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Effect of prenatal multiple micronutrient supplements and medium-quantity lipid-based nutritional supplements on maternal weight gain and infant birth weight in rural Niger: a cluster-randomised trial

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ABSTRACT

Introduction The risk of adverse birth outcomes, such as low birth weight (<2500 g, LBW), is associated with poor maternal nutrition and weight gain in pregnancy and can increase the risk of infant mortality. We evaluated the effect of three prenatal nutritional supplementation strategies to improve maternal nutrition and adverse pregnancy and birth outcomes.

Methods A cluster-randomised trial of three prenatal nutritional supplements was conducted in rural Niger. Villages (n=53) were randomised to receive either daily prenatal multiple micronutrient supplementation with 20 micronutrients and 30 mg iron (MMN), medium-quantity lipid-based micronutrient supplementation with 30 mg iron and 237 kcal (MQ-LNS), or routine iron folic acid supplementation with 60 mg of iron (IFA). Pregnant women were identified through monthly, community-based pregnancy surveillance. Study outcomes included infant birth weight, maternal weight gain during pregnancy (including total weight gain, rate of weight gain and adequacy of weight gain) and maternal haemoglobin (Hb) concentration and anaemia (Hb <110 g/L) in the second and third trimesters.

Results A total of 3332 pregnant women were enrolled between September 2015 and February 2017. Birth weight did not significantly differ by supplementation group (mean difference MMN vs IFA=39 g, 95% CI −55, 134; mean difference MQ-LNS vs IFA=50 g, 95% CI −55, 156). There was also no statistically significant effect of MMN or MQ-LNS compared with IFA on total weight gain in pregnancy, the rate of weight gain per week during the second and third trimesters or adequacy of gestational weight gain (p values >0.05). We found no effect of MMN or MQ-LNS on maternal haemoglobin concentration or anaemia in the second and third trimesters (p values >0.05).

Conclusion There was no statistically significant difference in birth weight, maternal weight gain or anaemia by prenatal nutritional supplementation strategy. However, statistical power in the trial was limited. A combination of strategies may be required to make large improvements in birth and pregnancy outcomes in rural Niger.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Provision of prenatal nutritional supplements to improve maternal nutrition, particularly in low- and middle-income countries, has been evaluated in randomised trials. However, the best format and composition for nutritional supplements has yet to be elucidated, particularly in diverse settings.

WHAT THIS STUDY ADDS

⇒ We compared three prenatal nutritional supplements in terms of infant birth weight, maternal weight gain and maternal haemoglobin and anaemia status. We found no statistically significant difference between standard iron folic acid compared with a multiple micronutrient supplement or a lipid-based nutrient supplement in terms of pregnancy or birth outcomes. However, it is important to note that our trial was underpowered to detect the moderate to small effect sizes on birth outcomes that would be expected for these interventions.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Given the many factors influencing poor health for women in Niger, an integrated package of interventions may produce larger effects as compared with targeting nutrition alone.

INTRODUCTION

Adverse birth outcomes, including low birth weight (birth weight <2500 g, LBW), preterm birth and stillbirth, remain highly prevalent in low- and middle-income countries.[1–4] LBW

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affects nearly 20 million children each year[5 6] and is an important risk factor for infant mortality, morbidity and suboptimal developmental outcomes.[7–11] Strategies to reduce the risk and consequences of LBW are essential to reduce infant mortality and promote healthy child growth and development.

During pregnancy, nutritional requirements for micronutrients and macronutrients are increased to meet the needs of both the mother and the growing fetus.[12] In food-insecure settings, such as Niger, malnourished women can enter pregnancy with low nutritional reserves due to nutrient-poor traditional diets, and nutritional deficiencies can be exacerbated by the high nutritional demands in pregnancy.[13] Iron-deficiency anaemia, which is prevalent in over half of women in Niger, has been associated with increased risk of LBW and infant mortality.[14] Chronic infections, such as HIV, and acute infections, including malaria and diarrhoeal disease, can increase energy and nutrient demands, reduce appetite and cause nutrient malabsorption.[15] Infection during pregnancy can affect gestational weight gain (GWG), a widely used indicator of macronutritional adequacy during pregnancy that can contribute to LBW and other adverse birth outcomes.[16 17]

To improve micronutrient status and GWG during pregnancy and decrease the risk of adverse birth outcomes, one potential strategy is the provision of prenatal nutritional supplementation. Multiple micronutrient supplementation (MMN) has shown beneficial effects on pregnancy and birth outcomes, including LBW,[18–21] small for gestational age[22] and GWG,[23] with stronger effects among undernourished and anaemic women.[24] Lipid-based nutrient supplements (LNS) provide multiple micronutrients as well as varying amounts of macronutrients and essential fatty acids, with small-quantity LNS (SQ-LNS) providing 100–120 kcal/day and medium-quantity LNS (MQ-LNS) providing 259–500 kcal/day.[25] SQ-LNS in pregnancy may decrease the risk of inadequate weight gain and increase newborn size, although prior studies are not conclusive.[26–28] Additional evidence is needed to understand the effectiveness of prenatal nutritional supplementation in food-insecure populations with a high burden of maternal undernutrition and poor birth outcomes, such as Niger.

We nested a cluster-randomised controlled trial of prenatal MMN, MQ-LNS and routine IFA supplementation within a phase III placebo-controlled oral rotavirus vaccine trial in Madarounfa, Niger. Here, we conducted a secondary analysis to evaluate the effect of prenatal nutritional supplementation on maternal weight gain, anaemia in pregnancy and infant birth weight.

METHODS

Study design and population

A randomised, double-blind, placebo-controlled trial was conducted to assess the efficacy of a live oral rotavirus vaccine (Rotasiil; Serum Institute of India) to prevent severe rotavirus gastroenteritis.[29–31] The parent trial was conducted in the Madarounfa Health District, Niger, a setting with high average fertility (7.1 live births per woman) and high infant mortality (84 deaths per 1000 live births).[32] The study design and procedures of the parent efficacy trial have been published previously.[29]

Immunogenicity of oral vaccines is known to be lower in low- and middle-income countries.[30 33 34] This could be due to the inhibitory effects of poor nutrition, particularly in pregnancy and infancy, on immune development in children.[35] To test this hypothesis, a cluster-randomised nutrition substudy was nested within the parent vaccine efficacy trial to test the effect of prenatal nutritional supplementation on infant immune response to oral rotavirus vaccination (see online supplemental table 1 for supplement composition).[30] We found that prenatal nutritional supplementation had no effect on infant immune response.[30] The present analysis reports on the effect of prenatal nutritional supplementation on pregnancy and birth outcomes.

Substudy randomisation and masking

Village clusters (n=53) were randomly assigned to one of three prenatal nutritional supplements (MMN, MQ-LNS or IFA) in a 1:1:1 ratio, stratified by village size. Randomised village assignment was made by the head of each village, who selected the name of one of three supplements from an opaque jar after providing consent for village participation. Participants and study investigators were unblinded to the randomised intervention assignment.

