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SUPPLEMENT ARTICLE

Feasibility of integrating calcium and iron–folate supplementation to prevent preeclampsia and anemia in pregnancy in primary healthcare facilities in Kenya

Moshood O. Omotayo[1] | Katherine L. Dickin[1] | David L. Pelletier[1] | Stephanie L. Martin[1] | Jacqueline K. Kung'u[2] | Rebecca J. Stoltzfus[1]

[1] Program in International Nutrition, Cornell University, Ithaca, New York, USA

[2] Africa Regional Office - Nutrition International, Nairobi, Kenya

Correspondence
Moshood O. Omotayo, Rm 270, Farber Hall, Department of Epidemiology and Environmental Health, State University of New York at Buffalo, Buffalo, NY 14214.
Email: momotayo@buffalo.edu

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Abstract

Calcium (Ca) supplementation to prevent preeclampsia can save maternal and newborn lives, but there are no program models for integration into existing antenatal care platforms. We used a program impact pathway model to guide the design of integrated Ca and iron–folate (IFA) supplementation in Kenya. We provided healthcare providers with job aids (posters and counseling cards), trained them on counseling techniques and supplementation guidelines, and developed behavior change materials for pregnant women (pill-taking calendars). We allocated health facilities to prescribe either 1.0 or 1.5 g/day Ca, with standard IFA. We collected implementation data from 16 facilities and 990 women. We also explored effects of supplementation on percentage of the population meeting recommended daily allowance. Supplements and job aids were available during 90% of facility spot-check episodes; calendar availability was lower (78%). Over 98% of clients received Ca and IFA supplements, but only 76% received enough Ca supplements to last between antenatal care visits. Among clients that still had pills by return date, adherence was 77% and 83% for the IFA and Ca regimen, respectively. When 1.5 g/day of Ca supplements were prescribed, over 75% of participants met recommended daily allowance. Only 54% met the recommended daily allowance when 1.0 g was prescribed. This study illustrates a systematic approach for integrating Ca supplementation into primary healthcare and demonstrates that such integration is feasible when contextual bottlenecks are addressed. Policy makers and program planners should pay attention to supply chain, healthcare worker dispensing behavior, and appropriateness of regimen for their settings.

KEYWORDS

anemia, calcium, preeclampsia, program impact pathway

1 | INTRODUCTION

A primary challenge in improving global maternal, neonatal, and child health is the sustainable and effective delivery of high impact interventions for pregnant women. Public health programs fail to achieve impact because of two main reasons: (a) lack of validity of the program theory (i.e., flawed assumptions linking program inputs and activities to the problem in a particular context) and (b) inadequate implementation of core activities in the program model (Mbuya et al., 2015). Moreover, it is important in evaluation design to differentiate these two types of potential failures, because they require different strategies for effective course correction. Analytical approaches useful for guiding these types of evaluations include the logic model, logical framework, results framework, value chain analysis, theory of change, and program impact pathway (PIP) analysis (Habicht & Pelto, 2014; Kim, Habicht, Menon, & Stoltzfus, 2011). All are variants of theory-based analytical approaches for program evaluation.

Compared to other theory-based approaches applied at the project level, PIP analysis is particularly suited for evaluating implementation of the core activities in a supplementation program. This is due to its emphasis on detailed tracking of resource transfer activities among the different players in a program. Resources in this context may be material (supplements, food, posters, calendars, etc.) or nonmaterial (knowledge, motivation, self-efficacy, etc.), and they are typically

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made explicit on a finer scale than other approaches, such as in a logic model. When appropriate theories in the biological, social, behavioral, and organizational sciences are employed to specify and investigate potential influences on resource transfer activities in the PIP, it can serve as a useful conceptual tool for design and evaluation of nutrition programs. The PIP has been generally defined as "the explicit representation of the pathways by which the program (activities) achieves its intended outcomes" (Kim et al., 2011). For nutrition programs, the PIP has been specifically defined as "the flow from a nutrient's introduction into a program to its biological outcome" (Habicht & Pelto, 2014). We employed the integrated behavior model to identify relevant modifying variables for investigation, during our formative research and specification of potential influences on the PIP (Glanz, Rimer, & Viswanath, 2008).

Micronutrient supplementation in developing countries has a strong evidence base, but limited programmatic success (Palacios, n.d.; Darnton-Hill & Mkparu, 2015) and integration of new supplementation programs into existing platforms might require more comprehensive theory-based programming and evaluation. For instance, iron supplementation is an efficacious intervention to prevent and treat iron-deficiency anemia, and several low-income countries have policies supporting antenatal iron supplementation (Stoltzfus, 2011), yet iron deficiency remains a major cause of maternal morbidity globally (Kassebaum, 2016). Likewise, calcium (Ca) supplementation to prevent preeclampsia is supported by systematic reviews of randomized controlled efficacy trials and the World Health Organization (WHO) recommendations as part of antenatal care (ANC) programs, yet the recommendations are complex and there is potential for implementation failure (Omotayo, et al., 2016). For instance, a study in Brazil found that, in a sample with 210 mg/day mean Ca intake and 90% of individuals with inadequate Ca intake, only 5.1% of ANC clients received Ca supplementation prescriptions (Camargo et al., 2013). Integrating Ca supplementation into existing antenatal programs requires a comprehensive approach to reduce the likelihood of implementation failure, especially given the challenges faced by existing antenatal iron supplementation programs.

