Tablets Are Preferred and More Acceptable Than Powdered Prenatal Calcium Supplements among Pregnant Women in Dhaka, Bangladesh\textsuperscript{1–3}

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Abstract

Prenatal calcium supplementation is recommended by the WHO to decrease the risk of preeclampsia in women with low dietary calcium intake; yet, this recommendation has not been successfully implemented to date. One component of an effective population-based prenatal calcium intervention will be the selection of a widely accepted calcium vehicle to promote consistent, long-term consumption of the supplement. We aimed to evaluate preference and acceptability of 4 different options for delivering prenatal calcium (conventional tablets, chewable tablets, unflavored powder, and flavored powder) to pregnant women in urban Bangladesh. In a modified discrete-choice trial, pregnant women (n = 132) completed a 4-d “run-in period” in which each delivery vehicle was sampled once, followed by a 21-d “selection period” during which participants were instructed to freely select a single delivery vehicle of their choice each day. Preference was empirically defined as the probability that each delivery vehicle was selected on a given day, and measured from participants’ daily delivery vehicle selections; acceptability was assessed by using mid- and post-trial questionnaires. Conventional tablets demonstrated the highest probability of selection (62%); the probability of selection of chewable tablets (19%), flavored powder (12%), and unflavored powder (5%) were all significantly lower than for conventional tablets (P < 0.001). The palatability and product characteristics of the conventional tablets were more acceptable than for the other 3 delivery vehicles. Our rigorous methodologic approach used both quantitative and self-reported measures that consistently identified the most preferred and accepted prenatal calcium delivery form. Through observation of pregnant women’s actual supplement use, and perceptions of acceptability (i.e., ease of use, palatability), we demonstrated that conventional tablets are likely to be the most accepted and successful calcium delivery vehicle in future field studies and scale-up of the WHO recommendation in Bangladesh. This trial was registered at clinicaltrials.gov as NCT01676636.


Introduction

Hypertensive diseases of pregnancy (HDP) are among the most common causes of maternal and perinatal morbidity and mortality worldwide (1). In populations where dietary calcium intake is low, randomized, controlled trials have demonstrated that calcium supplementation during pregnancy significantly decreases the risk of HDP and HDP-associated adverse outcomes (2–6). Furthermore, prenatal calcium supplementation was identified as the only intervention to prevent HDP that may be feasibly delivered at the community level (7).

A 2011 WHO guideline for the prevention of preeclampsia included the recommendation of routine prenatal calcium supplementation with 1.5 to 2.0 g of elemental calcium per day in areas where dietary calcium intake is low (8). This was reiterated in a 2013 WHO guideline that focused specifically on calcium supplementation during pregnancy (9). To date, these WHO recommendations have not been widely adopted, likely because of practical impediments to implementation, including the size and number of units of conventional calcium tablets required to deliver the recommended dose of calcium (typically 3 to 4 tablets/d), and the need to separate the ingestion of calcium


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\textsuperscript{1} Supported by the Centre for Global Child Health and Department of Paediatrics at the Hospital for Sick Children, and the Sprinkles Global Health Initiative.

\textsuperscript{2} Author disclosures: S.H. Zlotkin reports having intellectual property rights to his invention known as Sprinkles, which includes 7) patent rights for the United States and Canada, which are held by Ped-Med Limited (a Canadian corporation of which S.H. Zlotkin is the sole shareholder), and 2) trademark rights in various jurisdictions to the name Sprinkles, which are held by either Ped-Med Limited or the Sprinkles Global Health Initiative, Inc. (a Canadian not-for-profit corporation of which S.H. Zlotkin is a member); holding a North American patent on micronutrient powders; having a nonexclusive agreement on micronutrient powders with New GPC Ltd. in Guyana; and receiving institutional funding from the UN Children’s Fund (UNICEF) for consultation meetings related to micronutrient powders.


\textsuperscript{4} Supplemental Tables 1–5 and Supplemental Figures 1–5 are available from the “Online Supporting Material” link in the online posting of the article and from the same link in the online table of contents at http://jn.nutrition.org.

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from prenatal iron because of the negative impact of calcium on iron absorption (10).

