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Supplemental Appendix. Preconception interventions to prevent low birth weight, preterm birth and small for gestational age – a systematic review and meta-analysis

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1. Preconception interventions to prevent low birth weight, preterm birth and small for gestational age: Search strategy

(All searches run on 28 Nov 2020)

1.1. PubMed

1.1A. Combined search

Preconception + study type + LBW: ((1 AND 9) NOT 8) AND 2D = **2875 results**

1.1B. Search sub-blocks:

(1) **Preconception**

“preconception*”[tiab] OR “pre-conception*”[tiab] OR “periconception*”[tiab] OR “peri-conception*”[tiab] OR “conception*”[tiab] OR “pre-pregnancy”[tiab] OR “prepregnancy”[tiab] OR “pre pregnancy”[tiab] OR “before-pregnancy”[tiab] OR “before pregnancy”[tiab] OR “prior to pregnancy”[tiab] OR “pre-gestation”[tiab] OR “pre gestation”[tiab] OR “inter-pregnancy”[tiab] OR “inter pregnancy”[tiab] OR “inter-gestation”[tiab] OR “inter gestation”[tiab] OR “between pregnancy”[tiab] OR “between-pregnancy”[tiab] OR “interconception”[tiab] OR “inter-conception”[tiab] OR “inter conception”[tiab] OR “adolescen*”[tiab] OR “teenage*”[tiab]

Results: 375,166 on 28 Nov 2020

(2) Outcomes

“low birth weight”[tiab] OR “low birthweight”[tiab] OR “low-birthweight”[tiab] OR “LBW”[tiab] OR “birth weight”[tiab] OR “birthweight”[tiab] OR “weight at birth”[tiab] OR “preterm”[tiab] OR “pre-term”[tiab] OR “prematur*” OR “pre-matur*”[tiab] OR “PPROM”[tiab] OR “gestational age”[tiab] OR “gestational age at birth”[tiab] OR “fetal age”[tiab] OR “small for gestational age”[tiab] OR “small-for-gestational-age”[tiab] OR “small-for-gestational age”[tiab] OR “SGA”[tiab] OR “weight for gestational age”[tiab] OR “weight-for-gestational-age”[tiab] OR “weight-for-gestational age”[tiab] OR “birthweight for gestational age”[tiab] OR “birthweight-for-gestational-age”[tiab] OR “birthweight-for-gestational age”[tiab] OR ("weight"[tiab] AND "gestational age"[tiab]) OR ("birthweight"[tiab] AND "gestational age"[tiab]) OR ("birth-weight"[tiab] AND "gestational age"[tiab]) OR “intrauterine growth retardation”[tiab] OR “intra-uterine growth retardation”[tiab] OR “intrauterine growth restriction”[tiab] OR “intra-uterine growth restriction”[tiab] OR “IUGR”[tiab] OR “fetal growth retardation”[tiab] OR “fetal growth restriction”[tiab] OR “FGR”[tiab] OR "Infant, Low Birth Weight"[mh] OR "Birth Weight"[mh] OR "Premature Birth"[mh] OR "Fetal Membranes, Premature Rupture"[mh] OR "Gestational Age"[mh] OR "Infant, Small for Gestational Age"[mh] OR "Fetal Growth Retardation"[mh] OR (("maternal"[tiab] OR "mother*"[tiab] OR “pregnan*”[tiab]) AND (“underweight”[tiab] OR “under-weight”[tiab] OR “thin*”[tiab] OR “overweight”[tiab] OR “over-weight”[tiab] OR “obes*”[tiab] OR “undernourish*”[tiab] OR “under-nourish*”[tiab] OR “malnourish*”[tiab] OR “mal-nourish*”[tiab] OR “malnutrition”[tiab] OR “mal-nutrition”[tiab] OR “body mass index”[tiab] OR “body-mass index”[tiab] OR “BMI”[tiab] OR “body mass”[tiab] OR “anthropometr*”[tiab] OR "anaem*"[tiab] OR "anem*"[tiab] OR "haemoglobin"[tiab] OR "hemoglobin"[tiab] OR "Hb"[tiab] OR “deficien*”[tiab] OR “iron”[tiab] OR “hypertens*”[tiab] OR “blood pressure*”[tiab] OR “systolic”[tiab] OR “diastolic”[tiab] OR “SBP”[tiab] OR “DBP”[tiab] OR "proteinuria"[tiab] OR “diabet*”[tiab] OR “prediabet*”[tiab] OR “hyperglycemi*”[tiab] OR “dysglycemi*”[tiab] OR “blood glucose”[tiab] OR “fasting glucose”[tiab] OR “IGT”[tiab] OR “IFG”[tiab] OR “HbA1c”[tiab] OR “glycated hemoglobin”[tiab] OR “glycated haemoglobin”[tiab] OR “glucose tolerance”[tiab] OR “glucose intolerance”[tiab] OR “insulin”[tiab] OR “hyperinsulinaemia”[tiab] OR “hyperinsulinemia”[tiab])) OR “gestational hypertension”[tiab] OR "pre-eclampsia"[tiab] OR "preeclampsia"[tiab] OR "pre eclampsia"[tiab] OR "pregnancy-induced hypertension"[tiab] OR "pregnancy induced hypertension"[tiab] OR "gestational diabetes"[tiab] OR "stillbirth"[tiab] OR "still birth"[tiab] OR "still-birth"[tiab] OR "birth defect*"[tiab] OR "perinatal

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mortality"[tiab] OR "peri natal mortality"[tiab] OR "peri-natal mortality"[tiab] OR "large for gestational age”[tiab] OR “large-for-gestational-age”[tiab] OR “large-for-gestational age”[tiab] OR “LGA”[tiab]

Results: 517,610 on 28 Nov 2020

Sub-blocks 8 and 9. Inclusions and exclusions based on study type, in order to focus the search.

(8) **Exclusions**
(Address[ptyp] OR Autobiography[ptyp] OR Bibliography[ptyp] OR Biography[ptyp] OR pubmed books[filter] OR Case Reports[ptyp] OR Congress[ptyp] OR Consensus Development Conference[ptyp] OR Directory[ptyp] OR Duplicate Publication[ptyp] OR Editorial[ptyp] OR Festschrift[ptyp] OR Guideline[ptyp] OR Interview[ptyp] OR Lecture[ptyp] OR Legal Case[ptyp] OR News[ptyp] OR Newspaper Article[ptyp] OR Personal Narrative[ptyp] OR Portrait[ptyp] OR Retracted Publication[ptyp] OR Twin Study[ptyp] OR Video-Audio Media[ptyp])

Results: 3,323,471 on 28 Nov 2020

(9) **Inclusions for study type**. Based on the Cochrane sensitivity- and precision-maximising search for RCTs, and adding in the following possible study types: Clinical Study, Clinical Trial, Evaluation Study, Meta-Analysis, Pragmatic Clinical Trial, Preprint, Randomized Controlled Trial, Review, Systematic Review)
(randomized controlled trial[pt] OR controlled clinical trial[pt] OR Clinical Study[pt] OR Clinical Trial[pt] OR Meta-Analysis[pt] OR Pragmatic Clinical Trial[pt] OR Preprint[pt] OR Evaluation Study[pt] OR Systematic Review[pt] OR randomized[tiab] OR placebo[tiab] OR clinical trials as topic[mesh:noexp] OR randomly[tiab] OR trial[ti] NOT (animals[mh] NOT humans [mh]))

Results: 1,879,320 on 28 Nov 2020

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1.2. Embase

1.2A. Combined search

Search A: 1 and 2: **42 396 results**

Search B: limit A to (human and embase and (meta analysis or "systematic review" or clinical trial or randomized controlled trial or controlled clinical trial or multicenter study) and (article or article in press) and journal): **1260 results**

1.2B. Search sub-blocks

(1) **Preconception**

preconception*.ab,ti OR pre-conception*.ab,ti OR periconception*.ab,ti OR peri-conception*.ab,ti OR conception*.ab,ti OR pre-pregnancy.ab,ti OR prepregnancy.ab,ti OR pre pregnancy.ab,ti OR before-pregnancy.ab,ti OR before pregnancy.ab,ti OR prior to pregnancy.ab,ti OR pre-gestation.ab,ti OR pre gestation.ab,ti OR inter-pregnancy.ab,ti OR inter pregnancy.ab,ti OR inter-gestation.ab,ti OR inter gestation.ab,ti OR between pregnancy.ab,ti OR between-pregnancy.ab,ti OR interconception.ab,ti OR inter-conception.ab,ti OR inter conception.ab,ti OR adolescen*.ab,ti OR teenage*.ab,ti

Results: 456,304 (map term to subject heading on) on 28 Nov 2020

(2) **Low birth weight, small for gestational age, preterm birth**

low birth weight.ab,ti OR low birthweight.ab,ti OR low-birthweight.ab,ti OR LBW.ab,ti OR birth weight.ab,ti OR birthweight.ab,ti OR weight at birth.ab,ti OR preterm.ab,ti OR pre-term.ab,ti OR prematur*.ab,ti OR pre-matur*.ab,ti OR PPROM.ab,ti OR gestational age.ab,ti OR gestational age at birth.ab,ti OR fetal age.ab,ti OR small for gestational age.ab,ti OR small-for-gestational-age.ab,ti OR small-for-gestational age.ab,ti OR SGA.ab,ti OR weight for gestational age.ab,ti OR weight-for-gestational-age.ab,ti OR weight-for-gestational age.ab,ti OR birthweight for gestational age.ab,ti OR birthweight-for-gestational-age.ab,ti OR birthweight-for-gestational age.ab,ti OR (weight adj25 gestational age).ab,ti OR (birthweight adj25 gestational age).ab,ti OR (birth-weight adj25 gestational age).ab,ti OR intrauterine growth retardation.ab,ti OR intra-uterine growth retardation.ab,ti OR intrauterine growth restriction.ab,ti OR intra-uterine growth restriction.ab,ti OR IUGR.ab,ti OR fetal growth retardation.ab,ti OR fetal growth restriction.ab,ti OR FGR.ab,ti OR ((maternal OR mother* OR pregnan*).ab,ti AND (underweight OR under-weight OR thin* OR overweight OR over-weight OR obes* OR undernourish* OR under-nourish* OR malnourish* OR mal-nourish* OR malnutrition OR mal-nutrition OR body mass index OR body-mass index OR BMI OR body mass OR anthropometr* OR anaem* OR anem* OR haemoglobin OR hemoglobin OR Hb OR deficien* OR iron OR hypertens* OR blood pressure* OR systolic OR diastolic OR SBP OR DBP OR proteinuria OR diabet* OR prediabet* OR hyperglycemi* OR dysglycemi* OR blood glucose OR fasting glucose OR IGT OR IFG OR HbA1c OR glycated hemoglobin OR glycated haemoglobin OR glucose tolerance OR glucose intolerance OR insulin OR hyperinsulinaemia OR hyperinsulinemia).ab,ti) OR gestational hypertension.ab,ti OR pre-eclampsia.ab,ti OR preeclampsia.ab,ti OR pre eclampsia.ab,ti OR pregnancy-induced hypertension.ab,ti OR pregnancy induced hypertension.ab,ti OR gestational diabetes.ab,ti OR stillbirth.ab,ti OR still birth.ab,ti OR still-birth.ab,ti OR birth defect*.ab,ti OR perinatal mortality.ab,ti OR peri natal mortality.ab,ti OR peri-natal mortality.ab,ti OR large for gestational age.ab,ti OR large-for-gestational-age.ab,ti OR large-for-gestational age.ab,ti OR LGA.ab,ti OR exp low birth weight/ OR exp birth weight/ OR exp premature fetus membrane rupture/ OR exp premature labor/ OR exp "immature and premature labor"/ OR exp small for date infant/ OR exp intrauterine growth retardation/ OR exp gestational age/

Results: 661,217 (map term to subject heading on) on 28 Nov 2020

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1.3. Cochrane Library
(Also includes records from WHO ICTRP and ClinicalTrials.gov)

1.3A. Combined search

Overall search: 1 AND (2 OR 3), limits: Cochrane reviews or trials = 1245 results (101 reviews, 1144 trials)

1.3B. Search sub-blocks:

1 Preconception

Search in title, abstract, keyword: "preconception*" OR "pre-conception*" OR "periconception*" OR "peri-conception*" OR "conception*" OR "pre-pregnancy" OR "prepregnancy" OR "pre pregnancy" OR "before-pregnancy" OR "before pregnancy" OR "prior to pregnancy" OR "pre-gestation" OR "pre gestation" OR "inter-pregnancy" OR "inter pregnancy" OR "inter-gestation" OR "inter gestation" OR "between pregnancy" OR "between-pregnancy" OR "interconception" OR "inter-conception" OR "inter conception" OR "adolescen*" OR "teenage*"

Results: 3907 on 28 Nov 2020

2 Outcomes – non-MeSH terms

Search in title, abstract, keyword: "low birth weight" OR "low birthweight" OR "low-birthweight" OR "LBW" OR "birth weight" OR "birthweight" OR "weight at birth" OR "preterm" OR "pre-term" OR "prematur*" OR "pre-matur*" OR "PPROM" OR "gestational age" OR "gestational age at birth" OR "fetal age" OR "small for gestational age" OR "small-for-gestational-age" OR "small-for-gestational age" OR "SGA" OR "weight for gestational age" OR "weight-for-gestational-age" OR "weight-for-gestational age" OR "birthweight for gestational age" OR "birthweight-for-gestational-age" OR "birthweight-for-gestational age" OR ("weight" AND "gestational age") OR ("birthweight" AND "gestational age") OR ("birth-weight" AND "gestational age") OR "intrauterine growth retardation" OR "intra-uterine growth retardation" OR "intrauterine growth restriction" OR "intra-uterine growth restriction" OR "IUGR" OR "fetal growth retardation" OR "fetal growth restriction" OR "FGR" OR (("maternal" OR "mother*" OR "pregnan*") AND ("underweight" OR "under-weight" OR "thin*" OR "overweight" OR "over-weight" OR "obes*" OR "undernourish*" OR "under-nourish*" OR "malnourish*" OR "mal-nourish*" OR "malnutrition" OR "mal-nutrition" OR "body mass index" OR "body-mass index" OR "BMI" OR "body mass" OR "anthropometr*" OR "anaem*" OR "anem*" OR "haemoglobin" OR "hemoglobin" OR "Hb" OR "deficien*" OR "iron" OR "hypertens*" OR "blood pressure*" OR "systolic" OR "diastolic" OR "SBP" OR "DBP" OR "proteinuria" OR "diabet*" OR "prediabet*" OR "hyperglycemi*" OR "dysglycemi*" OR "blood glucose" OR "fasting glucose" OR "IGT" OR "IFG" OR "HbA1c" OR "glycated hemoglobin" OR "glycated haemoglobin" OR "glucose tolerance" OR "glucose intolerance" OR "insulin" OR "hyperinsulinaemia" OR "hyperinsulinemia")) OR "gestational hypertension" OR "pre-eclampsia" OR "preeclampsia" OR "pre eclampsia" OR "pregnancy-induced hypertension" OR "pregnancy induced hypertension" OR "gestational diabetes" OR "stillbirth" OR "still birth" OR "still-birth" OR "birth defect*" OR "perinatal mortality" OR "peri natal mortality" OR "peri-natal mortality" OR "large for gestational age" OR "large-for-gestational-age" OR "large-for-gestational age" OR "LGA" (title, abstract, keyword)

Results: 34,798 on 28 Nov 2020

3 Outcomes – MeSH terms

Entered directly in search box: mh "Infant, Low Birth Weight" OR mh "Birth Weight" OR mh "Premature Birth" OR mh "Fetal Membranes, Premature Rupture" OR mh "Gestational Age" OR mh "Infant, Small for Gestational Age" OR mh "Fetal Growth Retardation"

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Results: 470 on 28 Nov 2020

1.4. WHO Global Index Medicus

1.4A. Combined search

(1 AND (2 OR 3 OR 4))) AND 5 = 857 results

1.4B. Search sub-blocks

(1) Preconception

preconception* OR pre-conception* OR periconception* OR peri-conception* OR conception* OR pre-pregnancy OR prepregnancy OR pre pregnancy OR before-pregnancy OR before pregnancy OR prior to pregnancy OR pre-gestation OR pre gestation OR inter-pregnancy OR inter pregnancy OR inter-gestation OR inter gestation OR between pregnancy OR between-pregnancy OR interconception OR inter-conception OR inter conception OR adolescen* OR teenage* **(title, abstract, subject)**

Results: 1,404,188 28 Nov 2020

(2) Outcomes – LBW

low birth weight OR low birthweight OR low-birthweight OR LBW OR birth weight OR birthweight OR weight at birth OR preterm OR pre-term OR prematur* OR pre-matur* OR PPROM OR gestational age OR gestational age at birth OR fetal age OR small for gestational age OR small-for-gestational-age OR small-for-gestational age OR SGA OR weight for gestational age OR weight-for-gestational-age OR weight-for-gestational age OR birthweight for gestational age OR birthweight-for-gestational-age OR birthweight-for-gestational age OR (weight AND gestational age) OR (birthweight AND gestational age) OR (birth-weight AND gestational age) OR intrauterine growth retardation OR intra-uterine growth retardation OR intrauterine growth restriction OR intra-uterine growth restriction OR IUGR OR fetal growth retardation OR fetal growth restriction OR FGR **(title, abstract, subject)**

Results: 259 on 28 Nov 2020

(3) Outcomes – maternal 1

(maternal OR mother* OR pregnan*) AND (underweight OR under-weight OR thin* OR overweight OR over-weight OR obes* OR undernourish* OR under-nourish* OR malnourish* OR mal-nourish* OR malnutrition OR mal-nutrition OR body mass index OR body-mass index OR BMI OR body mass OR anthropometr* OR anaem* OR anem* OR haemoglobin OR hemoglobin OR Hb OR deficien* OR iron OR hypertens* OR blood pressure* OR systolic OR diastolic OR SBP OR DBP OR proteinuria OR diabet* OR prediabet* OR hyperglycemi* OR dysglycemi* OR blood glucose OR fasting glucose OR IGT OR IFG OR HbA1c OR glycated hemoglobin OR glycated haemoglobin OR glucose tolerance OR glucose intolerance OR insulin OR hyperinsulinaemia OR hyperinsulinemia) **(title, abstract, subject)**

Results: 4252 on 28 Nov 2020

(4) Outcomes – maternal 2 and other adverse outcomes

gestational hypertension OR pre-eclampsia OR preeclampsia OR pre eclampsia OR pregnancy-induced hypertension OR pregnancy induced hypertension OR gestational diabetes OR stillbirth OR still birth OR still-birth OR birth defect* OR perinatal mortality OR peri natal mortality OR peri-natal mortality OR large for gestational age OR large-for-gestational-age OR large-for-gestational age OR LGA **(title, abstract, subject)**

Results: 127 on 28 Nov 2020

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(5) Key words for study type

"trial" OR "randomized" OR "randomised" OR "intervention" OR "review" OR "meta-analysis"

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2. Preconception interventions to prevent low birth weight, preterm birth and small for gestational age: Additional details regarding data analysis

Use of estimates from studies

- Where studies reported median and interquartile range, estimates were approximated to mean and standard error in accordance with the Cochrane Handbook (Chapter 6.5.2.5).[1]
- Where two intervention or comparator groups were combined for the purposes of consistent comparisons, these were done in accordance with the Cochrane Handbook (Chapter 6.5.2.10).[1]
- For studies where the standard deviation or standard error for a continuous measure was reported to be 0 for any intervention or comparator group, the corresponding statistic for another group was used.
- Where studies reported risk ratios, the adjusted estimate was included in analyses. Where only categorical cell counts were reported, crude risk ratios were calculated. If odds ratios were reported, these were converted to risk ratios in accordance with the Cochrane Handbook (Chapter 15.4.4.4),[1] using the proportion of outcomes in the comparator group as the assumed comparator risk. If information on the proportion of outcomes in the comparator group was missing and could not be retrieved, the odds ratio was not included in meta-analysis and was reported separately.
- If studies did not report risk ratios and reported no outcomes in one or more groups, an approximate estimate for the risk ratio was calculated by adding 0.5 to each empty cell (Cochrane Handbook Chapter 10.4.4.1).[1] If studies reported no outcomes in both groups, the estimate was noted, but not included as part of meta-analyses (Cochrane Handbook Chapter 10.4.4.2).[1]
- For cluster-randomized trials or clustered studies, cluster-adjusted effect estimates as reported by the study or calculated independently were combined with other outcome data. If these were not available, to account for clustering, we contacted study authors for relevant data (e.g. number of clusters and ICC) to estimate the effective sample size or adjust estimates' standard errors (Cochrane Handbook Chapter 23.1.5).[1] If no information was forthcoming, we adjusted estimates assuming a design effect of 2, in line with previous reports on child health indicators.[2]

Synthesis of effect estimates

Where appropriate, similar intervention and comparator groups were combined for the purposes of meta-analysis, following procedures outlined in the Cochrane Handbook (Chapter 6.5.2.10);[1] disaggregated estimates were also noted and summarized. Where multiple similar outcomes from the same studies were reported (for example, distinct birth defects), we used the measure most consistent with other studies included in meta-analysis, and described any other measures.