Using the PIP approach, we developed and tested a program model to integrate Ca supplementation into ANC delivery at subnational levels. This approach involves three iterative steps: (a) developing a schematic representation of flow of resources, activities, and other factors that can influence program impact based on existing scientific and contextual knowledge (PIP model); (b) grounding the PIP model in a particular context through formative research to tailor design of the integration effort; and (c) empirically testing validity of key assumptions as well as adequacy of implementation of core activities and flow of resources in the program, using the PIP model as a guide for data collection and analysis.

Our primary objectives in this paper are (a) to describe the development of a comprehensive program for the integration of Ca supplementation into ANC platforms using the PIP approach and (b) to determine whether Ca supplementation can be feasibly integrated with antenatal IFA supplementation in primary ANC. This paper focuses on evaluating the implementation of key activities and flow of material resources. Specifically, we address the following questions: (a) Were nutritional supplements and other requisite materials (trained staff, job aids, and behavior change materials) for program impact available at the primary healthcare facilities? (b) Did healthcare workers (HCWs) carry out activities requisite for program impact? (c) Did ANC clients consume supplements and utilize other resources received from healthcare facilities? (d) What percentage of the sample population met the recommended daily allowance?

Key messages

- Calcium supplementation can be feasibly integrated into primary healthcare delivery in low-income countries.
- The program impact pathway approach is useful for systematic integration of micronutrient supplementation into primary healthcare in low-income countries.
- Current WHO-recommended supplementation regimen might lead to a higher percentage of the population meeting recommended daily allowance for calcium, compared to lower regimens.

2 | METHODS

2.1 | Study context

This study was conducted in Malava subcounty, Kakamega County in Western Kenya from September 2014 to June 2015. The Malava subcounty, located northeast of Kakamega County, is mainly rural with some suburban neighborhoods. Malava is the subcounty headquarters and largest town. One referral facility in Malava and 16 primary healthcare facilities throughout the subcounty were providing ANC services at the time of study design. These included three health centers and 13 dispensaries. Health centers had three to five clinical staff in addition to laboratory staff and were open 24 hr. They provided emergency medical services, inpatient services, outpatient services, and maternal and child health clinics. The dispensaries had two to three clinical staff and were open from 9:00 a.m. to 5:00 p.m. They provided outpatient services and maternal and child health clinics. The focus on delivery through facility-based consultations was informed by the Kenyan national policy of delivering micronutrient supplementation for control of deficiencies through facility-based healthcare providers.

2.2 | Development of program impact pathway model and district-wide program

Based on a literature review and consultation with experts, we developed a PIP model to guide integration of Ca supplementation into primary healthcare delivery. A simplified adaptation of our PIP is in Figure 1.

We conducted formative research in western Kenya to adapt the model to the local context, and we found poor ANC attendance beyond the first visit, erratic supply of iron–folate (IFA) supplements, inadequate knowledge of IFA recommendations, and poor counseling

