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MULTIPLE MICRONUTRIENT POWDERS FOR HOME (POINT OF USE) FORTIFICATION OF FOODS IN PREGNANT WOMEN: A SYSTEMATIC REVIEW

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ABSTRACT

Home (point of use) fortification of foods with multiple micronutrient powders consists of sprinkling a mixture of vitamins and minerals (which are supplied in powdered form in single-serving sachets) over any semi-solid food before consumption. Home fortification with multiple micronutrient powders of food consumed by pregnant women is being implemented in several countries, but its safety and effectiveness in relation to pregnancy outcomes has not been systematically evaluated. This review aimed to assess the effects and safety of antenatal home (point of use) fortification of foods with multiple micronutrient powders with regard to newborn and maternal health outcomes. Several databases, the Cochrane Central Register of Controlled Trials (*The Cochrane Library*), MEDLINE, EMBASE, CINAHL EBSCO, POPLINE and LILACS, were searched for studies that fulfilled the inclusion criteria, with no language or publication time restrictions. The International Clinical Trials Registry Platform (ICTRP) was searched for ongoing studies and relevant organizations were also contacted. The inclusion criteria were as follows: (i) randomized (both individual and cluster randomization) and quasi-randomized trials, and prospective non-randomized trials, interrupted time series (with at least three points) and observational studies having a control group; (ii) study participants needed to be apparently healthy pregnant women; and (iii) the study should have aimed to compare home fortification of foods with multiple micronutrient powders (with at least three micronutrients, one of them being iron) with no intervention, iron-only supplements, iron and folic acid supplements, or the same multiple micronutrients in supplement form. Two review authors independently extracted data and assessed the quality of the trials potentially identified as suitable in the searches. However, no study satisfied the inclusion criteria, and the review concluded that despite the widespread implementation of interventions with multiple micronutrient powders, there have been no studies evaluating the effects of this intervention in pregnant women on maternal and newborn health outcomes. There is an urgent need for randomized controlled trials evaluating the effectiveness and safety of the use of multiple micronutrient powders in pregnant women to inform policy-making.

BACKGROUND

More than two billion people worldwide are estimated to be deficient in one or more vitamins or minerals (*1*). Pregnant women are particularly vulnerable to vitamin and mineral deficiencies because of their increased metabolic demands to meet fetal requirements for growth and development (*2*). Iron deficiency is the most common micronutrient deficiency and is the leading cause of anaemia, although folate, vitamin B_{12} and vitamin A deficiencies, chronic inflammation, parasitic infections, and inherited blood disorders also contribute to anaemia (*3*). An estimated 41% of pregnant women are anaemic (*4*), and approximately 60% of the cases in non-malarial areas and 50% in malaria-endemic areas are assumed to be due to iron deficiency (*5*).

The increased micronutrient requirements of some pregnant women cannot be fulfilled through the normal diet, particularly in developing countries (*6*). Causes of the high burden of maternal micronutrient deficiencies include poor access to nutrient-adequate foods, cultural practices that discourage women from gaining weight, long hours of physical labour, and recurrent infections (*2*). Inadequate intakes and increased metabolic requirements during pregnancy further exacerbate pre-existing maternal micronutrient deficiencies (*7*).

Vitamin and mineral deficiencies in pregnancy are associated with adverse health outcomes in both the mother and the baby. Anaemia in pregnancy is considered a risk factor for maternal mortality (*4*) and is associated with prematurity and low birth weight (*8*). Iodine deficiency is the leading cause of preventable brain damage in childhood (*9*) and leads to thyroid under-function and goitrogenesis in adults (*10*). Nearly two billion people have insufficient iodine intake, and even subclinical iodine deficiency during pregnancy increases the risk of miscarriage and fetal growth restriction (*11*). Vitamin A deficiency affects 19 million pregnant women worldwide and is associated with an increased risk of complications and death during pregnancy and in the postpartum period (*12–14*). Severe vitamin A deficiency in the mother can also lead to low amounts of vitamin A reserves in the baby, which can negatively affect lung development and the survival of the child in the first year of life (*13, 15*).