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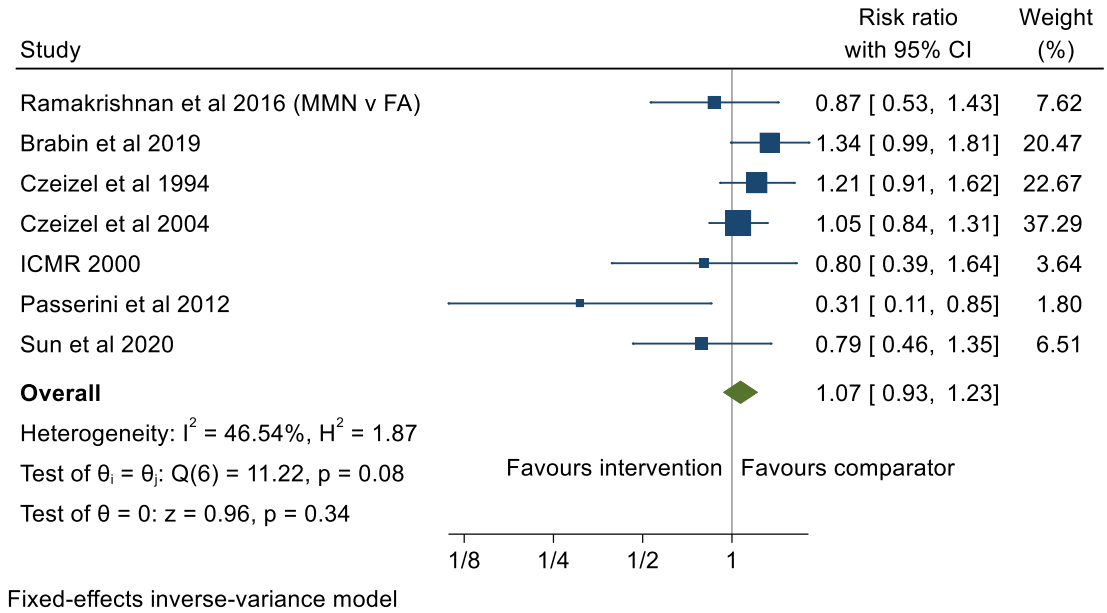
3. Preconception interventions to prevent low birth weight, preterm birth and small for gestational age: Meta-analyses for primary outcomes

3.1. Low birth weight

3.1A. Interventions in nutrition - overall



Supplementary Figure 1. Meta-analysis of reported estimates: any general population-based nutritional intervention in the pre- and periconception period compared with FA supplementation, supplementation with other micronutrients (not FA), standard or routine care, or no intervention to prevent low birth weight.

7 studies, N=13,973: Ramakrishnan et al 2016 (MMN supplementation v FA supplementation) [3], Czeizel et al 1994 (MMN supplementation v supplement containing only copper, manganese, zinc and Vitamin C) [4], Czeizel et al 2004 (MMN supplementation v no supplementation) [5], ICMR 2000 (MMN supplementation v supplement containing only iron and calcium; population: women with previous birth with neural tube defect) [6], Brabin et al 2019 (IFA supplementation v FA supplementation) [7], Passerini et al 2012 (IFA supplementation with deworming v no supplementation or deworming) [8], and Sun et al 2020 (100g mushroom daily v standard or routine care [normal diet]) [9].

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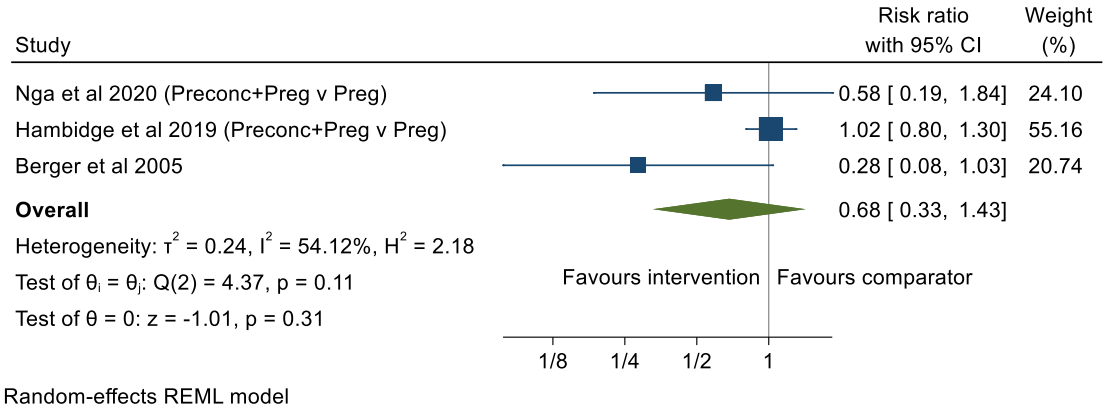

Supplementary Figure 2. Meta-analysis of reported estimates: any general population-based nutritional intervention <u>from preconception throughout pregnancy</u> compared with pregnancy-only intervention to prevent low birth weight.

3 studies, N=1334: Berger et al 2005 (preconception throughout pregnancy IFA supplementation v pregnancy-only supplementation) [10], Nga et al 2020 (preconception throughout pregnancy food supplement containing dark-green leafy vegetables and animal source foods v pregnancy-only supplementation) [11], Hambidge et al 2019 (preconception throughout pregnancy Nutriset [and additional lipid-based protein energy supplement for women with BMI <20 kg/m^2 or gestational weight gain <Institute of Medicine recommendations] v pregnancy-only supplementation) [12].

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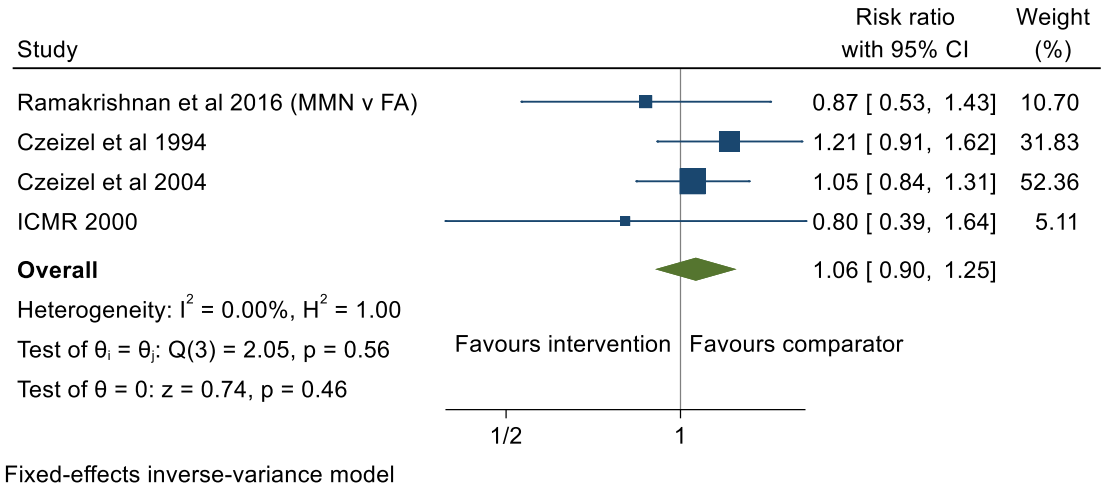
3.1B. Multiple micronutrient supplementation including IFA



Supplementary Figure 3. Meta-analysis of reported estimates: pre- and periconception MMN including IFA versus pre- and periconception FA supplementation, supplementation with other micronutrients (not FA), or no intervention to prevent low birth weight.

4 studies, N=12,054: Ramakrishnan et al 2016 (MMN supplementation v FA supplementation) [3], Czeizel et al 1994 (MMN supplementation v supplement containing only copper, manganese, zinc and Vitamin C) [4], Czeizel et al 2004 (MMN supplementation v no supplementation) [5], ICMR 2000 (MMN supplementation v supplement containing only iron and calcium; population: women with previous birth with neural tube defect) [6].

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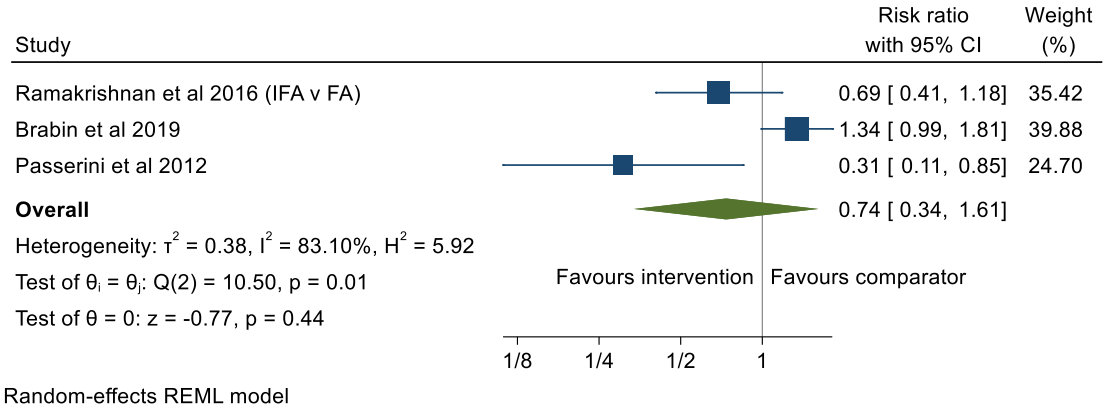
3.1C. Iron and folic acid supplementation



Supplementary Figure 4. Meta-analysis of reported estimates: pre- and periconception IFA supplementation versus pre- and periconception FA supplementation or no intervention to prevent low birth weight.
3 studies, N=1831: Brabin et al 2019 (IFA supplementation v FA supplementation) [7], Ramakrishnan et al 2016 (IFA supplementation v FA supplementation) [3], Passerini et al 2012 (IFA supplementation with deworming v no supplementation or deworming) [8].

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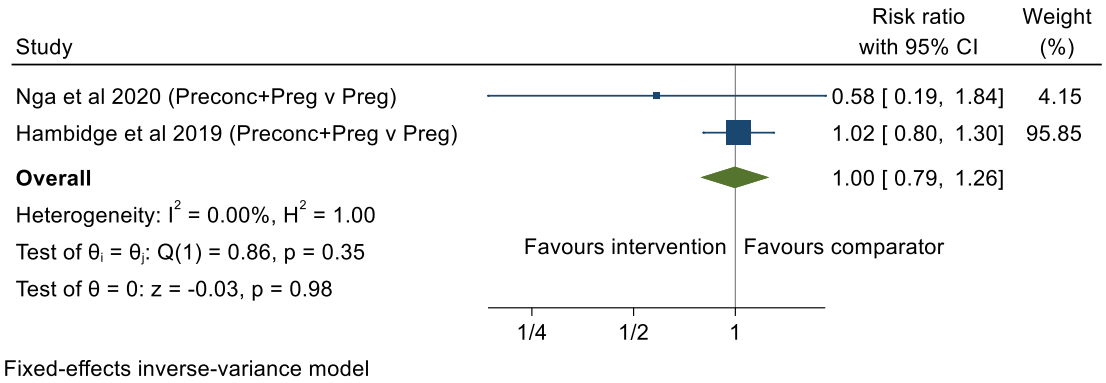
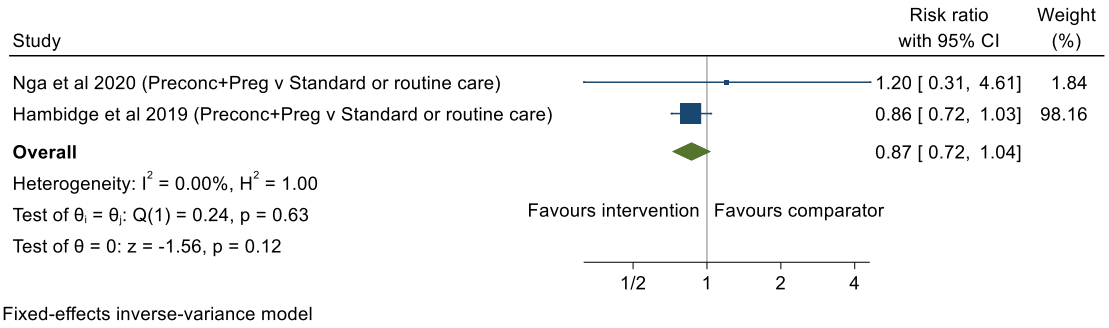
3.1D. Food supplementation



Supplementary Figure 5. Meta-analysis of reported estimates: preconception and pregnancy food supplementation versus pregnancy-only food supplementation to prevent low birth weight.
2 studies, N=1134: Nga et al 2020 (preconception throughout pregnancy food supplement containing dark-green leafy vegetables and animal source foods v pregnancy-only supplementation) [11], Hambidge et al 2019 (preconception throughout pregnancy Nutriset [and additional lipid-based protein energy supplement for women with BMI <20 kg/m^2 or gestational weight gain <Institute of Medicine recommendations] v pregnancy-only supplementation) [12].



Supplementary Figure 6. Meta-analysis of reported estimates: preconception and pregnancy food supplementation versus standard or routine care to prevent low birth weight.
2 studies, N=1078: Nga et al 2020 (preconception throughout pregnancy food supplement containing dark-green leafy vegetables and animal source foods v standard or routine care) [11], Hambidge et al 2019 (preconception throughout pregnancy Nutriset [and additional lipid-based protein energy supplement for women with BMI <20 kg/m^2 or gestational weight gain <Institute of Medicine recommendations] v standard or routine care) [12].

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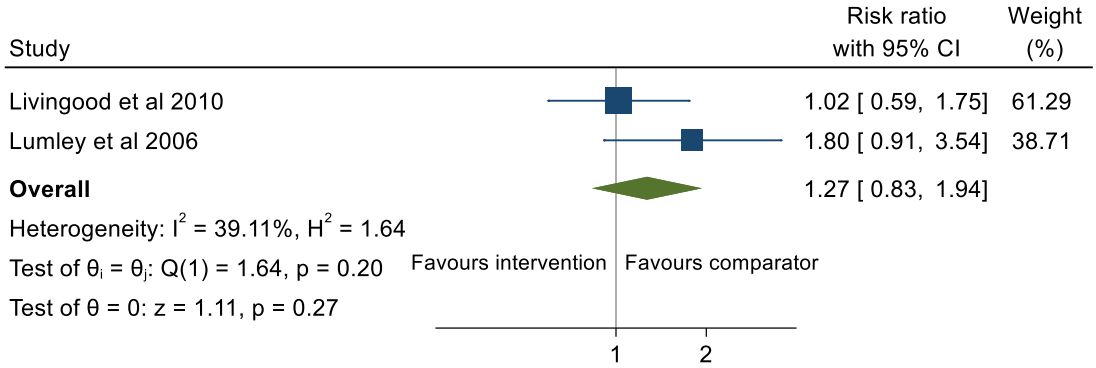
3.1E. General health interventions

General health interventions are those that provide care aiming to directly address aspects of preconception health. As examples, such interventions include preconception counseling, or a package of care comprising of services such as counseling, screening, vaccination, and linkage with appropriate clinical or community resources.



Supplementary Figure 7. Meta-analysis of reported estimates: pre- and periconception general health interventions versus pre- and periconception standard or routine care to prevent low birth weight.

2 studies, N=1188: Lumley et al 2006 (postpartum home visit offering comprehensive preconception care v standard or routine care; population: low income women) [13], Livingood et al 2010 (preconception care including goal plan to build resilience to negative social determinants v standard or routine care; population: low income women) [14].

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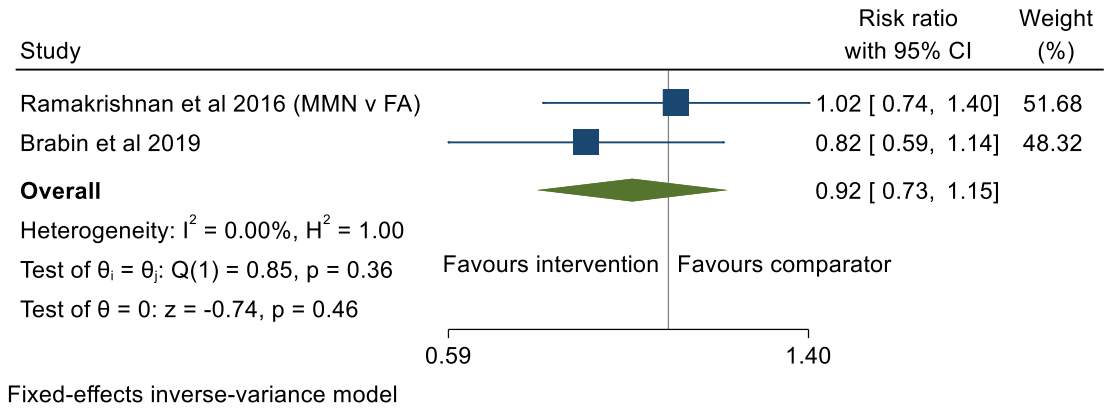
3.2. Small for gestational age

3.2A. Interventions in nutrition - overall



Supplementary Figure 8. Meta-analysis of reported estimates: any general population-based nutritional intervention in the pre- and periconception period compared with FA supplementation to prevent small for gestational age.

2 studies, N=1361: Ramakrishnan et al 2016 (MMN supplementation v FA supplementation) [3], Brabin et al 2019 (IFA supplementation v FA supplementation) [7].

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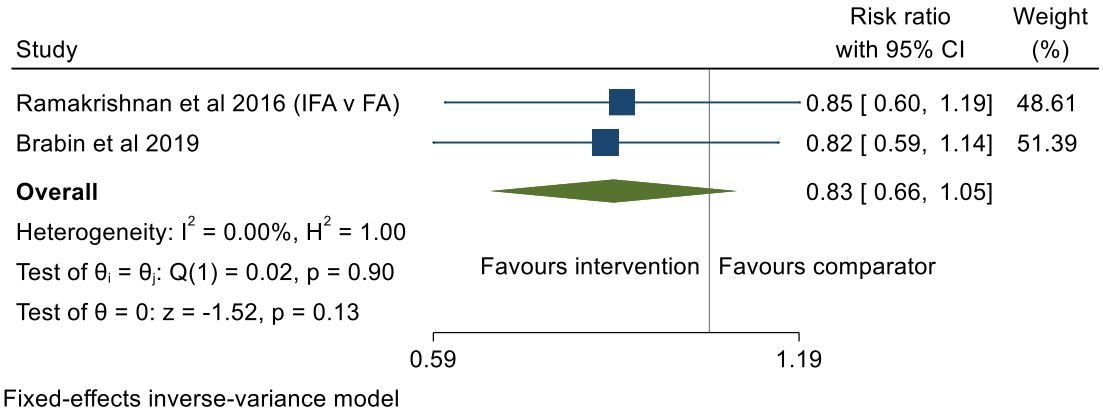
3.2B Iron and folic acid supplementation



Supplementary Figure 9. Meta-analysis of reported estimates: pre- and periconception IFA supplementation versus pre- and periconception FA supplementation to prevent small for gestational age.
2 studies, N=1351: Brabin et al 2019 (IFA supplementation v FA supplementation) [7] and Ramakrishnan et al 2016 (IFA supplementation v FA supplementation) [3].

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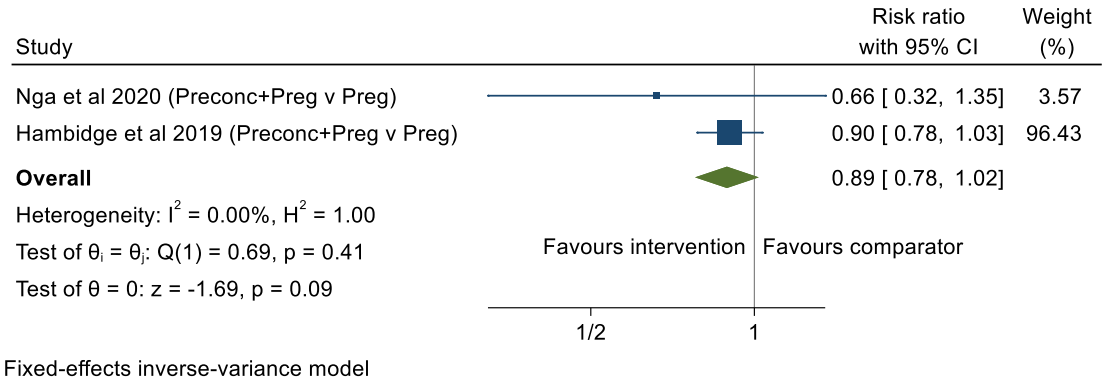
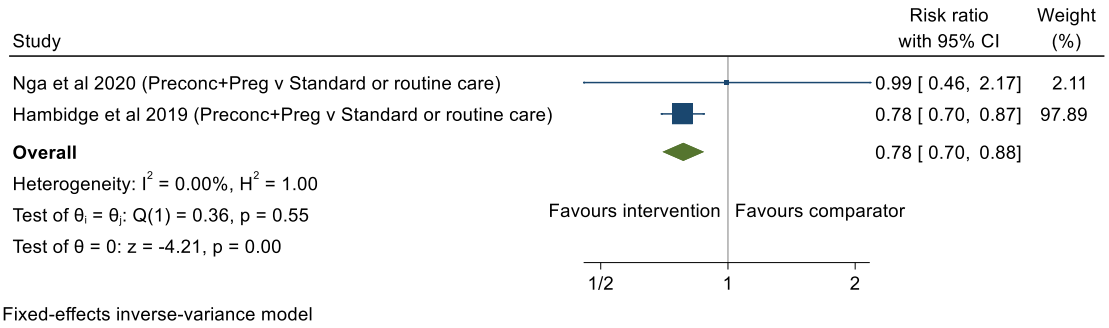
3.2C. Food supplementation



Supplementary Figure 10. Meta-analysis of reported estimates: preconception and pregnancy food supplementation versus pregnancy-only food supplementation to prevent small for gestational age.
2 studies, N=1161: Hambidge et al 2019 (preconception throughout pregnancy Nutriset [and additional lipid-based protein energy supplement for women with BMI <20 kg/m^2 or gestational weight gain <Institute of Medicine recommendations] v pregnancy-only supplementation) [12] and Nga et al 2020 (preconception throughout pregnancy food supplement containing dark-green leafy vegetables and animal source foods v pregnancy-only supplementation) [11].