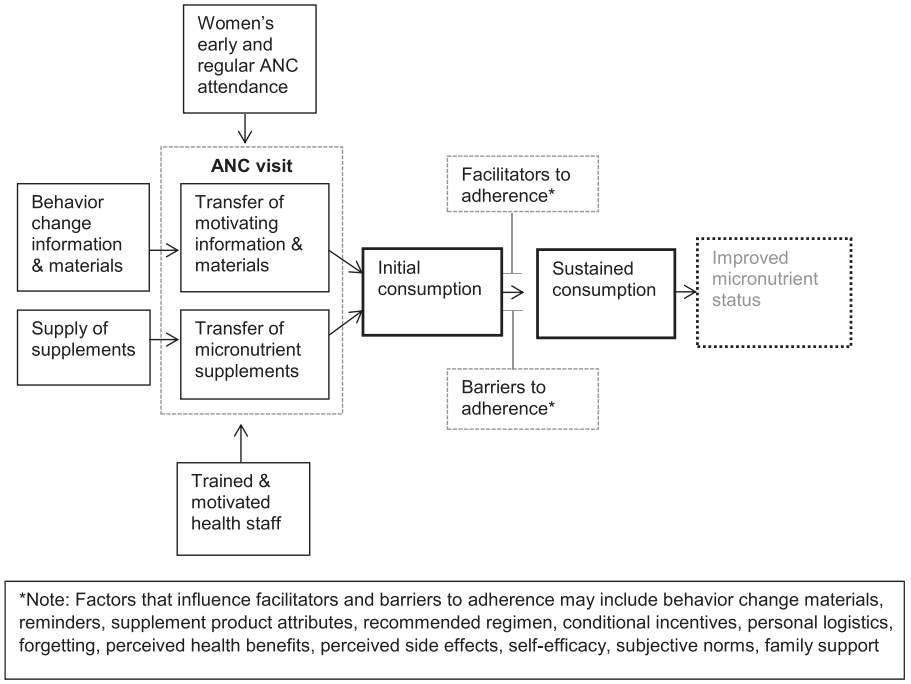

FIGURE 1 Program impact pathway for integrating calcium supplementation into primary care delivery. ANC = antenatal care

of clients about benefits and side effects (Martin et al., 2017a). We further conducted a desk review of policy documents and informal interviews with policy actors. Multiple national policies and programmatic guidelines emphasized routine antenatal IFA supplementation for prevention and treatment of anemia. We also conducted trial of improved practices to gain insight into factors that influence pill-taking among pregnant women taking iron and Ca supplements (Dickin et al, 1997; Omotayo, Martin, et al., 2017). The trial of improved practices indicated the importance of product and regimen characteristics as well as counseling of clients about benefits, side effects, and reminder strategies (Omotayo, 2016).

Based on the formative findings, we developed a district-wide pilot program to integrate Ca supplementation into facility-based ANC and strengthen delivery of IFA supplementation. Activities were aimed to ensure that pregnant women attended ANC clinics, and supplements, behavior change resources, and well-equipped HCWs were consistently available in primary healthcare facilities. We identified six intervention delivery activities: (a) one-off training for ANC providers on Ca supplementation guidelines and counseling techniques; (b) continuous mobilization of pregnant women to attend ANC clinics through training and motivation of community health workers (CHWs); (c) stop-gap provision of IFA supplements to district pharmacy and distribution to all facilities to avoid stock-outs throughout program duration; (d) provision of Ca supplements to the district pharmacy and distribution to all facilities to avoid stock-outs throughout program duration; (e) development and distribution of take-home behavior change communication materials (i.e., calendar with illustrated messages) to healthcare facilities to facilitate pregnant women's adherence to recommendations and encourage familial support; and (f) development and distribution of appropriate counseling guides and job aids to all facilities.

2.3 | Training and motivation of HCWs

We trained facility-based HCWs in the district on Ca supplementation recommendations and counseling techniques, during four training sessions that took place on four different days at the same venue. Each training session lasted 6 to 8 hrs. All sessions contained modules covering purpose, rationale, prescription regimen, benefits, and side effects of Ca and IFA supplementation as well as training on counseling techniques. The sessions were similar in content except for recommended supplementation regimen for which there were two options. The recommended regimen differed because a cluster-randomized non-inferiority trial of the impact of recommended regimen on supplement consumption was background of the pilot program, the design of which are reported elsewhere (Omotayo et al., 2015). In brief, half of the facilities in the study were randomly allocated to prescribe a two-dose regimen (1.0 g elemental Ca as calcium carbonate [$CaCO_3$] in two pill-taking events with 500 mg Ca per pill and IFA 60 mg Fe + 400 μg folic acid taken with the evening dose) and the other half were allocated to prescribing a three-dose regimen (1.5 g elemental Ca as $CaCO_3$ in three pill-taking events with 500 mg Ca per pill and IFA 60 mg Fe + 400 μg folic acid taken with the evening dose). The primary analysis of the non-inferiority trial will be reported elsewhere (Omotayo, Dickin, et al., 2017).

The recommended regimen in each of the training sessions was consistent with the regimen allocation for invited attendees for that session. The same set of facilitators, which included two members of the subcounty health management team and two members of the investigating team, delivered all training sessions. Make-up sessions were facilitated for 13 HCWs who were newly recruited by the government during the course of the program and one of the two HCWs who missed the original training. The make-up training sessions were

also consistent with the original training protocols but were delivered by the program coordinator and research staff.

2.4 | Training and motivating CHWs to improve ANC attendance

We also trained selected CHWs to track and mobilize pregnant women to ANC clinics and reinforce program-related messages. The design and logistics of the training was similar to that of the facility-based healthcare providers, but the emphasis was on mobilization of pregnant women to ANC visits. We met with CHWs on a monthly basis to troubleshoot problems and address their concerns throughout the study.

