

Toward a Better Understanding of Adherence to Micronutrient Powders: Generating Theories to Guide Program Design and Evaluation Based on a Review of Published Results

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Abstract

Background: The Global Alliance for Improved Nutrition is conducting theory-driven process evaluations of micronutrient powder (MNP) programs.

Objective: The aim was to generate preliminary theories about factors affecting adherence to recommendations with regard to point-of-use fortification of foods with MNPs.

Methods: A literature search was conducted to identify documents with content related to adherence to MNPs as an intervention provided at home to children 6–59 mo of age. Thirty-five studies and 6 program descriptions were identified. We used thematic analyses to generate a comprehensive list of factors that could influence adherence, followed by content analysis to quantify the results. We developed a Program Impact Pathway to concretize the points at which the factors identified affect the process of adherence.

Results: In the set of documents reviewed ($n = 41$), the most influential factors, measured by number of documents reporting the factor having effect, were 1) caregivers' perception of positive changes as a result of MNP use ($n = 14$), 2) caregivers' perceived child acceptance of food with MNPs ($n = 12$), and 3) caregivers' forgetfulness ($n = 11$). Behavior change communication channels ($n = 13$) and messages ($n = 12$) were the most frequently reported program design features influencing caregiver knowledge and subsequent adherence. Administration regimen ($n = 10$), which may be related to caregivers' capacity to remember to give MNPs, was also a frequently cited program design feature affecting adherence.

Conclusions: The preponderance of knowledge and perception factors may reflect an underlying theoretical bias among researchers as to what they measure. To achieve programs that support greater adherence, we need to adopt a cultural-ecological perspective to inform program design in order to address a broader set of determinants. Studies that assess progress across the impact pathway, particularly from adherence to biological outcomes, would also provide guidance for evaluation studies, particularly when time or other constraints limit the potential to measure biological outcomes. CDN 2017;1:e001123.

Introduction

In addition to the well-known structural and economic constraints on achieving nutrient adequacy in low-income populations, adequacy during the period of complementary feeding (age 6–24 mo) is particularly challenging because infants and young children eat in small amounts and nutrient adequacy can be achieved only through the consumption of nutrient-dense foods (1–3). In many low-resource populations, access to nutrient-dense complementary foods is limited. One intervention recommended by the WHO to improve micronutrient content of infant and young child (IYC) diets is point-of-use fortification of foods with micronutrient powders (MNPs) (4, 5). MNPs are single-dose sachets of dry powder



Keywords: micronutrient powders, adherence, infant and young child nutrition, complementary feeding, micronutrient deficiency, cultural-ecological

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Supplemental Table 1 is 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://cdn.nutrition.org>.

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Abbreviations used: CERQual, Confidence in the Evidence from Reviews of Qualitative research; GAIN, Global Alliance for Improved Nutrition; IYC, infant and young child; MNP, micronutrient powder; PIP, Program Impact Pathway.

containing lipid-encapsulated iron and other micronutrients that can be sprinkled onto any semisolid food (6). Studies have shown that adding MNPs to complementary foods reduces the risk of iron deficiency anemia and retinol deficiency among infants and young children (7, 8). As of 2014, UNICEF reports that 50 countries are implementing MNP programs, including 9 at the national level (9).

The Global Alliance for Improved Nutrition (GAIN), with funding from the Ministry of Foreign Affairs of The Netherlands, is supporting the Federal Ministry of Health in Ethiopia and the Mozambique Ministry of Health to pilot the delivery of MNPs for the first time in these countries. In Ethiopia, the lessons learned will inform the scale-up of MNP delivery through the Federal Ministry of Health's Health Extension Program, which, since 2003, has deployed government-salaried female health extension workers to provide primary health care services in rural communities (10, 11). In Mozambique, free vouchers redeemable at local stores are used to facilitate MNP distribution through the Ministry of Health's health facilities and community health volunteers (*activistas*), who are organized by the nongovernmental organization Save the Children Netherlands. Theory-driven process evaluations, which are designed to generate learning about factors affecting program delivery systems and how MNP outcomes are achieved or not achieved (12–15), are integral to the projects in both countries.

As part of the preparation for the evaluations, we carried out a study to better understand what is currently known about the factors that affect MNP adherence. As described below, we sought to generate a comprehensive list of factors that could influence adherence and then developed a Program Impact Pathway (PIP) to concretize the points at which the factors identified affect the process of adherence (16, 17). This article presents the results of our analysis of the published and accessible gray literature. The findings are used to generate preliminary theories, conceptualized in a revised and expanded PIP, about how these factors could limit or facilitate adherence. The PIP provides a blueprint to guide MNP program evaluations to be undertaken by GAIN or others and includes a priori hypotheses to test determinants of program impacts to generate evidence to guide planning and decision-making.

Nutrition-specific interventions, including MNPs, have biological objectives that are mediated through households, and specifically caregivers. PIPs developed for nutrition-specific programs therefore need to consist of 2 components representing the processes of 1) program delivery, the pathway from program inputs to the handover points (points of interaction) during which caregivers receive the intervention, and 2) household utilization, the sequence of behaviors by household members, predominantly caregivers, that are required to lead to a biological impact on child nutritional status. Similar to procedures in other nutrition program evaluations, we mapped program delivery in collaboration with program staff (16–18). This approach provided the basis for assessing the flow of program delivery and generating hypotheses about factors that could affect implementation fidelity or program integrity.

In the context of MNP interventions, the process of household utilization is grounded in adherence, which can be defined as the extent to which a caregiver's behavior and child's consumption are congruent with recommendations with regard to MNPs (19, 20). Adherence to MNP recommendations involves 3 basic elements:

initiation (caregiver determination to feed MNPs and starting to do so), appropriate use (caregiver preparing and child consuming MNPs as directed), and continued use (caregiver providing and child consuming the minimum number of MNP sachets over a recommended time period). We diagrammed the sequence of caregiver behaviors for the 3 elements on the basis of the specific instructions provided in the Ethiopia and Mozambique programs (as shown in **Figure 1** for Ethiopia) augmented by interviews with program staff. (There is no universal set of standardized instructions for MNP use. The instructions provided to caregivers in Mozambique and Ethiopia varied. For example, caregivers in Mozambique were instructed to use MNPs every day, whereas in Ethiopia, caregivers were instructed to use the MNP every other day.) This 2-pronged approach produced a depiction of the flow of the intervention from the caregiver to the child. However, the diagram that was generated was insufficient to derive hypotheses about factors that influence adherence. Therefore, we turned to the literature to learn from programs that have implemented MNP interventions in other contexts and report on their experiences and evaluation results.

