HEALTHY MOTHERS HEALTHY BABIES

Micronutrient FORUM

Join us for a virtual Coffee & Chai Chat!

Improving MMS Effectiveness through High Adherence: Evidence and Country Insights

Mai A. Hoang

Nutrition Advisor & Technical Coordinator, Asia

Helen Keller Intl

Emily Smith

Associate Professor

Milken Institute of Public Health, GWU

15 OCTOBER 2025

9:00 AM EDT | 3:00 PM CEST | 6:30 PM IST

bit.ly/HMHBchats

Adherence and Acceptability of Multiple Micronutrient Supplements (MMS) during pregnancy in Cambodia

HMHB Webinar: Coffee and Chai Chats

October 15, 2025

The American Journal of Clinical Nutrition 122 (2025) 166–173

The American Journal of CLINICAL NUTRITION

journal homepage: https://ajcn.nutrition.org/

Original Research Article

Assessing the adherence and acceptability to iron and folic acid compared with multiple micronutrient supplements during pregnancy: a cluster-randomized noninferiority trial in Cambodia

Cassandra Sauer [1,2], Mai-Anh Hoang [3], Hou Kroeun [4], Aman Sen Gupta [5], Rem Ngik [4], Meng Sokchea [4], Jocelyne M Labonté [6], Mary Chea [7], Rolf Klemm [3,8], Ashutosh Mishra [9], Aishwarya Panicker [9], Vin Sokhal [9], Crystal D Karakochuk [1,2,*]

[1] *Food, Nutrition & Health, The University of British Columbia, Vancouver, BC, Canada;* [2] *Healthy Starts, BC Children's Hospital Research Institute, Vancouver, BC, Canada;* [3] *Helen Keller International, New York, NY, United States;* [4] *Helen Keller International, Phnom Penh, Cambodia;* [5] *Helen Keller International, Lalitpur, Nepal;* [6] *Interdisciplinary School of Health Sciences, University of Ottawa, Ottawa, Canada;* [7] *National Nutrition Program, Ministry of Health, Phnom Penh, Cambodia;* [8] *International Health, John Hopkins Bloomberg School of Public Health, Baltimore, MD, United States;* [9] *Vitamin Angel Alliance, Santa Barbara, CA, United States*

A B S T R A C T

Background: The Cambodian Ministry of Health is exploring transitioning from iron and folic acid (IFA) to multiple micronutrient supplements (MMS) during pregnancy and is seeking rigorous evidence to inform this policy change.
Objective: We aimed to assess the adherence and acceptability of MMS compared with IFA supplementation during pregnancy.
Methods: We conducted an open-label cluster-randomized noninferiority trial across 48 health centers in Cambodia. A total of 1546 healthy pregnant individuals (18–45 y) were recruited at their first antenatal care (ANC) visit (<14 weeks of gestation) and randomized to 1 of 3 arms at the health center level: *1*) IFA for 90 d (IFA-90, $n = 515$), the current standard of care; *2*) MMS for 180 d via 1 180-tablet bottle (MMS-180, $n = 516$); or 3) MMS for 180 d via 2 90-tablet bottles (MMS-90, $n = 515$). Our primary outcome was the noninferiority of adherence rates of MMS-180 compared with IFA-90, assessed by tablet counts and compared against a predefined noninferiority margin of −15%. Mixed-effects linear regression models were used to estimate the mean difference (95% confidence interval [95% CI]) in adherence rates. Our secondary outcomes included the mean difference in ANC attendance between the MMS groups and the acceptability of MMS across 6 domains.
Results: Overall, 88% of participants completed the trial, with high mean adherence rates across arms (91% for IFA-90, 95% for MMS-180, and 95% for MMS-90). The adjusted mean (95% CI) difference in adherence rates between MMS-180 and IFA-90 groups was 3.9% (1.7, 6.2). The adjusted mean (95% CI) difference in ANC visits for MMS-180 and MMS-90 groups was 0.0 (−0.1, 0.2) visits. The acceptability of MMS was positive (90%–100% "agreement" across 6 domains).
Conclusions: Both IFA and MMS were highly acceptable, yet adherence to MMS was superior to IFA. These findings support the transition from IFA to MMS in Cambodia.
This trial was registered at Clinicaltrials.gov as NCT05867836.