2.5 | Delivery of behavior change materials and supply of supplements to healthcare facilities

We delivered Ca and IFA supplements to the district pharmacy. Study staff worked with the district pharmacy staff to design and implement a distribution and notification plan to prevent Ca and IFA stock-outs during the study period. This involved a complementary push and pull mechanism. The healthcare facility manager was mandated to notify the district pharmacy or designated study staff when stock-outs were imminent. Pharmacy staff and designated study staff visited all facilities at approximately 8-week intervals to replenish facility stores irrespective of notification. The Ca supplements used in the trial were Ostocal Calcium and Vitamin D3 film-coated tablets manufactured by Eskayef Bangladesh Limited and purchased through Madawa Pharmaceuticals, Nairobi, Kenya. Calcium supplements contained 500 mg elemental Ca as $CaCO_3$ with 200 IU of vitamin D3 per pill. The pills were hard, tasteless, and white.

Calcium supplementation counseling guides for healthcare providers and take-home behavior change materials for pregnant women were developed to be consistent with existing IFA materials, which had been recently rolled out nationally. The materials were pretested with pregnant women and healthcare providers in the subcounty (Martin et al., 2017a). The job aids were delivered to healthcare facilities at the beginning of the program. Behavior change materials, which included calendars with illustrated regimen, motivating messages and spaces for tracking consumption with daily marking were periodically delivered to the healthcare facilities by study staff at regular intervals through the course of the program but were not included in the pull and push delivery mechanism.

2.6 | Data collection

Monitoring and evaluation data were collected by study staff and included (a) unannounced spot-checks to track availability of resources at the healthcare facility; (b) exit surveys with ANC clients and; (c) midline and end line surveys with healthcare providers (Table 1). These were supplemented with other sources of program data including facility ANC registers and district pharmacy bin cards. We developed the instruments by generating questions and checklists or adapting existing scales and questionnaires when available. Research assistants translated and back-translated the questionnaires before pretesting in the communities and facilities. We pretested and cognitively tested data collection instruments as needed and consequently made alterations to improve reliability and validity of the instruments (Martin et al., 2017b). We developed a template for facility tracking of Ca and IFA inventory, ANC traffic, and counseling guide use during spot checks. We also measured whether the clinician providing care had been trained on Ca recommendations using this template, altogether providing data on program fidelity at the healthcare facility level.

For the facility spot-checks, a research assistant visited each of the 16 participating facilities at an average of four times during the course of the study to collect information to fill out the facility-tracking templates, providing information about availability of supplements and behavior change materials.

For ANC client exit interviews, a team of seven trained interviewers recruited 990 ANC clients from (479 and 511 women from facilities allocated to the two- and three-dose regimen, respectively) the 16 participating facilities. We collected data from each participant at up to three time points when possible. Recruitment days for each participating facility were scheduled and communicated to staff and communities in advance. All ANC clients attending the facility on the designated day were screened and consent was sought from those found eligible for the study, prior to their ANC consultations. Eligibility criteria were (a) maternal age at least 15 years, (b) gestational age 16 to 30 weeks based on self-reports and clinician judgement, (c) not planning to relocate from the community prior to delivery, and (d) inadequate habitual Ca intake as measured by a screening tool that requested information about frequency and estimated serving size of local dietary Ca sources. Consenting clients were enrolled; then, demographic surveys were administered, and clients were asked to participate in exit interviews to assess what transpired during the ANC consultations, including pill count. After the exit interview, enrolled participants were requested to grant follow-up interviews at the return ANC visit approximately 4 weeks later. At the follow-up interviews, we interviewed participants prior to their ANC consultations and their

TABLE 1 Data collection schedule for implementation analysis in district-wide antenatal calcium supplementation program in Kenya

	Data collection activity	Timing	Observation unit	Instrument	Data source
1	Spot-checks and program data	Once in 2 months	Healthcare facility	Monitoring template	Administrative records
2	Training data (e.g., Knowledge assessment)	Pre- and post-training events	HCW and CHW	Structured questionnaire	HCW and CHW
3	HCW surveys	Midline and end line	HCW	Structured questionnaire	HCW
4	ANC exit interviews	Initial ANC consultation and return visits	ANC client	Structured questionnaire	ANC client

Note. ANC = antenatal care; CHW = community health worker; HCW = healthcare worker.

remaining pills were counted. We also conducted exit interviews after the ANC consultation. We collected similar data at a subsequent and final follow-up visit. Where clients did not attend on the scheduled day, arrangements were made for follow-up on the earliest possible later date.

2.7 | Data management and analysis

We entered ANC exit interview data and HCW surveys into REDCap electronic data management tool hosted at Cornell University. REDCap is a secure, web-based data collection tool designed to support data capture for research studies (Harris et al., 2009). We exported the data into Stata statistical software for further processing and analysis (StataCorp., 2015). The facility tracking data were cleaned in Microsoft Excel.

We developed a table of metrics and scoring protocols for key activities in the PIP. We calculated values for the key indicators of availability of resources (supplements, counseling guides, and behavior change materials) at the facility and activities of HCWs, as ratios, percentages and absolute values, using Microsoft Excel and Stata as appropriate.

