**: 180 tablets of MMS and wall calendars with health information and motivational messages will be provided.
- **Intervention C (MMS + Social media posts and videos)**: 180 tablets of MMS and 2-3 times/weekly social media posts and videos educational and motivational messages from healthcare providers delivered through social media posts and videos. Messages will emphasize its benefits and offer encouragement.

Figure 2: Weeks 1-14, Testing of interventions across all study arms and participant FGDs

Intervention	*Week 1-3*	*Week 4*	*Week 5-7*	*Week 8*	*Week 9-11*	*Week 12*	*Week 13-14*
	Intervention A	**Focus Group Discussion A**	**Intervention B**	**Focus Group Discussion B**	**Intervention C**	**Focus Group Discussion C**	**Participatory Workshop**
A	**X**	**X**					**X**
B			**X**	**X**			**X**
C					**X**	**X**	**X**

7d. Conduct of focus group discussions

Recruitment and scheduling: In each province, all pregnant women who have completed the specific intervention period (e.g., all used wall calendars for 3-4 weeks) will be invited to participate in an FGD. The research team will schedule a convenient time for a 70-minute discussion in a convenient, private, comfortable location.

Moderator and notetaker: The research team will identify a trained moderator familiar with MMS and the project's interventions. Additionally, the research team will identify a trained notetaker present to capture key points and nonverbal cues.

Discussion Guide: The research team will use the intervention-specific semi-structured discussion guide(s) with open-ended questions for each intervention (See Annex D for a discussion guide for Intervention A; Annex E for a Discussion guide for Intervention B; and Annex E for a Discussion guide for Intervention F). For each intervention, explore the following themes:

- Acceptability of the intervention (e.g., ease of use, cultural appropriateness)
- Explore fit-for-purpose, such as the intervention's ability to support adherence to MMS during the intervention period.
- Perceived pros and cons of the intervention
- Suggestions for improvement

Conduct of the FGD: Start with introductions, explain the purpose of the discussion, and establish ground rules for respectful communication and confidentiality. Ensure informed written consent. Inform participants that the FGD will be audio-recorded. The moderator will guide the conversation using the discussion guide, ensuring all participants have a chance to share their experiences. Encourage open discussion and probing for details and insights. The moderator will practice active listening techniques, and the notetaker will capture key points, quotes, and nonverbal cues for later analysis.

7e. Conduct of participatory workshops

Recruitment process:

- All women who previously participated in the TIPS program within the targeted provinces will be contacted by phone. During the call, invite the woman's partner/husband to attend the workshop with her. Explain that their joint perspectives are valuable.
- Briefly explain the workshop purpose, eligibility criteria, and incentive.
- If interested, obtain verbal consent to participate and schedule the workshop.
- Confirm availability of the proposed date, time and location of workshop.

Pre-workshop preparation:

- Develop three prototype MMS packaging designs with variations in color scheme, logo, brand name, and box features.
- Brainstorm key messages related to the benefits of MMS use during pregnancy.

Workshop Structure (70 minutes):

- **Introduction** (5 minutes): Welcome participants, provide an overview of the workshop's objectives, and obtain written informed consent. Inform participants that the FGD will be audio-recorded.
- **Icebreaker activity** (5 minutes): An engaging activity to create a comfortable atmosphere for participation.
- **Presentation** (10 minutes): Briefly explain the importance of MMS and its benefits for mothers and babies.
- **Group Discussion and prototype presentation** (30 minutes):

    - Participants will be asked guided questions using a semi-structured discussion guide. Themes focus on preferred colors, logos, brand names, and information they want to be included on the packaging.
    - Three prototypes of MMS packaging designs will be shared and the facilitator will guide participants through their visual elements (color, logo, brand name, box features).
    - Participants will be asked to “vote” on different aspects, using a prepared paper form to record their “vote” on different elements of colors, logos, brand names, and preferred prototypes.
- **Brainstorming session** (20 minutes): As a whole group, brainstorm key messages that should be included on the packaging to promote MMS use.

Moderator and notetaker: The research team will identify a trained moderator familiar with MMS and the project’s interventions. Additionally, the research team will identify a trained notetaker present to capture key points and nonverbal cues.