Keywords: pregnancy, global health, policy, prenatal supplements, nutrition, iron and folic acid, multiple micronutrient supplements, Cambodia

Introduction

Current guidelines in Cambodia recommend the consumption of iron and folic acid (IFA) supplements during pregnancy for 90 d, starting as early as possible [1]. However, there has been a global push based on evidence showing its superiority to replace IFA with multiple micronutrient supplements (MMS), which include IFA and 13 other vitamins and minerals [2,3]. A 2019 review concluded that prenatal supplementation with MMS reduced risk of low birth weight by 12% and risk of small for gestational age by 8%, compared with

Abbreviations: ANC, antenatal care; CI, confidence interval; DHS, Demographic and Health Survey; IFA, iron and folic acid; IFA-90, IFA for 90 d; MMS, multiple micronutrient supplements; MMS-180, MMS for 180 d via 1 180-tablet bottle; MMS-90, MMS for 180 d via 2 90-tablet bottles; MoH, Ministry of Health; UNIMMAP MMS, United Nations International Multiple Micronutrient Antenatal Preparation Multiple Micronutrient Supplements.

* Corresponding author.
E-mail address: crystal.karakochuk@ubc.ca (C.D. Karakochuk).

https://doi.org/10.1016/j.ajcnut.2025.04.033
Received 1 December 2024; Received in revised form 25 April 2025; Accepted 29 April 2025; Available online 5 May 2025

Principal Investigator: Crystal D. Karakochuk, Food, Nutrition & Health, The University of British Columbia, Vancouver, BC, Canada

Authors: Cassandra Sauer [1], Mai-Anh Hoang [2], Hou Kroeun [3], Aman Sen Gupta [4], Rem Ngik [3], Meng Sokchea [3], Jocelyne M Labonté [5], Mary Chea [6], Rolf Klemm [7], Ashutosh Mishra [8], Aishwarya Panicker [8], Vin Sokhal [8], Crystal D Karakochuk [9]

Overarching Aim & Objectives

Aim: To conduct rigorous research in the Cambodian context to inform and provide recommendations to the MoH MMS Steering Committee to effectively transition from IFA to MMS, as part of routine ANC services.

Objectives:

1. Assess the adherence of MMS vs. IFA in pregnant women.
2. Assess the impact of 1 vs. 2 bottles of MMS tablets on ANC attendance.
3. Assess acceptability of IFA and MMS supplements.
4. Evaluate factors that influence adherence of MMS.
5. Develop recommendations for the MoH to transition from IFA to MMS.

Study Design

Cluster Randomized Non-inferiority Trial

Province:
Kampong Thom

Operational Districts (OD):
Kampong Thom, Baray Santuk, Staung

Health Centers (clusters):
48 in total (16 in each study arm)

Three Intervention Arms

IFA-90

Two bags (60 tablets at ANC 1 & 30 tablets at ANC 2)