Supplementary Figure 11. Meta-analysis of reported estimates: preconception and pregnancy food supplementation versus preconception and pregnancy standard or routine care to prevent small for gestational age.
2 studies, N=1108: Hambidge et al 2019 (preconception throughout pregnancy Nutriset [and additional lipid-based protein energy supplement for women with BMI <20 kg/m^2 or gestational weight gain <Institute of Medicine recommendations] v standard or routine care) and Nga et al 2020 (preconception throughout pregnancy food supplement containing dark-green leafy vegetables and animal source foods v standard or routine care).

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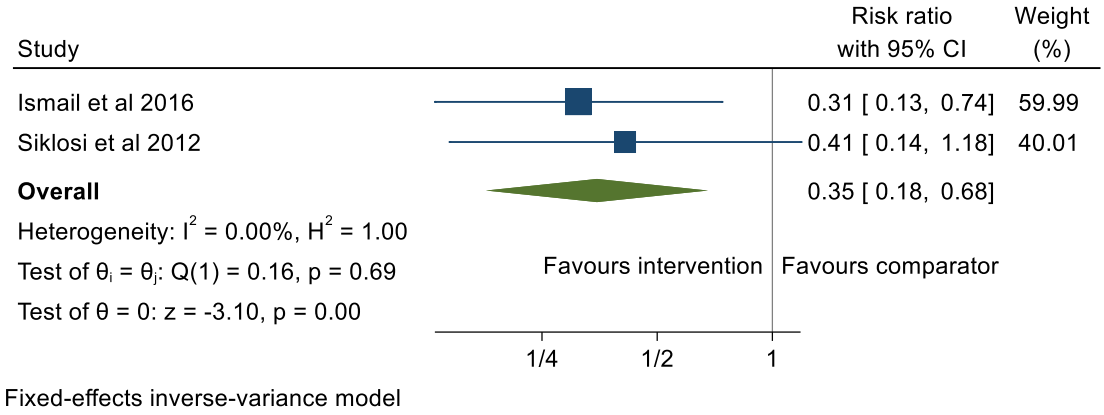
3.2D. Interventions to prevent adverse outcomes in early pregnancy

Early adverse pregnancy outcome interventions include studies aiming primarily to prevent miscarriage or other early adverse outcomes in subsequent pregnancies in populations of women with at least one previous miscarriage.



Supplementary Figure 12. Meta-analysis of reported estimates: pre- and periconception early adverse pregnancy outcome prevention interventions versus placebo to prevent small for gestational age.

2 studies, N=208: Ismail et al 2016 (oral aspirin + subcutaneous heparin v placebo; population: women with ≥2 previous miscarriages and antiphospholipid syndrome) [15] and Siklosi et al 2012 (clomiphene citrate v placebo; population: women with ≥3 previous miscarriages) [16].

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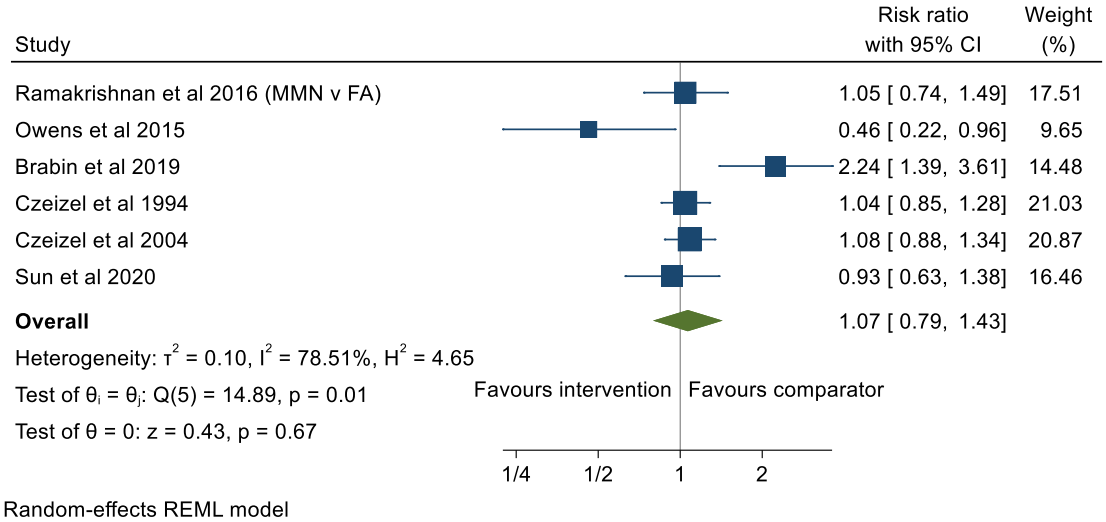
3.3. Preterm birth

3.3A. Interventions in nutrition – overall



Supplementary Figure 13. Meta-analysis of reported estimates: any general population-based nutritional intervention in the pre- and periconception period compared with FA supplementation, supplementation with other micronutrients (not FA), placebo, standard or routine care, or no intervention to prevent preterm birth.
6 studies, N=13,683: Ramakrishnan et al 2016 (MMN supplementation v FA supplementation) [3], Czeizel et al 1994 (MMN supplementation v supplement containing only copper, manganese, zinc and Vitamin C) [4], Czeizel et al 2004 (MMN supplementation v no supplementation) [5], Owens et al 2015 (MMN supplementation v placebo) [17], Brabin et al 2019 (IFA supplementation v FA supplementation) [7], Sun et al 2020 (100g mushroom daily v standard or routine care [normal diet]) [9].

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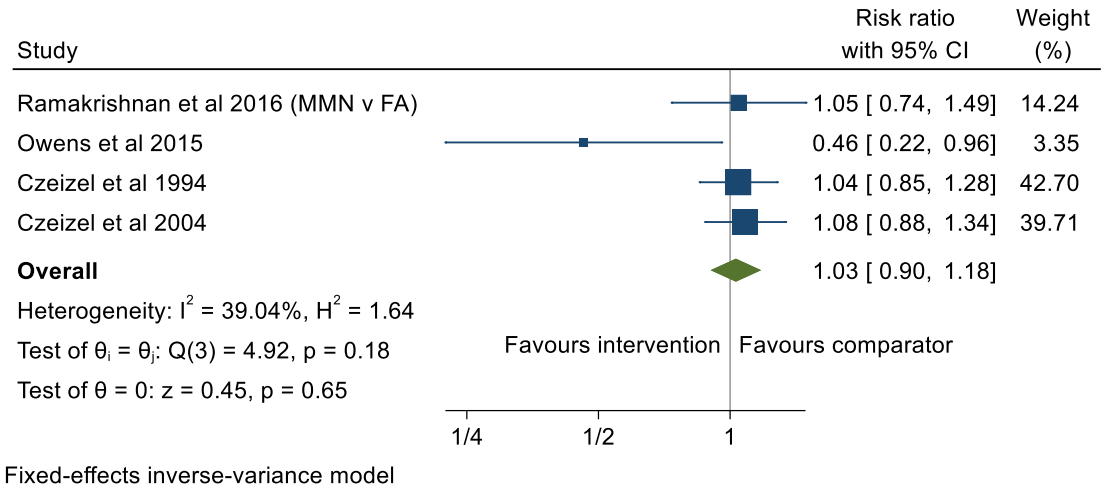
3.3B. Multiple micronutrient supplementation including IFA



Supplementary Figure 14. Meta-analysis of reported estimates: pre- and periconception MMN supplementation including IFA versus pre- and periconception FA supplementation, supplementation with other micronutrients (not FA), placebo or no intervention to prevent preterm birth.
4 studies, N=12,235: Ramakrishnan et al 2016 (MMN supplementation v FA supplementation) [3], Czeizel et al 1994 (MMN supplementation v supplement containing only copper, manganese, zinc and Vitamin C) [4], Czeizel et al 2004 (MMN supplementation v no supplementation) [5], Owens et al 2015 (MMN supplementation v placebo) [17].

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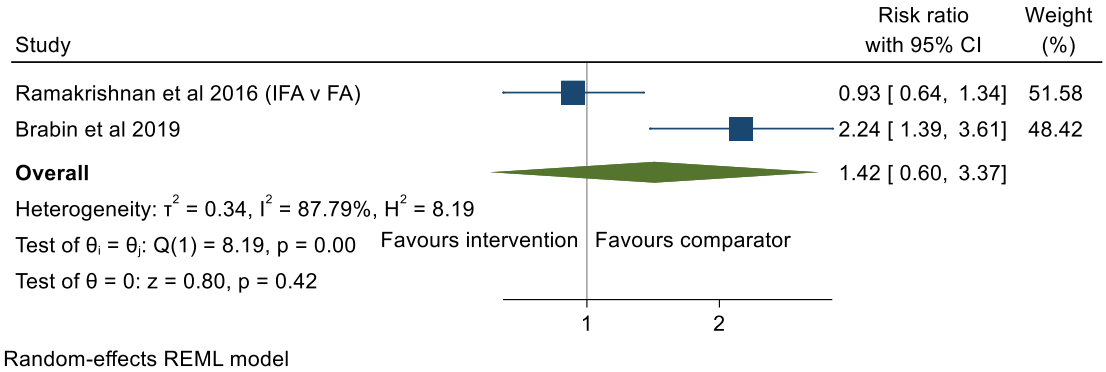
3.3C. Iron and folic acid supplementation



Supplementary Figure 15. Meta-analysis of reported estimates: pre- and periconception IFA supplementation versus pre- and periconception FA supplementation to prevent preterm birth.
2 studies, N=1360: Brabin et al 2019 (IFA supplementation v FA supplementation) [7], Ramakrishnan et al 2016 (IFA supplementation v FA supplementation) [3].

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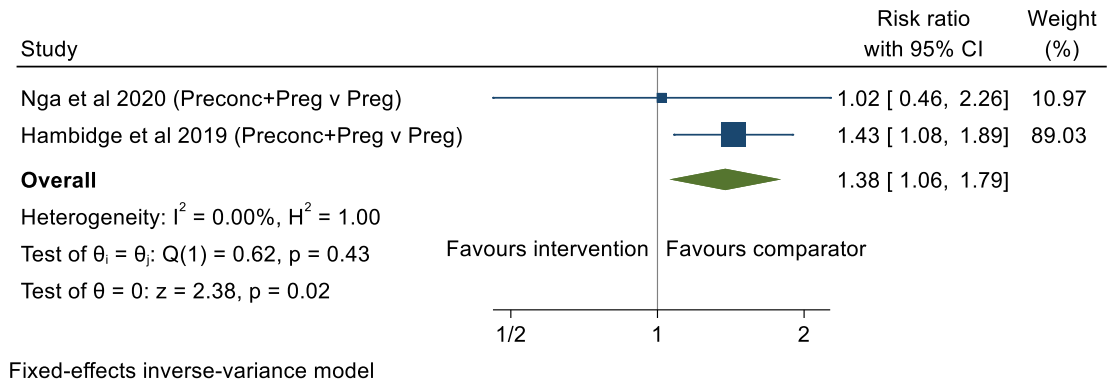
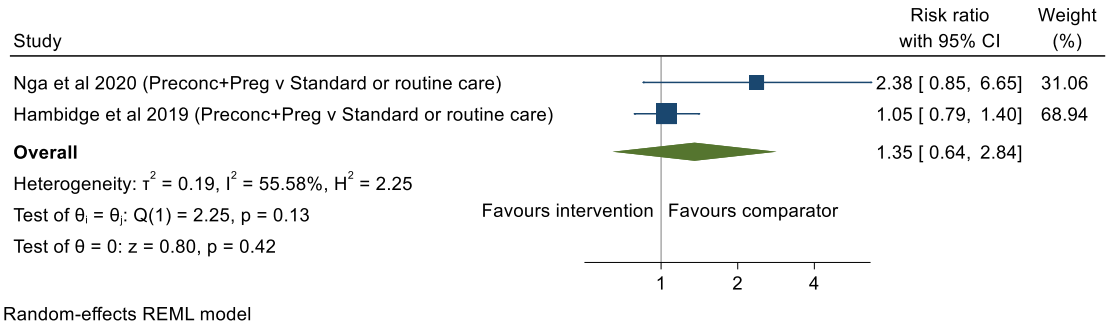
3.3D. Food supplementation



Supplementary Figure 16. Meta-analysis of reported estimates: preconception and pregnancy food supplementation versus pregnancy-only food supplementation to prevent preterm birth.
2 studies, N=1163: Nga et al 2020 (preconception throughout pregnancy food supplement containing dark-green leafy vegetables and animal source foods v pregnancy-only supplementation) [11], Hambidge et al 2019 (preconception throughout pregnancy Nutriset [and additional lipid-based protein energy supplement for women with BMI <20 kg/m^2 or gestational weight gain <Institute of Medicine recommendations] v pregnancy-only supplementation) [12].



Supplementary Figure 17. Meta-analysis of reported estimates: preconception and pregnancy food supplementation versus preconception and pregnancy standard or routine care to prevent preterm birth.
2 studies, N=1110: Nga et al 2020 (preconception throughout pregnancy food supplement containing dark-green leafy vegetables and animal source foods v standard or routine care) [11], Hambidge et al 2019 (preconception throughout pregnancy Nutriset [and additional lipid-based protein energy supplement for women with BMI <20 kg/m^2 or gestational weight gain <Institute of Medicine recommendations] v standard or routine care) [12].

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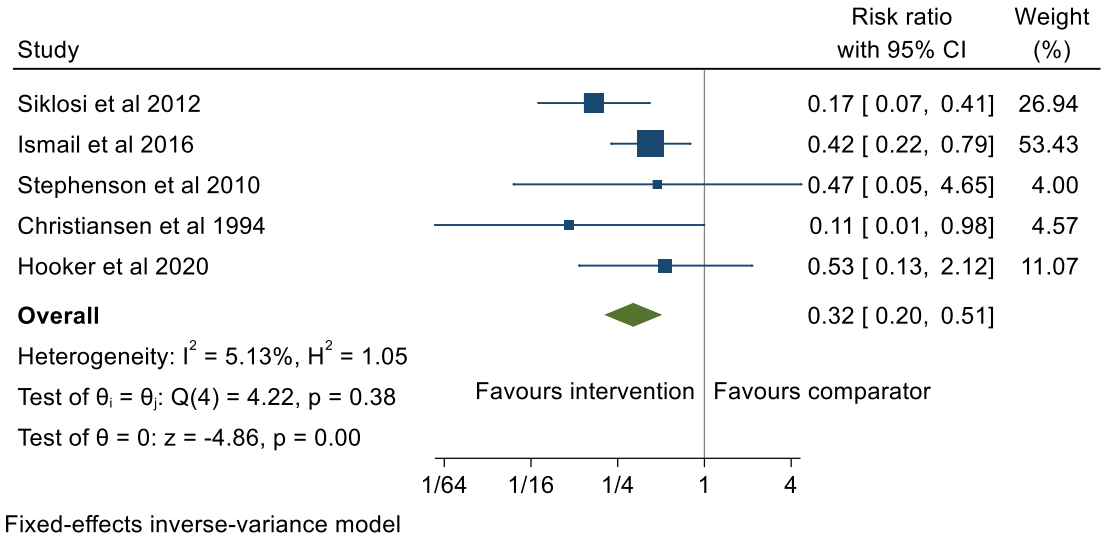
3.3E. Interventions to prevent adverse outcomes in early pregnancy

Early adverse pregnancy outcome interventions include studies aiming primarily to prevent miscarriage or other early adverse outcomes in subsequent pregnancies in populations of women with at least one previous miscarriage.



Supplementary Figure 18. Meta-analysis of reported estimates: pre- and periconception early adverse pregnancy outcome prevention interventions versus pre- and periconception placebo or no intervention to prevent preterm birth.

5 studies, N=382: Siklosi et al 2012 (clomiphene citrate v placebo; population: women with ≥3 previous miscarriages) [16], Ismail et al 2016 (oral aspirin + subcutaneous heparin v placebo; population: women with ≥2 previous miscarriages and antiphospholipid syndrome) [15], Hooker et al 2020 (intrauterine hyaluronic acid gel v no intervention following dilation and curettage; population: women with miscarriage undergoing dilation and curettage) [18], Stephenson et al 2010 (intravenous immunoglobulin v placebo [normal saline solution]; population: women with ≥3 consecutive previous miscarriages) [19], Christiansen et al 1994 (active immunization with third party leukocytes v placebo [participant's own blood, drawn immediately before transfusion]; population: women with ≥3 consecutive previous miscarriages) [20].

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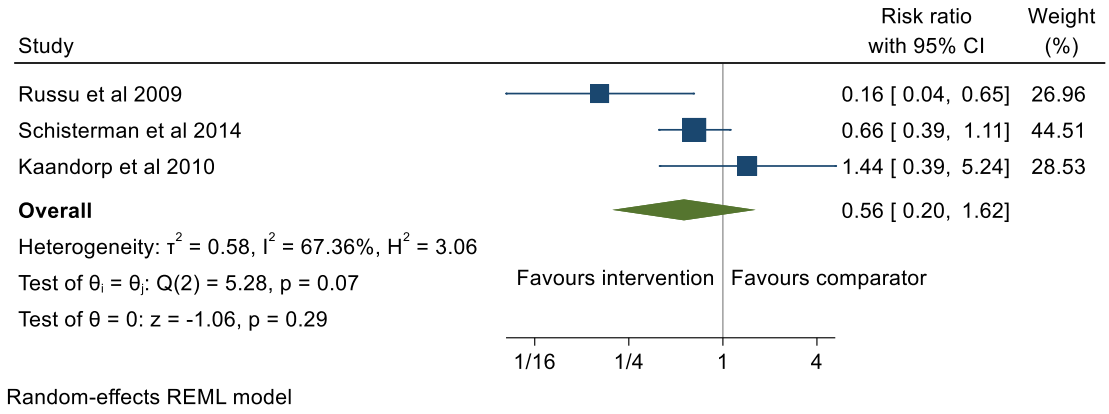

Supplementary Figure 19. Meta-analysis of reported estimates: preconception and pregnancy early adverse pregnancy outcome prevention interventions versus placebo and/or no intervention to prevent preterm birth.
3 studies, N=864: Russu et al 2009 (vaginal micronized progesterone v placebo [muscle relaxant]; population: women with 2 previous miscarriages) [21], Schisterman et al 2014 (oral aspirin v placebo; population: women with 1-2 previous miscarriages) [22], Kaandorp et al 2010 (oral aspirin or oral aspirin + subcutaneous heparin v placebo [for aspirin only]; population: women with ≥2 previous miscarriages) [23].