We computed daily IFA consumption as difference between pills received and pills returned, divided by number of days in the assessment period. We defined adherence to IFA as mean daily consumption of 0.8–1.2 pills per day. Percentage adherence for subgroups was computed as percentage number of individuals meeting the adherence definition.

We computed daily Ca supplement consumption as difference between pills received and pills returned, divided by number of days in the assessment period. We assessed adherence to Ca regimen for subgroups, by computing average of mean daily consumption for individuals in the subgroups and divided by daily prescription (1.0 or 1.5 mg).

We explored the percentage of participants that met the recommended daily allowance in each interval by regimen subgroup, taking estimated average dietary intake into account. We did not have individual dietary Ca intake data so we used the estimated averages from a recent national survey, whose reports and details have been published (Kenya National Micronutrient Survey 2011, 2016). We added the point estimate for daily dietary intake in the national survey to daily supplemental intake of each participant, to calculate total Ca intake. To account for intake variation, we examined additional scenarios (a) an optimistic scenario in which we added the upper limit of the 95% confidence interval (CI) from the survey estimate, rather than the point estimate, to each participant's supplemental intake and (b) a conservative scenario in which we added the lower limit of the 95% CI from the survey estimate to each participant's supplemental intake. Then we estimated the percentage of clients that consumed up to an average of 800 mg/day, 1,000 mg, and 2,500 mg/day of Ca supplements in each interval and regimen subgroup in all three scenarios, because this approximates meeting the estimated average requirement, recommended dietary allowance (RDA), and the upper limit, respectively. We excluded clients that had follow-up periods exceeding the dispensed amount of pills from the analyses, if they did not return with any leftover pills, as it was not possible to assess their consumption using pill-counts.

2.8 | Ethical aspects

This study was reviewed and approved by the Institutional Review Board at Cornell University and Kenyatta National Hospital and University of Nairobi Ethics and Research Review Committee. All respondents were given detailed information about the objectives and purpose of the study and written informed consent was obtained from each respondent before enrolment.

3 | RESULTS

a. Were nutritional supplements and other requisite materials (trained staff, job aids, and behavior change materials) for program impact available at the primary healthcare facilities?

We carried out unannounced spot-checks at the facilities to determine the extent to which nutritional supplements, counseling guides, and behavior change materials were regularly available. All metrics reflecting availability of supplements and other resources at the facility level were higher, compared to availability of behavior change materials. As part of program design, we instituted a mixed push and pull mechanism for facility-level supplement forecasting and stock replenishment, but this was not extended to behavior change materials. The healthcare facility manager was mandated to notify the district pharmacy or designated study staff when stockouts were imminent. Pharmacy staff and designated study staff were also scheduled to visit all facilities at approximately 8-week intervals to replenish facility stores, irrespective of notification calls. As shown in Table 2, requisite materials were mostly available at the facilities (>90% of spot check episodes), except for the behavior change materials. Calcium and IFA supplements were available during 94% and 98% of assessment spot-checks, respectively, indicating regular supply of supplements. Healthcare provider counseling guides were also found in the facilities during 97% of assessment episodes. However, take-home behavior change materials were found during 78% of spot-check episodes only.

b. Did facility-based HCWs and CHWs appropriately carry out activities and utilize resources requisite for program impact?

We examined exit interview data to understand the extent to which HCWs counseled clients with job aids and dispensed supplements and behavior materials during ANC consultations. Over 80% of clients reported being counseled about Ca and IFA supplementation with counseling guides.

Although over 98% of ANC clients received some Ca and IFA supplements, only 76% and 89% of clients respectively, received the amount of supplements needed to meet their prescriptions until the scheduled return date. All indicators of frontline worker activity exceeded 80% as shown in Table 2, except ANC consultations during which the client received adequate Ca supplements. Eighty-one percent of ANC clients attended follow-up ANC visits on scheduled return dates. Clients received Ca supplements during almost all (>98%) consultations, despite the amount received being sufficient in only 76% of consultations.

TABLE 2 Supplies and implementation of antenatal calcium supplementation through primary healthcare facilities in Kenya

Activity	Indicator	Value
Availability of program materials at primary healthcare facilities		
Ca supplements	% spot-check episodes during which Ca supplements were available	98.1% *N* = 53[b]
IFA supplements	% spot-check episodes during which IFA supplements were available	93.8% *N* = 64
Take-home behavior change communication materials	% spot-check episodes with behavior change materials seen at facility	78.1% *N* = 64
Counseling guides and job aids	% spot-check episodes counseling guides seen	96.8% *N* = 63
HCWs and CHWs implementation of program activities		
Dispensing Ca supplements	% ANC consultations during which client received adequate calcium supplements	76.4%
Dispensing IFA supplements	% ANC consultations during which pregnant women received adequate iron supplements (≥28 pills)	88.5%
Giving take-home behavior change materials	% ANC consultations during which pregnant women received (shown to exit interviewer) posters and calendars	89.4% (poster) 91.4% (calendar)
Using counseling guides	% ANC consultations during which HCWs used counseling guide (as reported at recruitment ANC exit interview)	82.9%
Mobilizing pregnant women by CHWs	% ANC clients that attended follow-up visits at recommended times (28 days)	81%

Note. Ca = calcium; IFA = iron–folate; *N* = number of spot-check episodes; ANC = antenatal care; CHWs = community health workers; HCWs = healthcare workers.