Substudy sample size

The substudy sample size was calculated to evaluate the impact of a prenatal nutritional supplement (MMN or MQ-LNS) compared with IFA on the immune response to three doses of Rotasiil. To achieve 90% power to detect an absolute difference of 20% in the proportion of children who seroconverted (defined as a ≥3-fold increase in rotavirus IgA) between groups, 660 infants were needed per nutritional intervention group. A baseline seroconversion rate of 30%, an attrition rate of 20%, exclusion of 30% due to rotavirus infection detection before 28 days post dose 3, and a design effect of 1.2 were assumed for the sample size calculation. Posthoc power calculations for the current analysis showed that the available sample size, the observed SD in birth weight of 969 g and intracluster correlation of 0.09 and 80% power, allowed us to detect a mean difference in birth weight of 296 g. Meta-analyses of the effect of prenatal MMS and LNS on birth weight have found a pooled effect size of approximately +50 g.[24 36] Therefore, our trial is likely underpowered and should be interpreted with caution.

Substudy enrolment

Monthly, community-based pregnancy surveillance was conducted among all non-pregnant women of reproductive age in the study area who provided individual

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written informed consent. Following an at-home positive pregnancy test (Wondfo Biotech; Guangzhou, China), mothers were referred to the nearest health facility, where a study midwife assessed trial eligibility. Participants were eligible for substudy enrolment if they were ≤30 weeks gestation using the date of the last menstrual period and intended to remain in the region for delivery and the following 2 years. Exclusion criteria included the need for regular medical attention due to chronic or severe illness, history of allergy to peanuts or pregnancy complications evident at enrolment (moderate to severe oedema; blood haemoglobin <70 g/L or diastolic blood pressure >90 mm Hg). Infants born to women enrolled in the prenatal nutritional supplementation substudy were evaluated for eligibility in the parent trial at 6–8 weeks of age, as per the parent trial protocol.

Prenatal nutritional interventions

Enrolled pregnant women received supplements from enrolment until delivery based on randomised cluster assignment of their village. Pregnant women receiving IFA (standard of care) were provided tablets containing 60 mg iron and 400 µg folic acid (Remedica; Limassol, Cyprus). Pregnant women randomised to MMN received capsules containing 30 mg iron, 400 µg folic acid and 20 additional micronutrients (DSM Nutritional Products; Isando, South Africa). Pregnant women randomised to the MQ-LNS group received 40 g of a fortified, ready-to-use food consisting of peanuts, dried skimmed milk powder, sugar and oil with the same micronutrient composition as the MMN (Nutriset S.A.S; Malaunay, France). MQ-LNS was a new 40 g LNS formulation developed in collaboration with Nutriset to meet the nutritional needs of pregnant women in rural Niger.[37] It was a modified form of the 20 g LNS developed by the iLiNS Project for supplementation of pregnant and lactating women in Ghana and Malawi.[38] In this study, the dose was increased from 20 g to 40 g based on findings from Burkina Faso, where a higher-dose prenatal MMN-fortified food supplement was shown to increase birth length compared with MMN supplementation alone.[39] Pregnant women in the MMN and LNS arms did not receive additional standard-of-care IFA tablets, as iron and folic acid were included in these products.

Data collection

At enrolment, a complete physical and obstetric exam was performed, including the calculation of gestational age based on the date of the last menstrual period and anthropometric assessment (eg, weight, height and mid-upper arm circumference (MUAC). A background questionnaire was administered, including questions on maternal age, education, reproductive history (eg, parity and age of first delivery), sociodemographic characteristics, household size and household food security assessed using the Food and Nutrition Technical Assistance Household Food Insecurity Access Scale.[40]

Scheduled follow-up took place at the health facility at 24-, 32- and 37-week gestation and at 1-week, 6-week and 6-month post partum. Facility visits included a physical and obstetric exam as well as standard antenatal care as per the national protocol,[41] including assessment of blood pressure, proteinuria and urinary infection by urine dipstick, malaria rapid test (SD Bioline Malaria Ag *Pf* (HRP-2)), haemoglobin (HemoCue Hb 301) and maternal anthropometry (weight, height and MUAC). Community health assistants conducted weekly at-home visits to distribute a 10-day supply of the assigned prenatal nutritional supplements, discuss health events and concerns since the last distribution and review supplement adherence assessed through collection of supplements unused since the last distribution. Serious adverse events (SAEs) in pregnancy were monitored through facility- and home-based surveillance from the time of first supplement distribution through 6 months post partum. SAEs were defined as any adverse event that resulted in death, was life-threatening, required inpatient hospitalisation or prolongation of existing hospitalisation, resulted in persistent or significant disability or incapacity or was a medically important event/reaction that may have jeopardised the subject and required medical or surgical intervention to prevent one of the outcomes listed above. Standard prenatal and postnatal care services, including diagnostic and therapeutic services, were provided free of charge up to 6 months post partum as per national guidelines.

Participants were encouraged by study personnel to deliver at a health facility. A study nurse conducted a visit within 48 hours of a live birth, either at home or at the health facility, to record birth outcomes, including fetal death (defined as a fetus showing no sign of life (breathing, heartbeat, pulsation of the umbilical cord, movement of voluntary muscles), irrespective of the duration of pregnancy) and measure maternal and child anthropometry. Weight was taken using a Salter scale for mothers and a SECA scale for infants to the nearest 10 g and MUAC with non-stretchable plastic tape to the nearest 1 mm.

Statistical analysis

Baseline maternal and household characteristics for study participants were examined by the prenatal nutritional supplementation group, expressed as counts and percentages or mean and SE.

Study outcomes included infant birth weight (continuous and LBW), maternal weight gain and maternal anaemia. LBW was defined as a birth weight of <2500 g.[42] Birth weight and LBW were analysed for singleton live births only.

GWG was defined for all women with a singleton pregnancy and known birth outcome in three ways: total weight gain, rate of weight gain (grams/week) and adequacy of weight gain as per the Institute of Medicine (IOM) implementation guidelines.[43] Total weight gain was defined as the difference between the mother's last measurement during follow-up and first trimester weight. The rate of

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weight gain in grams per week was calculated using the last recorded weight measurement in the third trimester and the first recorded weight in the second trimester for all women. Adequacy of weight gain was determined using the first-trimester weight to define the prepregnancy body mass index (BMI) category (underweight, normal, overweight or obese) and the IOM expected weight gain according to first-trimester BMI category and gestational week of the last measurement.[43] Observed weight gain was considered inadequate if <90% of the expected weight gain, adequate if between 90% and 125% and excess if greater than 125%.[23] First-trimester weight was defined as any observed measurement in the first trimester, or for women without a measurement in the first trimester, the imputed weight at 9 weeks was calculated using a mixed-effects model, as shown by Yang *et al*.[44]

Maternal haemoglobin was evaluated up to three times during pregnancy at 24-, 32- and 37-week gestation. Maternal haemoglobin was considered at any time point, as well as in the second and third trimesters, among all enrolled mothers with at least one haemoglobin measurement. Anaemia was defined as any measurement of haemoglobin <110 g/L.

Safety and adherence were also examined. SAEs in pregnancy were evaluated in all enrolled women. Fetal deaths were evaluated among all enrolled women with a known birth outcome. The percentage of supplements consumed was calculated as the sum of weekly counts of used supplement divided by the number of supplements that should have been consumed from trial enrolment through delivery. Adherence was then defined as consuming 75% or more of the total supplements given and was calculated in all enrolled pregnant women.

The intention-to-treat principle was used for all analyses. Pairwise differences in maternal and birth outcomes between supplementation groups (MMN vs IFA and MQ-LNS vs IFA) were assessed using log-binomial regression to estimate relative risk and 95% CIs for binary variables and using linear regression to estimate mean differences and 95% CIs for continuous variables. The effect of the nutrition supplements on haemoglobin was examined using generalised linear mixed models with a random intercept to account for repeated measures. All models accounted for clustering by village.