Methods

Research approach

Systematic analysis of research evidence is commonly used to inform nutrition policies and programs, including MNPs (7). Well-established procedures for quantitative, epidemiologic analyses, particularly the establishment of the GRADE (Grading of Recommendations Assessment, Development, and Evaluation) approach, has facilitated a consistent and reproducible assessment of quantitative evidence of effectiveness (21). More recently, the Confidence in the Evidence from Reviews of Qualitative research (CERQual) approach was developed to support analyses to examine a range of implementation issues. It is intended to provide a method for assessing confidence in findings from studies that are based on qualitative evidence syntheses (22). We considered the use of the CERQual approach to synthesize the evidence on factors affecting adherence to recommendations with regard to MNPs. However, in contrast to the purpose for which the CERQual was developed, our objectives were to create a comprehensive taxonomy of factors reported by researchers and program implementers and to generate hypotheses that could be tested through future research. We expect that, as more nutrition implementation research is conducted, the qualitative CERQual approach will be increasingly applied to assess the relations of factors identified in adherence study outcomes. At this preliminary stage of evidence building, we felt that a combination of thematic and content analysis, following recommended procedures for qualitative data analysis, would be more productive (23, 24).

Systematic search and selection of literature

In 2015, on behalf of the US Agency for International Development, the SPRING (Strengthening Partnerships, Results, and Innovations in Nutrition Globally) project convened a consultation of policy makers, program implementers, donors, and global experts to share evidence and experience related to MNP programs (25). As part of

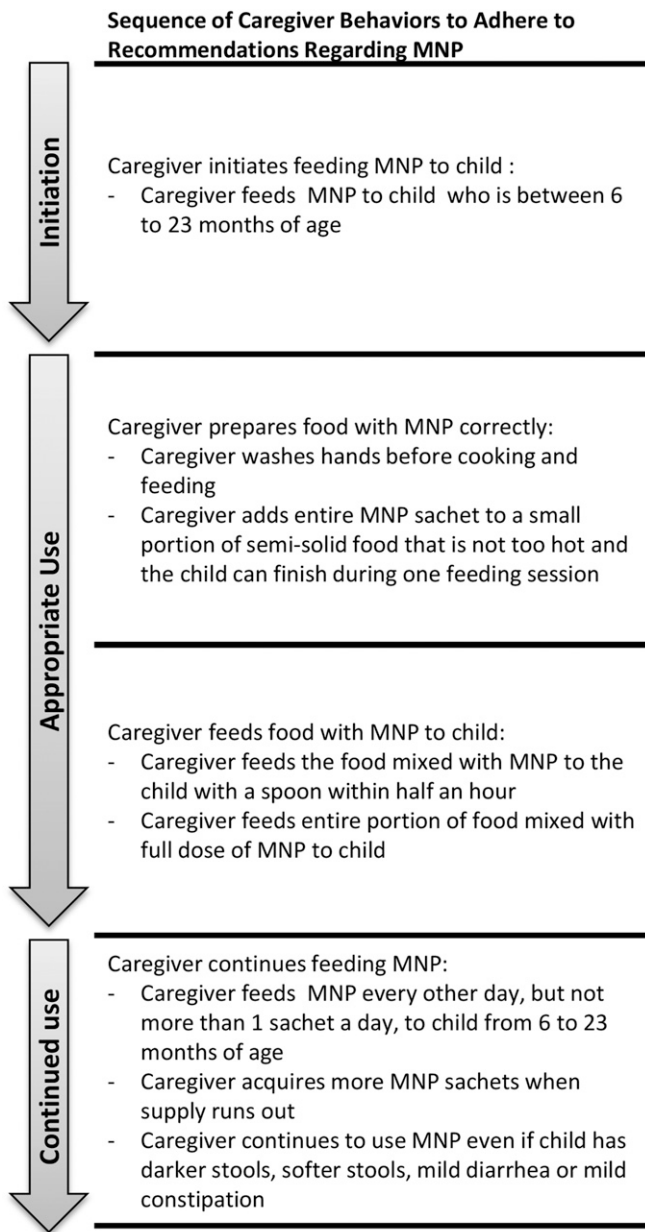


FIGURE 1 Program Impact Pathway depicting household utilization of MNPs. Caregiver behaviors are based on key messages communicated as part of the Ethiopia program. MNP, micronutrient powder.

the consultation and the subsequent preparation of manuscripts, an extensive systematic literature search was conducted to identify articles that had any relevance to MNP programs. Two of the authors of the current article (AT and LMN) participated in this process, which used the following inclusion criteria: 1) MNPs as an intervention provided at home to children 6–59 mo of age, 2) relevant learning for MNP intervention implementation, and 3) full text available in English. Details of the search strategy are described elsewhere (25). As a result of the consultation’s systematic literature search, 81 peer-reviewed articles, 19 guidance documents, and 55 program reports or conference presentations were identified with information

on program implementation experiences. In the analysis for this article, we excluded presentations, review articles, and guidance documents and added 3 studies identified through an additional search of PubMed, resulting in a potential database of 55 documents.

The first author (AT) read the 55 documents to determine whether they contained content related to the sequence of behaviors involved in adherence to MNPs (see Figure 1). For the present study, articles were excluded only if they did not contain any content related to adherence as depicted in Figure 1. We purposely chose not to exclude publications based on a rating of quality. In this step, we identified 41 documents—35 published studies (26–60) and 6 program descriptions (61–66)—that constituted the database for our analysis.

Data analysis

Thematic analysis of a data set (individual studies or a set of studies) is a standard approach for analyzing qualitative data (67–69). When thematic analyses are coupled with coding, by using content analysis procedures, the dual approach permits quantitative assessment, as well as a comparison of themes across the studies in a database. We used QSR International’s NVivo version 11 qualitative data analysis software to organize data and facilitate coding (70). The first author read and coded the 41 documents, with all documents revisited as new codes were created. The process of revising codes as analysis proceeds is standard good practice in qualitative coding (71). The aim of this step was to generate a comprehensive list of factors that could influence adherence and a matrix of quotations that could be used to compare themes across documents. The identification of factors and themes emerged from the content of the documents, not from a preset list of codes. This step produced a comprehensive list of factors, including those that were theorized by researchers or program implementers to have influenced MNP intervention outcomes.