[a]The values indicate availability of materials (no stock-outs) at the facility and do not indicate utilization or dispensing of materials. The ideal requirement is that materials be available at all times because clients at all stages of gestation and ANC attendance continuously visit the facilities; however, there is no known availability threshold for a well-functioning program.

[b]There was a total of 64 spot-checks (four per facility), but data on availability of calcium supplements were not recorded for 11 facilities in the first wave of spot-checks.

c. Did ANC clients consume supplements and utilize other resources received from primary healthcare facilities?

Table 3 shows characteristics of participants providing exit interview data. They were mostly married women in their third and fourth decades of life, who had not completed secondary education and were in their second and third trimesters of pregnancy.

Overall, 77% and 83% adherence was recorded for the IFA and Ca regimen, respectively. Initial mean adherence to Ca supplementation regimen at first follow-up was 90% across the board, but reduced significantly at the second follow-up in both regimen groups.

A nationally representative survey indicated that the average daily dietary Ca intake in Kenya was 511 mg/day (95% CI = 422, 600; Kenya National Micronutrient Survey 2011, 2016). We explored the impact of supplementation on percentage of the population meeting Ca dietary reference intakes for pregnant women by regimen and time interval, taking dietary intake into account. In the most conservative scenario (using lower limit of 95% CI of average dietary intake estimate in Table 4) for participants prescribed 1.5 g/day, over 75% of the population would meet the daily recommended intake for pregnant women with ages 19 to 50 years. However, in the same scenario for participants prescribed 1.0 g/day, only 55% would meet the daily recommended intake for pregnant women with ages 19 to 50 years.

4 | DISCUSSION

Calcium supplementation is a key component of the strategy for addressing perinatal mortality due to preeclampsia (Omotayo, Dickin,

TABLE 3 Characteristics of participants providing exit interview data in district-wide antenatal calcium supplementation program in Kenya

Characteristics	[b]Regimen A, *N* = 479[a]	[c]Regimen B, *N* = 511[a]
Age, mean (*SD*)	25.10 (5.96)	24.81 (5.72)
Adolescent, %15–19 years	17.39	18.38
Gestational Age, months (*SD*)	5.5 (1.1)	5.4 (1.1)
Education, %Completed secondary	21.98	24.58
Marital status, %Never married	11.39	11.89
Primigravid, %	24.12	26.97

[a]These are number of women recruited into the study in facilities allocated to each regimen. These numbers differ from numbers the number of women contributing data to average intakes at each study interval.

[b]1.0 g elemental Ca as calcium carbonate in two pill-taking events with 500 mg Ca per pill and IFA 60 mg Fe + 400 μg folic acid taken with the evening dose.

[c]1.5 g elemental Ca as calcium carbonate in three pill-taking events with 500 mg Ca per pill and IFA 60 mg Fe + 400 μg folic acid taken with the evening dose.

TABLE 4 Consumption and adherence to calcium supplementation in district-wide antenatal calcium supplementation program in Kenya

	1.0 g		1.5 g	
	1st interval $N = 301^d$	2nd interval $N = 291^d$	1st interval $N = 319^d$	2nd interval $N = 225^d$
Mean adherence	91.5% (29.6)	69.3% (36.3)	89.9% (24.0)	67.6% (31.8)
Average daily supplemental intake (mg/day; *SD*)	915 (296)	693 (363)	1,349 (359)	1,014 (477)
≥500[a]	91.43%	61.79%	96.93%	84.33%
≥1,000[b]	29.52%	16.07%	85.89%	50.00%
≥1,500[c]	4.44%	2.5%	27.30%	16.79%
Lower limit of 95%CI of average daily dietary intake + supplemental intake				
Average daily intake (mg/day; *SD*)	1,337 (296)	1,115 (363)	1,771 (359)	1,436 (477)
≥800	94.92%	78.93%	98.77%	88.43%
≥1,000	85.71%	54.64%	94.79%	76.12%
≥2,500	0.32%	0.00%	1.84%	0.75%
Point estimate of average daily dietary intake + supplemental intake				
Average daily intake (mg/day; *SD*)	1,426 (296)	1,204 (363)	1,860 (359)	1,525 (477)
≥800	96.51%	85.36%	99.39%	92.54%
≥1,500	92.70%	62.50%	96.93%	85.82%
≥2,500	0.33%	0.00%	3.07%	1.49%
Upper limit of 95%CI of average daily dietary intake + supplemental intake				
Average daily intake (mg/day; *SD*)	1,515 (296)	1,293 (363)	1,949 (359)	1,614 (477)
≥800	97.78%	92.50%	99.39%	94.40%
≥1,000	94.60%	76.43%	98.77%	87.69%
≥2,500	0.32%	0.00%	4.39%	2.24%

[a]Percentage of the population consuming at least an average of 500 mg/day.