Effect modification of the supplementation regimen on outcomes was explored by prespecified factors: child sex, maternal parity, maternal BMI at enrolment, gestational age at enrolment, maternal haemoglobin at enrolment, maternal malaria infection at enrolment, season of enrolment and season of conception. Interactions were considered statistically significant using a Wald test at p<0.05.

Ethics

The trial was conducted in accordance with the Good Clinical Practice guidelines and registered with ClinicalTrials.gov (NCT02145000). The study protocol was approved by the Ethics Committee of the World Health Organisation (Geneva, Switzerland), the Western Institutional Review Board (Olympia, Washington, USA), the Comité Consultatif National d'Ethique (Niamey, Niger), the Comité de Protection des Personnes (Ile-de-France XI, France) and the Hôpitaux Universitaires de Génève (Geneva, Switzerland).

Patient and public involvement

Patients and members of the public were not involved in the design, conduct, reporting or dissemination plans of this research.

RESULTS

In total, 3332 pregnant women were randomised to prenatal nutritional supplementation from September 2015 to February 2017 (figure 1). Of these, 1083 were randomised to receive MMN, 1144 to receive MQ-LNS, and 1105 were randomised to receive IFA. Women were on average 26.8 (SD 6.9) years of age at enrolment, and over 85% had at least one previous pregnancy (table 1). The proportions of women who consumed >75% of supplements during pregnancy were similar between groups (66.5% MMN, 70.5% MQ-LNS and 65.5% IFA).

The effect of the prenatal nutritional supplement group on birth and safety outcomes is presented in table 2. There was no statistically significant difference in mean birth weight between MMN and IFA (mean difference: 39 grams, 95% CI −55, 134) or between MQ-LNS and IFA (mean difference: 50 grams, 95% CI −55, 156). We also found no effect of MMN or MQ-LNS compared with IFA on LBW (MMN vs IFA Relative Risk (RR)=0.90, 95% CI 0.53, 1.53; MQ-LNS vs IFA RR=0.98, 95% CI 0.58, 1.67). No effect of MMN or MQ-LNS was found on SAEs in pregnancy or fetal death.

The effect of the prenatal nutritional supplements on maternal weight gain outcomes is presented in table 3. There was no difference in total weight gain between the MMN and IFA groups (mean difference 0.27 kg, 95% CI −0.59, 0.06) nor between the MQ-LNS and IFA groups (mean difference 0.13 kg, 95% CI −0.33, 0.59). Neither MMN nor MQ-LNS had a significant effect compared with IFA supplementation on the rate of weight gain in trimesters 2 and 3 (MMN vs IFA mean difference 3.1 g/week, 95% CI −37.1, 30.7; MQ-LNS vs IFA mean difference 4.2 g/week, 95% CI −23.6, 32.0). Most women in this population gained an inadequate amount of weight as per IOM guidelines (89.1% in the MMN group, 88.9% in the MQ-LNS group and 87.5% in the IFA group). No effect of MMN or MQ-LNS supplementation was found compared with IFA supplementation on inadequate weight gain or excess weight gain.

Continuous haemoglobin was on average 111 g/L. There was no difference in continuous haemoglobin or anaemia comparing MMN or MQ-LNS with IFA overall or in the second or third trimester (table 3) (continuous haemoglobin overall: MMN vs IFA mean difference

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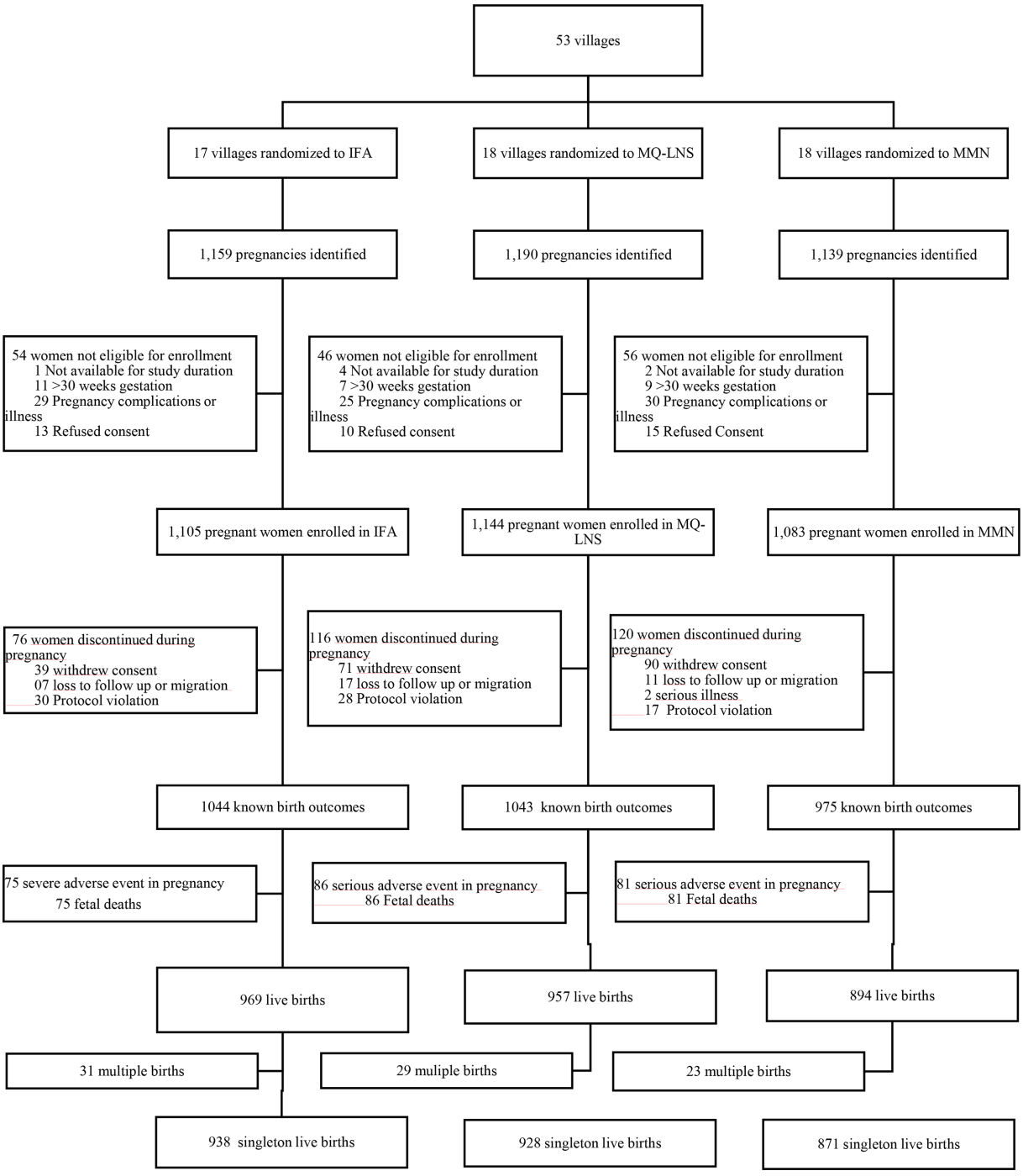

Figure 1 Flowchart of participants. IFA, iron folic acid; MQ-LNS, medium-quantity lipid-based micronutrient supplementation; MMN, multiple micronutrient supplementation.