In the next analytic step, the factors were categorized according to their described effect, or valence, on MNP adherence as follows: 1) factor reported to have a facilitating effect, 2) factor reported to have a limiting effect, 3) factor reported to have a facilitating or limiting effect depending on other conditions, 4) factor reported but authors stated that they did not find evidence of its effect on adherence, and 5) factor reported but authors did not comment on its effect. In this article, we compare the relative influence of factors in our database by counting the number of documents reporting that the factor has either a facilitating or limiting effect (i.e., factor effect categories 1–3). A coding framework was created to allow the second author (CHS) to validate coding on a subset (~10%) of randomly selected documents. The discrepancy rates between the first and second authors for both the identification of factors and their valence were <5%. The authors (AT and CHS) reviewed and discussed the discrepancies and agreed on coding definitions for the factors in question. Frequencies were analyzed by using IBM SPSS Statistics for Windows version 24.0 and graphed by using SigmaPlot version 13.0 (Systat Software, Inc.).

In the last analytic step, we categorized the factors, drawing on the “cultural-ecological framework,” a theoretical formulation that has been used previously to examine IYC feeding from an ethnographic perspective (72, 73). We modified and expanded the

framework and used it to classify the factors into broad categories, which are referred to in the original formulation as “domains.”

Results

A description of the documents and factors coded in each of the documents is presented in **Supplemental Table 1**. The documents include studies and program descriptions from 26 countries. Twenty-three of the studies used only quantitative research methods (26–30, 33–41, 44, 45, 47, 49, 51, 54, 55, 57, 58), 8 studies used only qualitative research methods (31, 32, 42, 43, 50, 53, 59, 60), and 4 studies used both quantitative and qualitative methods (46, 48, 52, 56). The qualitative and mixed-method studies were exploratory and permitted investigators to discover factors that were not predefined; the quantitative studies were focused on measuring coverage, utilization, or biological outcomes, and used close-ended questions and precoded answers. The average duration of the quantitative studies was 10 mo, ranging from 2 to 26 mo. Six of the quantitative studies (27, 33, 40, 41, 49, 57) statistically analyzed associations among child, caregiver, household factors, and adherence outcomes. Among the 12 exploratory studies, the average duration was 8 mo; 7 of the studies were short-duration (2 d–2 mo) formative research studies to assess the acceptability or feasibility of an MNP intervention.

Twenty-four factors are reported to potentially influence the sequence of behaviors involved in adherence to MNPs. **Figure 2** shows the number of documents that are coded for each factor and the factor’s categorization, according to the authors’ description of its effect on adherence. We also identified 16 program design features that were discussed in relation to their influence on the factors affecting adherence. **Figure 3** shows the number of documents that are coded for each program design feature.

In the set of documents in our database ($n = 41$), the most frequently reported factors for adherence to MNP recommendations are as follows: 1) caregivers’ perception of negative side effects ($n = 23$), 2) caregivers’ perception of positive changes in their children as a consequence of consuming MNPs ($n = 21$), and 3) caregivers’ perception of organoleptic changes associated with preparation of food with MNPs ($n = 20$). However, in the full sample of studies ($n = 41$), the list of most influential factors, based on the authors stating that they had either a facilitating or limiting effect, are as follows: 1) caregivers’ perception of positive changes as a result of MNP use ($n = 14$), 2) caregivers’ perceived child acceptance of food with MNPs ($n = 12$), and 3) caregivers’ forgetfulness ($n = 11$). Details of the main findings are described below.

Positive changes and negative side effects associated with MNP use

Positive changes and negative side effects that caregivers observed in their children that are linked to consuming MNPs are the most commonly investigated and reported factors by researchers and program implementers. Fourteen of the 41 documents analyzed reported that the perception of positive changes facilitates continued use, and 8 documents reported caregivers’ perception of negative side effects as limiting adherence. Only 2 studies, both in Nepal

and both conducted by the same research team, tested and presented the results of correlations between observed changes in children and MNP coverage and adherence (41, 49). The researchers found that caregivers who perceive ≥ 1 positive change in their child after MNP use are significantly more likely to obtain more sachets (≥ 2 batches of 60 MNP sachets in the previous 15 mo) (41) and to report greater adherence (i.e., to feed ≥ 45 sachets of MNPs to their children within the previous 60 d) (49). Neither study found correlations in the subsample of caregivers who perceived negative side effects.

Figure 4 shows the frequency of positive changes and negative side effects reported in our database of publications ($n = 41$). Caregivers’ perception that the child has improved health or immunity is the most influential positive change associated with MNP intake ($n = 14$). For the most part, the reports of health improvements consist of generalized statements without specification of how or for which illnesses MNPs improve outcomes: for example, “mothers also said they liked MNP[s] because it was easy to use and had beneficial health effects for the child” (53) and “caregivers reported perceived positive changes in their children’s health, energy levels and appetite after the children started receiving Vita-Mix-It [MNP]” (63). Two studies—1 in Peru and 1 in Kenya—provided more-detailed information, stating that caregivers observed less diarrhea (31, 42); the Kenya study also reported that “preexisting health problems” including “vomiting or swollen stomach (kwashiorkor)” resolved after using MNPs (42). Increased appetite is the second-most influential positive change associated with MNP intake ($n = 12$). However, in the context of household food insecurity, it is not always seen as a desirable change. Thus, 4 documents included accounts of difficulty with continuing MNP use due to the child’s increased appetite (42, 43, 53, 59). The most serious complaints about MNPs increasing appetite were reported during interviews in the Kakuma Refugee Camp in Kenya (43). In a setting in which food rations were inadequate, interviewees talked at length about the challenges that they faced as a result of their children having increased appetites.

In the set of documents reviewed for this article ($n = 41$), diarrhea or loose stools are the most reported ($n = 14$) and the most influential negative side effect ($n = 6$) associated with MNP intake. However, the influence of negative gastrointestinal events appears to be much less influential than the positive effect of perceived improvements in health or increased appetite; no authors reported the frequency or severity of diarrhea, and the range of its prevalence varied greatly (0–32%).

Caregiver knows MNP purpose and recommendations with regard to use and possible side effects

Main themes that emerged from the analysis are the positive influence on adherence of caregivers knowing the purpose and health benefits of MNPs ($n = 10$ of 41 documents), knowing how to prepare and feed MNPs ($n = 10$ of 41 documents), and knowing about negative side effects ($n = 6$ of 41 documents). Misunderstandings were common when caregivers were not well informed, potentially leading to poor adherence. In Peru, the use of MNPs was found to be limited by caregivers’ worry that MNPs would sterilize the girls, cause diarrhea and vomiting, or cause cognitive impairment (31).