Other micronutrients of concern during the gestational period include folic acid, vitamin D, zinc and vitamin B_{12}. Poor maternal folate status at conception increases the risk of neural tube and other birth defects, whereas low folate levels later in pregnancy are associated with haematological problems and possibly pre-eclampsia (*16,17*). The latter condition may also result from calcium and vitamin D deficiency. Zinc insufficiency has been associated with pregnancy complications, growth retardation, congenital abnormalities, and retarded neurobehavioural and immunological development in the fetus (*18*). Last but not the least, maternal B_{12} deficiency has also been implicated in neural tube defects and early fetal loss (*19*). Interventions to prevent and/or treat micronutrient malnutrition during pregnancy typically include dietary diversification to incorporate foods with highly absorbable vitamins and minerals, fortification of staple foods, and provision of supplements in the form of pills and tablets (*20*). Routine daily oral iron and folic acid supplements are recommended as part of an integrated programme for antenatal care to reduce the risk of having a low-birth-weight baby, and anaemia and iron deficiency at term (*21*), and is widely practised in many countries (*22–24*). Intermittent use of iron and folic acid supplements by non-anaemic pregnant women is also recommended to prevent anaemia and improve gestational outcomes among this group of women (*14*). Supplements containing vitamin and minerals as per the formulation of the United Nations Multiple Micronutrient Preparation (UNIMAPP) (*25*) can fulfil the increased maternal micronutrient needs in pregnancy (*26, 27*). Supplements containing other micronutrients in addition to iron and folic acid may have comparable benefits in reducing maternal anaemia and also benefit intrauterine growth as well as postnatal outcomes (*7, 28*).

The provision of supplements containing various vitamins and minerals has been shown to reduce micronutrient deficiencies in mothers, increase mean birth weight and reduce the incidence of low birth weight and small-for-gestational-age (SGA) births (*29, 30*). However, other trials have not found any significant impact of this intervention on birth length, duration of gestation and the risk of preterm delivery (*31*) or a reduction in stillbirths, perinatal mortality and neonatal mortality (*31*). A recent systematic review reported a significant benefit of multiple micronutrient supplementation in pregnancy with regard to reduction in SGA births compared with supplementation with iron and folic acid only (*32, 33*); however, there was no additional benefit of the former on maternal anaemia in the third trimester (*33*).

Adherence rates to routine supplementation regimens in pregnancy are reported to be about 50% because of the gastrointestinal side-effects associated with intake of supplemental iron, particularly constipation and nausea (*34*). Furthermore, poor compliance with supplementation programmes, the low bioavailability and tolerance of various iron preparations, and the sparse implementation of food fortification in many countries have all probably limited the effectiveness of this intervention (*35, 36*) in many settings, and alternative interventions are being sought to provide vitamins and minerals to pregnant women. A novel approach comprising "home" or "point of use" food fortification with multiple micronutrient powders has been developed to improve adherence. These powders, which consist of lipid-encapsulated iron and other micronutrients in dry powder form, are supplied as single-dose packets, the contents of which can be sprinkled onto any semi-solid food before consumption (*37*). The lipid coating prevents the iron and other nutrients from dissolving into the food, thereby preventing any change in colour, flavour or taste of the food. This method of delivery, along with the buffering effect of the foods to which the multiple micronutrient powders are added, also reduces the incidence of side-effects associated with iron supplementation, thus leading to increased adherence.

While the use of multiple micronutrient powders is similar to mass fortification in that the powder is added to a food matrix, the process is not carried out at industrial level but at the point of use, immediately before consumption. The advantages of this intervention include: the powders are light in weight and simple to store and transport; they are easy to use; the powder formulations can be customized, with different amounts and combinations of vitamin and minerals; and the intervention is unlikely to result in overdose and is associated with low production costs (*38*).

Although the primary motivation behind the use of multiple micronutrient powders has been to prevent and treat anaemia and iron deficiency in infants and young children aged 6–23 months (*37*), the powders are being distributed to other target groups including pregnant women. In some countries multiple micronutrient powders are being used in targeted regions, while in others they are being distributed as part of national programmes (*39*).