0.06 g/dL 95% CI −0.07, 0.18; MQ-LNS vs IFA mean difference 0.03 g/dL, 95% CI −0.10, 0.16).

In analyses of potential effect modification (table 4), we found some evidence that the effect of prenatal nutritional supplements on haemoglobin and anaemia may differ by malaria diagnosis and BMI at enrolment. The effect of MMN as compared with IFA on maternal anaemia during the second or third trimester appeared to be more protective among mothers who had a malaria diagnosis at baseline as compared with those who did not have a malaria diagnosis (RR with malaria=0.66, 95% CI 0.43, 1.01; RR without malaria=1.11, 95% CI 0.94, 1.33). The effect of MQ-LNS on continuous maternal haemoglobin concentration during the third trimester as compared with IFA appeared more negative for mothers whose BMI at enrolment was <18.5 kg/m^2 as compared 18–24.9 and ≥25 kg/m^2 (MQ-LNS vs IFA BMI <18.5 kg/m^2 mean difference −1.45 g/dL, 95% CI −2.40 to −0.50; MQ-LNS vs IFA BMI 18–24.9 kg/m^2 mean difference 0.06 g/dL, 95% CI −0.14, 0.26; MQ-LNS vs IFA BMI ≥25 kg/m^2 mean difference 0.24 g/dL, 95% CI 0.04, 0.44).

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Table 1 Baseline maternal and household characteristics in nutrition cohort

	IFA	MMN	MQ-LNS
N	1105	1083	1144
Maternal age, mean (SD)	26.5 (6.8)	26.8 (6.8)	27.0 (7.2)
Completed primary school, n (%)	61 (5.5)	80 (7.4)	66 (5.8)
Age at first pregnancy, mean (SD)	17.1 (1.8)	17.2 (1.9)	17.3 (2.1)
Number of pregnancies, mean (SD)	4.8 (2.9)	4.9 (2.8)	4.8 (2.9)
Primiparous, n (%)	135 (12.4)	120 (11.3)	144 (12.7)
Number of children <5 years in household, mean (SD)	2.2 (1.9)	2.4 (2.0)	2.5 (1.9)
Maternal BMI at enrolment (kg/m^2), n (%)			
BMI <18.5	39 (3.9)	37 (3.7)	62 (5.9)
BMI 18.5–24.9	753 (74.6)	796 (79.8)	858 (81.0)
BMI ≥25	218 (21.6)	165 (16.5)	139 (13.1)
Maternal anaemia (haemoglobin <110 g/L) at enrolment, n (%)	320 (32.5)	317 (32.7)	397 (38.4)
Maternal malaria diagnosis at enrolment, n (%)	162 (16.2)	150 (15.3)	229 (21.9)
Enrolment during the lean season (May–September), n (%)	482 (43.7)	363 (33.5)	573 (50.1)
Gestational age at enrolment, mean (SD)	18.1±3.9	18.3±4.1	18.3±4.1

IFA, iron folic acid; MMN, multiple micronutrient supplementation; MQ-LNS, medium-quantity lipid-based nutrient supplementation.

DISCUSSION

In this cluster-randomised trial in Niger, we evaluated the impact of MMN and MQ-LNS supplementation during pregnancy on infant birth weight, maternal weight gain and maternal anaemia as compared with standard IFA supplementation. We found no statistically significant difference in terms of infant birth weight (including continuous birth weight and risk of LBW), maternal weight gain measures (including total weight gain, rate of weight gain and adequacy of weight gain) or the risk of maternal anaemia in the second or third trimester. However, the trial was statistically underpowered to detect small to moderate effect sizes. This is the first study of prenatal nutritional supplementation to be conducted in rural Niger, where fertility is high, maternal nutritional status is poor and infectious diseases are common.[32]

Approximately 20 million children per year are born with LBW, which is associated with both immediate risks, such as neonatal mortality, as well as long-term adverse outcomes, including impaired growth and development and increased risk of chronic disease.[6 8–11] Trials of prenatal supplementation with MMN to date have found positive effects on the risk of LBW compared with IFA.[45–47] The most recent Cochrane review that included data on 20 trials and nearly 150 000 participants found that MMN supplementation reduced the incidence of LBW by 12%.[48] Our finding of a non-significant 10% decrease in the risk of LBW with MMN supplementation compared with IFA is therefore consistent with the effects found in the Cochrane review. Further, the estimated effect of MMS on continuous birth weight in meta-analyses was +48 g,[24] which is consistent with our trial effect size of +50 g, although it was not statistically significant. As a result of limited statistical power, our results should not be interpreted as a definitive null finding.

In 2016, the WHO recommended balanced energy and protein supplements (BEP), defined as supplements with protein providing <25% of energy content, for populations with a prevalence of undernourished pregnant women >20%.[49] A meta-analysis from low- and middle-income countries found BEP, as compared with either placebo, no supplement or MMN, significantly increased the birth weight of children born to undernourished women.[50] MQ-LNS as formulated in our study met the criteria for formulation of BEP (<25% of total energy from protein) and provided multiple micronutrients as well as macronutrients and essential fatty acids that may contribute to improved maternal and infant outcomes.[51] We found no significant difference in birth weight or LBW with MQ-LNS compared with IFA, which is consistent with systematic reviews of BEP.

Inadequate GWG, which was identified in more than 90% of our population in rural Niger, has been associated with poor birth outcomes, including an increased risk of LBW.[52]

The provision of MMN has been hypothesised to increase GWG, potentially through multiple mechanisms, including improving maternal immune function and reducing infection risk.[53–55] Several studies in Africa found no effect of MMN as compared with IFA on total weight gain, similar to the results in our trial.[23 56–58] However, a larger global meta-analysis that included 17 studies across Latin America, Southeast Asia and Africa found that MMN led to a small increase in maternal weight gain compared with IFA.[59] A subgroup analysis by region, which may have explained this discrepancy, was

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Table 2 Effect of maternal supplementation regimens on birth and safety outcomes

	IFA	MMN	MQ-LNS	P value	MMN vs IFA	MQ-LNS vs IFA
	Mean (95% CI)	Mean (95% CI)	Mean (95% CI)	(df=2)	Difference in means (95% CI)	Difference in means (95% CI)
Birth weight*, g	3004 (2945, 3062)	3043 (2969, 3117)	3054 (2966, 3142)	0.56	39 (−55, 134)	50 (−55, 156)
	n/N (%)	n/N (%)	n/N (%)		RR (95% CI)	RR (95% CI)
Low birth weight (<2500 g)	71/872 (8.1)	55/794 (6.9)	64/826 (7.8)	0.91	0.90 (0.53, 1.53)	0.98 (0.58, 1.67)
Serious adverse event in pregnancy	75/1075 (7.0)	83/1066 (7.8)	86/1116 (7.7)	0.79	1.13 (0.80, 1.59)	1.07 (0.76, 1.50)
Fetal death any time in pregnancy	75/1044 (7.2)	81/975 (8.3)	86/1043 (8.3)	0.70	1.16 (0.82, 1.64)	1.11 (0.78, 1.56)

*N=872 for IFA; 794 for MMN; 826 for MQ-LNS.
IFA, iron folic acid; MMN, multiple micronutrient supplementation; MQ-LNS, medium-quantity lipid-based nutrient supplementation.