Programmatic success in public health depends on ensuring effective delivery of efficacious interventions to a targeted population (11). For prenatal calcium supplementation, this has not yet been achieved. An important component of a successful population-based prenatal calcium intervention will be the selection of a widely accepted, ingestible calcium vehicle, which will thereby promote consistent, long-term consumption of the supplement. Population-based nutrient supplementation programs can be substantially influenced by end-user preference (the expression of appeal for a product) and acceptability (the extent to which a product is perceived to be suitable for its intended use) (12,13). Major determinants of preference and acceptability are a product’s palatability (taste, mouth feel, aftertaste, and smell) and other product characteristics such as the vehicle size, shape, formulation, and dosing frequency (14). Few studies have looked at pregnant women’s perceptions or preferences for micronutrient supplements (15–17), and only one study has compared the acceptance of different delivery forms during pregnancy (12). There is a paucity of literature on the implementation of micronutrient interventions in pregnancy, and virtually no studies that have examined specific factors that may influence the implementation of prenatal calcium supplements.

In the present study, we aimed to assess the preference and acceptability of 4 alternative delivery vehicles for prenatal calcium supplementation at the WHO-recommended dose among pregnant women in urban Bangladesh by using a novel discrete-choice experimental design.

Participants and Methods

Study site and participants. This study was conducted at the Shimantik Maternity Centre, a nongovernmental, not-for-profit facility that provides basic antenatal and obstetric services in the urban, low-income neighborhood of Khilgaon, Dhaka, Bangladesh, from November 2012 to March 2013.

Pregnant women attending the Centre for clinical services were screened for eligibility on the basis of the following inclusion criteria: aged 18 to 39 y; gestational age of 13 to 30 completed wk (based on recalled day 1 of the last menstrual period); residence in Dhaka at a fixed address; and self-reported intent to remain in Dhaka for the duration of the study. Exclusion criteria included reported complications during the current pregnancy, history of medical or obstetric complications, or moderate or severe anemia [hemoglobin concentration <90 g/L; assessed by using a handheld hemoglobinometer (Hb 201; HemoCue)]. Demographic and socioeconomic data were collected via a structured interview following enrollment at the Centre. All subsequent supplement administration, monitoring, and data collection activities were conducted in the participants’ homes. The study protocol was reviewed and approved by the Research Ethics Board at the Hospital for Sick Children (Toronto, Canada) and the Ethical Review Committee at the International Centre for Diarrhoeal Disease Research (Dhaka, Bangladesh). All participants provided written informed consent.

Sample size. The sample size was calculated by estimating the number of individuals needed to detect a 20% minimum difference between the proportion of days on which the least and most preferred delivery vehicles were selected. Although there was a lack of published evidence to guide sample size calculations, a 20% minimum difference was considered to be an effect size that would be large enough to have programmatic implications. With an α of 0.05, 80% power, and an estimated attrition of 20%, a total of 140 individuals were targeted for enrollment.

Prenatal calcium supplements. Participants were provided with 4 distinct prenatal calcium supplement options (“delivery vehicles”), including conventional tablets, chewable tablets, unflavored powder, and flavored powder (Supplemental Fig. 1). The composition, daily dose size, and mode of use of each supplement are outlined in Table 1. Each supplement option provided a daily dose of 1500 mg of elemental calcium, consistent with the WHO recommendation for pregnant women in settings where dietary calcium intake is low (8). The powdered supplement options additionally contained iron and folic acid in amounts consistent with the WHO recommendations for supplementation during pregnancy (18).

Conventional tablets (i.e., those intended to be swallowed intact) were purchased off-the-shelf in Dhaka (Sandolco 500; Novaris) and were provided in blister packs of 3 tablets each. The chewable tablets (Life Brand extra-strength calcium antacid, assorted fruit-flavors variety; Perrigo International) were purchased in Canada because chewable tablets are not available as a retail product in Bangladesh. A daily dose of 5 chewable tablets was provided in a single small plastic vial. The supplement powders were manufactured by the Toronto Institute of Pharmaceutical Technology (Toronto, Canada) for a parallel research study investigating the impact of this novel powdered formulation on in vivo calcium absorption (Encapsulated Calcium Absorption in Pregnancy; clinicaltrials.gov, NCT01678079). Each powder dose was provided to participants in a plastic vial sealed with a desiccant-filled cap. For the unflavored powder, participants were instructed to add the contents of 1 vial to a semi-liquid food or drink. The flavored powder had a mild orange flavor (N-C juicy orange flavor; FONA International), and participants were instructed to add the contents of 1 vial to half a cup of potable water.