7f. Pill counts

At each FGD, pregnant women will be asked to bring with them their MMS bottle. At the end of each FGD, the research team will conduct a tablet count. The research team will explain that they will quickly count the woman's remaining MMS tablets by transferring the pills to a clean bag, counting them, and then returning them without touching them. After putting on fresh gloves, the trained researcher will open the medication bottle, pour the pills into a sealed bag, and place all pills flat with pills on one side. Using gloved hands, the researcher will count the pills, moving them one by one or grouping them by ten for easier counting. The count will be recorded twice. If the counts differ, they will repeat the process once more and record the final number. Finally, a small corner of the bag will be snipped, and the pills with the desiccant will be carefully poured back into the bottle before securing the lid. See Annex G for the tablet count sheet.

7g. Acceptability survey

During the FGD with pregnant women, all participants will be asked to fill out a survey to gather their opinions on various sensory aspects of the MMS. The survey will inquire about their preferences regarding the taste, smell, size, color, and ease of swallowing the pill. Participants will be asked to rate their opinions on a scale ranging from "strongly disagree" to "strongly agree," with options including "disagree," "neutral," and "agree." Each option will be represented by a corresponding mood emoji on the survey form. The survey is designed to be completed within 5 minutes and will be administered at the conclusion of the FGD. See Annex H for a copy of the acceptability survey form.

7h. Inventives for participants

Mobile data (KHR 15,000) will be provided for all women to see the social media posts and videos. In addition, a sarong, a towel, local fruits, or local nutritious food products (e.g. fish powder, dried fish) will be provided after each FGD and/or participatory workshop to respect participants' time and valuable participation in the FGDs and/or participatory workshop. These items were selected as incentives as they are believed to be valuable enough to show appreciation to respondents for their time, but not so valuable that they will cause undue influence in study participation.

8. Data collection methods and tools

Tool	Purpose	Annex No.
Enrollment Form	To obtain information on demographics, gestational age at enrollment, maternal age, maternal BMI, maternal Hb, parity, as well as contact information	A
Written Informed consent form for TIPS	To ensure that the participant is informed about the study; that participation is completely voluntary; and to understand any associated risks, benefits, and knowledge that she can withdraw at any time	B
Written informed consent form for participatory workshops for MMS product packaging	To ensure that the participant is informed about the study; that participation is completely voluntary; and to understand any associated risks, benefits, and knowledge that she can withdraw at any time	C
Intervention A FGD guide	• Acceptability of the intervention (e.g., ease of use, cultural appropriateness) • Explore fit-for-purpose, such as the intervention's ability to support adherence to MMS during the intervention period. • Perceived pros and cons of the intervention • Suggestions for improvement	D
Intervention B FGD guide		E
Intervention C FGD guide		F
Pill count form	To assess the participant's level of adherence and compliance to one tablet per day regimen	G
Acceptability form	To assess the participant's level of acceptability to several sensory aspects of MMS	H
Participatory workshop discussion guide		I

9. Data management plan

To ensure the quality and security of your focus group data, we'll follow these procedures:

Recording and Taking Notes:

- Discussions will be recorded digitally for future reference. Each recording will have a clear name, location, study group, intervention type, and date (e.g., Rattanakiri, Intervention A, May 16, 2024).
- A designated note-taker will capture key points during each discussion. These notes will also be named to match the corresponding recording for easy reference.

Data Storage:

- All recordings and notes will be securely stored in a dedicated folder on the Helen Keller International SharePoint site.
- Paper forms used to collect pill counts after each discussion will be returned to Helen Keller for separate storage.

Confidentiality:

- The research team will take steps to anonymize all data during analysis, meaning any information that could identify you will be removed.
- The research team will strictly follow the institutional privacy policy to protect your information.
- Paper notes will be kept safe in a locked cabinet, accessible only to the lead researchers (Principal Investigator and Co-Principal Investigator).

- Digital recordings will be password-protected and only authorized personnel can access them.

10. Data analysis plan

10a. Qualiatitive data analysis

Transcription and translation. All FGDs and the participatory workshops will be digitally recorded using ipads. Additionally, notetakers will be present to provide contextual notes and ensure accurate documentation of different speakers. The audio recordings from the FGDs and participatory workshops will be transcribed verbatim in English. Translation will be done simultaneously during transcription for interviews conducted in local languages. Transcribers will listen to the audio recordings in Khmer and translate and transcribe the interviews into English. The transcripts will be checked for quality by comparing them with the recorded audio and the notes taken by the notetakers.

After transcription is completed, a team of transcribers and coders will clean all FGD data. This cleaning process will involve tidying up partial sentences or words and writing out any abbreviations or acronyms. Any typos or abbreviations used in transcribing will be corrected directly in the text. All final transcripts will be reviewed for completeness and clarity before the analysis.