not performed. MQ-LNS may provide a greater effect on GWG due to the provision of additional macronutrients. While one study in Ghana found that a 20 g SQ-LNS provided during pregnancy reduced the risk of inadequate GWG compared with MMN,[23] a recent meta-analysis including this study found no overall effect on GWG of SQ-LNS compared with IFA.[59] We hypothesised the provision of greater energy with MQ-LNS would increase GWG, but we found no effect. These results suggest that MMN and MQ-LNS may be insufficient to fully address suboptimal maternal weight gain in the setting of rural Niger. More research is needed to explore effective dosages of nutritional supplementation and alternative delivery strategies, such as care packages that include nutrition, infection and other intervention components to comprehensively support healthy maternal weight gain in pregnancy.[60–62]

Over 50% of women of childbearing age in Niger are anaemic,[63] and 59.0% of women in our population had anaemia during their pregnancy. Maternal anaemia in pregnancy has been associated with adverse birth outcomes, including LBW, preterm birth and infant mortality.[14] Standard care of daily prenatal supplementation with IFA can be provided to reduce the risk of LBW and maternal anaemia.[64] Two large studies of prenatal MMN and SQ-LNS supplementation compared with standard IFA supplementation, one in Ghana[18] and one in Malawi,[65] found that mothers who received SQ-LNS containing 20 mg iron had significantly lower haemoglobin levels compared with those receiving 60 mg iron. In our study in Niger, we provided MMN and MQ-LNS, each containing 30 mg of iron daily, and IFA, containing 60 mg daily. We observed no difference in the risk of anaemia in mothers who received MMN or MQ-LNS compared with IFA, suggesting that 30 mg of daily iron may be an adequate dose for pregnant women in Niger. We also found the effect of prenatal nutritional supplements on the risk of maternal anaemia may differ by individual-level characteristics, including malaria diagnosis and first-trimester BMI. Iron provision during malaria infection may lead to more severe malaria disease,[66] and therefore the lower dose of iron provided by MMN compared with IFA in our study may have been more beneficial to mothers with malaria at baseline. The higher dose of iron found in IFA in our study also may have had a stronger effect on haemoglobin levels in women with a low BMI, as these pregnant women may be more likely to be iron deficient.[67] Additional research is needed to determine the optimal iron dose in prenatal nutritional supplements to safely reduce the risk of anaemia in settings with a high infectious disease burden.

Our trial has several limitations. First, we observed that only two-thirds of participants consumed >75% of the supplements provided. While adherence did not differ by group, suboptimal intake would bias the results to the null. Second, comprehensive data on dietary intake was not available in the present analysis. Third, due to the form of prenatal supplements, blinding of participants

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Table 3 Effect of maternal supplementation on gestational weight gain and anaemia

	IFA	MMN	MQ-LNS	P value	MMN vs IFA	MQ-LNS vs IFA
	Mean (95% CI)	Mean (95% CI)	Mean (95% CI)		Mean difference (95% CI)	Mean difference (95% CI)
Total weight gain (kg)*	4.9 (4.6, 5.1)	4.6 (4.4, 4.8)	5.0 (4.6, 5.4)	0.12	–0.27 (–0.59, 0.06)	0.13 (–0.33, 0.59)
Rate of weight gain in trimesters 2 and 3 (g/week)*	396.4 (380.3, 412.6)	393.3 (363.6, 423.1)	400.6 (378.0, 423.3)	0.92	–3.1 (–37.0, 30.7)	4.2 (–23.6, 32.0)
Continuous haemoglobin (g/dL)						
Trimester 2+3†	11.1 (11.0, 11.2)	11.1 (11.1, 11.2)	11.1 (11.0, 11.2)	0.71	0.06 (-0.07, 0.18)	0.03 (-0.10, 0.16)
Trimester 2‡	11.0 (10.9, 11.2)	11.1 (11.0, 11.2)	11.1 (11.0, 11.2)	0.50	0.08 (-0.06, 0.23)	0.01 (-0.13, 0.16)
Trimester 3§	11.2 (11.1, 11.3)	11.2 (11.0, 11.3)	11.2 (11.1, 11.3)	0.82	–0.01 (-0.19, 0.16)	0.04 (-0.13, 0.22)
	n (%)	n (%)	n (%)		RR (95% CI) MMN vs IFA	RR (95% CI) MQ-LNS vs IFA
Adequacy of weight gain*						
Inadequate	826 (87.5)	812 (89.1)	855 (88.9)	0.93	1.02 (0.92, 1.12)	1.01 (0.92, 1.12)
Adequate	88 (9.3)	74 (8.1)	79 (8.2)			
Excess	30 (3.2)	25 (2.7)	28 (2.9)	0.94	0.90 (0.49, 1.65)	0.95 (0.53, 1.71)
Anaemia Trimester 2+3†				0.91	0.97 (0.85, 1.11)	0.99 (0.86, 1.12)
Hb<11	575 (56.9)	596 (60.1)	631 (59.9)			
Hb≥11	436 (43.1)	395 (39.9)	422 (40.1)			
Anaemia Trimester 2‡				0.79	0.94 (0.80, 1.12)	0.98 (0.83, 1.16)
Hb<11	444 (45.3)	460 (48.3)	508 (49.6)			
Hb≥11	536 (54.7)	493 (51.7)	517 (50.4)			
Anaemia Trimester 3§				0.52	1.05 (0.83, 1.32)	0.91 (0.72, 1.16)
Hb<11	279 (36.9)	282 (40.8)	278 (35.8)			
Hb≥11	478 (63.1)	410 (59.3)	498 (64.2)			

*N=947 for IFA; 912 for MMN; 965 for MQ-LNS.
†N=1011 for IFA; 991 for MMN; 1053 for MQ-LNS.
‡N=980 for IFA; 953 for MMN; 1025 for MQ-LNS.
§N=757 for IFA; 692 for MMN; 776 for MQ-LNS.
IFA, iron folic acid; MMN, multiple micronutrient supplementation; MQ-LNS, medium-quantity lipid-based nutrient supplementation.

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Table 4 Exploratory analysis of effect modification of the effect of supplementation regimen on birth outcomes and maternal weight gain