MMS-180

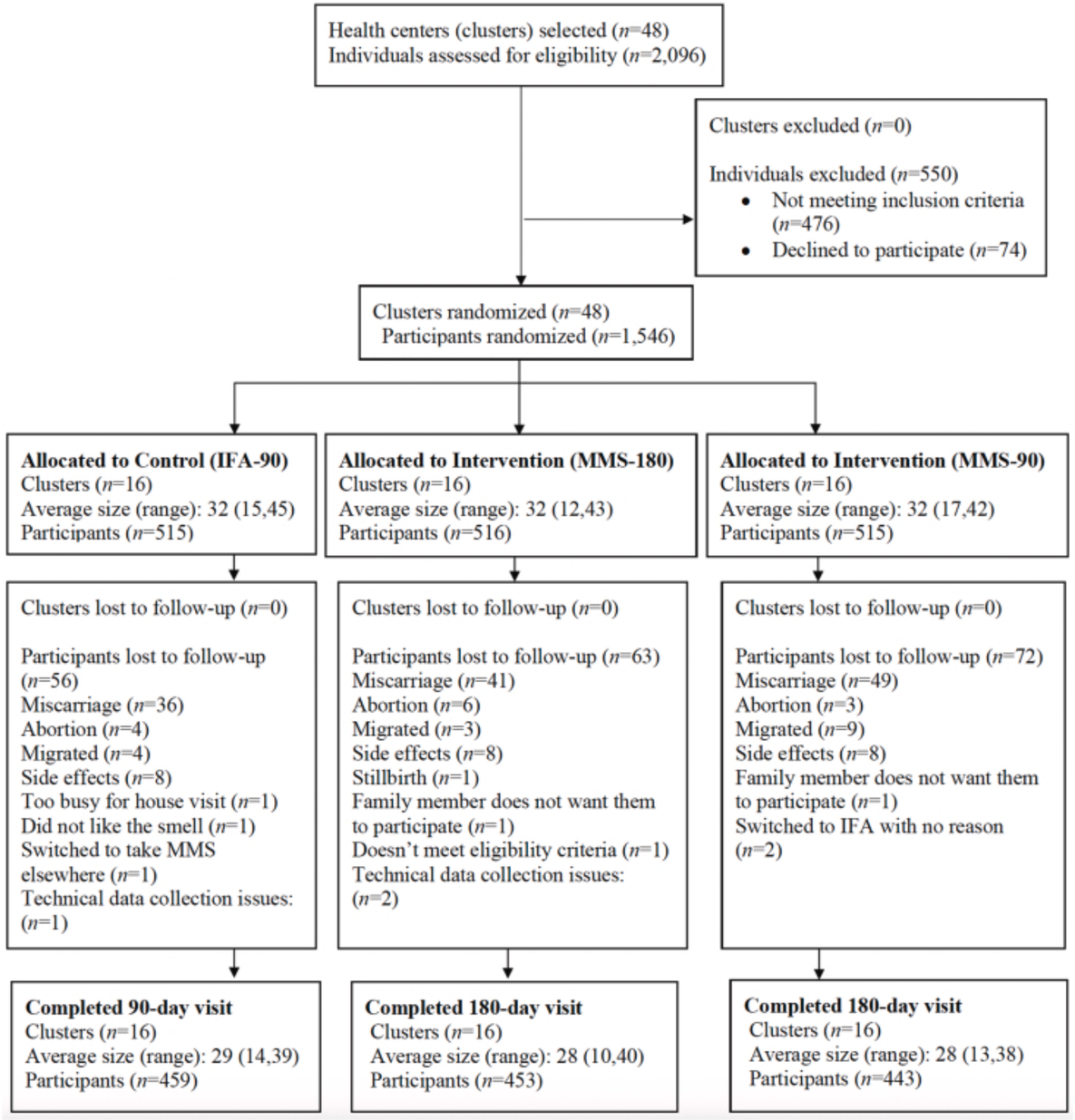
One 180 tablet bottle at ANC 1

MMS-90

Two 90 tablet bottles at ANC 1 & ANC 2

Participant Flow Chart

- **2096** Pregnant women were assessed for eligibility.
- **1546** Pregnant women were randomized at the health center-level (cluster).
- Overall, **87%** completed the trial.



Overview of Study Visits

Study Day	1	~ 7	30	~ 50	90	180 *
Gestational Age (weeks)	< 14	1 – 16	4 - 18	20 – 24	12 – 26	24 – 38
Location	Health Center ANC 1 Visit	Home Visit	Home Visit	Health Center ANC 2 Visit	Home Visit	Home Visit
Activity	Eligibility Criteria Verbal Consent Distribution of tablets	Study Overview Written Consent Demographic Survey	Tablet Count Quantitative Survey	Prenatal check up Tablet refill: IFA-90 & MMS-90 groups	Tablet Count Quantitative Survey	Tablet Count Quantitative Survey