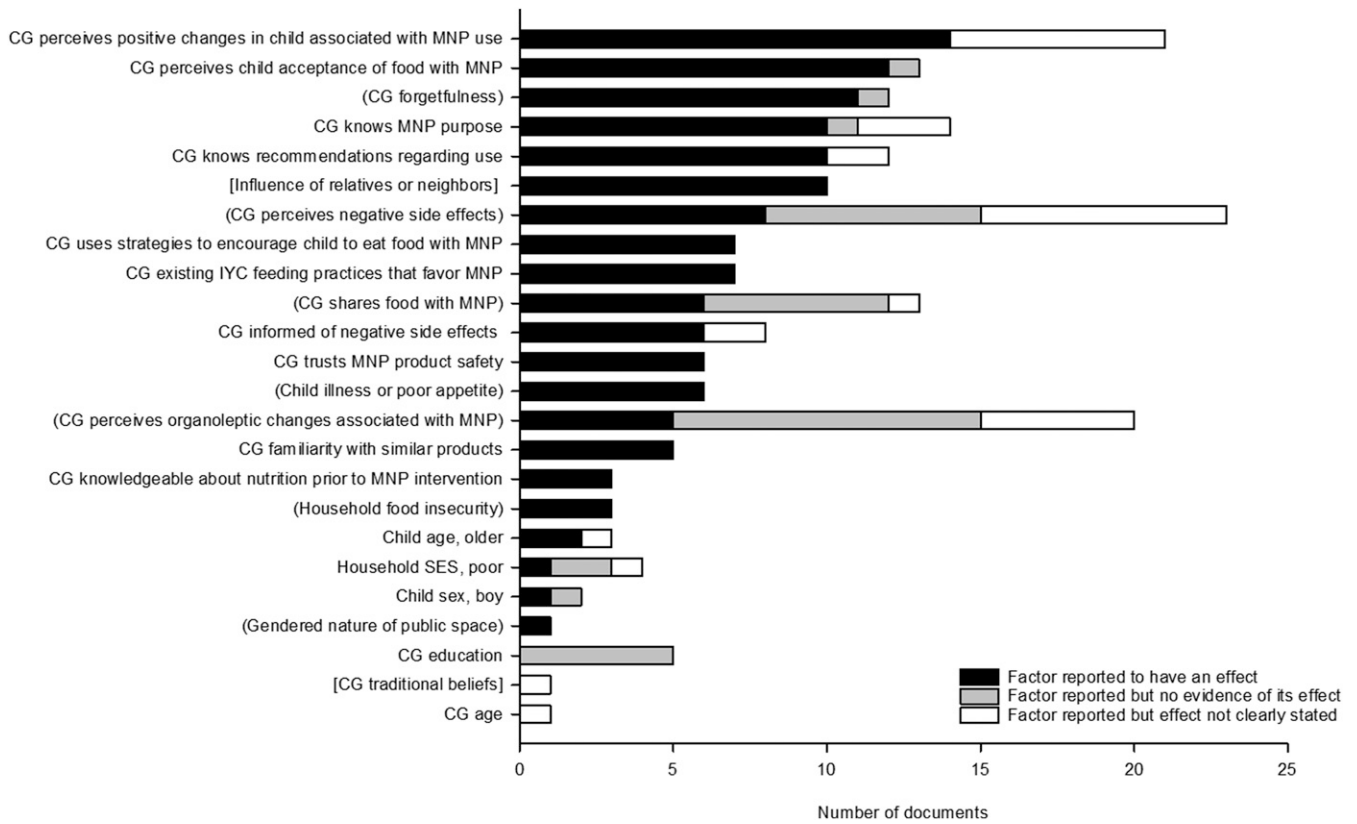


FIGURE 2 Number of documents ($n = 41$) that reported factors affecting adherence to MNP recommendations. Factors not in parentheses or brackets are facilitating factors. Factors in parentheses are limiting factors. Factors in brackets are factors that could be facilitating or limiting depending on other conditions. CG, caregiver; IYC, infant and young child; MNP, micronutrient powder; SES, socioeconomic status.

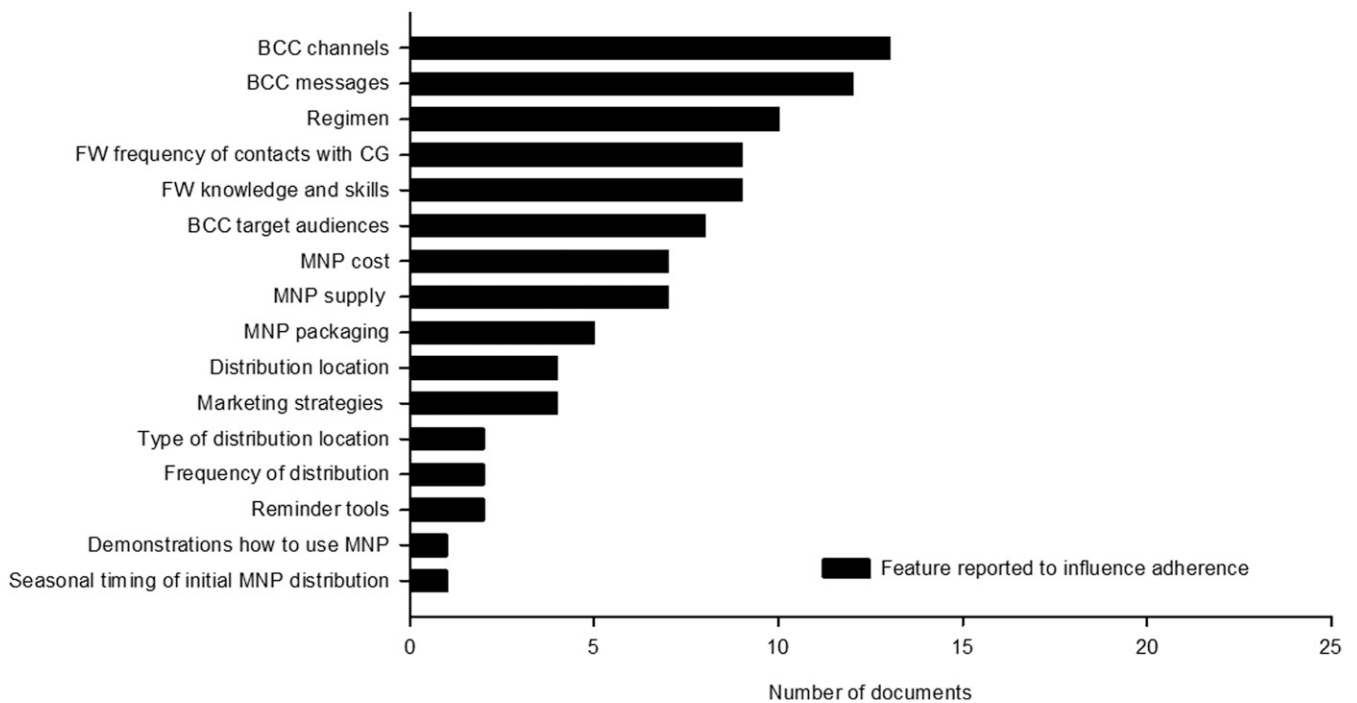


FIGURE 3 Number of documents ($n = 41$) that reported program design features affecting factors that influence adherence to MNP recommendations. BCC, behavior change communication; CG, caregiver; FW, frontline worker; MNP, micronutrient powder.