In malaria-endemic areas, provision of iron supplements has been a long-standing controversy due to concerns that iron therapy may exacerbate the severity of infections (*40*). Approximately 40% of the world population is vulnerable to malaria, and it is endemic in over 100 countries (*41*). Of all the complications associated with malaria, anaemia is the most common and causes the highest number of malaria-related deaths. Malaria in a pregnant woman increases the risk of maternal death, miscarriage, stillbirth and low birth weight (with associated risk of neonatal death) (*41*). While there has been limited research on the safety of iron supplementation among pregnant women in malarial areas, antenatal iron/folic acid supplementation combined with intermittent preventive treatment of malaria during pregnancy has been shown to reduce neonatal mortality in malaria-endemic regions (*42*).

Although the mechanisms by which supplemental iron can benefit the parasite are far from clear, hypotheses include high peak concentrations of serum iron, in particular non-transferrin-bound iron, which increase adhesion of the malarial parasite to the vascular endothelium (*43, 44*). Multiple micronutrient powders, which are mixed with food and thus absorbed more slowly, yielding lower peak concentrations of unbound iron in the circulation, may thus be less likely to increase the risk of infection (*45*). Currently, the World Food Programme (WFP) and the United Nations International Children's Fund (UNICEF) have designed modified formulations that contain less iron for use in malaria-endemic areas. The safety and effects of these modified multiple micronutrient powder preparations are still being evaluated.

The provision of vitamins and minerals to pregnant women through multiple micronutrient powders for home fortification may be associated with higher acceptability and adherence to dosing regimens compared with routine supplementation programmes. Use of multiple micronutrient powders is probably influenced by their organoleptic qualities, ease of use and storage, reduced side-effects, and perceived positive effects, such as increased energy and strength (*46*). Because they are ingested with a semi-solid food, the absorption and utilization of the powder contents by the body may be different from the same micronutrients supplied as supplements, depending on food habits and practices (e.g. reduced iron absorption because of the high phytate content of maize). Therefore, evaluation of the effects and safety of the use of multiple micronutrient powders in pregnant women at community level, and versus routine iron and folic acid or multiple micronutrient supplementation provided through antenatal care programmes, is warranted.

Home fortification of foods with multiple micronutrient powders in young children has been shown to be effective in reducing anaemia and iron deficiency (*47*), and multiple micronutrient powder programmes targeting infants and children are being planned or implemented in several countries. The initial success of this intervention in infants and children has encouraged its use in pregnant women. To date, however, there has been no systematic assessment of the provision of multiple micronutrient powders among pregnant women to inform policy-making.

Various Cochrane reviews or protocols have evaluated studies on the effects of supplementation with different vitamins and minerals in pregnant women. The effectiveness of daily and intermittent iron and folic acid supplementation in pregnant women includes trials providing these regimens with additional vitamins and minerals (*48*). These reviews include studies on a range of interventions providing daily or intermittent oral supplementation (e.g. tablets, capsules) containing iron alone, iron + folic acid or iron + other vitamins and minerals. The effects of multiple vitamin and mineral supplementation in pregnancy have also been reviewed elsewhere (*32*) as has the impact of multiple micronutrient supplementation in pregnancy, defined as supplementation with at least five micronutrients including the UNIMMAP formulation (*25*) or those with comparable composition versus standard iron and folic acid supplements, on specific maternal and pregnancy outcomes (*33*).

AIM AND OBJECTIVE

The aim was to assess the effect and safety of prenatal home (point of use) fortification of foods with multiple micronutrient powders with regard to newborn and maternal health.

The objective was to conduct a systematic review of published and ongoing trials that fulfilled the selection criteria (see Methods).

METHODS

Study eligibility criteria

Types of studies

We aimed to include randomized controlled trials (both individual and cluster randomization) and quasi-randomized trials, prospective non-randomized trials, interrupted time series (with at least three points) and observational studies having a control group.

Types of participants

We considered trials that involved apparently healthy pregnant women of any gestational age and parity, and who may or may not have had one or several micronutrient deficiencies, including those living in malaria settings. Studies specifically targeting human immunodeficiency virus (HIV)-positive women were excluded.