*Only the MMS groups had a 180-day visit

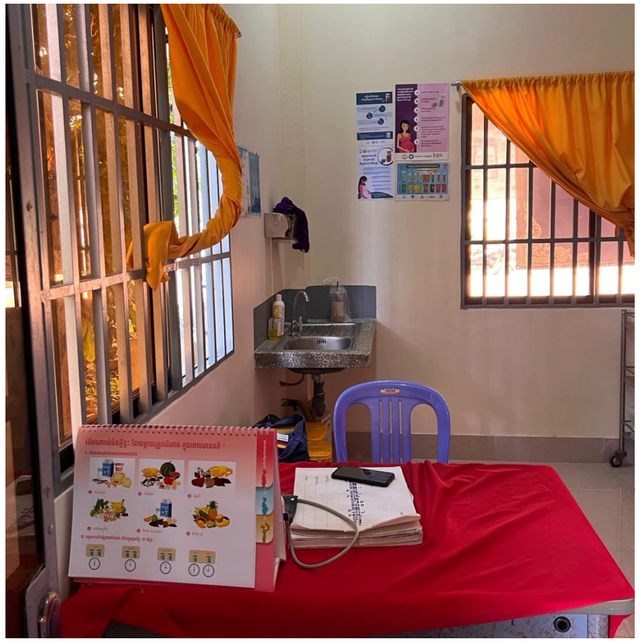
Study Timeline

March – June 2023

March – December 2023

January – February 2024

Enrolment



Data Collection

Data Analysis

Assessing Adherence

- **Primary Outcome:** Mean difference of adherence rates between MMS-180 and IFA-90
- **Adherence Measure:** Adherence %, based on tablet counts
- **Adherence Calculation:**

$$\frac{\text{Tablets consumed}}{\text{Tablets eligible to be taken}} \times 100$$

- **Eligibility Period:**

  First ANC – (last study visit OR delivery date)*

  *Whichever came first

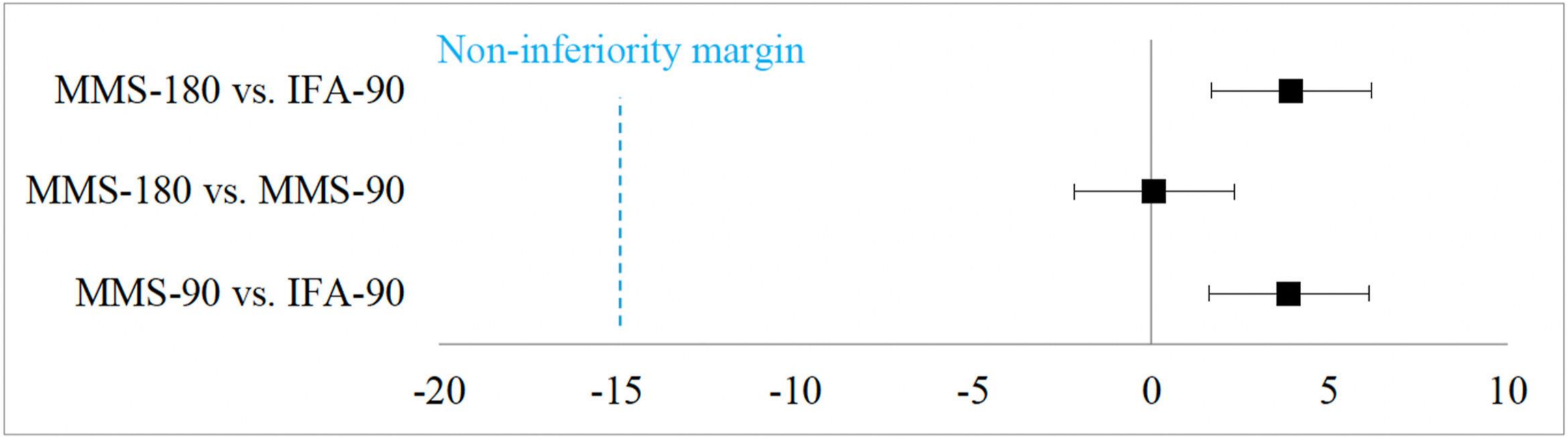
Results: Adherence Rate

IFA-90	MMS-180		MMS-90	
90 days n = 459	90 days n = 444	180 days n = 454	90 days n = 435	180 days n = 444
91% (90, 92)	94% (93, 96)	95% (94, 96)	95% (94, 96)	95% (94, 96)

Adjusted mean difference (95% CI) in adherence rates between the MMS-180- and IFA-90 groups was **3.9% (1.7, 6.2).**

Conclusion: Adherence to MMS was significantly higher than adherence to IFA (95% vs 91%).

Results: Non-inferiority of Adherence Rate



Results: ANC Attendance

MMS bottles received	1 x 180	2 x 90
Number of ANC visits attended	5 ± 1.5	5 ± 1.4

Conclusion:
There was no difference in ANC attendance when MMS was distributed in 1 vs. 2 bottles.