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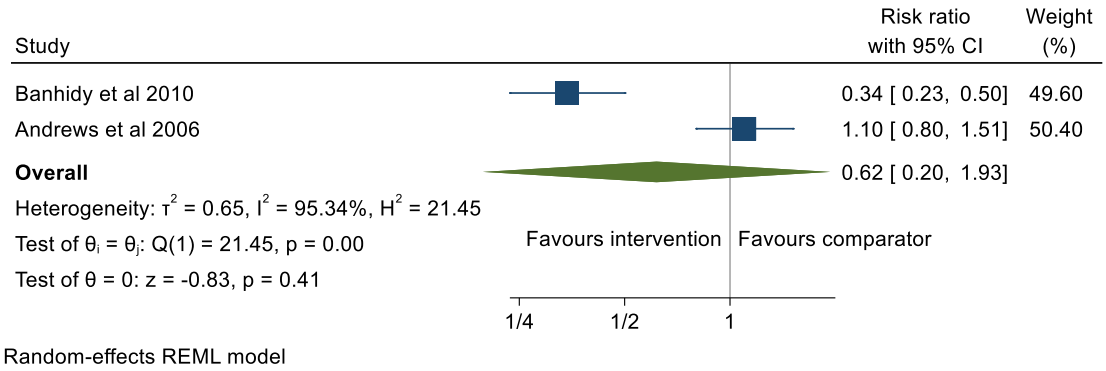
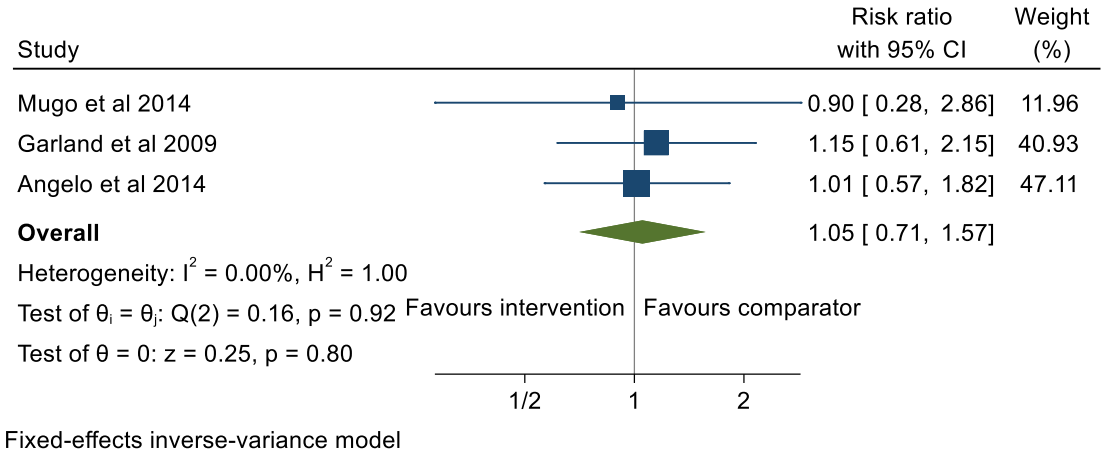
3.3F. Interventions to prevent or manage infectious diseases



Infectious disease interventions include studies examining interventions to prevent infectious diseases in the preconception period (e.g. HIV prevention or HPV vaccination), and studies examining interventions to manage infectious diseases in preconception (e.g. HIV management with ART).

Supplementary Figure 20. Meta-analysis of reported estimates: pre- and periconception infectious disease interventions versus placebo or no intervention to prevent preterm birth.
2 studies, N=2275: Andrews et al 2006 (azithromycin + metronidazole v placebo; population: women with a previous spontaneous preterm birth) [24], Banhidy et al 2010 (treatment of sexually transmitted diseases and/or vaginal candidiasis v no treatment; population: women with sexually transmitted diseases or vaginal candidiasis) [25].
Risk ratio for Andrews et al if restricted to spontaneous preterm births only: 1.12 (95% CI: 0.76, 0.64) (27/52 babies in intervention group and 26/56 in comparator group born spontaneously preterm).



Supplementary Figure 21. Meta-analysis of reported estimates: pre- and periconception infectious disease interventions versus pre- and periconception placebo or alternative intervention that may affect preterm birth.
4 studies, 3 included in meta-analyses (N=3666): Mugo et al 2014 (TDF+FTC or TDF v placebo; population: women with partners with HIV) [26], Garland et al 2009 (HPV vaccine [Gardasil] v placebo) [27], Angelo et al 2014 (HPV vaccine [Cervarix] v placebo or other vaccine) [28].

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Makanani et al 2018 (dapivirine vaginal ring v placebo vaginal ring), N=181: reported separately as no preterm birth cases [29]: 0/87 preterm births among women assigned to use a dapivirine vaginal ring (HIV PreP) pre- and periconceptionally compared with 9/94 preterm births among women assigned to a placebo ring (calculated RR: 0.06 [95% CI: 0.00, 0.96]) (Makanani et al 2018) [29].

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4. Preconception interventions to prevent low birth weight, preterm birth and small for gestational age: summary of estimates for all outcomes

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Supplementary Table 1. Summary of evidence from included studies – nutrition interventions for low birth weight.

Period	Any nutrition	MMN supplementation including IFA	IFA supplementation	FA supplementation	Food supplementation	Other nutritional
Pre- + Periconc	7 studies, N=13,973[3–9] Comp: FA, other micronutrients (not FA), standard care, no int Popn: 1 study: previous NTD birth RR: 1.07 (95% CI: 0.93, 1.23), I^2: 46.54% **GRADE: Very low certainty**	4 studies, N=12,054[3–6] Comp: FA, other micronutrients (not FA), no int Popn: 1 study: previous NTD birth RR: 1.06 (95% CI: 0.90, 1.25), I^2: 0.00% **GRADE: Low certainty**	3 studies, N=1831[3,7,8] RR: 0.74 (95% CI: 0.34, 1.61), I^2: 83.10% Int: 1 study: IFA+deworming Comp: FA, no int **GRADE: Very low certainty**	No studies	1 study, N=529[30] 5-7 months v 0-2 months Popn: Low-income OR: 0.40 (95% CI: 0.14, 1.12) *(No case ns to calculate assumed comparator risk & RR)* **GRADE: Very low certainty**	(1) 1 study, N=507[31] Popn: previous pre-eclampsia Calcium supp v placebo RR: 1.00 (95% CI: 0.76, 1.30) (2) 1 study, N=1162[9] Mushroom in diet v standard care RR: 0.79 (95% CI: 0.46, 1.35)
Preconc + Preg v Preg only int	3 studies, N=1334[10–12] RR: 0.68 (95% CI: 0.33, 1.43), I^2: 54.12% **GRADE: Very low certainty**	No studies	1 study, N=200[10] RR: 0.28 (95% CI: 0.08, 1.03) **GRADE: Very low certainty**	No studies	2 studies, N=1134[11,12] RR: 1.00 (95% CI: 0.79, 1.26), I^2: 0.00% **GRADE: Very low certainty**	No studies
Preconc + Preg v Other (specified)	NA	1 study, N=108[32] Comp: Placebo (Preconc) and IFA (Preg) RR: 0.05 (95% CI: 0.00, 0.82)	No studies	No studies	(1) 1 study, N=1360[33] High v Low nutrition value snack (Preconc+Preg) RR: 0.89 (95% CI: 0.76, 1.03) (2) 2 studies, N=1078[11,12] Comp: Standard care (Preconc+Preg) RR: 0.87 (95% CI: 0.72, 1.04), I^2: 0.00	No studies

NTD: Neural tube defect, MMN: Multiple micronutrient, IFA: Iron and folic acid, FA: Folic acid, Supp: Supplementation, Preconc: Preconception, Periconc: Periconception, Preg: Pregnancy, Int: Intervention, Comp: Comparator, Popn: Population, No int: No intervention, Standard care: Standard or routine care, RR: relative risk, 95% CI: 95% confidence interval.
Grey shaded and yellow shaded cells indicate statistically notable results (95% CIs not overlapping 1) from single studies and meta-analyses respectively.

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Supplementary Table 2. Summary of evidence from included studies – health and social interventions for low birth weight.

	Health interventions				Social interventions
Period	**General health**	**Prevention of early adverse pregnancy outcomes**	**Prevention or management of non-communicable disease**	**Prevention or management of infectious disease**	**Reproductive planning**
Pre- + Periconc	2 studies, N=1188[13,14] Popn: Low income Int: Preconc health care Comp: Standard care RR: 1.27 (95% CI: 0.83, 1.94), I^2: 39.11% **GRADE: Very low certainty**	1 study, N=82[16] Popn: Previous miscarriage Clomiphene citrate v placebo RR: 0.23 (95% CI: 0.11, 0.51) **GRADE: Very low certainty**	No studies	1 study, N=39[34] H1N1 vaccine v placebo RR: 4.96 (95% CI: 0.27, 89.87) **GRADE: Very low certainty**	No studies
Preconc + Preg v Preg only int	No studies	No studies	1 study, N=149[35] Popn: T1DM Int: Intensive DM management RR: 4.34 (95% CI: 0.55, 34.34) **GRADE: Very low certainty**	1 study, N=186[36] Popn: HIV Int: Antiretroviral therapy RR: 2.65 (95% CI: 1.20, 5.81) **GRADE: Very low certainty**	No studies
Preconc + Preg v Other (specified)	1 study, N=349[37] Int: Integrated preconc and antenatal care Comp: Standard care (Preconc+Preg) RR: 0.44 (95% CI: 0.19, 0.97)	1 study, N=69[21] Popn: Previous miscarriage Int: Vaginal micronized progesterone Comp: Placebo (Preconc+Preg) RR: 0.09 (95% CI: 0.01, 0.65)	1 study, N=134[35] Popn: T1DM Int: Intensive DM management Preconc+Preg; 40 v 7 months Preconc RR: 1.60 (95% CI: 0.35, 7.37)	1 study, N=196[38] Popn: HIV Int: Isoniazid Comp: Placebo (Preconc+Preg), Outcome: Composite including LBW RR: 0.72 (95% CI: 0.43, 1.05)	No studies

DM: Diabetes mellitus, T1DM: Type 1 diabetes mellitus, Preconc: Preconception, Periconc: Periconception, Preg: Pregnancy, Int: Intervention, Comp: Comparator, Popn: Population, Standard care: Standard or routine care, RR: relative risk, 95% CI: 95% confidence interval.
Grey shaded and yellow shaded cells indicate statistically notable results (95% CIs not overlapping 1) from single studies and meta-analyses respectively.

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Supplementary Table 3. Summary of evidence from included studies – nutrition interventions for birth weight.

Period	Any nutrition	MMN supplementation including IFA	IFA supplementation	FA supplementation	Food supplementation	Other nutritional
Pre- + Periconc	8 studies, N=15,040[3–5,7–9,39,40] Comp: FA, other micronutrients (not FA), standard care, placebo, no int MD: -13.98g (95% CI: -51.69, 23.74), I^2: 67.42%	4 studies, N=11,926[3–5,39] Comp: FA, other micronutrients (not FA), placebo, no int MD: -18.26g (95% CI: -62.15, 25.62), I^2: 74.28%	3 studies, N=1831[3,7,8] Int: 1 study: IFA+deworming Comp: FA, no int MD: 6.59g (95% CI: -116.54, 129.72), I^2: 81.09%	1 study, N=234[41] Popn: Oral cleft, previous oral cleft birth 4mg FA v 0.4 mg FA MD: -69g (SE: 62)	1 study, N=529[30] Popn: low-income 5-7 months v 0-2 months MD: 131g (SE: 43)	(1) 1 study, N=1195[40] Iodine supp v no supp MD: 200g (SE: 283) (2) 1 study, N=1162[9] Mushroom in diet v standard care MD: -4g (SE: 23) (3) 1 study, N=551[40] Iodine supp Preconc v Preg MD: 0g (SE: 283)
Preconc + Preg v Preg only int	3 studies, N=1971[10–12] MD: 7.03g (95% CI: -30.19, 44.25), I^2: 10.66%	No studies	1 study, N=200[10] MD: 81g (SE: 53)	No studies	2 studies, N=1771[11,12] MD: -3.76g (95% CI: -43.60, 36.08), I^2: 0.00%	No studies
Preconc + Preg v Other (specified)	NA	2 studies, N=127[32,42] Comp: Placebo (Preconc+Preg), Placebo (Preconc) and IFA (Preg) MD: 295.96g (95% CI: 158.55, 433.37), I^2: 0.00%	No studies	No studies	(1) 1 study, N=1360[33] High v Low nutrition value snack (Preconc+Preg) MD: 26g (SE: 21) (2) 2 studies, N=1745[11,12] Comp: Standard care (Preconc+Preg) MD: 41.86g (95% CI: 1.36, 82.37), I^2: 0.00	No studies

MMN: Multiple micronutrient, IFA: Iron and folic acid, FA: Folic acid, Supp: Supplementation, Preconc: Preconception, Periconc: Periconception, Preg: Pregnancy, Int: Intervention, Comp: Comparator, Popn: Population, No int: No intervention, Standard care: Standard or routine care, MD: mean difference, 95% CI: 95% confidence interval, SE: standard error.
Yellow shaded cells indicate statistically notable results (95% CIs not overlapping 0) from meta-analyses.

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Supplementary Table 4. Summary of evidence from included studies – health and social interventions for birth weight.

	Health interventions				Social interventions
Period	**General health**	**Prevention of early adverse pregnancy outcomes**	**Prevention or management of non-communicable disease**	**Prevention or management of infectious disease**	**Reproductive planning**
Pre- + Periconc	1 study, N=781[13] Popn: Low income Int: Preconc health care Comp: Standard care MD: -97g (SE: 36)	3 studies, N=269[15,18,20] Popn: Previous miscarriage, 1 study: APS Aspirin + heparin v placebo, Intrauterine hyaluronic acid gel v no int post D&C, Third party leukocytes transfusion v placebo MD: 279.46g (95% CI: -292.95, 851.87), I^2: 91.80%	1 study, N=157[43] Popn: T1DM or T2DM Counseling session for DM v standard care MD: 99g (SE: 139)	1 study, N=108[44] Popn: Previous PTB Azithromycin+Metronidazole v placebo MD: -418g (SE: 220)	No studies
Preconc + Preg v Preg only int	No studies	No studies	1 study, N=149[35] Popn: T1DM Int: Intensive DM management MD: 45g (SE: 112)	No studies	No studies
Preconc + Preg v Other (specified)	No studies	2 studies, N=664[21,22] Popn: Previous miscarriage Int: Aspirin, Vaginal micronized progesterone Comp: Placebo (Preconc+Preg) MD: 299.67g (95% CI: -294.28, 893.61), I^2: 93.75%	(1) 1 study, N=134[35] Popn: T1DM Int: Intensive DM management Preconc+Preg; 40 v 7 months Preconc MD: -21g (SE:126) (2) 1 study, N=25[45] Popn: T1DM Int: Continuous glucose monit Comp: Standard care (Preconc+Preg) MD: -327g (SE: 244) (3) 2 studies, N=289[46,47] Popn: Overweight/obese and/or previous GDM Int: Lifestyle change counseling Comp: Standard care (Preconc+Preg) MD: -81.15g (95% CI: -205.97, 43.67), I^2: 0.00%	No studies	No studies

DM: Diabetes mellitus, T1DM: Type 1 diabetes mellitus, T2DM: Type 2 diabetes mellitus, GDM: Gestational diabetes mellitus, APS: Antiphospholipid syndrome, D&C: Dilation and curettage, Continuous glucose monit: Continuous glucose monitoring, Preconc: Preconception, Periconc: Periconception, Preg: Pregnancy, Int: Intervention, Comp: Comparator, Popn: Population, Standard care: Standard or routine care. MD: mean difference, 95% CI: 95% confidence interval, SE: standard error.
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Supplementary Table 5. Summary of evidence from included studies – nutrition interventions for small for gestational age.

Period	Any nutrition	MMN supplementation including IFA	IFA supplementation	FA supplementation	Food supplementation	Other nutritional
Pre- + Periconc	2 studies, N=1361[3,7] Comp: FA RR: 0.92 (95% CI: 0.73, 1.15), I^2: 0.00% **GRADE: Low certainty**	1 study, N=1084[3] Comp: FA RR: 1.02 (95% CI: 0.74, 1.40) **GRADE: Very low certainty**	2 studies, N=1351[3,7] Comp: FA RR: 0.83 (95% CI: 0.66, 1.05), I^2: 0.00% **GRADE: Low certainty**	No studies	No studies	No studies
Preconc + Preg v Preg only int	No studies	No studies	No studies	No studies	2 studies, N=1161[11,12] RR: 0.89 (95% CI: 0.78, 1.02), I^2: 0.00% **GRADE: Low certainty**	No studies
Preconc + Preg v Other (specified)	NA	No studies	No studies	No studies	(1) 1 study, N=1360[33] High v Low nutrition value snack (Preconc+Preg) RR: 0.96 (95% CI: 0.88, 1.04) (2) 2 studies, N=1108[11,12] Comp: Standard care (Preconc+Preg) RR: 0.78 (95% CI: 0.70, 0.88), I^2: 0.00%	No studies

MMN: Multiple micronutrient, IFA: Iron and folic acid, FA: Folic acid, Supp: Supplementation, Preconc: Preconception, Periconc: Periconception, Preg: Pregnancy, Int: Intervention, Comp: Comparator, Popn: Population, No int: No intervention, Standard care: Standard or routine care, RR: relative risk, 95% CI: 95% confidence interval.
Grey shaded and yellow shaded cells indicate statistically notable results (95% CIs not overlapping 1) from single studies and meta-analyses respectively.

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Supplementary Table 6. Summary of evidence from included studies – health and social interventions for small for gestational age.

Period	Health interventions				Social interventions
	General health	**Prevention of early adverse pregnancy outcomes**	**Prevention or management of non-communicable disease**	**Prevention or management of infectious disease**	**Reproductive planning**
Pre- + Periconc	1 study, N=760[13] Popn: Low income Int: Preconc health care Comp: Standard care RR: 1.13 (95% CI: 0.57, 2.14) **GRADE: Very low certainty**	2 studies, N=208[15,16] Popn: Previous miscarriage, 1 study: APS Clomiphene citrate v placebo, Aspirin + heparin v placebo RR: 0.35 (95% CI: 0.18, 0.68), I^2: 0.00% **GRADE: Low certainty**	No studies	1 study, N=2871[27] HPV vaccine v placebo RR: 1.23 (95% CI: 0.33, 4.57) **GRADE: Very low certainty**	No studies
Preconc + Preg v Preg only int	No studies	No studies	No studies	No studies	No studies
Preconc + Preg v Other (specified)	No studies	1 study, N=200[23] Popn: Previous miscarriage Int: Aspirin or Aspirin + heparin Comp: Placebo + standard care (Preconc+Preg) RR: 1.40 (95% CI: 0.52, 3.77)	(1) 1 study, N=25 (no SGA cases)[45] Popn: T1DM Int: Continuous glucose monit Comp: Standard care (Preconc+Preg) RR: 1.45 (95% CI: 0.03, 67.95) (2) 1 study, N=161[46] Popn: Overweight/obese Int: Lifestyle change counseling Comp: Standard care (Preconc+Preg) RR: 5.37 (95% CI: 0.67, 29.82)	No studies	No studies

T1DM: Type 1 diabetes mellitus, APS: Antiphospholipid syndrome, Continuous glucose monit: Continuous glucose monitoring, Preconc: Preconception, Periconc: Periconception, Preg: Pregnancy, Int: Intervention, Comp: Comparator, Popn: Population, Standard care: Standard or routine care, RR: relative risk, 95% CI: 95% confidence interval.

Grey shaded and yellow shaded cells indicate statistically notable results (95% CIs not overlapping 1) from single studies and meta-analyses respectively.

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Supplementary Table 7. Summary of evidence from included studies – nutrition interventions for birth weight for gestational age.

Period	Any nutrition	MMN supplementation including IFA	IFA supplementation	FA supplementation	Food supplementation	Other nutritional
Pre- + Periconc	No studies	No studies	No studies	No studies	No studies	No studies
Preconc + Preg v Preg only int	No studies	No studies	No studies	No studies	No studies	No studies
Preconc + Preg v Other (specified)	NA	No studies	No studies	No studies	No studies	No studies

Preconc: Preconception, Periconc: Periconception, Preg: Pregnancy.

Supplementary Table 8. Summary of evidence from included studies – health and social interventions for birth weight for gestational age.

	Health interventions				Social interventions
Period	**General health**	**Prevention of early adverse pregnancy outcomes**	**Prevention or management of non-communicable disease**	**Prevention or management of infectious disease**	**Reproductive planning**
Pre- + Periconc	No studies	No studies	No studies	No studies	No studies
Preconc + Preg v Preg only int	No studies	No studies	No studies	No studies	No studies
Preconc + Preg v Other (specified)	No studies	No studies	(1) 1 study, N=25[45] Popn: T1DM Int: Continuous glucose monit Comp: Standard care (Preconc+Preg) MD: -3.90 centiles (SE: 4.48) (2) 1 study, N=161[46] Popn: Overweight/obese Int: Lifestyle change counseling Comp: Standard care MD: -0.10 centiles (SE: 0.15)	No studies	No studies

T1DM: Type 1 diabetes mellitus, Continuous glucose monit: Continuous glucose monitoring, Preconc: Preconception, Periconc: Periconception, Preg: Pregnancy, Int: Intervention, Comp: Comparator, Popn: Population, Standard care: Standard or routine care, MD: mean difference, 95% CI: 95% confidence interval, SE: standard error.
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Supplementary Table 9. Summary of evidence from included studies – nutrition interventions for preterm birth.