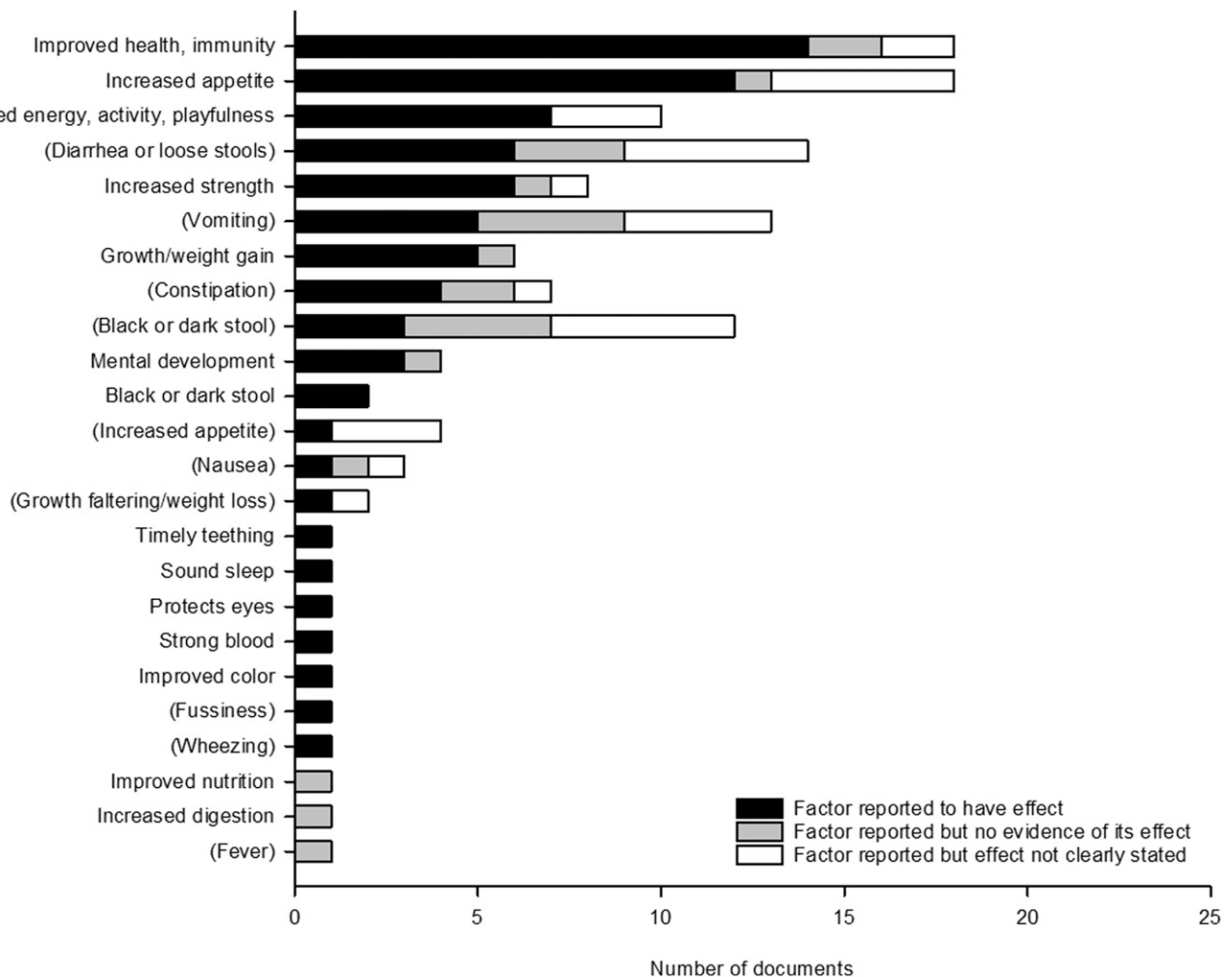


FIGURE 4 Number of documents ($n = 41$) that reported positive changes or negative side effects in children associated with MNP intake and reported effect on adherence to MNP recommendations. Factors not in parentheses are facilitating factors. Factors in parentheses are limiting factors. “Black or dark stool” is in the figure twice because some mothers thought that it was a positive sign that the MNP was working, and so facilitated its use (facilitating factor), whereas other mothers were alarmed because they were not forewarned that it was a side effect (limiting factor). “Increased appetite” is also in the figure twice because it was reported as both a facilitating and limiting factor. MNP, micronutrient powder.

In the Kakuma Refugee Camp in Kenya, some beneficiaries thought that MNPs might be a contraceptive for women, some believed it had been derived from deleterious ingredients, and others thought it was a medicine (43). Conversely, in Nepal, caregivers who knew of ≥ 1 consequence of anemia had greater odds of seeking additional MNP sachets than did caregivers who did not know of any consequences (41). We review evidence later in this article that child acceptance of food with MNPs may be dependent on caregivers following recommendations.

The influence of negative side effects on adherence appears to depend on the counseling received by caregivers. When caregivers are forewarned about the possible negative side effects of MNPs, it seems less likely that experiencing them deters continued MNP use and, paradoxically, their appearance may even encourage continued use (28, 42, 46, 47, 49, 52, 53, 59, 63). For example, in Haiti, caregivers mentioned dark stools and constipation as positive

aspects of MNP consumption because they were told about it at mothers’ meetings (46) and saw these as indications that the MNPs were working. Similarly, in Nigeria, several mothers reported at the start of the study that their child had darker stools and some mild diarrhea, but that this did not worry them because they were told it might happen (59). In this study, some mothers expressed the idea that the diarrhea was a sign the body was getting rid of “bad blood.” However, in Kyrgyzstan, program implementers received reports that caregivers who were not informed of side effects abandoned the use of MNPs because they attributed their children’s diarrhea episodes to MNP consumption (64).