Key Messages

- MMS adherence was significantly higher than IFA adherence (95% vs 91%).
- No difference in ANC attendance when MMS tablets were distributed via 1 vs. 2 bottles.
- Overall acceptability of MMS was high.

Thank you

Why Women Took or Skipped Their MMS

❌ Barriers

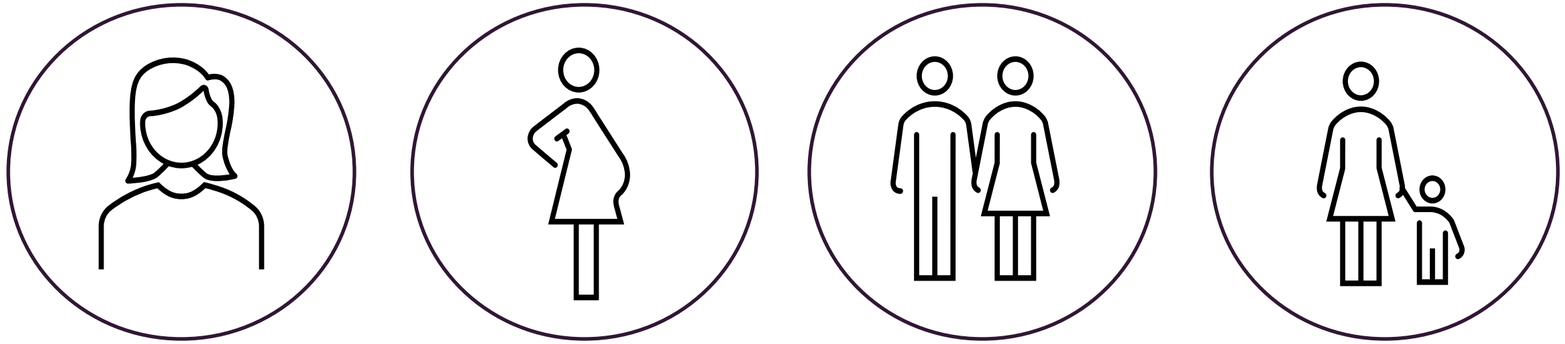
- Felt unwell or had side effects
- Migrated or moved during pregnancy
- Distracted with chores or forgot
- Not used to taking pills

✅ Enablers

- Built routines (bedtime, after meals)
- Kept MMS visible (e.g. kitchen shelf)
- Believed MMS helped self and baby

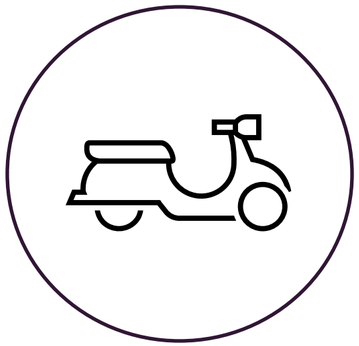
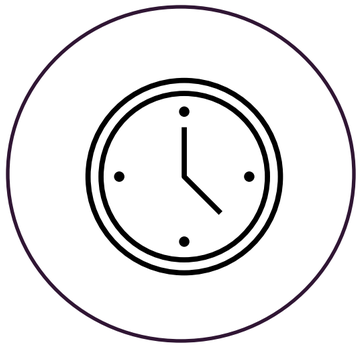
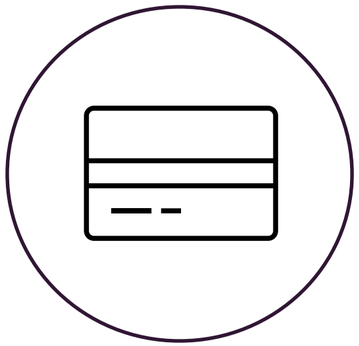
"After meals, I keep the bottle next to the kitchen door. Therefore, I could see it and take it." – High Adherer

Background Characteristics



Age	Gestational Age at ANC 1	Married	Multigravida
28 ±6 years old	8 ±3 weeks	99%	70%

Background Characteristics


Take a motorcycle to ANC visits	Time to get to health center	ID Poor	Completed Primary School
96%	18 ±12 minutes	15%	94%

Thank you for joining our Coffee and Chai Chat! Stay tuned for more chats with experts on maternal nutrition, MMS and BEP interventions.

bit.ly/HMHBchats