Data coding. The qualitative analysis team will read all typed transcripts and use a deductive-inductive approach for thematic content analysis. Initially, coding schemes will be developed based on the research questions and published literature for each intervention type (e.g. Intervention A, B, C) before data collection. These coding schemes will be refined and finalized after the lead researchers review a small set of transcripts and another small set by the assigned coders for accuracy and comprehensiveness. The coding schemes will then be shared and discussed with the rest of the research team before the assigned coders independently code the remaining transcripts. QSR NVivo software will be used to facilitate the coding and analysis of the data.

Data analysis. The qualitative analysis team will observe general patterns in the code summaries, focusing on context, descriptions, language, and narratives from the respondents' viewpoints. The analysis will include narratives and excerpts from focus group discussions to illustrate common themes, opinions, and viewpoints.

10b. Tablet counts

From pill count data, descriptive analysis will be performed to measure daily adherence to MMS. During each focus group discussion, we will count the MMS tablets for each participant and calculate the eligible period for consumption from the 1st ANC date (pill received date) to the date of the focus group discussion. The mean number of tablets consumed will be calculated based on the eligibility of the consumption period. Adherence e will be measured after the completion of each intervention, and differences in the mean will be measured. However, due to a very low sample size, no statistical test will be applied.

10c. Acceptability data

At the first focus group discussion, data collectors will ask pregnant women a quantitative acceptability questionnaire about MMS. A descriptive analysis will be conducted to determine the level of agreement (%) with each statement. However, due to a very low sample size, no statistical test will be applied.

11. Data custody, security, and protection of subject confidentiality

All data gathered during the study will be connected to identifiers and treated with the utmost confidentiality throughout and beyond the study period. Only the study's PIs and Co-PIs will have access to the data linked to the identifiers. The results of any analyses, presentations, or papers will be presented in aggregate to prevent individual disclosure. The survey will collect names of pregnant women only to ensure the accountability of the study team and to avoid duplication in the data collection/interviewing process. This information will be replaced with anonymous ID numbers for analysis, and the original data will be disposed of. Only members of the study team will be given access to the data.

Any paper notes collected during interviews will be kept in a locker until the final analysis is done. Once the analysis is done, all paper forms will be cut into pieces using a paper shredder machine. The data entry web-based platform will be password protected, and only a designated person can enter data. The data focal person will only have access to download and clean.

12. Risks and Benefits

Overall, the potential benefits of this study outweigh the minimal risks.

Benefits:

- Improved micronutrient status and improved birth outcomes: MMS is a proven effective intervention that improves maternal micronutrient status as well as improves birth outcomes, specifically reduces low birth weight, small for gestational weight, and pre-term births.

- Contribution to supportive interventions for pregnant women: The study will contribute valuable data to inform future interventions to improve optimal prenatal supplementation.

Risks:

- Minimal: The study involves minimal risks to the participants. MMS is a proven safe prenatal supplement that has been recommended by the World Health Organization to add to country's Essential Medicines List.

13. Plan for reporting unanticipated problems/adverse events

The study has been designed with minimal risks, but unanticipated situations may occur. In the event of an adverse incident, reporting will be directed as follows:

- **Midwife and/or physician:** Any immediate health concerns of a participant should be reported directly to the participant's midwife and/or health physician. This includes any perceived side effects from taking MMS or participating in any aspect of the study, including the FGD.

Additionally, reports to:

- **Principal Investigator:** Inform the principal investigator of all unanticipated risks to ensure data integrity and participant safety. The investigator will determine the next steps, which may involve modifying study procedures or informing the ethics board.

- **Helen Keller Country Director:** Depending on the severity and nature of the unanticipated risk, all adverse events should be reported to the Helen Keller Country Director.

14. Other IRBs/Ethics Review Boards

In the current study, a Serious Adverse Events Committee or a Data Safety Monitoring Board (DSMB) is deemed unnecessary because of the minimal risk of adverse effects.

The study protocol will be submitted to the National Ethics Committee for Health Research for ethical approval.

National Ethic Committee for Heath Research (NECHR) Phnom Penh, Cambodia
Address: Lot#80, Samdach Penn Nouth Blvd(289), Sangkat Boeung Kok2, Khan Tuo Kork Phnom Penh, Cambodia.
Tel: (855-012) 842 442, (855-012) 203 382

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