In the set of documents reviewed ($n = 41$), behavior change communication (BCC) channels ($n = 13$) and messages ($n = 12$) were the most frequently reported program design features influencing caregiver knowledge and subsequently adherence. (“BCC channels” denotes the various means (e.g. frontline workers,

radio) through which information is transmitted and “BCC messages” refers to the content, clarity, and cultural appropriateness of the information.) For example, the less-than-expected effectiveness of MNPs to improve iron status and anemia in the Kakuma Refugee Camp is theorized to be a result of poor quality of BCC activities and subsequent misconceptions about MNPs (43, 74). In Haiti, the program’s success in reducing anemia is attributed to a well-designed communication strategy and, in turn, “excellent” maternal knowledge of the benefits and appropriate use of MNPs (46, 75).

Our analysis also highlights the prominent role of interpersonal communication carried out by frontline workers whose activities may include cooking demonstrations, home visits, and counseling. The frontline worker is often the primary person responsible for program delivery. In some cases, this is a health professional, such as a nurse; however, in most settings, the frontline worker is either a minimally trained, paid community resident or a community volunteer. Researchers and program implementers frequently cite the knowledge, skill, and accessibility of frontline workers as critical for adherence; 2 of the most-cited program design features are frontline worker frequency of contact with caregivers ($n = 9$ of 41 documents) and frontline worker knowledge and skill ($n = 9$ of 41 documents). For example, in Bangladesh, children whose mothers had frequent contact with BRAC (formerly known as Bangladesh Rural Advancement Committee) *Shasthya Shebikas* (female community health volunteers trained to provide health services and sell essential health commodities) were significantly more likely to have high adherence (27). In Peru, researchers found that there was greater acceptance and use of MNPs by caregivers when frontline workers appropriately adapted their interaction, rapport, and counseling with caregivers to the local culture, taking time to understand their situation, explaining more about the MNPs to absolve their doubts, and inserting their use into the family’s and child’s feeding routines (31).

Caregivers’ perceived child acceptance of food with MNPs, perceived organoleptic changes, and strategies to encourage the child to eat food with MNPs

Caregivers’ perception of children’s acceptance of food with MNPs plays a large role in the feeding process and positively influencing its continued use ($n = 12$ of 41 documents). In Nepal, mothers who reported that their children did not like food mixed with MNPs had significantly lower odds of high intake adherence than did mothers who did not report this (49). Child refusal of food with MNPs could be a sign of incorrect preparation of food with MNPs and subsequent undesirable organoleptic changes. For example, in Peru, caregivers who reported that their children refused MNPs also reported mixing them with soups or other liquids (31). In Indonesia, program implementers reported that mothers considered MNPs not suitable for children because they did not understand that MNPs should be added to semisolid foods that are not too hot (62). Another problem discussed in the reports is that some caregivers added MNPs to a very small amount of food or gave the MNPs without food (53), which would result in a detectable metallic taste due to their high mineral concentration. In theory, an MNP is a bland powder that can be added to any food, provided that it is not a liquid (because

encapsulated ferrous fumarate does not dissolve or disperse) and that the food is not so hot as to melt the lipid layer that protects the iron from interacting with the food. Twenty documents were coded for caregivers who reported organoleptic changes; however, only 5 of those documents reported that those changes had a limiting effect and the prevalence of caregivers who reported this greatly varies (0–46%). The reported organoleptic changes include alterations in taste ($n = 7$), color ($n = 5$), smell ($n = 5$), or texture ($n = 3$), or a combination of these. One study reported that the MNP was perceived as a medicine due to its flavorless nature and powder form, which discouraged its use in the absence of illness (43).

Child acceptance can also be a consequence of the child’s appetite or the strategies that caregivers use to encourage children to eat food mixed with MNPs. In Peru, a caregiver stated, “I do better with banana because he eats more; with potato he hardly eats any, it must be because it has a taste” (31). Similarly, in India, a caregiver stated, “When I mix it [MNP] with rice and curry, nobody identifies that something is added to food. [The child] eats without any complaint” (50). Other strategies included giving the MNP “when the child is most hungry” at the first meal of the day (31), not giving snacks before the meal with the MNP (39), adding it without the child’s knowledge (42), and splitting one sachet of MNP over several meals during the day (42, 53, 60).

Caregiver forgetfulness

Caregivers forgetting to give their children MNPs is the most influential limiting factor for continued intake of MNPs ($n = 11$ of 41 documents). Two studies statistically examined the association of factors related to caregiver forgetfulness and adherence. In a randomized clinical trial of adherence with the ferrous fumarate Supplefer Sprinkles (MNP; Sprinkles Global Health Initiative) compared with ferrous sulfate drops, caregivers in either group who reported difficulty integrating the supplement into their daily routine were more likely to have low adherence (33). In Nepal, children of caregivers who received a reminder card had double the odds of meeting the criteria for high intake adherence than did children whose mothers who did not receive a reminder card (49).

Administration regimen, which may be related to caregivers’ capacity to remember to give MNPs, also seems to be a critical program design feature affecting adherence ($n = 10$ of 41 documents coded for “regimen”). A fixed schedule is defined as giving the MNP according to a prescribed frequency (e.g., daily or every other day), whereas with the use of a flexible schedule, caregivers are given the option of choosing their own intake frequency, as long as a fixed number of sachets are consumed within a given time period. Ip et al. (40) tested different MNP regimens in Bangladesh and found that a flexible schedule (consuming 60 MNP sachets over a period of 4 mo) was associated with higher adherence and improved anemia status than a fixed daily schedule. Caregivers in the flexible schedule group reported preferring more time to give all prescribed MNP sachets, more autonomy to decide on which day to give MNPs, and less anxiety associated with missing a daily dose. In another study in Bangladesh, caregivers reported different administration regimen preferences: approximately three-quarters preferred the program’s recommended daily schedule, whereas a quarter of caregivers preferred to feed MNPs every other day (27). Furthermore,

flexibility in terms of the number of times per day that the MNP is added to foods may affect adherence. A self-initiated strategy that some caregivers adopt to ensure that their children consume the full daily dosage is to split the MNP sachet contents over several meals during the day. In Guatemala, formative research on the feasibility of feeding MNPs 2 times/d showed that some caregivers would be willing to give their children the MNP 2 times/d, but a few caregivers reported that they would not be able to because either they were “strong vitamins” or they did not have time. Other mothers reported that they would give the MNP 3 times/d, because this is the number of times that they feed their children and because it will help them grow bigger and stronger more quickly (52).