	IFA	MMN	MQ-LNS	MMN vs IFA	MQ-LNS vs IFA
	Mean (95% CI)	Mean (95% CI)	Mean (95% CI)	Difference in means (95% CI)	Difference in means (95% CI)
Birth weight (g) by season of conception*					
Lean season of conception	3041 (2978, 3103)	3115 (3010, 3219)	3034 (2948, 3120)	74.1 (–47.7, 195.9)	–6.4 (–112.6, 99.8)
Non-lean season of conception	2989 (2914, 3064)	3013 (2934, 3093)	3080 (2972, 3189)	24.4 (–85.0, 133.8)	91.2 (–40.8, 223.3)
Haemoglobin trimester 2+3 by BMI†					
<18.5	11.1 (10.7, 11.5)	11.2 (10.8, 11.5)	10.9 (10.6, 11.3)	0.03 (–0.49, 0.55)	–0.18 (–0.66, 0.31)
18.5–<25	11.1 (10.9, 11.2)	11.1 (11.0, 11.2)	11.1 (11.0, 11.2)	0.07 (–0.10, 0.23)	0.03 (–0.14, 0.19)
≥25	11.1 (11.0, 11.2)	11.3 (11.2, 11.4)	11.3 (11.2, 11.4)	0.24 (0.07, 0.41)	0.19 (0.03, 0.35)
Second trimester haemoglobin by BMI‡					
<18.5	11.0 (10.6, 11.4)	11.1 (10.8, 11.5)	11.1 (10.9, 11.4)	0.12 (–0.41, 0.66)	0.10 (–0.36, 0.56)
18.5–<25	11.0 (10.9, 11.2)	11.1 (11.0, 11.2)	11.0 (10.9, 11.1)	0.09 (–0.08, 0.26)	0.00 (–0.16, 0.16)
≥25	11.0 (10.8, 11.3)	11.4 (11.2, 11.5)	11.2 (11.0, 11.4)	0.33 (0.05, 0.61)	0.19 (–0.11, 0.49)
Third trimester haemoglobin by BMI§					
<18.5	11.8 (11.2, 12.4)	11.3 (10.2, 12.4)	10.3 (9.6, 11.1)	–0.50 (–1.77, 0.76)	–1.45 (–2.40, –0.50)
18.5–<25	11.2 (11.0, 11.3)	11.1 (11.0, 11.3)	11.2 (11.1, 11.3)	–0.04 (–0.28, 0.19)	0.06 (–0.14, 0.26)
≥25	11.1 (10.9, 11.2)	11.3 (11.1, 11.4)	11.3 (11.2, 11.5)	0.16 (–0.06, 0.38)	0.24 (0.04, 0.44)
Second trimester haemoglobin by maternal malaria at baseline¶					
Malaria diagnosis	10.5 (10.3, 10.7)	10.9 (10.7, 11.1)	10.7 (10.5, 10.9)	0.36 (0.06, 0.66)	0.14 (–0.15, 0.43)
No malaria diagnosis	11.2 (11.0, 11.3)	11.2 (11.1, 11.3)	11.2 (11.1, 11.3)	0.06 (–0.09, 0.20)	0.04 (–0.11, 0.19)
Maternal weight gain (kg) by maternal malaria at baseline**					
Malaria diagnosis	4.5 (4.0, 5.1)	4.5 (3.9, 5.0)	4.6 (3.9, 5.3)	–0.07 (–0.86, 0.72)	0.04 (–0.88, 0.95)
No malaria diagnosis	4.9 (4.7, 5.2)	4.6 (4.4, 4.9)	5.1 (4.7, 5.5)	–0.28 (–0.63, 0.06)	0.18 (–0.27, 0.63)
	n/N (%)	n/N (%)	n/N (%)	RR (95% CI)	RR (95% CI)
Low birth weight by season of enrolment††					
Lean season of enrolment	22/327 (6.7)	22/196 (11.2)	32/399 (8.0)	1.75 (0.82, 3.74)	1.19 (0.57, 2.48)
Non-lean season of enrolment	49/545 (9.0)	33/598 (5.5)	32/427 (7.5)	0.63 (0.36, 1.09)	0.88 (0.51, 1.54)
Maternal anaemia by maternal malaria at baseline‡‡					
Malaria diagnosis	112/148 (75.7)	85/135 (63.0)	144/206 (69.9)	0.66 (0.43, 1.01)	0.81 (0.56, 1.18)
No malaria diagnosis	421/778 (54.1)	460/762 (60.3)	428/743 (57.6)	1.11 (0.94, 1.33)	1.04 (0.88, 1.25)
Maternal anaemia by season of enrolment§§					
Lea season off enrolment t	218/350 (62.3)	135/215 (62.8)	326/477 (68.3)	0.95 (0.67, 1.33)	1.09 (0.81, 1.47)
Non-lea season off enrolment t	326/597 (54.6)	418/697 (60.0)	253/488 (51.8)	1.06 (0.84, 1.34)	0.90 (0.70, 1.14)

*p for interaction=0.021.
†p for interaction ≤0.001.
‡p for interaction=0.044.
§p for interaction ≤0.001.
¶p for interaction=0.021.
**p for interaction ≤0.001.
††p for interaction=0.036.
‡‡p for interaction=0.033.
§§p for interaction=0.028.
IFA, iron folic acid; MMN, multiple micronutrient supplementation; MQ-LNS, medium-quantity lipid-based nutrient supplementation.

and investigators and the use of a placebo were not practical. In addition, we estimated first-trimester BMI to calculate GWG in pregnancy, as prepregnancy weight was not recorded. Our analysis therefore assumed minimal weight gain in the first trimester, and as a result, we may have underestimated total GWG even if weight gain in

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the first trimester is known to be substantially less than in the second and third trimesters.[68] Nevertheless, the approach of estimating first-trimester BMI has been validated and used in multiple studies that have evaluated GWG in resource-limited settings.[44 52] Last, we conducted the trial in rural Niger, and therefore the findings may not be generalisable to pregnant women in other contexts, particularly where food insecurity and infections are less prevalent.

Overall, we found that neither MMN nor MQ-LNS provided a statistically significant effect on pregnancy and birth outcomes, as compared with IFA. However, we had limited statistical power to detect moderate to small effect sizes that are likely for these nutritional interventions. Given many concurrent and potentially synergistic risk factors that may negatively impact women's health in Niger and similar contexts (high fertility, infectious disease burden and food insecurity),[63] integrated interventions may be required to produce a large benefit. A comprehensive intervention package implemented in India, delivered during preconception, pregnancy and early childhood, effectively reduced LBW and increased birth weight.[69] Further research in Ethiopia is currently underway exploring the effect of integrated infection, nutrition and educational interventions during pregnancy on newborn weight, which may provide key insight into potential interventions for pregnant women in Niger.[70] Therefore, integrating nutritional supplementation alongside other interventions may provide more comprehensive support for pregnant women in Niger and produce larger effects on maternal and infant outcomes.

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Contributors SI, CL and RG conceptualised the research; OG and IS conducted the investigation; SG curated the data; SI and CS designed the methodology; BP designed and implemented the computer programmes; BP and SMR conducted the formal analysis; SMR prepared the original manuscript draft; all authors reviewed and edited the manuscript. SI is responsible for the overall content as guarantor.

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Patient and public involvement Patients and/or the public were not involved in the design, conduct, reporting or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants. The study protocol was approved by the Ethics Committee of the World Health Organization (Geneva, Switzerland), the Western Institutional Review Board (Olympia, Washington, USA), the Comité Consultatif National d'Ethique (Niamey, Niger), the Comité de Protection des Personnes (Ile-de-France XI, France) and the Hôpitaux Universitaires de Genève (Geneva, Switzerland). Participants gave informed consent to participate in the study before taking part.

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Data availability statement Data are available upon reasonable request. The deidentified dataset supporting this research can be made available following a submitted request as per the Epicentre and General Data Protection Regulation (EU) 2016/679 data sharing policy. Additional information is available at https://epicentre.msf.org/en/ongoing-projects/study-data-access-request.