Period	Any nutrition	MMN supplementation including IFA	IFA supplementation	FA supplementation	Food supplementation	Other nutritional
Pre- + Periconc	6 studies, N=13,683[3–5,7,9,17] Comp: FA, other micronutrients (not FA), standard care, placebo, no int RR: 1.07 (95% CI: 0.79, 1.43), I^2: 78.51%) **GRADE: Very low certainty**	4 studies, N=12,235[3–5,17] Comp: FA, other micronutrients (not FA), placebo, no int RR: 1.03 (95% CI: 0.90, 1.18), I^2: 39.04% **GRADE: Low certainty**	2 studies, N=1360[3,7] Comp: FA RR: 1.42 (95% CI: 0.60, 3.37), I^2: 87.79% **GRADE: Very low certainty**	No studies	No studies	(1) 1 study, N=579[31] Popn: Previous pre-eclampsia Calcium supp v placebo RR: 0.90 (95% CI: 0.74, 1.10) (2) 1 study, N=1162[9] Mushroom in diet v standard care RR: 0.93 (95% CI: 0.63, 1.38)
Preconc + Preg v Preg only int	No studies	No studies	No studies	No studies	2 studies, N=1163[11,12] RR: 1.38 (95% CI: 1.06, 1.79), I^2: 0.00% **GRADE: Very low certainty**	No studies
Preconc + Preg v Other (specified)	NA	1 study, N=112[48] Comp: Placebo (Preconc) and IFA (Preg) RR: 0.32 (95% CI: 0.07, 1.53)	No studies	No studies	(1) 1 study, N=1360[33] High v Low nutrition value snack (Preconc+Preg) RR: 1.08 (95% CI: 0.81, 1.43) (2) 2 studies, N=1110[11,12] Comp: Standard care (Preconc+Preg) RR: 1.35 (95% CI: 0.64, 2.84), I^2: 55.58%	1 study, N=17,373[49] Vit A supp or B carotene v Placebo (Preconc+Preg) Vit A prevalence: 314/1000 pregnancies B carotene prevalence: 284/1000 pregnancies Placebo prevalence: 282/1000 pregnancies

MMN: Multiple micronutrient, IFA: Iron and folic acid, FA: Folic acid, Supp: Supplementation, Preconc: Preconception, Periconc: Periconception, Preg: Pregnancy, Int: Intervention, Comp: Comparator, Popn: Population, No int: No intervention, Standard care: Standard or routine care, RR: relative risk, 95% CI: 95% confidence interval.

Grey shaded and yellow shaded cells indicate statistically notable results (95% CIs not overlapping 1) from single studies and meta-analyses respectively.

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Supplementary Table 10. Summary of evidence from included studies – health and social interventions for preterm birth.

	Health interventions				Social interventions
Period	**General health**	**Prevention of early adverse pregnancy outcomes**	**Prevention or management of non-communicable disease**	**Prevention or management of infectious disease**	**Reproductive planning**
Pre- + Periconc	(1) 1 study, N=786[13] Popn: Low income Int: Preconc health care Comp: Standard care RR: 1.41 (95% CI: 0.74, 2.69) **GRADE: Very low certainty** (2) 1 study, N=1816[50] Int: Preconc counselling Comp: Standard care Outcome: Composite including PTB RR: 0.96 (95% CI: 0.81, 1.14)	5 studies, N=382[15,16,18–20] Popn: Previous miscarriage, 1 study: APS Clomiphene citrate v placebo, Aspirin + heparin v placebo, Intrauterine hyaluronic acid gel v no int post D&C, Intravenous immunoglobulin v placebo, Third party leukocytes transfusion v placebo RR: 0.32 (95% CI: 0.20, 0.51), I^2: 5.13% **GRADE: Very low certainty**	No studies	(1) 2 studies, N=2275[25,44] Specific aim: reduce PTB Popn: 1 study: previous PTB Azithromycin+Metronidazole v placebo, Treatment of STD/VC v no int RR: 0.62 (95% CI: 0.20, 1.93), I^2: 95.34% **GRADE: Very low certainty** (2) 3 studies, N=3666[26–28] Popn: 1 study: partner with HIV HIV PreP (TDF or TDF+FTC) v placebo, HPV vaccine v placebo, HPV vaccine v placebo or alternative int RR: 1.05 (95% CI: 0.71, 1.57), I^2: 0.00% **GRADE: Very low certainty** (3) 1 study, N=181 (no PTB cases)[29] Dapivirine vaginal ring HIV PreP v placebo RR: 0.06 (95% CI: 0.00, 0.96) **GRADE: Very low certainty**	1 study, N=1140[51] Comp: Standard care RR: 0.79 (95% CI: 0.63, 0.99) **GRADE: Very low certainty**
Preconc + Preg v Preg only int	No studies	No studies	No studies	No studies	No studies
Preconc + Preg v Other (specified)	1 study, N=364[37] Int: Integrated preconc and antenatal care Comp: Standard care RR: 0.33 (95% CI: 0.13, 0.77)	3 studies, N=864[21–23] Popn: Previous miscarriage Int: Aspirin or Aspirin + heparin, Aspirin, Vaginal micronized progesterone Comp: Placebo and/or standard care (Preconc+Preg) RR: 0.56 (95% CI: 0.20, 1.62), I^2: 67.36%	(1) 1 study, N=25[45] Popn: T1DM Int: Continuous glucose monit Comp: Standard care (Preconc+Preg) RR: 1.88 (95% CI: 0.66, 5.32) (2) 1 study, N=161[46] Popn: Overweight/obese Int: Lifestyle change counseling Comp: Standard care (Preconc+Preg) RR: 1.37 (95% CI: 0.44, 3.85)	1 study, N=196[38] Popn: HIV Int: Isoniazid Comp: Placebo (Preconc+Preg), Outcome: Composite including PTB RR: 0.72 (95% CI: 0.43, 1.05)	No studies

PTB: Preterm birth, T1DM: Type 1 diabetes mellitus, APS: Antiphospholipid syndrome, D&C: Dilation and curettage, TDF: Tenofovir disoproxil fumarate, FTC: Emtricitabine, STD: Sexually transmitted disease, VC: Vaginal Candidiasis, Continuous glucose monit: Continuous glucose monitoring, Preconc:

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Preconception, Periconc: Periconception, Preg: Pregnancy, Int: Intervention, Comp: Comparator, Popn: Population, Standard care: Standard or routine care, RR: relative risk, 95% CI: 95% confidence interval.
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Supplementary Table 11. Summary of evidence from included studies – nutrition interventions for gestational age.

Period	Any nutrition	MMN supplementation including IFA	IFA supplementation	FA supplementation	Food supplementation	Other nutritional
Pre- + Periconc	5 studies, N=12,212[3–5,7,39] Comp: FA, other micronutrients (not FA), placebo, no int MD: -0.01wk (95% CI: -0.07, 0.05), I^2: 36.82%	4 studies, N=11,926[3–5,39] Comp: FA, other micronutrients (not FA), placebo, no int MD: 0.00wk (95% CI: -0.06, 0.06), I^2: 0.00%	2 studies, N=1360[3,7] Comp: FA MD: -0.32wk (95% CI: -1.05, 0.40), I^2: 81.58%	1 study, N=231[41] Popn: Oral cleft, previous oral cleft birth 4mg FA v 0.4 mg FA MD: 0.1wk (SE: 0.2)	1 study, N=533[30] Popn: Low income 5-7 months v 0-2 months MD: 0.1wk (SE: 0.2)	No studies
Preconc + Preg v Preg only int	No studies	No studies	No studies	No studies	1 study, N=157[11] MD: 0.1wk (SE: 0.3)	No studies
Preconc + Preg v Other (specified)	NA	1 study, N=112[32] Comp: Placebo (Preconc) and IFA (Preg) MD: 1.7wk (SE: 1.2)	No studies	No studies	(1) 1 study, N=1360[33] High v Low nutrition value snack (Preconc+Preg) MD: -0.10wk (SE: 0.08) (2) 1 study, N=162[11] Comp: Standard care (Preconc+Preg) MD: -0.5wk (SE: 0.3)	No studies

MMN: Multiple micronutrient, IFA: Iron and folic acid, FA: Folic acid, Supp: Supplementation, Preconc: Preconception, Periconc: Periconception, Preg: Pregnancy, Int: Intervention, Comp: Comparator, Popn: Population, No int: No intervention, Standard care: Standard or routine care, MD: mean difference, 95% CI: 95% confidence interval, SE: standard error.
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Supplementary Table 12. Summary of evidence from included studies – health and social interventions for gestational age.

Period	Health interventions				Social interventions
	General health	**Prevention of early adverse pregnancy outcomes**	**Prevention or management of non-communicable disease**	**Prevention or management of infectious disease**	**Reproductive planning**
Pre- + Periconc	1 study, N=786[13] Popn: Low income Int: Preconc health care Comp: Standard care MD: -0.2wk (SE: 0.1)	2 studies, N=230[15,18] Popn: Previous miscarriage, 1 study: APS Aspirin + heparin v placebo, Intrauterine hyaluronic acid gel v no int post D&C MD: 1.56wk (95% CI: -3.44, 6.55), I^2: 99.21%	1 study, N=157[43] Popn: T1DM or T2DM Counseling session for DM v standard care MD: -0.4wk (SE: 0.4)	1 study, N=124[44] Popn: Previous PTB Azithromycin+Metronidazole v placebo MD: -2.4wk (SE: 1.3)	No studies
Preconc + Preg v Preg only int	No studies	No studies	1 study, N=149[35] Popn: T1DM Int: Intensive DM management MD: -0.9wk (SE: 0.3)	No studies	No studies
Preconc + Preg v Other (specified)	No studies	2 studies, N=795[22,23] Popn: Previous miscarriage Int: Aspirin or Aspirin + heparin v placebo, Aspirin v placebo Comp: Placebo and/or standard care (Preconc+Preg) MD: -0.30wk (95% CI: -0.98, 0.38), I^2: 75.27%	(1) 1 study, N=134[35] Popn: T1DM Int: Intensive DM management Preconc+Preg; 40 v 7 months Preconc MD: -1.1wk (SE: 0.3) (2) 1 study, N=25[45] Popn: T1DM Int: Continuous glucose monit Comp: Standard care (Preconc+Preg) MD: -0.6wk (SE: 0.4)	No studies	No studies

DM: Diabetes mellitus, T1DM: Type 1 diabetes mellitus, T2DM: Type 2 diabetes mellitus, GDM: Gestational diabetes mellitus, APS: Antiphospholipid syndrome, D&C: Dilation and curettage, TDF: Tenofovir disoproxil fumarate, FTC: Emtricitabine, Continuous glucose monit: Continuous glucose monitoring, Preconc: Preconception, Periconc: Periconception, Preg: Pregnancy, Int: Intervention, Comp: Comparator, Popn: Population, Standard care: Standard or routine care, MD: mean difference, 95% CI: 95% confidence interval, SE: standard error.
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Supplementary Table 13. Summary of evidence from included studies – nutrition interventions for birth defects.

Period	Any nutrition	MMN supplementation including IFA	IFA supplementation	FA supplementation	Food supplementation	Other nutritional
Pre- + Periconc	(1) 10 studies, N=313,312[5,6,52–59] Popn: 6 studies: previous NTD birth Int: MMN including IFA, or FA Comp: MMN no FA, other micronutrients (not FA), placebo, no int RR: 0.37 (95% CI: 0.24, 0.55), I^2: 74.33% (2) 1 study, N=222,314[60] Dataset already included in (1) for different birth defect Comp: No int RR: 0.59 (95% CI: 0.33, 1.07)	6 studies, N=63,914[5,6,52–55] Popn: 3 studies: previous NTD birth Comp: MMN no FA, no int RR: 0.37 (95% CI: 0.22, 0.61), I^2: 63.89%	1 study, N=437[61] Comp: FA RR: 0.07 (95% CI: 0.00, 1.21)	(1) 4 studies, N=249,398[56–59] Popn: 3 studies: previous NTD birth Int: FA or MMN containing FA Comp: MMN no FA, other micronutrients (not FA), placebo, no int RR: 0.38 (95% CI: 0.18, 0.77), I^2: 77.58% (2) 1 study, N=222,314[60] Dataset already included in (1) for different birth defect Comp: No int RR: 0.59 (95% CI: 0.33, 1.07) (3) 1 study, N=213[62] Popn: Previous NTD birth Pre + periconc only v Early preg only FA RR: 0.13 (95% CI: 0.01, 2.34) (4) 1 study, N=224[41] Popn: Oral cleft or previous oral cleft birth 4mg FA v 0.4mg FA RR: 0.59 (95% CI: 0.10, 3.45)	No studies	No studies
Preconc + Preg v Preg only int	No studies	No studies	No studies	No studies	No studies	No studies
Preconc + Preg v Other (specified)	NA	No studies	No studies	No studies	No studies	No studies

NTD: Neural tube defect, MMN: Multiple micronutrient, IFA: Iron and folic acid, FA: Folic acid, Supp: Supplementation, Preconc: Preconception, Periconc: Periconception, Preg: Pregnancy, Int: Intervention, Comp: Comparator, Popn: Population, No int: No intervention, Standard care: Standard or routine care, RR: relative risk, 95% CI: 95% confidence interval.
Grey shaded and yellow shaded cells indicate statistically notable results (95% CIs not overlapping 1) from single studies and meta-analyses respectively.

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Supplementary Table 14. Summary of evidence from included studies – health and social interventions for birth defects.

Period	Health interventions				Social interventions
	General health	**Prevention of early adverse pregnancy outcomes**	**Prevention or management of non-communicable disease**	**Prevention or management of infectious disease**	**Reproductive planning**
Pre- + Periconc	1 study, N=786[13] Popn: Low income Int: Preconc health care Comp: Standard care RR: 2.51 (95% CI: 0.49, 12.87)	1 study, N=39[20] Popn: Previous miscarriage Third party leukocytes transfusion v placebo RR: 0.34 (95% CI: 0.02, 5.01)	1 study, N=187[43] Popn: T1DM or T2DM Counseling session for DM v standard care RR: 0.25 (95% CI: 0.04, 1.88)	4 studies, N=5300[26,27,29,63] Popn: 1 study: partner with HIV Dapivirine vaginal ring HIV PreP v placebo, HPV vaccine v placebo (2 studies), HIV PreP (TDF or TDF+FTC) v placebo, RR: 1.36 (95% CI: 0.93, 1.99), I^2: 0.00%	No studies
Preconc + Preg v Preg only int	No studies	No studies	1 study, N=149[35] Popn: T1DM Int: Intensive DM management RR: 0.15 (95% CI: 0.02, 1.35)	No studies	No studies
Preconc + Preg v Other (specified)	No studies	2 studies, N=269[21,23] Popn: Previous miscarriage Int: Aspirin or Aspirin + heparin, Vaginal micronized progesterone Comp: Placebo and/or standard care (Preconc+Preg) RR: 1.19 (95% CI: 0.34, 4.10), I^2: 42.91%	(1) 1 study, N=134[35] Popn: T1DM Int: Intensive DM management Preconc+Preg; 40 v 7 months Preconc RR: 0.11 (95% CI: 0.01, 0.99) (2) 1 study, N=25 (no BD cases)[45] Popn: T1DM Int: Continuous glucose monit Comp: Standard care (Preconc+Preg) RR: 1.45 (95% CI: 0.03, 67.95) (3) 2 studies, N=297[46,47] Popn: Overweight/obese and/or previous GDM Int: Lifestyle change counseling Comp: Standard care (Preconc+Preg) RR: 1.04 (95% CI: 0.37, 2.96), I^2: 0.00%	1 study, N=196[38] Popn: HIV Int: Isoniazid Comp: Placebo (Preconc+Preg), Outcome: Composite including BD RR: 0.72 (95% CI: 0.43, 1.05)	No studies

BD: Birth defects, DM: Diabetes mellitus, T1DM: Type 1 diabetes mellitus, T2DM: Type 2 diabetes mellitus, GDM: Gestational diabetes mellitus, TDF: Tenofovir disoproxil fumarate, FTC: Emtricitabine, Continuous glucose monit: Continuous glucose monitoring, Preconc: Preconception, Periconc: Periconception, Preg: Pregnancy, Int: Intervention, Comp: Comparator, Popn: Population, Standard care: Standard or routine care, RR: relative risk, 95% CI: 95% confidence interval.

Grey shaded and yellow shaded cells indicate statistically notable results (95% CIs not overlapping 1) from single studies and meta-analyses respectively.

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Supplementary Table 15. Summary of evidence from included studies – nutrition interventions for stillbirth.

Period	Any nutrition	MMN supplementation including IFA	IFA supplementation	FA supplementation	Food supplementation	Other nutritional
Pre- + Periconc	5 studies, N=12,684[4–6,31,57] Popn: 2 studies: previous NTD birth, 1 study: previous pre-eclampsia Comp: MMN no FA, other micronutrients (not FA), placebo, no int RR: 0.83 (95% CI: 0.57, 1.21), I^2: 0.00%	3 studies, N=11,844[4–6] Popn: 1 study: previous NTD birth Comp: Other micronutrients (not FA), no int RR: 1.03 (95% CI: 0.56, 1.90), I^2: 0.00%	1 study, N=437[61] Comp: FA RR: 0.68 (95% CI: 0.34, 1.37)	1 study, N=261[57] Popn: Previous NTD birth Int: FA or MMN containing FA Comp: MMN no FA RR: 0.10 (95% CI: 0.01, 2.14)	No studies	1 study, N=579[31] Popn: Previous pre-eclampsia Calcium supp v placebo RR: 0.78 (95% CI: 0.48, 1.27)
Preconc + Preg v Preg only int	No studies	No studies	No studies	No studies	No studies	No studies
Preconc + Preg v Other (specified)	NA	No studies	No studies	No studies	No studies	1 study, N=17,373[49] Vit A supp or B carotene v Placebo (Preconc+Preg) Outcome: Miscarriage + SB Vit A (N=11,723) RR: 1.06 (95% CI: 0.91, 1.25) B carotene (N=11,303) RR: 1.03 (95% CI: 0.87, 1.19)

NTD: Neural tube defect, MMN: Multiple micronutrient, IFA: Iron and folic acid, FA: Folic acid, Supp: Supplementation, Preconc: Preconception, Periconc: Periconception, Preg: Pregnancy, Int: Intervention, Comp: Comparator, Popn: Population, No int: No intervention, Standard care: Standard or routine care, RR: relative risk, 95% CI: 95% confidence interval.
Grey shaded and yellow shaded cells indicate statistically notable results (95% CIs not overlapping 1) from single studies and meta-analyses respectively.

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Supplementary Table 16. Summary of evidence from included studies – health and social interventions for stillbirth.

	Health interventions				Social interventions
Period	**General health**	**Prevention of early adverse pregnancy outcomes**	**Prevention or management of non-communicable disease**	**Prevention or management of infectious disease**	**Reproductive planning**
Pre- + Periconc	1 study, N=1816[50] Int: Preconc counselling Comp: Standard care Outcome: Composite including SB RR: 0.96 (95% CI: 0.81, 1.14)	No studies	No studies	4 studies, N=8656[27,29,63,64] Dapivirine vaginal ring HIV PreP v placebo, HPV vaccine v placebo (3 studies) RR: 1.20 (95% CI: 0.74, 1.93), I^2: 0.00%	No studies
Preconc + Preg v Preg only int	No studies	No studies	1 study, N=218[35] Popn: T1DM Int: Intensive DM management RR: 0.31 (95% CI: 0.03, 3.34)	1 study, N=266[65] Popn: HIV Int: Antiretroviral therapy RR: 2.70 (95% CI: 0.55, 13.14)	No studies
Preconc + Preg v Other (specified)	1 study, N=6275[66] Int: Women's groups on perinatal care Comp: Standard care (Preconc+Preg) RR: 1.06 (95% CI: 0.76, 1.45)	1 study, N=69[21] Popn: Previous miscarriage Int: Vaginal micronized progesterone Comp: Placebo (Preconc+Preg) RR: 0.73 (95% CI: 0.07, 7.69)	(1) 1 study, N=187[35] Popn: T1DM Int: Intensive DM management Preconc+Preg; 40 v 7 months Preconc RR: 0.39 (95% CI: 0.02, 6.05) (2) 1 study, N=25 (no SB cases)[45] Popn: T1DM Int: Continuous glucose monit Comp: Standard care (Preconc+Preg) RR: 1.45 (95% CI: 0.03, 67.95)	1 study, N=196[38] Popn: HIV Int: Isoniazid Comp: Placebo (Preconc+Preg), Outcome: Composite including SB RR: 0.72 (95% CI: 0.43, 1.05)	No studies

DM: Diabetes mellitus, T1DM: Type 1 diabetes mellitus, Continuous glucose monit: Continuous glucose monitoring, Preconc: Preconception, Periconc: Periconception, Preg: Pregnancy, Int: Intervention, Comp: Comparator, Popn: Population, Standard care: Standard or routine care, RR: relative risk, 95% CI: 95% confidence interval.

Grey shaded and yellow shaded cells indicate statistically notable results (95% CIs not overlapping 1) from single studies and meta-analyses respectively.

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Supplementary Table 17. Summary of evidence from included studies – nutrition interventions for large for gestational age.

Period	Any nutrition	MMN supplementation including IFA	IFA supplementation	FA supplementation	Food supplementation	Other nutritional
Pre- + Periconc	No studies	1 study, N=1084[3] Comp: FA RR: 1.06 (95% CI: 0.75, 1.51)	1 study, N=1074[3] Comp: FA RR: 1.05 (95% CI: 0.73, 1.49)	No studies	No studies	No studies
Preconc + Preg v Preg only int	No studies	No studies	No studies	No studies	No studies	No studies
Preconc + Preg v Other (specified)	NA	No studies	No studies	No studies	1 study, N=1360[33] High v Low nutrition value snack (Preconc+Preg) RR: 1.05 (95% CI: 0.21, 5.21)	No studies

MMN: Multiple micronutrient, IFA: Iron and folic acid, FA: Folic acid, Supp: Supplementation, Preconc: Preconception, Periconc: Periconception, Preg: Pregnancy, Int: Intervention, Comp: Comparator, Popn: Population, No int: No intervention, Standard care: Standard or routine care, RR: relative risk, 95% CI: 95% confidence interval.
Grey shaded and yellow shaded cells indicate statistically notable results (95% CIs not overlapping 1) from single studies and meta-analyses respectively.