[b]Percentage of the population consuming at least an average of 1,000 mg/day.

[c]Percentage of the population consuming at least an average of 1,500 mg/day.

[d]These are the number of women contributing data to the average consumption estimates for each regimen at each time point. These differ from the total number of women because many women contributed data to only time point.

& Stolzfus, 2016). The WHO issued global guidelines for integration of Ca supplementation for prevention of preeclampsia with IFA supplementation programs in ANC, but there has been no program model for implementation of these guidelines. Prenatal IFA supplementation programs continue to face implementation challenges. Reports of Ca supplementation programs are rare, but a study in Brazil reported that only 5% of ANC clients received Ca supplement prescriptions in a client population where over 90% individuals had inadequate habitual intake (Camargo et al., 2013). To our knowledge, this is the first study to design and evaluate a systematic program for implementing these guidelines.

4.1 | Facility-level availability of requisite resources for program impact

The few supplement stock-outs that were recorded resulted from notification delays from healthcare facilities to the district pharmacy during periods of unanticipated surges in ANC attendance. These could have been prevented with shorter intervals between scheduled replenishment visits by district officials or increasing the inventory threshold at which notification by facility managers was required. The relatively high level of stock-outs for behavior change materials is plausibly due to the absence of a well-coordinated notification plan for supply and replenishment of the materials to the facilities, but the design of this study does not permit a direct test of this hypothesis. Taken together, our findings underscore the importance of a well-coordinated push and pull mechanism for delivery of materials for program success.

4.2 | Adequacy of HCW activities

Prior studies and our formative research have shown limited fidelity to prescription and dispensing guidelines for pills and supplements among healthcare providers (Martin et al., 2017a). This 'rationing' is likely due to limited understanding of dispensing guidelines on the part of healthcare providers in our own study, rather than supplement stock-outs in the facilities, given the high supplement availability rates recorded during spot-checks. The lower rates of appropriate dispensing of IFA compared to Ca supplements might be because HCWs had been used to dispensing IFA with different protocols and their experiences prior to the study. Although our training sessions included information about prescription and dispensing guidelines, there could have been more emphasis and clarity about dispensing guidelines. Inclusion of dispensing guidelines in counseling guides and other job aids in addition to other reminders could have been helpful for reinforcement. Future studies should examine utility and impact of job aids and other tools for reinforcing dispensing guidelines.

4.3 | Supplementation adherence and behavior change material utilization by pregnant women

Most clients that received calendars reported using it. Our prior formative work revealed that pregnant women found calendars helpful as a reminder to consume their Ca supplements (Omotayo, 2016).

Cumulative supplement consumption depends on the balance between long-term adherence and recommended daily consumption. Adherence was defined as mean daily consumption as a percentage of prescribed daily consumption. Adherence to Ca supplementation reduced over time in this study. Similar findings have been reported for other pills and supplements in other settings. We found that a high proportion of (over 75%) participants were still able to meet the RDA, when prescribed 1.5 g/day, despite the drop in adherence. However, when prescribed with 1.0 g/day the percentage of participants that met the RDA might be as low as 55% in the second interval. Our findings provide empirical evidence suggesting that (a) we can conservatively expect 75% of the population to meet Dietary Reference Intakes (DRIs) if our program conditions are replicated in similar settings with current WHO regimen, (b) adherence to regimen reduces over time irrespective of regimen, and (c) lower regimen led to fewer people meeting DRIs.

4.4 | Supplement products and regimen

Average daily dietary Ca intake in a nationally representative Kenyan sample was 511 mg/day with standard deviation 281 mg/day, in an analysis reports submitted by Healthbridge to Micronutrient Initiatives (Kenya National Micronutrient Survey 2011, 2016). The minimal amount of Ca intake needed to prevent preeclampsia is yet to be determined. The WHO recommends 1.5 to 2.0 g/day of supplemental Ca based on meta-analysis of randomized trials; however, comparable benefit has been reported in meta-analysis of studies administering dosages below 1.0 g/day, but the primary studies were of poor quality and relevance (Hofmeyr, Lawrie, Atallah, Duley, & Torloni, 2014). The estimated average requirement and RDA for pregnant women are 800 mg/day and 1,000 mg/day, respectively (Institute of Medicine (US) Committee to Review Dietary Reference Intakes for Vitamin D and Calcium, 2011). Although these are based on skeletal end-points in a different population, it is believed that effect of Ca in preeclampsia prevention derives from filling the dietary Ca gap in populations with inadequate dietary intake (WHO Guideline: Calcium Supplementation in Pregnant Women, 2013). Therefore, the RDA was used as the criterion for adequacy of supplement intake in this study and findings indicate that prescribing 1.5 g/day is likely to have higher clinical impact. However, choosing prescription regimens in national programs can be more complex. It will be considered not only in light of clinical impact but also in light of implications for cost and supply chain logistics in large-scale programs, factors that might favor lower dosages.