Study design. Discrete-choice experimental designs involve providing participants with a “choice set” containing ≥2 alternative products or interventions that vary by characteristics of interest at a set point in time, and asking them to make a presumably “utility-maximizing” discrete choice (19). In the current study, we used a modified discrete-choice design by providing participants with 4 alternative calcium delivery vehicles and asking them to freely choose and ingest a single vehicle each day for a period of time. We assumed that the observation of participants’ unconstrained daily selection from among the 4 vehicles

TABLE 1 Nutrient content, portion size, and mode of use of 4 calcium (with or without iron and folic acid) supplement vehicles provided to pregnant Bangladeshi women in the study

<table>
<thead>
<tr>
<th></th>
<th>Conventional tablets</th>
<th>Chewable tablets</th>
<th>Unflavored powder</th>
<th>Flavored powder</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium, mg</td>
<td>1500</td>
<td>1500</td>
<td>1500</td>
<td>1500</td>
</tr>
<tr>
<td>Iron, mg</td>
<td>—</td>
<td>—</td>
<td>60</td>
<td>60</td>
</tr>
<tr>
<td>Folic acid, μg</td>
<td>—</td>
<td>—</td>
<td>400</td>
<td>400</td>
</tr>
<tr>
<td>Units required per day, n</td>
<td>3 × 500-mg tablets</td>
<td>5 × 300-mg tablets</td>
<td>1 container</td>
<td>1 container*</td>
</tr>
<tr>
<td>Mode of use⁵</td>
<td>Swallowed with a meal</td>
<td>Chewed before or after a meal</td>
<td>Added to 125 mL of semi-liquid food or drink</td>
<td>Added to 125 mL of potable water</td>
</tr>
</tbody>
</table>

¹ Amount shown is elemental calcium, provided as calcium carbonate.
² Amount shown is elemental iron, provided as ferrous fumarate.
³ One unit of unflavored powder weighed ~11 g.
⁴ One unit of flavored powder weighed ~19 g.
⁵ Tablet-based delivery vehicles were consumed at one time or throughout the day. Powder-based delivery vehicles were consumed at one time during the day.
over a prolonged period of time (3 wk) in a real-world setting (their homes) would reflect their actual preferences. The total study duration for each participant was 25 d, including a 4-d “run-in period” and a 21-d “selection period.” During the run-in period, each participant was exposed to all 4 delivery vehicles by assigning 1 vehicle to be consumed on each of the 4 d according to a random sequence. Participants were asked to consume each of the delivery vehicles during the run-in period to proceed to the selection period. During the subsequent selection period, participants were asked to freely select 1 of the 4 supplement delivery options on each day and record their selections (or missed doses) on a tracking form. A participant’s choice on any given day of the selection period was independent of her choice on other days; however, only 1 option was permitted on each day. At the start of each study week, research personnel provided participants with a 1-wk supply (7 doses) of each delivery vehicle. At the end of each study week, the number of consumed and unconsumed delivery vehicles was counted to verify reported consumption, and participants were asked if they had experienced any adverse events. A dose was considered to be consumed if ingested in its entirety (i.e., no units remained).

Assessment of preference and acceptability. Relative preference was operationally defined according to the proportion of days on which each delivery vehicle was selected during the 21-d selection period. In the primary analyses, preference was ranked at the group level by aggregating all days of observation contributed by all participants, irrespective of each individual’s distribution of selections. We also ascertained preference at the individual level by considering the proportion of days on which each participant selected each delivery vehicle (referred to as “revealed preference”).

To further understand the rationale for a participant’s choice, a semi-structured questionnaire was used at 2 time points: 1) following the run-in period (mid-trial), and 2) upon completion of the selection period (post-trial). Both questionnaires required participants to rate sensory (taste, mouth feel, aftertaste, and odor) and product-related (portion size, preparatory requirements, and ease of use) characteristics on a 5-point rating scale (ranging from “I really liked it” to “I really did not like it”). In the post-trial questionnaire, participants were asked to identify their most and least preferred delivery vehicles (referred to as “stated preference”) and indicate reasons why a supplement was not used or stopped.

Data collection. Questionnaires were written in English and translated into Bengali (the primary language in Bangladesh). Representative items were back-translated into English from Bengali to confirm the precision of the original translation; only selected items underwent formal back-translation because the wording was very similar across multiple items. Trained study personnel verbally administered the questionnaires to participants as structured interviews. All questionnaires were manually checked for completeness before data were entered into an electronic database (Microsoft SQL Server 2005) with the use of a custom interface (ASP.NET with C#).