Types of interventions

We included studies investigating interventions involving home (point of use) fortification of foods with multiple micronutrient powders provided to women during pregnancy. For the purposes of this review, home (point of use) fortification of foods refers to the addition of multiple micronutrient powders to semi-solid foods immediately before consumption; this can be done at home or in any other place where meals are consumed (e.g. schools, refugee camps). The powder formulations in the studies considered in the review were required to contain at least three micronutrients, one of them being iron.

Four comparison groups were considered:

- home (point of use) fortification of foods with multiple micronutrient powders versus no intervention/placebo;
- home (point of use) fortification of foods with multiple micronutrient powders versus use of iron-only supplements;
- home (point of use) fortification of foods with multiple micronutrient powders versus use of iron and folic acid supplements;
- home (point of use) fortification of foods with multiple micronutrient powders versus the use of the same multiple micronutrients as supplements.

The comparison groups could also include other co-interventions, such as education, provided they were applied in a similar manner in the intervention and control groups.

We did not include studies examining the effects of:

- other home (point of use) fortification interventions such as lipid-based supplements or crushed tablets;
- centrally processed fortified foods;
- oral supplement forms such as tablets or capsules (*49*).

Types of outcome measures

We aimed to evaluate the following outcomes.

Primary outcomes

Maternal outcomes

- Anaemia at term (haemoglobin less than 110 g/L).
- Iron deficiency at term (as defined by the trialists, based on any indicator of iron status).
- Iron deficiency anaemia at term (defined as haemoglobin less than 110 g/L and low levels of at least one other laboratory indicator of iron).
- All-cause maternal mortality (death in pregnancy or within 42 days of termination of pregnancy).
- Side-effects (any)[1].

[1] In trials reporting individual side-effects separately but not specifying the number of women reporting any side-effects, for our primary outcome we aimed to select the side-effect with the greatest number of women (in the intervention and control groups combined) reporting that particular problem.

Infant outcomes

- Low birth weight (less than 2500 g).
- Prematurity (less than 37 weeks' gestation).
- Birth weight (g).

Secondary outcomes

Maternal outcomes

- Haemoglobin at term (g/L).
- All-cause morbidity.
- Infection during pregnancy (including urinary tract infections and others as specified by the trialists).
- Antepartum haemorrhage (as defined by the trialists).
- Postpartum haemorrhage (intrapartum and postnatal, as defined by the trialists).
- Serum folate at term (nmol/L).
- Erythrocyte folate at term (nmol/L).
- Serum retinol concentrations at term (μmol/L).
- Miscarriage (as defined by the trialists).

Infant outcomes

- Serum ferritin concentration within the first 3 months of life (μg/L).
- Stillbirth (as defined by the trialists).
- Haemoglobin concentration within the first 3 months of life (g/L).
- Neonatal death (death occurring within day 0 to day 28 of life).
- Stunting at any time within the first 6 months of life (–2 Z-score or lower).
- Small-for-gestational-age (SGA) (birth weight less than 10% of weight in reference population of same age).

For populations in malaria-endemic areas, the following outcomes were sought:

- malaria incidence;
- malaria severity;
- placental malaria.

We aimed to assess the potential modifying effects of various factors by undertaking subgroup analyses of the primary outcomes:

- by anaemia status of participants at the start of the intervention;
- by iron status of the pregnant women at the start of the intervention;
- by malaria status in the study area: malaria present at the time of the trial;
- by regimen type;
- by duration of the intervention;
- by elemental iron content in the product used.

For the comparisons concerning malaria-endemic areas we planned to conduct a subgroup analysis by absence or presence of concurrent antimalarial measures (treatment and prevention).

Search methods

The following electronic databases were searched for relevant studies, with no language restrictions: Cochrane Central Register of Controlled Trials (The Cochrane Library), MEDLINE, EMBASE, CINAHL EBSCO, POPLINE and LILACS.

The search terms used for MEDLINE were modified as necessary when searching the other databases. No filter search as language or randomized controlled trials was used to prevent missing any relevant study. Bibliographies were also searched, and authors of the studies identified through the above search were asked for other studies that could be considered for inclusion.