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REFERENCES

1 Khan KS, Wojdyla D, Say L, *et al*. WHO analysis of causes of maternal death: a systematic review. *Lancet* 2006;367:1066–74.
2 Kinney MV, Kerber KJ, Black RE, *et al*. Sub-Saharan Africa's mothers, newborns, and children: where and why do they die? *PLoS Med* 2010;7:e1000294.
3 World Health Organization. Global nutrition targets 2025: low birth weight policy brief. 2014.6.
4 Black RE, Allen LH, Bhutta ZA, *et al*. Maternal and child undernutrition: global and regional exposures and health consequences. *Lancet* 2008;371:243–60.
5 United Nations Children's Fund (UNICEF), World Health Organization (WHO). UNICEF-WHO low birthweight estimates: levels and trends 2000-2015. Geneva: World Health Organization, 2019.
6 Okwaraji YB, Krasevec J, Bradley E, *et al*. National, regional, and global estimates of low birthweight in 2020, with trends from 2000: a systematic analysis. *Lancet* 2024;403:1071–80.
7 Katz J, Wu LA, Mullany LC, *et al*. Prevalence of small-for-gestational-age and its mortality risk varies by choice of birth-weight-for-gestation reference population. *PLoS One* 2014;9:e92074.
8 Martorell R, Ramakrishnan U, Schroeder DG, *et al*. Intrauterine growth retardation, body size, body composition and physical performance in adolescence. *Eur J Clin Nutr* 1998;52 Suppl 1:S43–52.
9 Woldehanna T, Behrman JR, Araya MW. The effect of early childhood stunting on children's cognitive achievements: Evidence from young lives Ethiopia. *Ethiop J Health Dev* 2017;31:75–84.
10 Rytter MJH, Kolte L, Briend A, *et al*. The immune system in children with malnutrition--a systematic review. *PLoS One* 2014;9:e105017.
11 Victora CG, Adair L, Fall C, *et al*. Maternal and child undernutrition: consequences for adult health and human capital. *Lancet* 2008;371:340–57.
12 Marangoni F, Cetin I, Verduci E, *et al*. Maternal Diet and Nutrient Requirements in Pregnancy and Breastfeeding. An Italian Consensus Document. *Nutrients* 2016;8:629.
13 Cisse-Egbuonye N, Ishdorj A, McKyer ELJ, *et al*. Examining Nutritional Adequacy and Dietary Diversity Among Women in Niger. *Matern Child Health J* 2017;21:1408–16.
14 Rahman MM, Abe SK, Rahman MS, *et al*. Maternal anemia and risk of adverse birth and health outcomes in low- and middle-income countries: systematic review and meta-analysis. *Am J Clin Nutr* 2016;103:495–504.
15 Katona P, Katona-Apte J. The interaction between nutrition and infection. *Clin Infect Dis* 2008;46:1582–8.

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16 Gondwe A, Ashorn P, Ashorn U, *et al*. Pre-pregnancy body mass index (BMI) and maternal gestational weight gain are positively associated with birth outcomes in rural Malawi. *PLoS One* 2018;13:e0206035.
17 Zhao R, Xu L, Wu ML, *et al*. Maternal pre-pregnancy body mass index, gestational weight gain influence birth weight. *Women Birth* 2018;31:e20–5.
18 Adu-Afarwuah S, Lartey A, Okronipa H, *et al*. Impact of small-quantity lipid-based nutrient supplement on hemoglobin, iron status and biomarkers of inflammation in pregnant Ghanaian women. *Matern Child Nutr* 2017;13:e12262.
19 Christian P, Lee SE, Donahue Angel M, *et al*. Risk of childhood undernutrition related to small-for-gestational age and preterm birth in low- and middle-income countries. *Int J Epidemiol* 2013;42:1340–55.
20 Changamire FT, Mwiru RS, Peterson KE, *et al*. Effect of multivitamin supplements on weight gain during pregnancy among HIV-negative women in Tanzania. *Matern Child Nutr* 2015;11:297–304.
21 West KP Jr, Shamim AA, Mehra S, *et al*. Effect of maternal multiple micronutrient vs iron-folic acid supplementation on infant mortality and adverse birth outcomes in rural Bangladesh: the JiVitA-3 randomized trial. *JAMA* 2014;312:2649–58.
22 Das JK, Hoodbhoy Z, Salam RA, *et al*. Lipid-based nutrient supplements for maternal, birth, and infant developmental outcomes. *Cochrane Database Syst Rev* 2018;2018:CD012610.
23 Adu-Afarwuah S, Lartey A, Okronipa H, *et al*. Maternal Supplementation with Small-Quantity Lipid-Based Nutrient Supplements Compared with Multiple Micronutrients, but Not with Iron and Folic Acid, Reduces the Prevalence of Low Gestational Weight Gain in Semi-Urban Ghana: A Randomized Controlled Trial. *J Nutr* 2017;147:697–705.
24 Smith ER, Shankar AH, Wu LS-F, *et al*. Modifiers of the effect of maternal multiple micronutrient supplementation on stillbirth, birth outcomes, and infant mortality: a meta-analysis of individual patient data from 17 randomised trials in low-income and middle-income countries. *Lancet Glob Health* 2017;5:e1090–100.
25 Dewey KG, Arnold CD, Wessells KR, *et al*. Lipid-based nutrient supplements for prevention of child undernutrition: when less may be more. *Am J Clin Nutr* 2023;118:1133–44.
26 Adu-Afarwuah S, Lartey A, Okronipa H, *et al*. Lipid-based nutrient supplement increases the birth size of infants of primiparous women in Ghana. *Am J Clin Nutr* 2015;101:835–46.
27 Hambidge KM, Westcott JE, Garcés A, *et al*. A multicountry randomized controlled trial of comprehensive maternal nutrition supplementation initiated before conception: the Women First trial. *Am J Clin Nutr* 2019;109:457–69.
28 Ashorn P, Alho L, Ashorn U, *et al*. The impact of lipid-based nutrient supplement provision to pregnant women on newborn size in rural Malawi: a randomized controlled trial. *Am J Clin Nutr* 2015;101:387–97.
29 Isanaka S, Guindo O, Langendorf C, *et al*. Efficacy of a Low-Cost, Heat-Stable Oral Rotavirus Vaccine in Niger. *N Engl J Med* 2017;376:1121–30.
30 Isanaka S, Garba S, Plikaytis B, *et al*. Immunogenicity of an oral rotavirus vaccine administered with prenatal nutritional support in Niger: A cluster randomized clinical trial. *PLoS Med* 2021;18:e1003720.
31 Isanaka S, Langendorf C, McNeal MM, *et al*. Rotavirus vaccine efficacy up to 2 years of age and against diverse circulating rotavirus strains in Niger: Extended follow-up of a randomized controlled trial. *PLoS Med* 2021;18:e1003655.
32 Institut National de la Statistique Niger. Enquête démographique et de santé et à indicateurs multiples 2012. Niamey, Niger, 2012.
33 John TJ, Jayabal P. Oral polio vaccination of children in the tropics. I. The poor seroconversion rates and the absence of viral interference. *Am J Epidemiol* 1972;96:263–9.
34 Levine MM. Immunogenicity and efficacy of oral vaccines in developing countries: lessons from a live cholera vaccine. *BMC Biol* 2010;8:129.
35 Moore SE, Jalil F, Ashraf R, *et al*. Birth weight predicts response to vaccination in adults born in an urban slum in Lahore, Pakistan. *Am J Clin Nutr* 2004;80:453–9.
36 Dewey KG, Wessells KR, Arnold CD, *et al*. Effects of prenatal small-quantity lipid-based nutrient supplements on pregnancy, birth, and infant outcomes: a systematic review and meta-analysis of individual participant data from randomized controlled trials in low- and middle-income countries. *Am J Clin Nutr* 2024;120:814–35.
37 Isanaka S, Kodish SR, Mamaty AA, *et al*. Acceptability and utilization of a lipid-based nutrient supplement formulated for pregnant women in rural Niger: a multi-methods study. *BMC Nutr* 2019;5:34.
38 Arimond M, Zeilani M, Jungjohann S, *et al*. Considerations in developing lipid-based nutrient supplements for prevention of undernutrition: experience from the International Lipid-Based Nutrient Supplements (iLiNS) Project. *Matern Child Nutr* 2015;11 Suppl 4:31–61.
39 Huybregts L, Roberfroid D, Lanou H, *et al*. Prenatal food supplementation fortified with multiple micronutrients increases birth length: a randomized controlled trial in rural Burkina Faso. *Am J Clin Nutr* 2009;90:1593–600.
40 Coates J, Swindale A, Bilinsky P. *Household Food Insecurity Access Scale (HFIAS) for measurement of food access: indicator guide*. Washington, D.C: Food and Nutrition Technical Assistance Project, Academy for Educational Development, 2007.
41 Ministère de la Santé du Niger, UNICEF, OMS. Protocole national de prise en charge intégrée de malnutrition aigue. 2016.
42 WHO. Global reference list of 100 core health indicators (plus health-related SDGs). Geneva World Health Organization; 2018.
43 Institute of Medicine, National Research Council of the National Academies. *Implementing guidelines on weight gain & pregnancy*. 2009.
44 Yang J, Wang D, Darling AM, *et al*. Methodological approaches to imputing early-pregnancy weight based on weight measures collected during pregnancy. *BMC Med Res Methodol* 2021;21:24.
45 Sunawang, Utomo B, Hidayat A, *et al*. Preventing low birthweight through maternal multiple micronutrient supplementation: a cluster-randomized, controlled trial in Indramayu, West Java. *Food Nutr Bull* 2009;30:S488–95.
46 Bhutta ZA, Rizvi A, Raza F, *et al*. A comparative evaluation of multiple micronutrient and iron-folic acid supplementation during pregnancy in Pakistan: impact on pregnancy outcomes. *Food Nutr Bull* 2009;30:S496–505.
47 Friis H, Gomo E, Nyazema N, *et al*. Effect of multimicronutrient supplementation on gestational length and birth size: a randomized, placebo-controlled, double-blind effectiveness trial in Zimbabwe. *Am J Clin Nutr* 2004;80:178–84.
48 Keats EC, Haider BA, Tam E, *et al*. Multiple-micronutrient supplementation for women during pregnancy. *Cochrane Database Syst Rev* 2019;3:CD004905.
49 World Health Organization. WHO recommendations on antenatal care for a positive pregnancy experience. Luxembourg World Health Organization; 2016.
50 Stevens B, Buettner P, Watt K, *et al*. The effect of balanced protein energy supplementation in undernourished pregnant women and child physical growth in low- and middle-income countries: a systematic review and meta-analysis. *Matern Child Nutr* 2015;11:415–32.
51 Ciulei MA, Smith ER, Perumal N, *et al*. Nutritious Supplemental Foods for Pregnant Women from Food Insecure Settings: Types, Nutritional Composition, and Relationships to Health Outcomes. *Curr Dev Nutr* 2023;7:100094.
52 Perumal N, Wang D, Darling AM, *et al*. Suboptimal gestational weight gain and neonatal outcomes in low and middle income countries: individual participant data meta-analysis. *BMJ* 2023;382:e072249.
53 Christian P, Mullany LC, Hurley KM, *et al*. Nutrition and maternal, neonatal, and child health. *Semin Perinatol* 2015;39:361–72.
54 Major GC, Doucet E, Jacqmain M, *et al*. Multivitamin and dietary supplements, body weight and appetite: results from a cross-sectional and a randomised double-blind placebo-controlled study. *Br J Nutr* 2008;99:1157–67.
55 Liu E, Wang D, Darling AM, *et al*. Multivitamin Supplementation Is Associated with Greater Adequacy of Gestational Weight Gain among Pregnant Women in Tanzania. *J Nutr* 2022;152:1091–8.
56 Moore SE, Fulford AJ, Darboe MK, *et al*. A randomized trial to investigate the effects of pre-natal and infant nutritional supplementation on infant immune development in rural Gambia: the ENID trial: Early Nutrition and Immune Development. *BMC Pregnancy Childbirth* 2012;12:107.
57 Roberfroid D, Huybregts L, Lanou H, *et al*. Effects of maternal multiple micronutrient supplementation on fetal growth: a double-blind randomized controlled trial in rural Burkina Faso. *Am J Clin Nutr* 2008;88:1330–40.
58 Ashorn P, Alho L, Ashorn U, *et al*. Supplementation of Maternal Diets during Pregnancy and for 6 Months Postpartum and Infant Diets Thereafter with Small-Quantity Lipid-Based Nutrient Supplements Does Not Promote Child Growth by 18 Months of Age in Rural Malawi: A Randomized Controlled Trial. *J Nutr* 2015;145:1345–53.
59 Liu E, Wang D, Darling AM, *et al*. Effects of prenatal nutritional supplements on gestational weight gain in low- and middle-income countries: a meta-analysis of individual participant data. *Am J Clin Nutr* 2022;116:1864–76.