Statistical analyses. The primary analysis of participant preference was based on daily delivery vehicle selections throughout the selection period, whereby the unit of analysis was a “discrete choice” (i.e., 1 delivery vehicle selection on 1 d). Participants had to have made a single selection per study day to be included in the primary analysis, which led to the exclusion of selections made by 1 participant on days 1 to 7 because she selected 2 delivery vehicles per day. Multinomial logistic regression was used to model the probability of selection of each discrete (categorical) outcome (with 95% CIs) (20), while employing cluster robust-SE to account for correlation among individual delivery vehicle selections (range of data points per participant: 7 to 21) (21). The reference category was conventional tablets. Associations between sociodemographic characteristics and delivery vehicle preference were also assessed by using multinomial logistic regression. In secondary analyses, each participant’s most frequently selected option was considered to be her most preferred (revealed preference), regardless of the magnitude of the difference in the proportion of days on which she selected her most preferred vehicle vs. others. To be included in this analysis, participants had to have made a single selection on each day of the selection period and completed the entire selection period, which led to the exclusion of 3 participants. Changes in preference patterns over time were also considered by calculating the proportion of participants who selected each delivery vehicle every day and every week. To observe whether progressive stabilization of delivery vehicle choices occurred over time, the cumulative proportion of selections was determined by study day.

The stated frequencies of participants’ most and least preferred delivery vehicles were summarized as proportions with 95% CIs. Other acceptability-related outcomes were based on summaries of ratings for the characteristics of different delivery vehicles at 2 time points; these ratings were compared by using the nonparametric Wilcoxon signed-rank test (22). For some characteristics, comparisons were separated by delivery form (tablet-based and powder-based) given the specificity of the characteristic to the form. The reasons why participants did not use or stopped using a delivery vehicle during the selection period, as determined from open-ended questions post-trial, were summarized.

Data were analyzed by using Stata/IC 12.0 (Stata Corporation), and P values of <0.05 were considered to be statistically significant. All graphs were generated with the use of Microsoft Excel 2010 (Microsoft).

Results

Recruitment and attrition. Of 269 pregnant women screened for enrollment, 149 were enrolled (Fig. 1). Of those enrolled, 17 withdrew prior to the selection period. Of the 132 participants who entered the selection period, 2 withdrew before completing follow-up and 130 completed the entire 21-d selection period. Participants who contributed at least 1 selection during the selection period were included in primary analyses (Table 2). At the time of enrollment, the mean age of study participants was 21.9 ± 3.7 y. They had completed 21.9 ± 5.2 wk of gestation, and 48% identified the current pregnancy as their first. Most participants reported having had some education (77%), and most identified themselves as housewives (90%).

![FIGURE 1 Screening, exclusion, and withdrawals of pregnant Bangladeshi women during the study period.](image-url)
TABLE 2  Selected demographic and socioeconomic characteristics at baseline of pregnant Bangladeshi women who contributed data during the selection period (n = 132)¹

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>21.9 ± 3.7</td>
</tr>
<tr>
<td>Gestational age at enrollment, wk</td>
<td>21.9 ± 5.2</td>
</tr>
<tr>
<td>Pregnancies, n (%)</td>
<td></td>
</tr>
<tr>
<td>1 (First)</td>
<td>63 (48)</td>
</tr>
<tr>
<td>2</td>
<td>43 (33)</td>
</tr>
<tr>
<td>3</td>
<td>16 (12)</td>
</tr>
<tr>
<td>≥4</td>
<td>10 (8)</td>
</tr>
<tr>
<td>Educational attainment, n (%)</td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>32 (24)</td>
</tr>
<tr>
<td>Primary</td>
<td>46 (35)</td>
</tr>
<tr>
<td>Secondary or higher</td>
<td>54 (41)</td>
</tr>
<tr>
<td>Ability to read, n (%)</td>
<td></td>
</tr>
<tr>
<td>Cannot</td>
<td>30 (23)</td>
</tr>
<tr>
<td>With difficulty</td>
<td>31 (23)</td>
</tr>
<tr>
<td>Easily</td>
<td>71 (54)</td>
</tr>
<tr>
<td>Occupation, n (%)</td>
<td></td>
</tr>
<tr>
<td>Homemaker</td>
<td>119 (90)</td>
</tr>
<tr>
<td>Salaried job</td>
<td>6 (5)</td>
</tr>
<tr>
<td>Day laborer</td>
<td>4 (3)</td>
</tr>
<tr>
<td>Private business</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Unemployed</td>
<td>2 (1)</td>
</tr>
<tr>
<td>Past experience with delivery vehicle² n (%)</td>
<td></td>
</tr>
<tr>
<td>Conventional tablet</td>
<td>123 (93)</td>
</tr>
<tr>
<td>Chewable tablet</td>
<td>97 (74)</td>
</tr>
<tr>
<td>Oral rehydration salts</td>
<td>124 (94)</td>
</tr>
<tr>
<td>Powder</td>
<td>13 (10)</td>
</tr>
</tbody>
</table>