For assistance in identifying ongoing or unpublished studies, we contacted the Sprinkles Global Health Initiative; the In-Home Fortification Technical Advisory Group; Nutrition Section; UNICEF; WFP; the Micronutrient Initiative; the Global Alliance for Improved Nutrition (GAIN); Hellen Keller International (HKI); Sight and Life Foundation; the World Health Organization (WHO) Department of Nutrition for Health and Development; and the US Centers for Disease Control and Prevention (CDC). The International Clinical Trials Registry Platform (ICTRP) was also searched for ongoing or planned trials. As in the database searches, we did not apply any language restrictions to trials.

Data collection and analysis

Assessment of study eligibility for inclusion in the review

Two review authors independently assessed all the potential studies identified through the search strategy described above for inclusion in the analysis. Disagreements were resolved through discussion.

If a possibly suitable study was published only as an abstract, or a study report contained little information on the methods used or the results were not clear, we contacted the study authors to obtain further details about the study design, population, intervention and results to allow full assessment of the study's eligibility for inclusion in the review.

Data extraction and management

We designed a form to extract the relevant data from the studies deemed eligible for inclusion. Two reviewers undertook this task, using the agreed form. Discrepancies were resolved through discussion or, if required, consultation with the other authors. We then entered the data into the Review Manager software[1] and checked for accuracy.

If there was insufficient information in a report to assess the risk of bias, the study was filed as "awaiting assessment", which would be undertaken when either further information has been published or has been made available to us.

Assessment of risk of bias in included studies
Two review authors independently assessed the risk of bias for each study using the criteria outlined in the Cochrane handbook for systematic reviews of interventions (*50*):

1. sequence generation (checking for possible selection bias);
2. allocation concealment (checking for possible selection bias);
3. blinding (checking for possible performance bias and detection bias);
4. incomplete outcome data (checking for possible attrition bias through withdrawals, dropouts, protocol deviations);
5. selective reporting bias (checking if expected outcomes are reported);
6. other sources of bias (such as stopping the trial early or changing methods during the trial).

This assessment entails explicit judgements about whether studies are at high, low or unclear risk of bias (*50*). With reference to points (1) to (6) above, the likely magnitude and direction of the bias and whether it is considered likely to impact on the findings is determined and any disagreement is solved by discussion or by involving a third assessor.

RESULTS

The database search identified 2601 references, only two of which were potentially relevant to this review (*51–53*) but were subsequently excluded at full text assessment (see Appendix). The additional searches did not yield any studies for inclusion but two potentially relevant studies (*54–56*) were found. These studies are currently awaiting classification as no reports describing their methods and full results are available (see Appendix). The relevant organization has been contacted for more information. None of the studies evaluating the effectiveness and safety of home multiple micronutrient powders in pregnant women met the inclusion criteria.

One of the excluded trials mentioned above assessed supplementation with powders containing only two micronutrients (iron and folic acid) in women who were not pregnant at enrolment (*52*,53). The second excluded trial evaluated the relative bioavailability of iron and folic acid from a powdered supplement that can be sprinkled on semi-solid foods or beverages compared with that from a traditional tablet supplement. Evaluation of the nutritional or haematological response to the powders was beyond the scope of the study (*51*). See Appendix for a detailed description of these studies and the reasons for exclusion.

No relevant data were found to evaluate the effect of interventions with multiple micronutrient powders in pregnant women.

1. Home (point of use) fortification of foods with multiple micronutrient powders versus no intervention/placebo

No studies were included in this comparison.

2. Home (point of use) fortification of foods with multiple micronutrient powders versus use of iron-only supplements

No studies were included in this comparison.

3. Home (point of use) fortification of foods with multiple micronutrient powders versus use of iron and folic acid supplements

No studies were included in this comparison.

4. Home (point of use) fortification of foods with multiple micronutrient powders versus use of the same multiple micronutrients as supplements

A trial in Mexico (*55,56*) evaluated this comparison but sufficient data were not available in the report for extraction. The authors have been contacted for additional information. For a description of the study, see the Appendix.

None of the studies on home (point of use) fortification with multiple micronutrient powders in pregnant women met our eligibility criteria.