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Supplementary Table 18. Summary of evidence from included studies – health and social interventions for large for gestational age.

Period	Health interventions				Social interventions
	General health	**Prevention of early adverse pregnancy outcomes**	**Prevention or management of non-communicable disease**	**Prevention or management of infectious disease**	**Reproductive planning**
Pre- + Periconc	No studies	No studies	No studies	No studies	No studies
Preconc + Preg v Preg only int	No studies	No studies	No studies	No studies	No studies
Preconc + Preg v Other (specified)	No studies	No studies	(1) 1 study, N=25[45] Popn: T1DM Int: Continuous glucose monit Comp: Standard care (Preconc+Preg) RR: 0.82 (95% CI: 0.45, 1.48) (2) 1 study, N=161[46] Popn: Overweight/obese Int: Lifestyle change counseling Comp: Standard care (Preconc+Preg) RR: 0.97 (95% CI: 0.47, 1.82)	No studies	No studies

T1DM: Type 1 diabetes mellitus, Continuous glucose monit: Continuous glucose monitoring, Preconc: Preconception, Periconc: Periconception, Preg: Pregnancy, Int: Intervention, Comp: Comparator, Popn: Population, Standard care: Standard or routine care, RR: relative risk, 95% CI: 95% confidence interval.
Grey shaded and yellow shaded cells indicate statistically notable results (95% CIs not overlapping 1) from single studies and meta-analyses respectively.

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Supplementary Table 19. Summary of evidence from included studies – nutrition interventions for maternal anaemia.

Period	Any nutrition	MMN supplementation including IFA	IFA supplementation	FA supplementation	Food supplementation	Other nutritional
Pre- + Periconc	2 studies, N=1060[67,68] Int: MMN including IFA or FA Comp: FA Trimester: 1 RR: 1.01 (95% CI: 0.83, 1.24), I^2: 0.00%	(1) 1 study, N=972[67] Comp: FA Trimester: 1 RR: 1.01 (95% CI, 0.77, 1.32) (2) 1 study, N=973[67] Comp: FA Trimester: 2 RR: 0.95 (95% CI: 0.81, 1.11) (3) 1 study, N=974[67] Trimester: 3 Comp: FA RR: 1.07 (95% CI: 0.89, 1.28)	(1) 2 studies, N=1060[67,68] Comp: FA Trimester: 1 RR: 1.13 (95% CI: 0.93, 1.37), I^2: 0.00% (2) 1 study, N=971[67] Comp: FA Trimester: 2 RR: 1.02 (95% CI: 0.88, 1.19) (3) 1 study, N=986[67] Comp: FA Trimester: 3 RR: 1.05 (95% CI: 0.87, 1.25)	No studies	1 study, N=368[30] Popn: Low income 5-7 months v 0-2 months OR: 0.65 (95% CI: 0.45, 1.07) *(No case ns to calculate assumed comparator risk & RR)*	No studies
Preconc + Preg v Preg only int	(1) 2 studies, N=307[10,11] Int: Food supp or IFA Trimester: 2 RR: 0.61 (95% CI: 0.47, 0.80), I^2: 0.00% (2) 2 studies, N=289[10,11] Int: Food supp or IFA Trimester: 3 RR: 0.67 (95% CI: 0.47, 0.96), I^2: 0.00%	No studies	(1) 1 study, N=191[10] Trimester: 1 RR: 0.50 (95% CI: 0.31, 0.78) (2) 1 study, N=201[10] Trimester: 2 RR: 0.60 (95% CI: 0.45, 0.79) (3) 1 study, N=175[10] Trimester: 3 RR: 0.64 (95% CI: 0.43, 0.94)	No studies	(1) 1 study, N=106[11] Trimester: 2 RR: 0.78 (95% CI: 0.30, 2.03) (2) 1 study, N=114[11] Trimester: 3 RR: 0.89 (95% CI: 0.37, 2.14)	No studies
Preconc + Preg v Other (specified)	NA	No studies	No studies	No studies	(1) 1 study, N=112[11] Trimester: 2 Comp: Standard care (Preconc+Preg) RR: 0.77 (95% CI: 0.30, 1.98) (2) 1 study, N=123[11] Trimester: 3 Comp: Standard care (Preconc+Preg) RR: 1.03 (95% CI: 0.43, 2.49)	No studies

MMN: Multiple micronutrient, IFA: Iron and folic acid, FA: Folic acid, Supp: Supplementation, Preconc: Preconception, Periconc: Periconception, Preg: Pregnancy, Int: Intervention, Comp: Comparator, Popn: Population, No int: No intervention, Standard care: Standard or routine care, RR: relative risk, 95% CI: 95% confidence interval.

Grey shaded and yellow shaded cells indicate statistically notable results (95% CIs not overlapping 1) from single studies and meta-analyses respectively.

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	Supplementary Table 20. Summary of evidence from included studies – health interventions for maternal anaemia.			
Period	**General health**	**Prevention of early adverse pregnancy outcomes**	**Prevention or management of non-communicable disease**	**Prevention or management of infectious disease**
Pre- + Periconc	No studies	No studies	No studies	No studies
Preconc + Preg v Preg only int	No studies	No studies	No studies	No studies
Preconc + Preg v Other (specified)	No studies	No studies	No studies	No studies
Preconc: Preconception, Periconc: Periconception, Preg: Pregnancy.				

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Supplementary Table 21. Summary of evidence from included studies – nutrition interventions for maternal haemoglobin.

Period	Any nutrition	MMN supplementation including IFA	IFA supplementation	FA supplementation	Food supplementation	Other nutritional
Pre- + Periconc	(1) 2 studies, N=1060[67,68] Int: MMN including IFA or FA Comp: FA Trimester: 1 MD: 0.14g/dL (95% CI: -0.02, 0.31), I^2: 43.61% (2) 2 studies, N=1259[7,67] Int: MMN including IFA or FA Comp: FA Trimester: 2 MD: -0.06g/dL (95% CI: -0.20, 0.09), I^2: 0.00% (3) 2 studies, N=1217[7,67] Int: MMN including IFA or FA Comp: FA Trimester: 3 MD: -0.08g/dL (95% CI: -0.22, 0.07), I^2: 0.00%	(1) 1 study, N=972[67] Comp: FA Trimester: 1 MD: 0.18g/dL (SE: 0.09) (2) 1 study, N=973[67] Comp: FA Trimester: 2 MD: -0.07g/dL (SE: 0.08) (3) 1 study, N=974[67] Comp: FA Trimester: 3 MD: -0.07g/dL (SE:0.08)	(1) 2 studies, N=1060[67,68] Comp: FA Trimester: 1 MD: -0.04g/dL (95% CI: -0.20, 0.11), I^2: 0.00% (2) 2 studies, N=1257[7,67] Comp: FA Trimester: 2 MD: -0.07g/dL (95% CI: -0.21, 0.07), I^2: 0.00% (3)2 studies, N=1229[7,67] Comp: FA Trimester: 3 MD: -0.06g/dL (95% CI: -0.21, 0.09), I^2: 0.00%	No studies	1 study, N=368[30] Popn: Low income 5-7 months v 0-2 months MD: 0.29g/dL (SE: 0.11)	No studies
Preconc + Preg v Preg only int	(1) 2 studies, N=307[10,11] Int: Food supp or IFA Trimester: 2 MD: 0.29g/dL (95% CI: -0.48, 1.05), I^2: 85.97% (2) 2 studies, N=289[10,11] Int: Food supp or IFA Trimester: 3 MD: 0.06g/dL (95% CI: -0.64, 0.77), I^2: 85.44%	No studies	(1) 1 study, N=191[10] Trimester: 1 MD: 0.83g/dL (SE: 0.21) (2) 1 study, N=201[10] Trimester: 2 MD: 0.68g/dL (SE: 0.21) (3) 1 study, N=175[10] Trimester: 3 MD: 0.42g/dL (SE: 0.19)	No studies	(1) 1 study, N=106[11] Trimester: 2 MD: -0.10g/dL (SE: 0.20) (2) 1 study, N=114[11] Trimester: 3 MD: -0.30g/dL (SE: 0.20)	No studies
Preconc + Preg v Other (specified)	NA	No studies	No studies	No studies	(1) 1 study, N=112[11] Trimester: 2 Comp: Standard care (Preconc+Preg) MD: 0.00g/dL (SE: 0.21) (2) 1 study, N=123[11] Trimester: 3 Comp: Standard care (Preconc+Preg) MD: -0.10g/dL (SE: 0.19)	No studies

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MMN: Multiple micronutrient, IFA: Iron and folic acid, FA: Folic acid, Supp: Supplementation, Preconc: Preconception, Periconc: Periconception, Preg: Pregnancy, Int: Intervention, Comp: Comparator, Popn: Population, No int: No intervention, Standard care: Standard or routine care, MD: mean difference, 95% CI: 95% confidence interval, SE: standard error.
Yellow shaded cells indicate statistically notable results (95% CIs not overlapping 0) from meta-analyses.

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	Supplementary Table 22. Summary of evidence from included studies – health interventions for maternal anaemia.			
Period	**General health**	**Prevention of early adverse pregnancy outcomes**	**Prevention or management of non-communicable disease**	**Prevention or management of infectious disease**
Pre- + Periconc	No studies	No studies	No studies	No studies
Preconc + Preg v Preg only int	No studies	No studies	No studies	No studies
Preconc + Preg v Other (specified)	No studies	No studies	No studies	No studies
Preconc: Preconception, Periconc: Periconception, Preg: Pregnancy.				

	Supplementary Table 23. Summary of evidence from included studies – nutrition interventions for maternal gestational diabetes mellitus.					
Period	**Any nutrition**	**MMN supplementation including IFA**	**IFA supplementation**	**FA supplementation**	**Food supplementation**	**Other nutritional**
Pre- + Periconc	No studies	No studies	No studies	No studies	No studies	1 study, N=1162[9] Mushroom in diet v standard care RR: 0.72 (95% CI: 0.42, 1.21)
Preconc + Preg v Preg only int	No studies	No studies	No studies	No studies	No studies	No studies
Preconc + Preg v Other (specified)	NA	No studies	No studies	No studies	1 study, N=1008[69] High v Low nutrition value snack (Preconc+Preg) RR: 0.81 (95% CI: 0.55, 1.17)	No studies
MMN: Multiple micronutrient, IFA: Iron and folic acid, FA: Folic acid, Supp: Supplementation, Preconc: Preconception, Periconc: Periconception, Preg: Pregnancy, Int: Intervention, Comp: Comparator, Popn: Population, No int: No intervention, Standard care: Standard or routine care, RR: relative risk, 95% CI: 95% confidence interval. Grey shaded and yellow shaded cells indicate statistically notable results (95% CIs not overlapping 1) from single studies and meta-analyses respectively.						

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Supplementary Table 24. Summary of evidence from included studies – health interventions for maternal gestational diabetes mellitus.

Period	General health	Prevention of early adverse pregnancy outcomes	Prevention or management of non-communicable disease	Prevention or management of infectious disease
Pre- + Periconc	No studies	No studies	No studies	No studies
Preconc + Preg v Preg only int	No studies	No studies	No studies	No studies
Preconc + Preg v Other (specified)	No studies	(1) 1 study, N=69 (No GDM cases)[21] Popn: Previous miscarriage Int: Vaginal micronized progesterone Comp: Placebo (Preconc+Preg) RR: 1.45 (95% CI: 0.03, 70.93) (2) 1 study, N=728[22] Popn: Previous miscarriage Int: Aspirin Comp: Placebo (Preconc+Preg) RR: 0.93 (95% CI: 0.41, 2.11)	2 studies, N=297[46,47] Popn: Overweight/obese and/or previous GDM Int: Lifestyle change counseling Comp: Standard care (Preconc+Preg) RR: 1.01 (95%CI: 0.78, 1.31), I^2: 36.92%	No studies

GDM: Gestational diabetes mellitus, APS: Antiphospholipid syndrome, Preconc: Preconception, Periconc: Periconception, Preg: Pregnancy, Int: Intervention, Comp: Comparator, Popn: Population, Standard care: Standard or routine care, RR: relative risk, 95% CI: 95% confidence interval.
Grey shaded and yellow shaded cells indicate statistically notable results (95% CIs not overlapping 1) from single studies and meta-analyses respectively.

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Supplementary Table 25. Summary of evidence from included studies – nutrition interventions for maternal gestational hypertension.

Period	Any nutrition	MMN supplementation including IFA	IFA supplementation	FA supplementation	Food supplementation	Other nutritional
Pre- + Periconc	(1) 2 studies, N=1741[9,31] Popn: 1 study: previous pre-eclampsia Comp: Placebo, standard care RR: 0.72 (95% CI: 0.39, 1.32), I^2: 84.54% (2) 1 study, N=243 (no GHT cases)[7] Comp: FA RR: 0.98 (95% CI: 0.02, 48.79) (3) 1 study, N=363 (Pregnancy HT; unclear if GHT specifically)[17] Comp: Placebo RR: 1.15 (95% CI: 0.49, 2.57)	1 study, N=363 (Pregnancy HT; unclear if GHT specifically)[17] Comp: Placebo RR: 1.15 (95% CI: 0.49, 2.57)	1 study, N=243 (no GHT cases)[7] Comp: FA RR: 0.98 (95% CI: 0.02, 48.79)	No studies	No studies	(1) 1 study, N=579[31] Popn: Previous pre-eclampsia Calcium supp v placebo RR: 0.94 (95% CI: 0.84, 1.05) (2) 1 study, N=1162[9] Mushroom in diet v standard care RR: 0.50 (95% CI: 0.31, 0.80)
Preconc + Preg v Preg only int	No studies	No studies	No studies	No studies	No studies	No studies
Preconc + Preg v Other (specified)	NA	No studies	No studies	No studies	No studies	No studies

MMN: Multiple micronutrient, IFA: Iron and folic acid, FA: Folic acid, Supp: Supplementation, Preconc: Preconception, Periconc: Periconception, Preg: Pregnancy, Int: Intervention, Comp: Comparator, Popn: Population, No int: No intervention, Standard care: Standard or routine care, RR: relative risk, 95% CI: 95% confidence interval.
Grey shaded and yellow shaded cells indicate statistically notable results (95% CIs not overlapping 1) from single studies and meta-analyses respectively.

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Supplementary Table 26. Summary of evidence from included studies – health interventions for maternal gestational hypertension.

Period	General health	Prevention of early adverse pregnancy outcomes	Prevention or management of non-communicable disease	Prevention or management of infectious disease
Pre- + Periconc	No studies	No studies	No studies	1 study, N=39[34] Int: H1N1 vaccine RR: 2.13 (95% CI: 0.09, 49.08)
Preconc + Preg v Preg only int	No studies	No studies	No studies	No studies
Preconc + Preg v Other (specified)	No studies	2 studies, N=797[21,22] Popn: Previous miscarriage Int: Vaginal micronized progesterone, Aspirin Comp: Placebo (Preconc+Preg) RR: 0.76 (95% CI: 0.17, 3.53)	(1) 1 study, N=25[45] Popn: T1DM Int: Continuous glucose monit Comp: Standard care (Preconc+Preg) RR: 0.30 (95% CI: 0.04, 2.20) (2) 2 studies, N=297[46,47] Popn: Overweight/obese and/or previous GDM Int: Lifestyle change counseling Comp: Standard care (Preconc+Preg RR: 1.05 (95% CI: 0.55, 2.03), I^2: 0.00%	No studies

T1DM: Type 1 diabetes mellitus, GDM: Gestational diabetes mellitus, Continuous glucose monit: Continuous glucose monitoring, Preconc: Preconception, Periconc: Periconception, Preg: Pregnancy, Int: Intervention, Comp: Comparator, Popn: Population, Standard care: Standard or routine care, RR: relative risk, 95% CI: 95% confidence interval.
Grey shaded and yellow shaded cells indicate statistically notable results (95% CIs not overlapping 1) from single studies and meta-analyses respectively.

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Supplementary Table 27. Summary of evidence from included studies – nutrition interventions for maternal pre-eclampsia.

Period	Any nutrition	MMN supplementation including IFA	IFA supplementation	FA supplementation	Food supplementation	Other nutritional
Pre- + Periconc	3 studies, N=2156[9,17,31] Popn: 1 study: previous pre-eclampsia Comp: Placebo, standard care RR: 0.78 (95% CI: 0.60, 1.01), I^2: 29.53%	1 study, N=415[17] Comp: Placebo RR: 1.39 (95% CI: 0.31. 5.89)	No studies	1 study, N=233[41] Popn: Oral cleft or previous oral cleft birth 4mg FA v 0.4 mg FA RR: 1.30 (95% CI: 0.38, 4.47)	No studies	(1) 1 study, N=579[31] Popn: Previous pre-eclampsia Calcium supp v placebo RR: 0.80 (95% CI: 0.61, 1.06) (2) 1 study, N=1162[9] Mushroom in diet v standard care RR: 0.33 (95% CI: 0.11, 1.02)
Preconc + Preg v Preg only int	No studies	No studies	No studies	No studies	No studies	No studies
Preconc + Preg v Other (specified)	NA	No studies	No studies	No studies	No studies	No studies

MMN: Multiple micronutrient, IFA: Iron and folic acid, FA: Folic acid, Supp: Supplementation, Preconc: Preconception, Periconc: Periconception, Preg: Pregnancy, Int: Intervention, Comp: Comparator, Popn: Population, No int: No intervention, Standard care: Standard or routine care, RR: relative risk, 95% CI: 95% confidence interval.
Grey shaded and yellow shaded cells indicate statistically notable results (95% CIs not overlapping 1) from single studies and meta-analyses respectively.

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	Supplementary Table 28. Summary of evidence from included studies – health interventions for maternal pre-eclampsia.			
Period	**General health**	**Prevention of early adverse pregnancy outcomes**	**Prevention or management of non-communicable disease**	**Prevention or management of infectious disease**
Pre- + Periconc	No studies	2 studies, N=208[15,16] Popn: Previous miscarriage, 1 study: APS Clomiphene citrate v placebo, Aspirin + heparin v placebo RR: 0.39 (95% CI: 0.20, 0.74), I^2: 0.00%	No studies	1 study, N=39[34] Int: H1N1 vaccine RR: 3.54 (95% CI: 0.18, 69.18)
Preconc + Preg v Preg only int	No studies	No studies	No studies	No studies
Preconc + Preg v Other (specified)	No studies	2 studies, N=928[22,23] Popn: Previous miscarriage Int: Aspirin or Aspirin + heparin, Aspirin Comp: Placebo and/or standard care (Preconc+Preg) RR: 1.01 (95% CI: 0.63, 1.61), I^2: 0.00%	(1) 1 study, N=25[45] Popn: T1DM Comp: Standard care (Preconc+Preg) RR: 0.48 (95% CI: 0.02, 10.84) (2) 1 study, N=128[47] Popn: Obese and/or previous GDM Comp: Standard care RR: 0.48 (95% CI: 0.05, 5.21)	No studies

T1DM: Type 1 diabetes mellitus, GDM: Gestational diabetes mellitus, APS: Antiphospholipid syndrome, Preconc: Preconception, Periconc: Periconception, Preg: Pregnancy, Int: Intervention, Comp: Comparator, Popn: Population, Standard care: Standard or routine care, RR: relative risk, 95% CI: 95% confidence interval.
Grey shaded and yellow shaded cells indicate statistically notable results (95% CIs not overlapping 1) from single studies and meta-analyses respectively.

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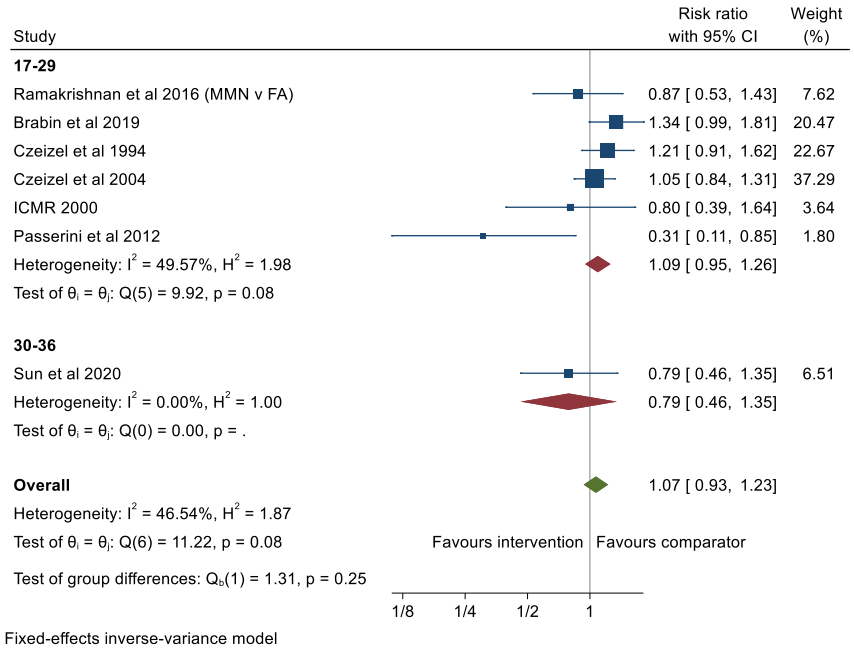
5. Preconception interventions to prevent low birth weight, preterm birth and small for gestational age: Subgroup and sensitivity analyses for primary outcomes and nutrition interventions

Note: subgroup and sensitivity analyses were only conducted for meta-analyses including ≥4 studies.