1 Values are means ± SDs or n (%).
2 Did not have to be in the context of pregnancy and could refer to consumption of a nutritional supplement and/or medication.

Delivery vehicle preference. Participants contributed a total of 2737 delivery vehicle selection days for analysis. In the primary analysis, the probability of selecting conventional tablets was highest (62%; 95% CI: 57–65%), followed by chewable tablets (19%; 95% CI: 18–20%), flavored powder (12%; 95% CI: 11–15%), unflavored powder (5%; 95% CI: 3–6%), and no delivery vehicle (2%; 95% CI: 2–3%). The selection probabilities for conventional tablets, flavored powder, unflavored powder, or no vehicle were significantly lower than for conventional tablets (P < 0.001 for all comparisons). To account for possible bias on the days that participants were visited by study personnel, the data were analyzed excluding study personnel home visit days (i.e., not including selection days 1, 8, and 15). There was still a strong preference for conventional tablets (P < 0.001), and the selection probabilities changed minimally.

TABLE 3  Delivery vehicle preferences of pregnant Bangladeshi women during the selection period

<table>
<thead>
<tr>
<th>Preference characteristics</th>
<th>Conventional tablets</th>
<th>Chewable tablets</th>
<th>Flavored powder</th>
<th>Unflavored powder</th>
<th>Missed dose, n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Most frequently selected delivery vehicle¹</td>
<td>91</td>
<td>74 (66, 82)</td>
<td>22</td>
<td>18 (11, 25)</td>
<td>9</td>
</tr>
<tr>
<td>Stated most preferred delivery vehicle²</td>
<td>100</td>
<td>77 (70, 84)</td>
<td>17</td>
<td>13 (7, 19)</td>
<td>12</td>
</tr>
<tr>
<td>Stated least preferred delivery vehicle²</td>
<td>2</td>
<td>2 (0, 4)</td>
<td>26</td>
<td>20 (13, 27)</td>
<td>26</td>
</tr>
</tbody>
</table>

1 Among participants who contributed 21 selections and did not have a tie for their most frequently selected delivery vehicle (n = 123).
2 Among all participants who completed the selection period (n = 130).
3 Participants’ stated most and least preferred delivery vehicle were determined post-trial.

Nearly all participants (93%) selected the conventional tablets at least once during the selection period, whereas about half ever used the chewable tablets (53%), and a minority ever used the flavored powder (45%) or the unflavored powder (31%). Doses were missed on 62 d (2% of all days for analysis), and 76% of participants reported missing no doses. Among those who had missed a dose, the number of doses missed ranged from 1 to 8. The most frequent reasons for missing a dose were “forgetting” (73% of missed doses) or “feeling unwell” (25% of missed doses). Participant sociodemographic characteristics were not significantly associated with preference (Supplemental Table 1).

In the analysis based on individual-level ascertainment of revealed preference, conventional tablets were the most preferred (i.e., most frequently selected) vehicle (74% of participants), followed by chewable tablets (18%), flavored powder (7%), and unflavored powder (1%) (Table 3). Six participants ended up selecting 2 vehicles with equal frequency for their first choice (4 had conventional tablets and chewable tablets; 2 had conventional tablets and flavored powder). Stated preferences for the delivery vehicles were evaluated in the post-trial questionnaire by asking participants which delivery vehicles they preferred most and least. The majority of participants (77%) reported that they liked conventional tablets the most, and 58% reported liking the unflavored powder the least (Table 3). Revealed (most frequently selected) and stated delivery vehicle preferences were consistent in 87% of participants.