CONCLUSIONS

Despite the implementation of interventions using multiple micronutrient powders in pregnant women in several countries, no published studies have evaluated their effects on maternal and infant nutritional status and health outcomes. Thus currently, there is no evidence base for directly analysing the potential benefits or harms derived from the use of multiple micronutrient powders in pregnant women for improvement of maternal and infant health outcomes. It seems reasonable to assume that this form of supplementation has the same effects as multiple micronutrient supplementation in pregnant women, but there is a need for further evaluation of this intervention before it can be recommended as an alternative to interventions using tablets. Evidence about the effects of home (point of use) fortification of foods given to other target groups (e.g. children)

[1]Review Manager (RevMan) [Computer program]. Version 5.1.1. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2011.

could be used to continue exploring the feasibility of this intervention for women in pregnancy. Other factors such as acceptability would also need to be considered.

The Iron and Malaria Technical Working Group (TWG) report concluded that home fortification mixtures with appropriate amounts of absorbable iron compounds can be used to improve or maintain the iron status of infants, children, and pregnant and non-pregnant women (*43*). However, we consider that the limited evidence available does not support this conclusion in pregnant women.

IMPLICATIONS FOR RESEARCH

This review highlights the need for well-conducted, randomized controlled trials evaluating the effectiveness and safety of home (point of use) fortification with multiple micronutrient powders of foods consumed by women during pregnancy. Trials should measure population-relevant health outcomes, including side-effects of this intervention in pregnant women, and other maternal and infant health outcomes.

The dosing regimens, rationale for use, and distribution of this form of supplementation are different from the standard forms of multiple micronutrient supplementation. These factors are likely to influence absorption and utilization, and ultimately the effectiveness of the intervention. Therefore there is a need for thorough separate evaluations of interventions with multiple micronutrient powders in women during pregnancy.

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DECLARATION OF INTERESTS

The authors have no affiliations with or involvement in any organization or entity with a direct financial interest in the subject matter of the review (e.g. employment, consultancy, stock ownership, honoraria, expert testimony).

APPENDIX: CHARACTERISTICS OF EXCLUDED STUDIES AND THOSE AWAITING CLASSIFICATION

Excluded studies

Study	Hartman-Craven 2009 (*51*)	Khambalia 2009 (*52, 53*)
Methods	Randomized trial (using a cross-over design)	Randomized trial
Participants	18 healthy pregnant women (*24–32* weeks gestation) recruited from staff and visitors at the Hospital for Sick Children, Toronto, Canada	272 married, nulliparous non-pregnant women in Kaliganj, central Bangladesh (Note: Women who were not married, had previously given birth, were more than 40 years old, were not a permanent household member (living in household less than 6 months), not living in same household as their husband, using an implant form of birth control, had previous surgery to prevent pregnancy, had used iron supplements within the previous 3 months, were known to be pregnant at enrolment, or were identified as severely anaemic at baseline (haemoglobin concentration less than 70 g/L) were excluded)
Interventions	The participants were randomly assigned to one of two groups Group 1 received a powdered supplement containing 30 mg of elemental iron (as micronized dispersible ferric pyrophosphate with an emulsifier coating) and 600 µg (0.6 mg) folic acid Group 2 received a tablet containing 27 mg elemental iron (as ferrous fumarate and 1000 µg (1 mg) folic acid	The participants were randomly assigned to one of two groups Group 1 received Sprinkles® containing 60 mg elemental iron (as ferrous fumarate) and 400 µg (0.4 mg) folic acid) periconceptionally daily Group 2 received Sprinkles® containing 400 µg (0.4 mg) folic acid alone daily in the form of a powdered supplement to be added to food Each woman was given 35 sachets at enrolment and at each monitoring visit (30 sachets for a 1-month daily supply and five extra sachets) Participants were followed up monthly for 9 months or until they became pregnant
Outcomes	Absorption and bioavailability of iron and folic acid from a powdered supplement that can be sprinkled on semi-solid foods or beverages were assessed by measuring changes in serum iron and folate over 8 hours and compared with those from a traditional tablet supplement	Haemoglobin concentration among women who became pregnant (iron and folic acid compared with folic acid).
Reasons for exclusion	No primary or secondary outcomes for determination of safety or effectiveness were assessed The powdered micronutrient supplement only contained two micronutrients (iron and folic acid) and did not meet our criteria for a "multiple" micronutrient powder, containing at least three micronutrients The types of intervention used in this study did not allow for comparisons within the scope of the present review	The types of participant and intervention did not allow for comparisons within the scope of this review