5.1. Any general population-based nutritional intervention in the pre- and periconception period compared with FA supplementation, supplementation with other micronutrients (not FA), standard or routine care, or no intervention to prevent low birth weight

7 studies, N=13,973: Ramakrishnan et al 2016 (MMN supplementation v FA supplementation) [3], Czeizel et al 1994 (MMN supplementation v supplement containing only copper, manganese, zinc and Vitamin C) [4], Czeizel et al 2004 (MMN supplementation v no supplementation) [5], ICMR 2000 (MMN supplementation v supplement containing only iron and calcium; population: women with previous birth with neural tube defect) [6], Brabin et al 2019 (IFA supplementation v FA supplementation) [7], Passerini et al 2012 (IFA supplementation with deworming v no supplementation or deworming) [8], and Sun et al 2020 (100g mushroom daily v standard or routine care [normal diet]) [9].



Supplementary Figure 22. Any general population-based nutritional intervention in the pre- and periconception period compared with FA supplementation, supplementation with other micronutrients (not FA), standard or routine care, or no intervention to prevent low birth weight: subgroup effects by age (as two categories: 17-29 and 30-36 years).

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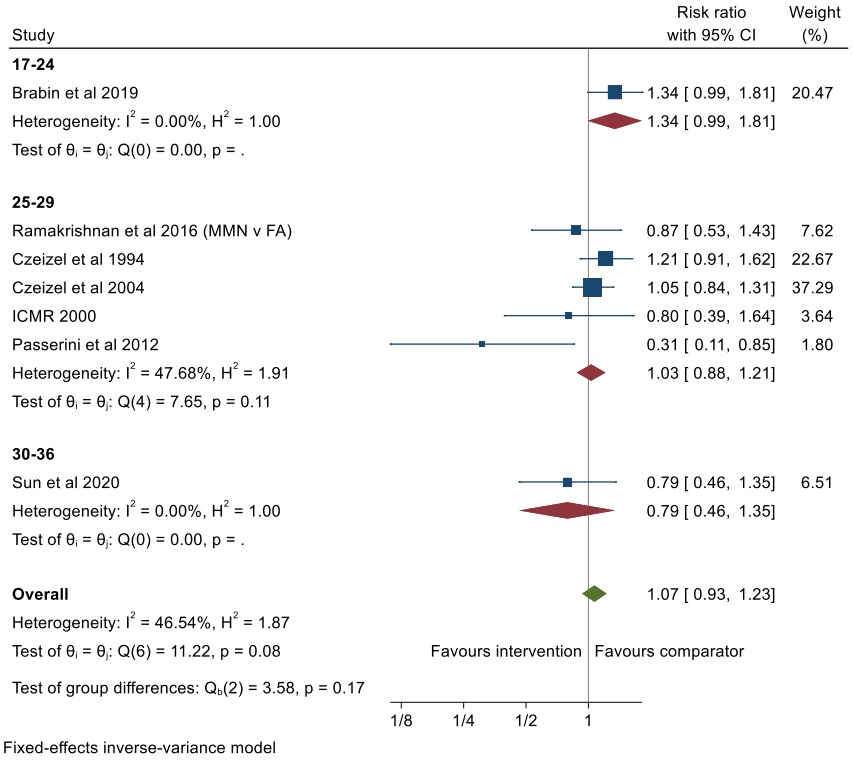

Supplementary Figure 23. Any general population-based nutritional intervention in the pre- and periconception period compared with FA supplementation, supplementation with other micronutrients (not FA), standard or routine care, or no intervention to prevent low birth weight: subgroup effects by age (as three categories: 17-24, 25-29 and 30-36 years).

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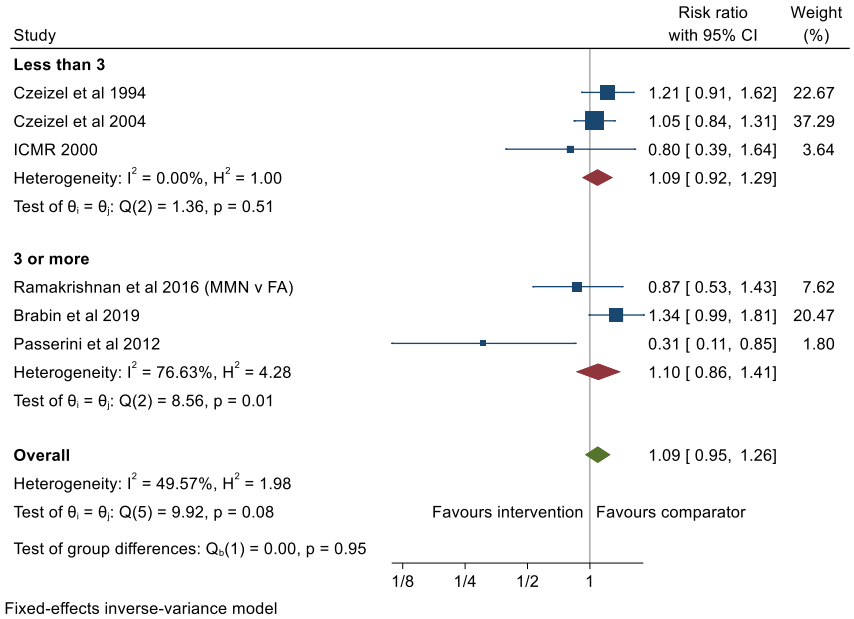

Supplementary Figure 24. Any general population-based nutritional intervention in the pre- and periconception period compared with FA supplementation, supplementation with other micronutrients (not FA), standard or routine care, or no intervention to prevent low birth weight: subgroup effects by months prior to conception intervention started (no information for Sun et al 2020).

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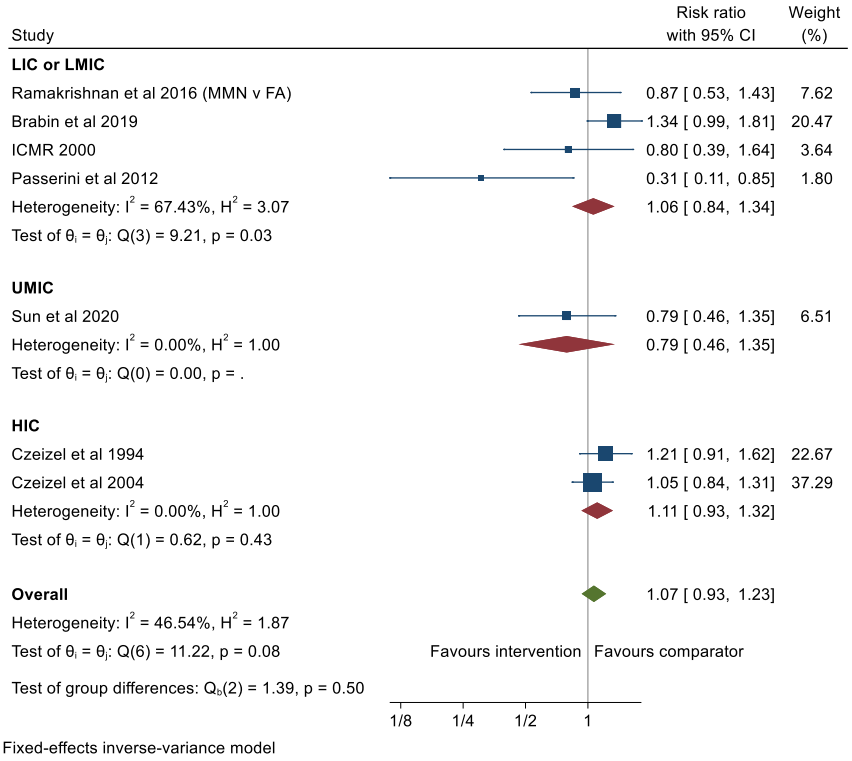

Supplementary Figure 25. Any general population-based nutritional intervention in the pre- and periconception period compared with FA supplementation, supplementation with other micronutrients (not FA), standard or routine care, or no intervention to prevent low birth weight: subgroup effects by country income status.

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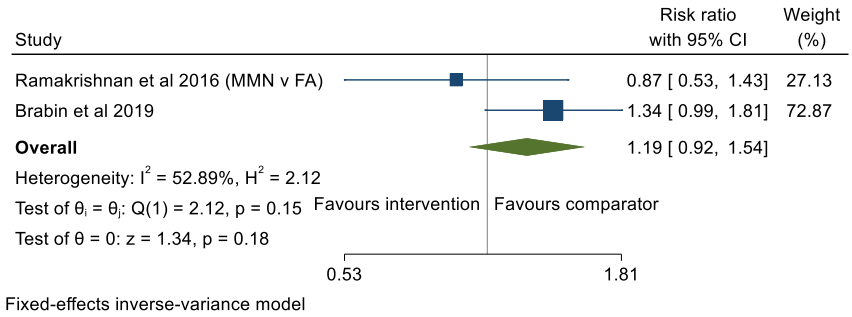

Supplementary Figure 26. Any general population-based nutritional intervention in the pre- and periconception period compared with FA supplementation, supplementation with other micronutrients (not FA), standard or routine care, or no intervention to prevent low birth weight: sensitivity analysis – including only studies at low risk of bias.

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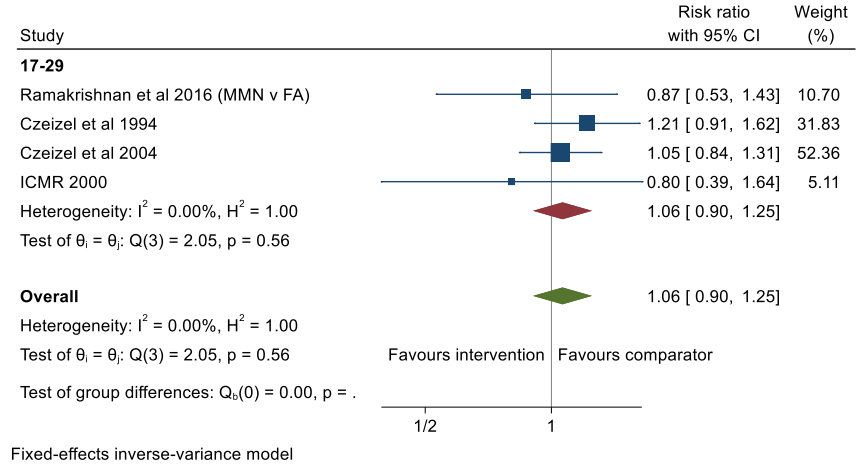
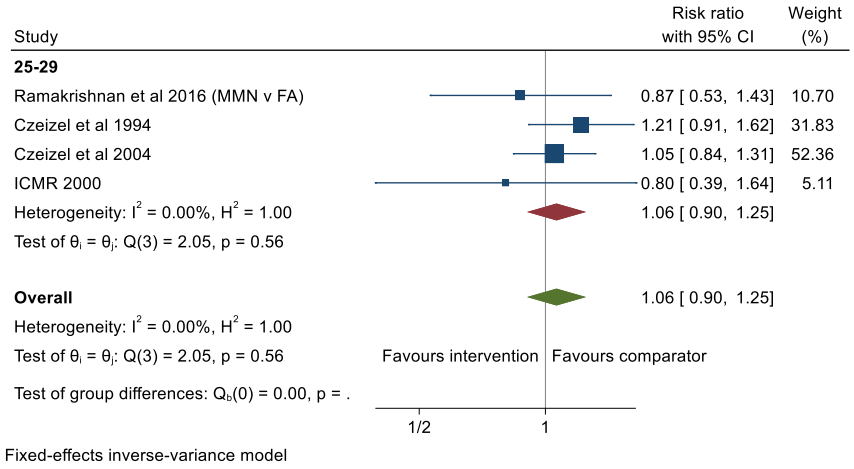
5.2. Pre- and periconception MMN including IFA versus pre- and periconception FA supplementation, supplementation with other micronutrients (not FA), or no intervention to prevent low birth weight.

4 studies, N=12,054: Ramakrishnan et al 2016 (MMN supplementation v FA supplementation) [3], Czeizel et al 1994 (MMN supplementation v supplement containing only copper, manganese, zinc and Vitamin C) [4], Czeizel et al 2004 (MMN supplementation v no supplementation) [5], ICMR 2000 (MMN supplementation v supplement containing only iron and calcium; population: women with previous birth with neural tube defect) [6].



Supplementary Figure 27. Pre- and periconception MMN including IFA versus pre- and periconception FA supplementation, supplementation with other micronutrients (not FA), or no intervention to prevent low birth weight: subgroup effects by age (as two categories: 17-29 and 30-36 years).



Supplementary Figure 28. Pre- and periconception MMN including IFA versus pre- and periconception FA supplementation, supplementation with other micronutrients (not FA), or no intervention to prevent low birth weight: subgroup effects by age (as three categories: 17-24, 25-29 and 30-36 years).

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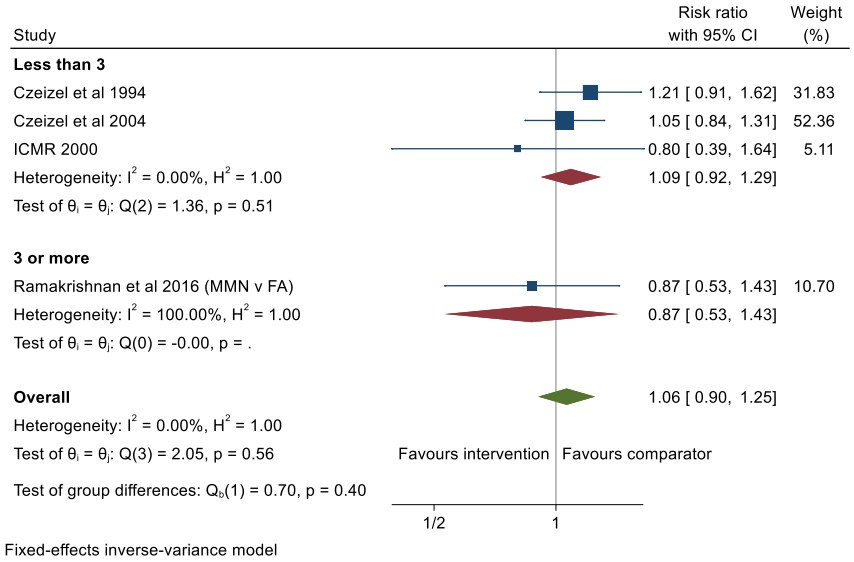
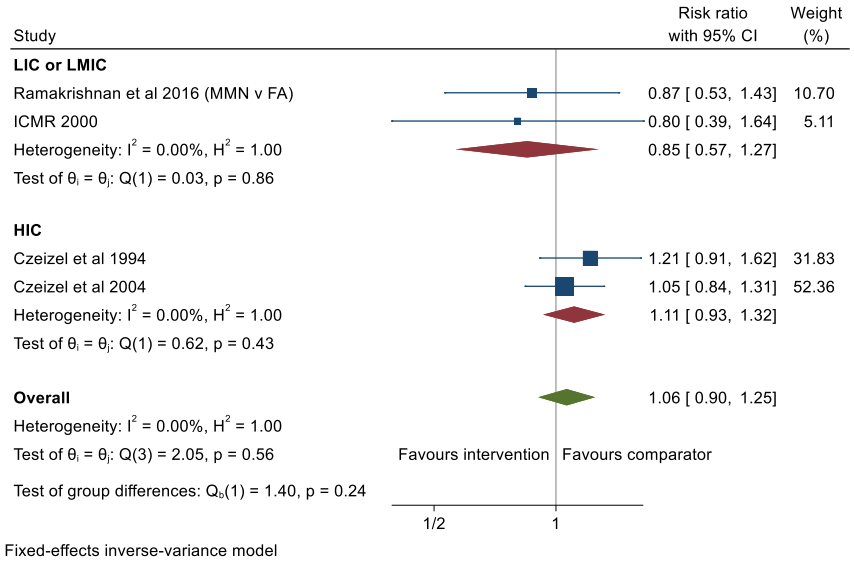


Supplementary Figure 29. Pre- and periconception MMN including IFA versus pre- and periconception FA supplementation, supplementation with other micronutrients (not FA), or no intervention to prevent low birth weight: subgroup effects by months prior to conception intervention started.



Supplementary Figure 30. Pre- and periconception MMN including IFA versus pre- and periconception FA supplementation, supplementation with other micronutrients (not FA), or no intervention to prevent low birth weight: subgroup effects by country income status.

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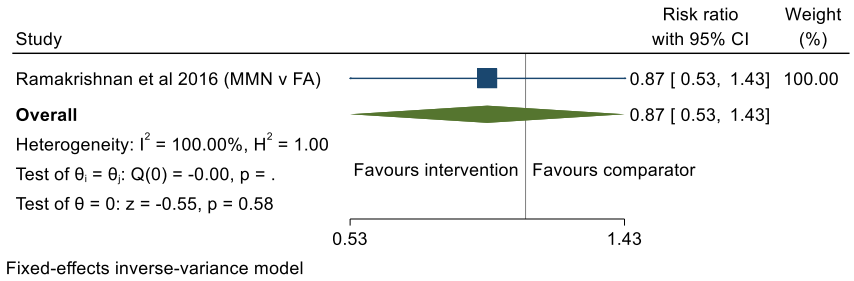

Supplementary Figure 31. Pre- and periconception MMN including IFA versus pre- and periconception FA supplementation, supplementation with other micronutrients (not FA), or no intervention to prevent low birth weight: sensitivity analysis – including only studies at low risk of bias.

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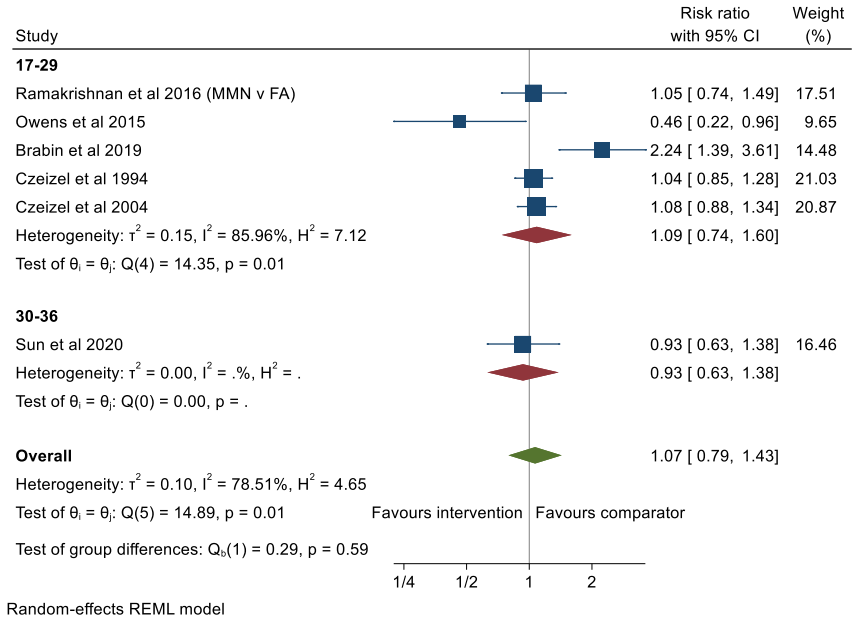
5.3. Any general population-based nutritional intervention in the pre- and periconception period compared with FA supplementation, supplementation with other micronutrients (not FA), placebo, standard or routine care, or no intervention to prevent preterm birth

6 studies, N=13,683: Ramakrishnan et al 2016 (MMN supplementation v FA supplementation) [3], Czeizel et al 1994 (MMN supplementation v supplement containing only copper, manganese, zinc and Vitamin C) [4], Czeizel et al 2004 (MMN supplementation v no supplementation) [5], Owens et al 2015 (MMN supplementation v placebo) [17], Brabin et al 2019 (IFA supplementation v FA supplementation) [7], Sun et al 2020 (100g mushroom daily v standard or routine care [normal diet]) [9].



Supplementary Figure 32. Any general population-based nutritional intervention in the pre- and periconception period compared with FA supplementation, supplementation with other micronutrients (not FA), placebo, standard or routine care, or no intervention to prevent preterm birth: subgroup effects by age (as two categories: 17-29 and 30-36 years).