Delivery vehicle selections over time. Of the possible delivery vehicle selection combinations observed throughout the selection period, the greatest number of participants exclusively selected conventional tablets (29%; 38 of 129 participants), followed by a combination of all 4 delivery vehicles (22%; 29 of 129), and interspersed conventional and chewable tablet selection (20%; 26 of 129). Conventional tablets were most frequently selected regardless of the day (Supplemental Fig. 2). The proportion of delivery vehicle selections made on days corresponding with home visits by study personnel was significantly different from non-home visit days (P < 0.001) (Supplemental Fig. 3). The selection of conventional tablets increased between weeks 1 and 3, whereas the selection of flavored and unflavored powder decreased during this time (Supplemental Fig. 4). The cumulative proportion of conventional tablet selections declined somewhat during the first 7 d of the selection period, although it was relatively stable thereafter (Fig. 2).

Delivery vehicle acceptability. At midtrial, median and interquartile ranges of ratings for sensory characteristics were more favorable for conventional tablets compared with the other delivery vehicles (Table 4). The distribution of responses tended to be predominantly favorable for the conventional tablets; moderately favorable, yet widely distributed, for the
chewable tablets and flavored powder; and generally unfavorable for the unflavored powder (Supplemental Fig. 5). Post-trial responses appeared more favorable for all delivery vehicles relative to midtrial, with a notable absence of unfavorable responses for all sensory characteristics pertaining to conventional tablets.

In comparing the responses for conventional vs. chewable tablets, participants reported that the conventional tablets were easier to consume and swallow. The number of units required per day was reported to be more convenient for conventional tablets (3 tablets/d) than chewable tablets (5 tablets/d) (Supplemental Table 2). There were no differences in the perceived mixability of the flavored vs. unflavored powder, nor the degree to which they settled or adhered to the sides of the serving container (Supplemental Table 3). Distributions of ratings for the tablet-based and powder-based characteristics did not differ from mid- to post-trial, although post-trial responses tended to be more favorable for the tablet-based delivery vehicles.

The most frequently reported reasons for not using or stopping the use of a single delivery vehicle during the selection period included dislike of a vehicle’s taste; difficulty consuming a delivery vehicle; and feeling unwell after taking a delivery vehicle (Supplemental Table 4). Few participants reported having experienced any adverse events (e.g., nausea, vomiting, constipation) during the study period (Supplemental Table 5).

### Discussion

The selection of an acceptable supplement delivery vehicle by targeted end-users is believed to be a critical yet under-researched step in the path to scale-up of population-based nutritional interventions (12). In light of the recent WHO recommendation for prenatal calcium supplementation, this study evaluated preference and acceptability of 4 different options (conventional tablets, chewable tablets, unflavored powder, and flavored powder) for delivering the WHO-recommended dose of calcium to pregnant women in urban Bangladesh. Our consistent results, based on both revealed and stated measures, demonstrated that there was a strong preference for conventional calcium tablets, compared with the other delivery forms in this study population.

The present study employed a design that yielded estimates of both revealed and stated delivery vehicle preference, in addition to assessing perceptions of delivery vehicle characteristics. Importantly, the revealed preference for conventional tablets was consistent with most participants’ stated preference of conventional tablets as their “most preferred” option at the end of the study. There were 2 prominent trends in delivery vehicle selection: 1) an increase in the number of participants selecting the conventional tablets with the progression of each study week; and 2) an increase in conventional tablet selection on day 1 of each study week (when research personnel conducted home visits). It is possible that study personnel influenced the choices made by participants at their weekly interactions; however, the proportion of conventional tablet selections on home-visit days (77%) was closely aligned with the proportion of participants whose stated delivery vehicle preference was conventional tablets (74%), suggesting that selections made on home-visit days may have represented actual delivery vehicle preference. Notably, average preferences appeared to stabilize after about 1 wk of selection. This may indicate that in future applications of this novel study design, observing participants’ delivery vehicle selections for a 1-wk period may be sufficient.