Studies awaiting classification

Study	de Pee 2009 (*54*)	Neufeld et al. 2008 (*55, 56*)
Methods	Unclear. Two cross-sectional surveys before and after in intervention and control area	Cluster randomized trial, implemented in the context of the Oportunidades programme, a conditional cash transfer programme implemented in rural areas in 1997 and urban areas in 2002 with authorization of Oportunidades officials at the federal, state and local levels, National Institute of Public Health Ethics Commission, in Mexico. The study was designed to guide decisions within the programme to maintain distribution of a whole-milk-based fortified food for pregnant and lactating women or change to a micronutrient-only supplement (tablet or micronutrient powder). Statistical analysis: Estimates were made using multilevel modelling, with cluster as level one, woman as level two and the measurement (e.g. haemoglobin concentration) as level three, using the gllamm command in Stata
Participants	Pregnant and lactating women (and children) receiving food assistance in nine districts in the southern coastal region of India severely affected by cyclone Sidr	694 Oportunidades beneficiary pregnant women, recruited before 25th week of pregnancy and given supplements until 3 months postpartum Note: The trial did not include a placebo control group
Interventions	Micronutrient powder (MixMe®), provided by UN World Food Programme, to be consumed as two sachets every other day (total 200 sachets, 7 months' supply)	Communities were randomly assigned (18 communities per supplement) to one of three interventions Group 1 (n=235 women) received one daily tablet (Laboratorios Zerboni, S.A.) containing 15 mg elemental iron, 400 µg (0.4 mg) folic acid and 5 additional micronutrients (zinc, iodine, vitamin E, vitamin C, vitamin B12) Group 2 (n=224 women) received 44 g daily of whole-milk-based, sweetened fortified beverage for pregnant and lactating women (Nutrivida®) containing 15 mg elemental iron, 400 µg (0.4 mg) folic acid and the same 5 additional micronutrients, and also provided energy, protein, lipids, carbohydrates and sodium Group 3 (n=235 women) received 1 g of multiple micronutrient powders (Sprinkles®) containing 15 mg elemental iron, 400 µg (0.4 mg) folic acid and the same 5 additional micronutrients daily Visits at 37 weeks of pregnancy and 1 and 3 months postpartum
Outcomes	Number of multiple micronutrient powders received and distributed, acceptance, consumption, storage Knowledge of anaemia and vitamins, haemoglobin (6 months, February 2009) at 2, 4 and 6 months after initiation of programme Interim results: consumption: 2 months: 87.2% had used more than 40 sachets (the amount to be consumed in about 1.5 months); 4 months: 80% had consumed the sachets	Weight gain, weight retention, anaemia, haemoglobin concentration at 37 weeks, and 1 and 3 months postpartum Results for serum zinc, ferritin, transferrin receptor and C-reactive protein (CRP) are pending

Notes	Start date: July–August 2008; expected completion: mid 2009 Contact person: Dr Saskia de Pee, UN World Food Programme; Nutrition and HIV/AIDS Policy Division; email: depee.saskia@gmail.com	Preliminary results available: Haemoglobin concentrations in g/L (mean ± standard error) At 37 weeks of pregnancy: iron tablets 122 ± 1, multiple micronutrient powders 123 ± 1 At 1 month postpartum: iron tablets 132 ± 1, multiple micronutrient powders 129 ± 1 At 3 months postpartum: iron tablets 133 ± 1, multiple micronutrient powders 133 ± 1 Contact person: Dr Lynnette Neufeld, Chief Technical Advisor, Micronutrient Initiative, 180 Elgin St Suite 1000, Ottawa ON K2P 2K3, Canada; email: lneufeld@micronutrient.org

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