Influence of relatives or neighbors

Across many cultural contexts, the influence of relatives and neighbors plays a role, in either facilitating or limiting caregivers' decisions related to use of MNPs ($n = 10$ of 41 documents). For example, in Bangladesh, the influence of family and household members commonly determines what and how an infant is fed (60, 61). In Peru, the majority of caregivers who were suspicious of MNPs eventually tried giving them to their child after receiving reassurance from a relative or neighbor who supported the idea that they are vitamins (31).

Careful targeting of BCC activities to influential audiences is reported to be an important program design feature ($n = 7$ of 41 documents). Target audiences include relatives and neighbors, as well as other members of the community and health system. For example, in Kyrgyzstan, investigators found that a few months after the start of the program, medical workers at the hospital level who were unaware of the MNP program were discouraging caregivers from using MNPs when these caregivers brought their children to the hospital for diarrhea or other health issues (64). Training sessions for medical workers at hospitals were necessary to resolve misconceptions that diarrhea or other problems were caused by MNPs. In Bangladesh, the program implementer, BRAC, included awareness-raising activities for the sales of MNPs targeting government and nongovernment officers, political and religious leaders, health officials, alternative health care providers, teachers, adolescents, and fathers (61).

Caregiver existing IYC feeding practices that favor appropriate utilization of MNPs

Several IYC feeding practices were found to positively influence how an MNP is integrated in the process of complementary feeding. The IYC practices coded in the database of publications ($n = 41$) under the factor “caregiver existing IYC feeding practices that favor MNP” include the following: caregiver prepares semisolid foods ($n = 6$), caregiver prepares special foods for infants and young children ($n = 1$), and caregiver introduces foods at 6 mo of age ($n = 1$). The successful introduction of MNPs into the IYC diet depends on having or adopting the custom to feed semisolid foods. For example, in Peru, there was greater acceptance of the MNP by caregivers who were accustomed to feeding semisolid or solid foods, whereas caregivers who customarily served diluted or liquid foods and added the MNP to these preparations showed less acceptance and often discontinued giving it to their children (31). In China, introducing MNPs was

hampered by the custom of feeding powdered soy milk with water. Many caregivers fed the MNP to their children in this fashion, despite recommendations to mix it with semisolid foods (58). In Timor-Leste, a few caregivers reported that feeding MNPs had affected the way that they prepared the child's porridge, in that they had to make it thicker so that the MNP could mix well (53). One mother said, “Now I cook the porridge thicker than usual because I am afraid that if it is cooked too thin [too much water], it won't mix well with MNP.”

Shifting to the results of the analysis that used the cultural-ecological framework, **Table 1** shows how the factors that emerged from our content analysis as determinants of adherence can be classified in relation to the domains of the modified and expanded cultural-ecological framework (72, 73). The domains of the framework consist of the following: the Physical Environment, Technology, Social Organization; the Ideational System (“culture”); and the Social Environment, all of which affect the food system and diet. The majority of the factors ($n = 22$ of 24 factors) identified by investigators can be characterized as pertaining to the “cultural” or “ideational systems” (72, 73). The term “ideational system” has been proposed by anthropologists to distinguish those aspects of culture that pertain to knowledge, beliefs, values, and perceptions, as contrasted with other domains. As shown in Table 1, in addition to the 22 factors that pertain to the “ideational system,” the other factors that investigators reported to affect adherence can be classified as follows: habit [$n = 3$ of 24 factors; involves automated behaviors that can be triggered by cues (76)], child biological needs ($n = 3$ of 24 factors; includes individual biological requirements conditioned by developmental stage, activity level, health, and nutritional status), social organization ($n = 3$ of 24 factors; includes household income and expenditures, sociodemographic features, health status, educational attainment, allocation of time to child care, and food acquisition), physical environment ($n = 2$ of 24 factors; especially in this context, water supply and sanitation), and social environment ($n = 1$ of 24 factors; especially in this context, markets, programs, and health services).

Discussion

On the face of it, adding a sachet of powdered nutrients to complementary foods and feeding it to a child once a day does not seem to be a difficult action for caregivers to take. In fact, compared with other potential complementary feeding interventions, the apparent simplicity of MNPs is a central feature of their attractiveness as an intervention. However, what we found leads to a different conclusion, namely, that preparing food with an MNP correctly and succeeding in getting a child to eat it depends on a complementary feeding process that requires a complex set of caregiver behaviors and caregiver-child interactions. From the caregiver's side, effective behaviors depend on knowledge about preparation; on foods and feeding patterns that provide appropriate foods for fortification, including semisolid foods; and on creative strategies to encourage a child to eat the full portion. The centrality of interactions between children and their caregivers for adherence to MNP intake presents

TABLE 1 Expanded PIP depicting household utilization of MNPs, factors identified in analysis, and their domains based on a cultural-ecological framework¹

Sequence of CG behaviors to adhere to recommendations with regard to MNPs	Facilitating and limiting factors identified in analysis ²	Domain(s) of identified factor
CG initiates feeding MNPs to child: CG feeds the MNP to child who is between 6 and 23 mo of age	CG knows MNP purpose	Ideational system
	[Influence of relatives and neighbors]	Ideational system, social organization
CG prepares food with the MNP correctly: CG washes hands before cooking and feeding CG adds entire MNP sachet to a small portion of semisolid food that is not too hot and that the child can finish during one feeding session	CG trusts MNP product safety	Ideational system
	CG familiarity with similar products	Ideational system
	CG knowledgeable about nutrition before MNP intervention	Ideational system
	[CG traditional beliefs]	Ideational system
	CG knows recommendations regarding use	Ideational system
CG feeds food with the MNP to child: CG feeds the food mixed with the MNP to the child with a spoon within half an hour of preparing it	CG uses IYC feeding practices that favor MNPs	Ideational system, habit
	(Household food insecurity)	Social organization, physical environment
CG feeds food with the MNP to child: CG feeds the food mixed with the MNP to the child with a spoon within half an hour of preparing it	CG perceives child acceptance	Ideational system
	CG knows recommendations with regard to use	Ideational system
CG feeds entire portion of food mixed with full dose of the MNP to child	CG uses IYC feeding practices that favor MNPs	Ideational system, habit
	CG uses strategies to encourage child to eat food with MNPs	Ideational system
CG continues feeding MNPs: Caregiver feeds the MNP every other day, but not >1 sachet/d, to child between 6 and 23 mo of age CG acquires more MNP sachets when supply runs out CG continues to use MNPs even if child has darker stools, softer stools, mild diarrhea, or mild constipation	(CG shares food with the MNP)	Ideational system, habit
	(Child illness or poor appetite)	Ideational system, child biological needs, physical environment
	(CG perceives organoleptic changes)	Ideational system
	CG perceives positives changes in child	Ideational system
CG acquires more MNP sachets when supply runs out	CG knows MNP purpose	Ideational system
	CG perceives child acceptance	Ideational system
CG continues to use MNPs even if child has darker stools, softer stools, mild diarrhea, or mild constipation	(CG forgetfulness)	Social organization, habit
	CG knows recommendations with regard to use	Ideational system
CG continues to use MNPs even if child has darker stools, softer stools, mild diarrhea, or mild constipation	(CG perceives negative side effects)	Ideational system
	(CG shares food with the MNP)	Ideational system, habit
CG continues to use MNPs even if child has darker stools, softer stools, mild diarrhea, or mild constipation	CG informed of side effects	Ideational system
	(Child illness or poor appetite)	Ideational system, child biological needs, physical environment
CG continues to use MNPs even if child has darker stools, softer stools, mild diarrhea, or mild constipation	[CG traditional beliefs]	Ideational system
	(Gendered nature of public space)	Ideational system, social environment