The cultural context of taking medicine and supplements may have influenced participants’ perception of the various delivery vehicles. Conventional tablets have been a standard delivery form for medications and in therapeutic and preventative mineral and vitamin supplementation regimens worldwide given their familiarity, ease of use, and long shelf-life; the general acceptability of tablets was previously documented in low-income settings (12,15,16). Familiarity with this common delivery form may have contributed to their relative preference compared with the powder-based options, which were a
relatively novel mechanism for micronutrient delivery. Two factors that likely contributed to the observed low acceptance of the powdered products among participants were the following: 1) the total mass of powder required to adhere to the WHO-dose recommendation, and to allow for additional excipients to prevent settling or sticking within the serving container (final weight of 11 and 19 g for the unflavored and flavored powder, respectively); and 2) the suboptimal organoleptic nature of the granules themselves.

The importance of broadening the concept of acceptability beyond palatability, particularly taste, was similarly demonstrated in a multiple micronutrient supplementation trial among pregnant women in Mexico. Young et al. (12) compared participants' perceptions of sensory characteristics, ease of use, and perceived health effects for conventional tablets, micronutrient powder (Sprinkles), and a fortified food (Nurtrividta). Micronutrient powder and tablets were strongly preferred over the fortified food because participants disliked the smell, taste, and texture of the fortified food and often found it difficult to store and prepare. Conventional tablets were marginally preferred over the micronutrient powder, mainly because of perceived differences in the simplicity of use. However, we acknowledge that our findings related to preference and acceptability over a short term (i.e., the period of study) may not necessarily predict adherence throughout the duration of pregnancy (12). Factors known to affect adherence to supplementation regimens include volume or number of units recommended, dosing frequency, cost per dose, and the understanding of appropriate use and potential side effects (14–16).

Our finding that conventional tablets were the preferred delivery vehicle for calcium in the current study may not apply similarly to all nutrients in all settings. Preference for conventional tablets was likely attributable in part to the nature of the other delivery vehicles used in the study, the number of units per delivery vehicle, and the bulk of the powder needed to deliver the calcium dose based on the WHO recommendation. Most micronutrients are required in smaller doses, in which case a powder or chewable tablet delivery vehicle may be more readily accepted by targeted users because of the lower mass and/or number of units required per day. Indeed, micronutrient powders for infants, which are typically delivered in sachets weighing between 0.5 and 1.0 g, are generally well accepted (23).

The current study highlights the challenges associated with implementing the WHO prenatal calcium supplementation recommendations. A major strength was the application of a novel trial methodology that included evaluation of preference by using both quantitative observations and participant self-reported. However, the study had some limitations. The number of conventional vs. chewable tablets was not identical; therefore, tablet number may have been a confounder of observed differences in preference. Because the calcium content of commonly available conventional vs. chewable calcium tablets differed, our design could not account for this. In addition, iron and folic acid were not incorporated into the tablets as they were in the powders, which may have influenced measures of acceptability. In-depth interviews were not conducted, which may have further informed the discussion of motivators and barriers to supplementation. We note that the low rates of reported adverse effects and very high adherence may have been partly a result of social desirability bias that would be less common outside of a research context. Participant demographics were similar to the urban Bangladeshi population (24); a high proportion of participants self-identified as housewives, which is expected for a pregnancy cohort. Therefore, we believe that the present findings can be generalized to Bangladesh and potentially other jurisdictions and cultural contexts in which prenatal calcium supplementation is considered for programmatic implementation.

Although our study was not intended to examine the programmatic implications of the recent WHO calcium recommendations, we believe that high rates of coverage and adherence would be difficult to achieve if implementing agencies were to promote calcium at a dose of 3 tablets/d (500 mg each) plus a separate daily iron-folic acid tablet, as suggested by the WHO (9). Unless a range of delivery-related barriers to implementation are comprehensively addressed, there will be a high risk of persistent disconnect between what the WHO recommends in terms of prenatal calcium supplementation and what is actually implemented. The present study demonstrated that user preferences for calcium delivery vehicles can be evaluated by using a rigorous methodology that yields an informative combination of revealed and stated outcome measures. A large majority of participants (74%) demonstrated preference for conventional tablets, yet the availability of both conventional and chewable tablets would result in >90% of women having access to their most preferred delivery vehicle. Furthermore, the availability of 2 delivery forms may be a practical solution to improve overall adherence to calcium supplementation regimens. Future research in communities with low dietary calcium intakes should address the feasibility of calcium tablet supply chains, the determinants of long-term adherence to calcium supplementation during pregnancy, and the integration of both prenatal calcium and iron-folic acid supplementation into antenatal care programs in resource-poor settings.

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Preference and acceptability of prenatal calcium