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60 Jones L, de Kok B, Moore K, *et al*. Acceptability of 12 fortified balanced energy protein supplements - Insights from Burkina Faso. *Matern Child Nutr* 2021;17:e13067.
61 Lama TP, Khatry SK, Isanaka S, *et al*. Acceptability of 11 fortified balanced energy-protein supplements for pregnant women in Nepal. *Matern Child Nutr* 2022;18:e13336.
62 Gernand AD, Gallagher K, Bhandari N, *et al*. Harmonization of maternal balanced energy-protein supplementation studies for individual participant data (IPD) meta-analyses - finding and creating similarities in variables and data collection. *BMC Pregnancy Childbirth* 2023;23:107.
63 Institut Nationale de la Statistique. Evaluation nationale de la situation nutritionnelle par la methodologie SMART. 2019.
64 Peña-Rosas JP, De-Regil LM, Garcia-Casal MN, *et al*. Daily oral iron supplementation during pregnancy. *Cochrane Database Syst Rev* 2015;2015:CD004736.
65 Jorgensen JM, Ashorn P, Ashorn U, *et al*. Effects of lipid-based nutrient supplements or multiple micronutrient supplements compared with iron and folic acid supplements during pregnancy on maternal haemoglobin and iron status. *Matern Child Nutr* 2018;14:e12640.
66 Sazawal S, Black RE, Ramsan M, *et al*. Effects of routine prophylactic supplementation with iron and folic acid on admission to hospital and mortality in preschool children in a high malaria transmission setting: community-based, randomised, placebo-controlled trial. *Lancet* 2006;367:133–43.
67 Kamruzzaman M. Is BMI associated with anemia and hemoglobin level of women and children in Bangladesh: A study with multiple statistical approaches. *PLoS One* 2021;16:e0259116.
68 Gilmore LA, Redman LM. Weight gain in pregnancy and application of the 2009 IOM guidelines: toward a uniform approach. *Obesity (Silver Spring)* 2015;23:507–11.
69 Taneja S, Chowdhury R, Dhabhai N, *et al*. Impact of a package of health, nutrition, psychosocial support, and WaSH interventions delivered during preconception, pregnancy, and early childhood periods on birth outcomes and on linear growth at 24 months of age: factorial, individually randomised controlled trial. *BMJ* 2022;379:e072046.
70 Lee AC, Abate FW, Mullany LC, *et al*. Enhancing Nutrition and Antenatal Infection Treatment (ENAT) study: protocol of a pragmatic clinical effectiveness study to improve birth outcomes in Ethiopia. *BMJ Paediatr Open* 2022;6:e001327.

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