¹CG behaviors are based on key messages communicated as part of the Ethiopia program. Factors not specific to a particular behavior but that could affect adherence are as follows: child age (child biological needs, culture or idea system), child sex (child biological needs, culture or idea system), household socioeconomic status (social organization), CG education (culture or idea system, social organization), and CG age (culture or idea system, social organization). CG, caregiver; IYC, infant and young child; MNP, micronutrient powder; PIP, Program Impact Pathway.

²Factors not in parentheses or brackets are facilitating factors. Factors in parentheses are limiting factors. Factors in brackets are factors that could be facilitating or limiting depending on other conditions.

challenges and opportunities that call attention to the importance of equipping caregivers with knowledge, skills, and environments that are conducive to successfully feeding foods with MNPs. It is likely that communications designed to support better use of MNPs will have positive spin-off effects on complementary feeding behaviors in general, including encouraging timely initiation of complementary foods, appropriate consistency of complementary foods, and active or responsive feeding.

Adherence is widely recognized as a critical intermediate step for achieving impact in long-term therapies in the treatment of

disease (19) and micronutrient supplements (33, 77–80). In this review of existing evidence, we found that all of the factors affecting MNP adherence are common to other interventions that include new products or medications. The most influential factor facilitating adherence, measured by the number of documents reporting the factor as having an effect, was the positive changes that caregivers observed in their children as a result of giving MNPs. This is an example of “perceived benefit,” a construct that has been extensively studied. This is a key construct in the Health Belief Model and has been shown to influence behavior across a variety

of contexts and interventions (81), including other forms of micro-nutrient supplements for children (33, 79).

Further study of caregivers' perceptions is likely to provide more in-depth knowledge to inform the development of behavior change messages to encourage MNP use. Measuring and quantifying caregivers' perceptions about their children's health, appetite, and activity levels that are biologically plausible consequences of MNP consumption may also serve to provide evidence to advocate successfully for programs to scale-up MNP interventions. Policy and program decision makers often want evidence that adherence to MNPs improves health and nutrition outcomes in their locality. Unfortunately, measuring biological impact often presents difficult practical and economic challenges. New studies to address the relation between factors that have been identified with caregiver adherence and biological outcomes will be helpful to determine the adequacy of caregiver MNP perceptions as substitutes for difficult-to-measure biological outcomes in the context of program evaluations.

Turning to the implications of the findings for theory development, we begin by noting that the database created through our content analysis broadly reflects the focus of issues of concern for investigators or program implementers, as well as their relative frequency in publications and reports. It is probable that the preponderance of knowledge and perception factors in the MNP studies reflects an underlying assumption by investigators that caregiver behavior is primarily driven by the domain of cultural and ideational systems. In other words, the results may reflect an underlying theoretical bias among researchers as to what they measure. Taking a more cultural-ecological perspective leads us to recognize determinants that have been understudied. For example, results of a focused ethnographic study in Bangladesh found that cultural prohibitions on women traveling unaccompanied outside the home meant that women faced critical barriers to accessing products from the market (60). The highly gendered nature of public space constrains caregivers' actions in many diverse contexts (82), but this is not generally considered in evaluations of nutrition programs, including in evaluations of MNP adherence. Another aspect of culture that was not examined in the MNP studies is how conflicts and complementarities in caregivers' knowledge systems (i.e., between biomedical ideas and traditional knowledge) affect adherence, although studies in nutritional anthropology have shown their significance for responses to intervention efforts (83, 84).

In the sample, the studies that identified infrequently reported factors used an ethnographic approach, which allowed investigators to observe realities from an emic or insider's perspective. Thus, the application of ethnographic data collection techniques, coupled with a theoretical framework that encourages the examination of a wider range of potential determinants, provides opportunities to discover conditions, values, and behaviors that were not foreseen by the investigators (85). To achieve greater impact we need to adopt a more cultural-ecological perspective and draw on theories to inform the design of programs that take into account a broader set of determinants. For example, new, innovative approaches—adherence partners (86) and strategic use of social networks (87)—show the value of interventions that capitalize on aspects of the social organization of household and communities.

There are several methodologic issues concerning our database of studies that need to be noted (88):

1. Authors of the documents included in our analysis may have "misinterpreted" their data or used a labeling convention that obscured factors that should have been identified.
2. There is a possibility that we did not find all of the available studies and that, within the studies we analyzed, we missed specific factors. Double-coding a subsample of studies helps limit the potential for the latter but not the former.
3. Within a document, the number of times a factor is mentioned and how thoroughly it was investigated are also likely to affect whether or not it is coded.
4. The likelihood that the frequency with which factors are reported may also be influenced by what authors choose to present, as contrasted with what they examined.

Generalizations based on our database are further constrained, because it includes a small number of exploratory studies and many of those were focused on the initiation of the MNP and its appropriate use, not its continued use. It is likely that a wider range of factors affecting adherence would have been identified if there were more publications that used ethnographic approaches and of longer duration.

A primary motivation for the research reported here was to identify questions to include in the GAIN's process evaluations for the MNP intervention studies in Ethiopia and Mozambique. In this study we found that the approach we used to structure the analysis—creating a PIP, coupled with examining the results in relation to the cultural-ecological framework—facilitated the identification of hypotheses, as well as potentially significant gaps. Our analysis provides a theoretically sound basis on which to specify a priori expectations about MNP intervention outcomes. It permits an increased level of plausibility in planning quantitative studies for hypothesizing a causal role for individual factors in facilitating or limiting adherence (89). It also directs attention to the importance of using more exploratory approaches that will broaden the scope of our understanding about determinants of adherence.

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