Formative research revealed preference for sweet chewable Ca supplement tablets among pregnant women; however, we used hard tasteless pills in the pilot program because this form costs approximately 25% as much as sweet chewable tablets. It is unlikely that large-scale programs will use the chewable tablets with the current price regime. However, the drivers of differential cost between the pill types might not be related to attributes driving consumer preferences. Hence, it might be possible to produce new pill types that will balance consumer preferences with program cost thereby improving adherence and consumption. Future studies should examine this trade-off in detail.

4.5 | Strengths and limitations

This study has certain key strengths. (a) It is the first study to examine programmatic design for integration of Ca supplementation with IFA supplementation in primary healthcare facilities, in a low- or middle-income country. This is important because of high prevalence of dietary Ca inadequacy and incidence of preeclampsia in such countries globally. (b) Our program design was based on a rigorous program model grounded in established behavioral theories. (c) We carried out extensive formative research that grounded the program model in the local sociocultural and health systems context, providing us with relevant insight to interpret the findings and lessons from our study. (d) We address issues of key relevance to program planners and policy makers in several countries.

Our findings should be interpreted with caution. First, our analysis of HCW activities was based on self-reported data from exit interviews. Classically, social desirability and recall problems are potential sources of bias in this situation. However, data from exit interviews in this analysis involved receipt of materials that were also directly verified during the exit interviews, except for use of job aids by HCW during consultation. Second, our adherence and consumption estimates are aggregates based on pill counts. This might obscure distributional characteristics that are biologically relevant. The pill count was done after 4 to 8-week time intervals. This might obscure within-person fluctuations, such as periods of over- and under-consumption by the individual. The group adherence aggregates might also obscure the influence of outlier individuals. Although we are unable to rule out within-person fluctuations, graphical analysis of subgroup distributions and analysis of influence of outliers suggest that our conclusions are not driven by this factor. In addition, our operationalization of adherence is essentially arbitrary, without strong biological or clinical basis. Operationalization can influence inferences drawn from adherence estimates, but our definition of consumption is robust, consistent, and based on considerations of global clinical guidelines. Third, there is potential for measurement error in dietary intake values used in our study. We did not measure individual dietary intake but used averages from a national survey. In addition, we used the dietary reference intakes for pregnant women older than 18 years in our study, which is less than the reference intake for adolescents, but 17% of our participants were adolescents. This might bias our estimates of percentage population meeting recommended dietary intake. However, our conclusion about relative effect of prescription regimen on the percentage population meeting recommended dietary intake is likely robust to the potential errors in our estimates, given that facilities were randomly assigned to the prescription regimens. Fourth, sociocultural and health system factors are complex and heterogeneous across low- and middle-income countries, which limit the external validity of our findings. Further studies are needed to delineate the inferential boundaries of our conclusions in terms of geographical, sociocultural, and health systems conditions. Fifth, our study was well

implemented over a period of 9 months. It is plausible that over time the effect of the interventions might wane, as suggested by the decrease in adherence shown here. Finally, there is a broader range of factors that need be considered in national programs than we were able to examine in this study. National programs will require a sustained support system whose focus transcend operational bottlenecks that we investigated in the delivery system, but also work with managers to address organizational and political economic constraints (Meyers et al., 2012). Our study is a first step in elucidating key program delivery issues; further research and programmatic experience will refine our conclusions.

5 | CONCLUSION

In conclusion, this study illustrates a systematic approach to integrating primary prevention of preeclampsia and anemia into ANC delivery, guided by a PIP approach. Availability of requisite resources at primary healthcare facilities, activities of HCWs and CHWs, and population proportion meeting RDA among ANC clients were relatively high, suggesting that Ca integration is feasible under the conditions of this study. Policy makers and program planners should pay careful attention to supply chain, HCW dispensing behavior, and appropriateness of regimen and supplement products for their settings.

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CONFLICTS OF INTEREST

All authors do not have conflicts of interests to declare.

CONTRIBUTIONS

Study conception: MOO, RJS, and KLD; study design: MOO, RJS, KLD, SLM, and JKK.

Supervised data collection: MOO; data analysis: MOO; data interpretation: MOO, RJS, KLD, and DLP.

First draft: MOO; critically reviewed manuscript and approved final version: all authors.

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