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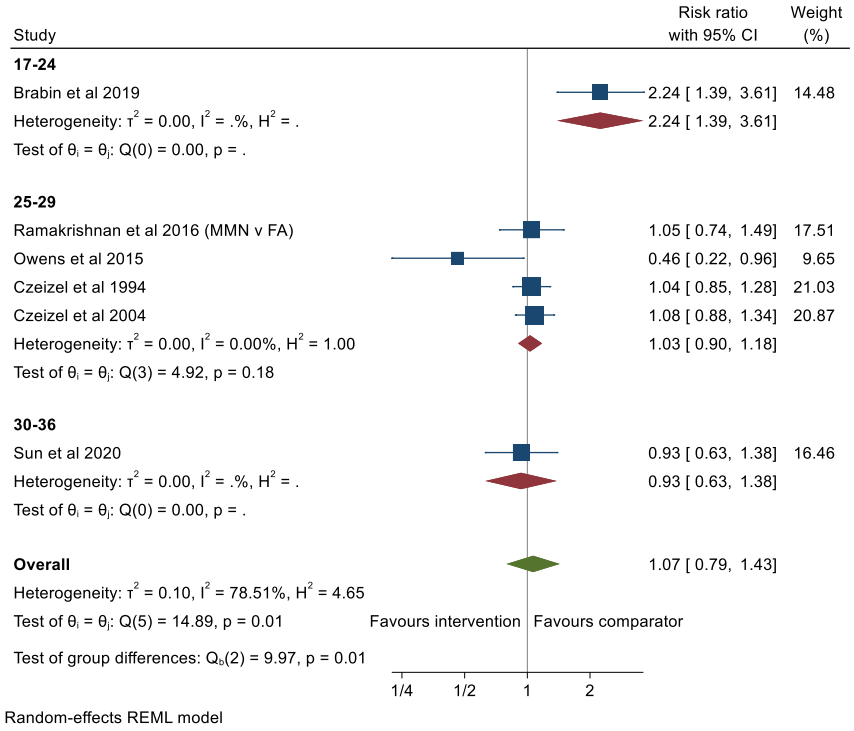

Supplementary Figure 33. Any general population-based nutritional intervention in the pre- and periconception period compared with FA supplementation, supplementation with other micronutrients (not FA), placebo, standard or routine care, or no intervention to prevent preterm birth: subgroup effects by age (as three categories: 17-24, 25-29 and 30-36 years).

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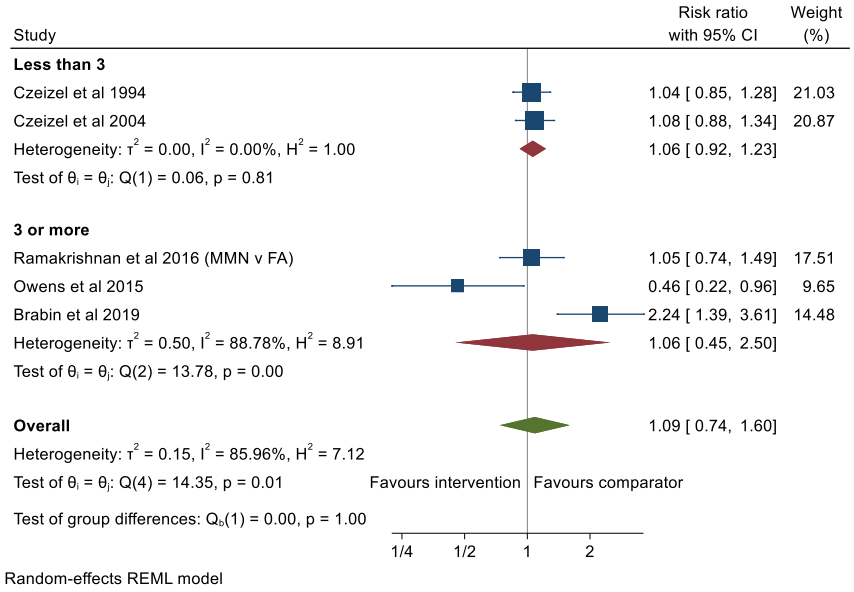

Supplementary Figure 34. Any general population-based nutritional intervention in the pre- and periconception period compared with FA supplementation, supplementation with other micronutrients (not FA), placebo, standard or routine care, or no intervention to prevent preterm birth: subgroup effects by months prior to conception intervention started (no information for Sun et al 2020).

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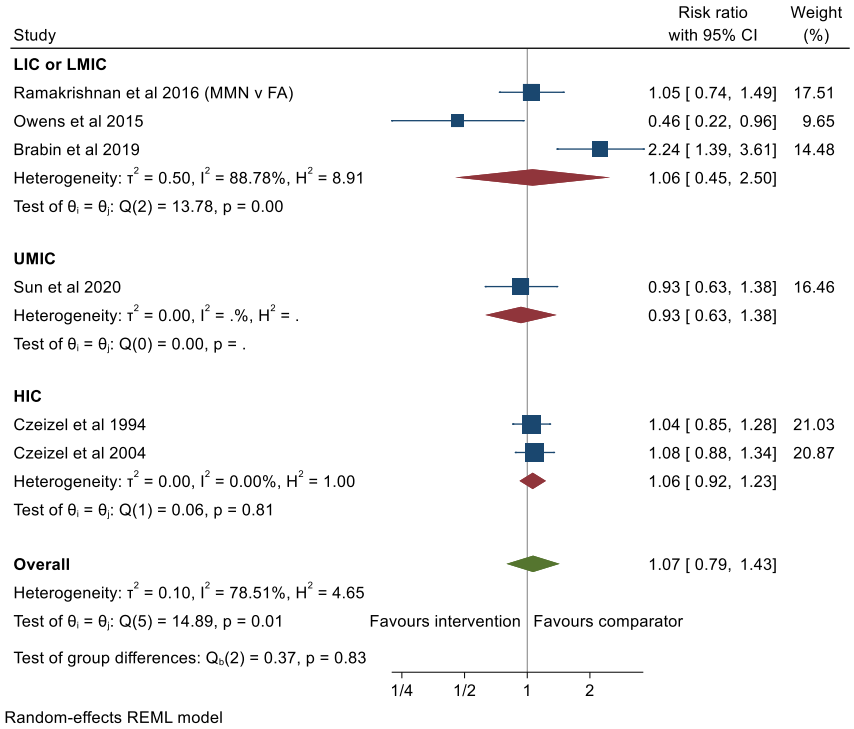

Supplementary Figure 35. Any general population-based nutritional intervention in the pre- and periconception period compared with FA supplementation, supplementation with other micronutrients (not FA), placebo, standard or routine care, or no intervention to prevent preterm birth: subgroup effects by country income status.

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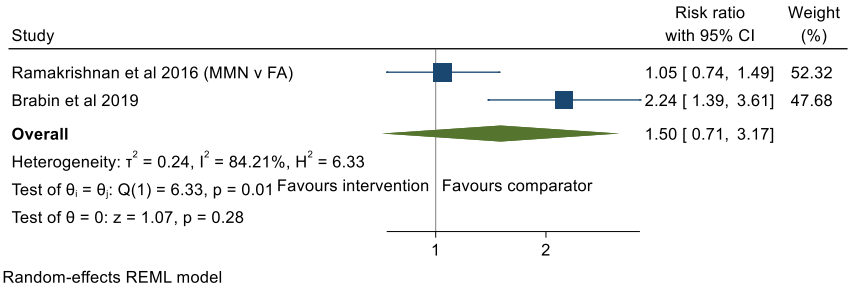

Supplementary Figure 36. Any general population-based nutritional intervention in the pre- and periconception period compared with FA supplementation, supplementation with other micronutrients (not FA), placebo, standard or routine care, or no intervention to prevent preterm birth: sensitivity analysis – including only studies at low risk of bias.

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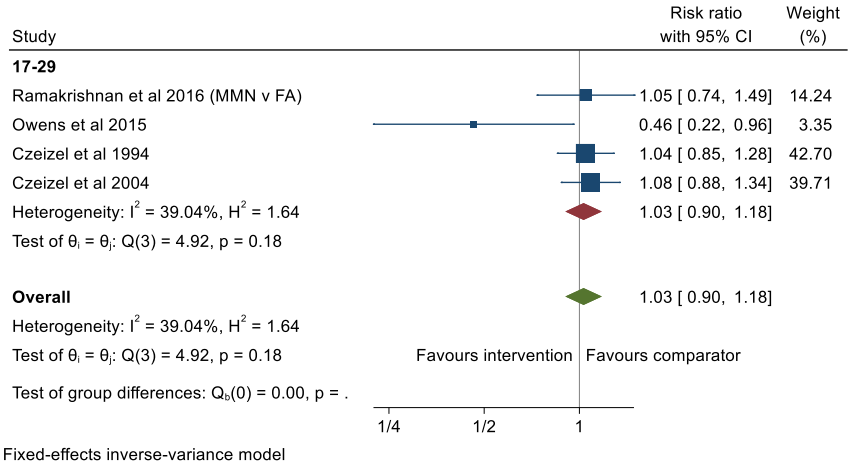
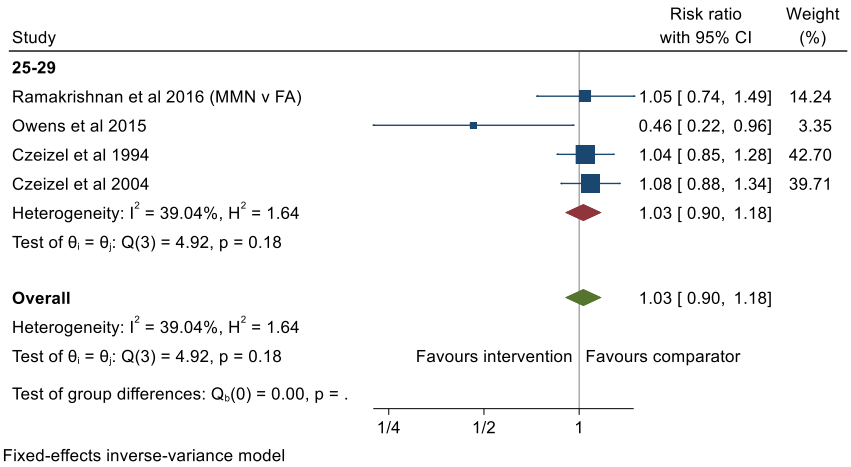
5.4. Pre- and periconception MMN supplementation including IFA versus pre- and periconception FA supplementation, supplementation with other micronutrients (not FA), placebo or no intervention to prevent preterm birth.

4 studies, N=12,235: Ramakrishnan et al 2016 (MMN supplementation v FA supplementation) [3], Czeizel et al 1994 (MMN supplementation v supplement containing only copper, manganese, zinc and Vitamin C) [4], Czeizel et al 2004 (MMN supplementation v no supplementation) [5], Owens et al 2015 (MMN supplementation v placebo) [17].



Supplementary Figure 37. Pre- and periconception MMN supplementation including IFA versus pre- and periconception FA supplementation, supplementation with other micronutrients (not FA), placebo or no intervention to prevent preterm birth: subgroup effects by age (as two categories: 17-29 and 30-36 years).



Supplementary Figure 38. Pre- and periconception MMN supplementation including IFA versus pre- and periconception FA supplementation, supplementation with other micronutrients (not FA), placebo or no intervention to prevent preterm birth: subgroup effects by age (as three categories: 17-24, 25-29 and 30-36 years).

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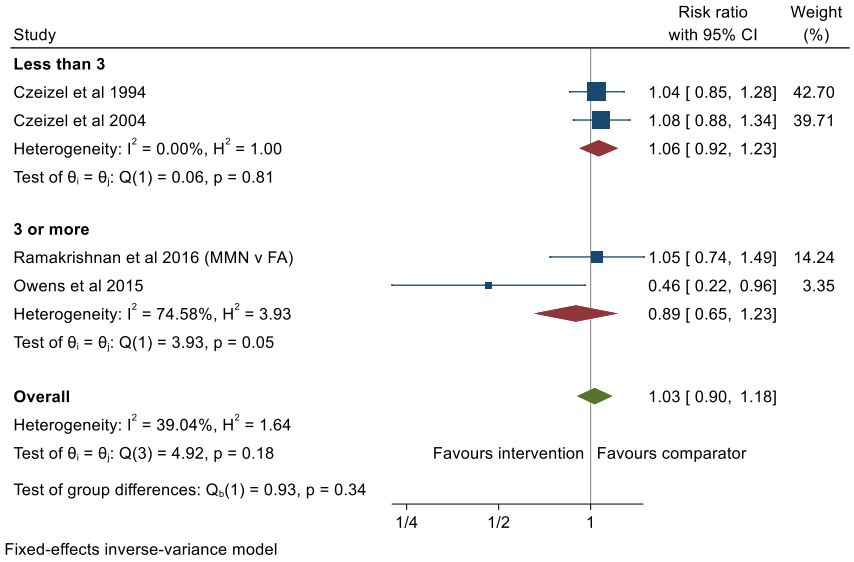
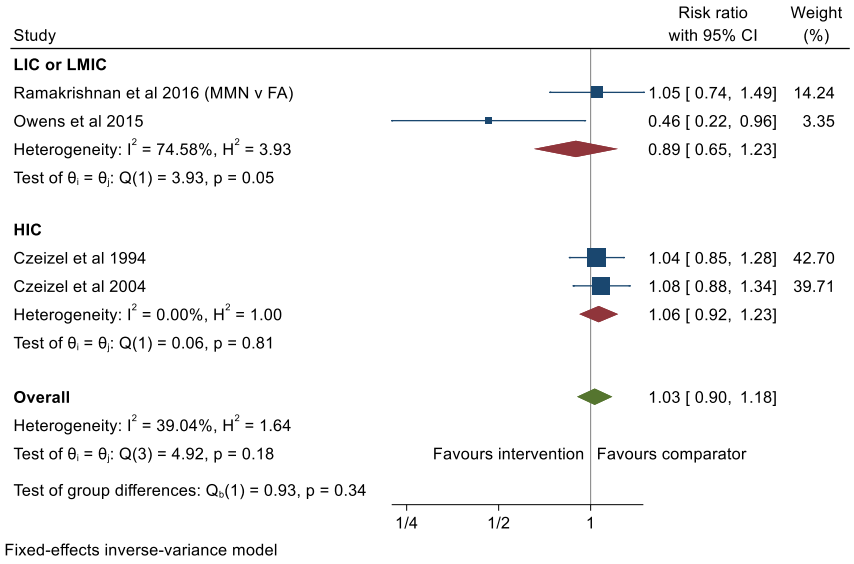


Supplementary Figure 39. Pre- and periconception MMN supplementation including IFA versus pre- and periconception FA supplementation, supplementation with other micronutrients (not FA), placebo or no intervention to prevent preterm birth: subgroup effects by months prior to conception intervention started.



Supplementary Figure 40. Pre- and periconception MMN supplementation including IFA versus pre- and periconception FA supplementation, supplementation with other micronutrients (not FA), placebo or no intervention to prevent preterm birth: subgroup effects by country income status.

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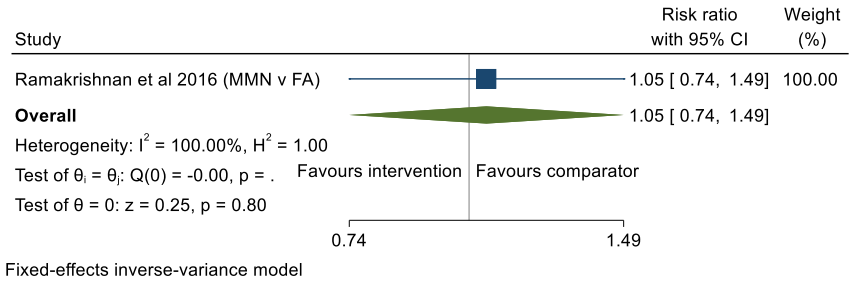

Supplementary Figure 41. Pre- and periconception MMN supplementation including IFA versus pre- and periconception FA supplementation, supplementation with other micronutrients (not FA), placebo or no intervention to prevent preterm birth: sensitivity analysis – including only studies at low risk of bias.

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6. Preconception interventions to prevent low birth weight, preterm birth and small for gestational age: Risk of bias assessments

Notes

1. Risk of bias assessments for RCTs were undertaken using the Revised Cochrane risk-of-bias tool for randomized trials (RoB 2) (v 22Aug2019) tool[70], assessments for cluster RCTs were done using the Revised Cochrane risk-of-bias tool for cluster-randomized trials (RoB 2 CRT) (v 10Nov2020) tool[71], and assessments for qRCTs were done using Risk Of Bias In Non-randomized Studies of Interventions (ROBINS-I) (v 01Aug2016) tool[72].

2. Traffic light plots and summary plots were generated using the robvis tool (https://mcguinlu.shinyapps.io/robvis/) [73].

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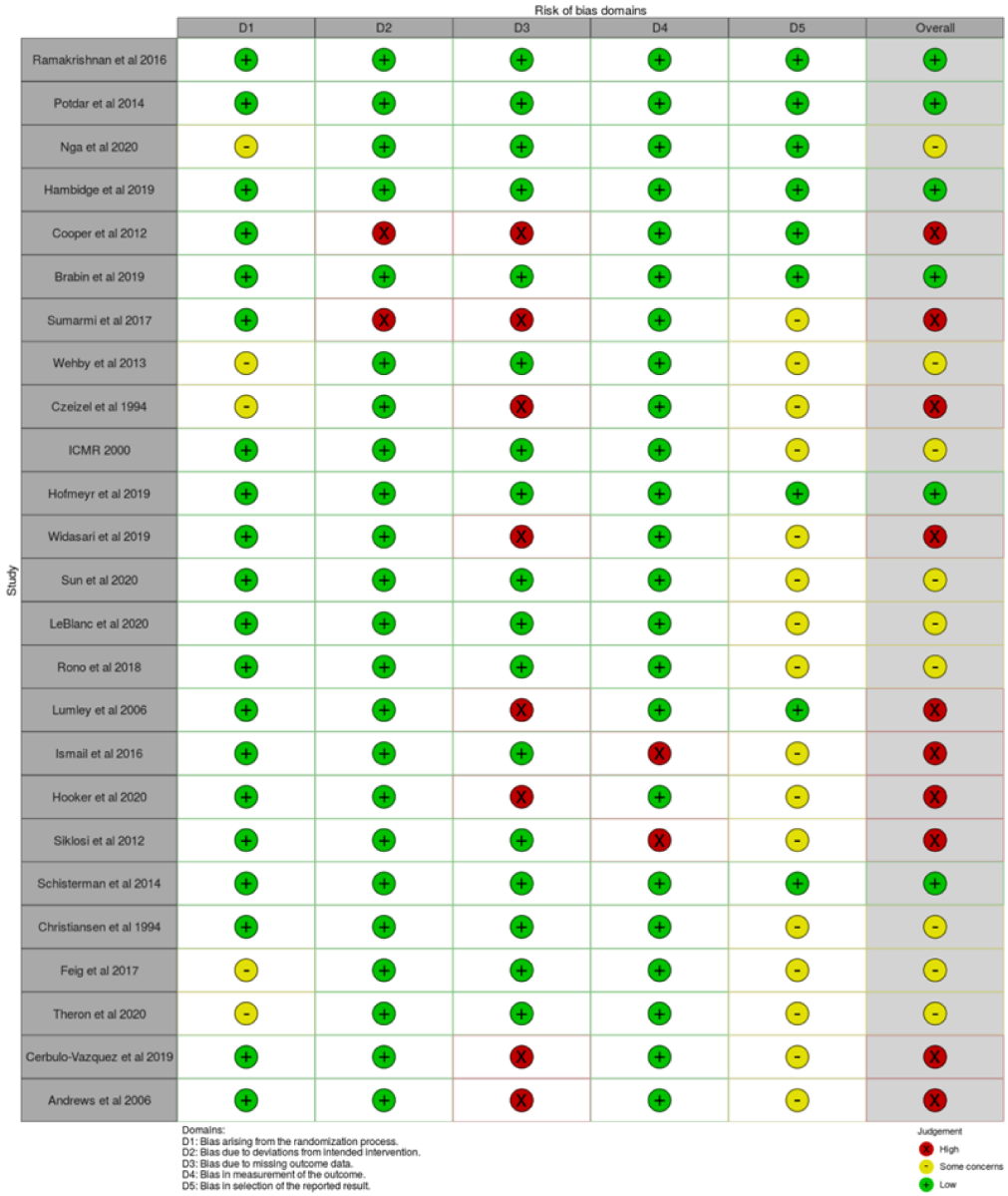
6.1. Low birth weight and birth weight

6.1A. Revised Cochrane risk-of-bias tool for randomized trials (RoB 2) (v 22Aug2019)



Supplementary Figure 42. RoB2 assessment for studies assessing low birth weight and birth weight: traffic light plot.

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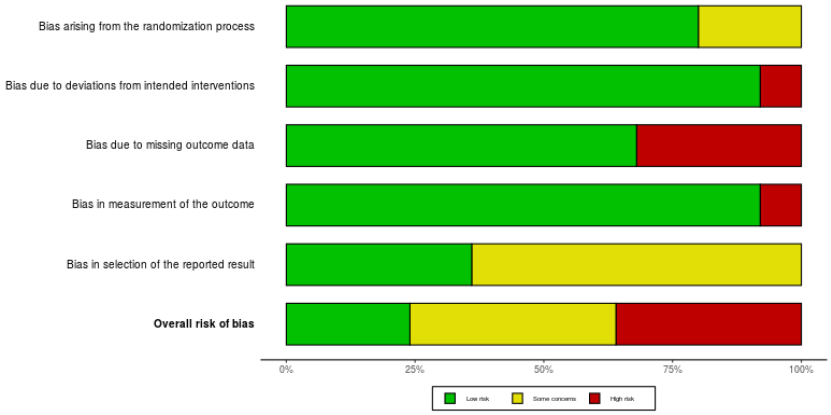

Supplementary Figure 43. RoB2 assessment for studies assessing low birth weight and birth weight: summary plot.

6.1B. Revised Cochrane risk-of-bias tool for cluster-randomized trials (RoB 2 CRT) (v 10Nov2020)

No studies

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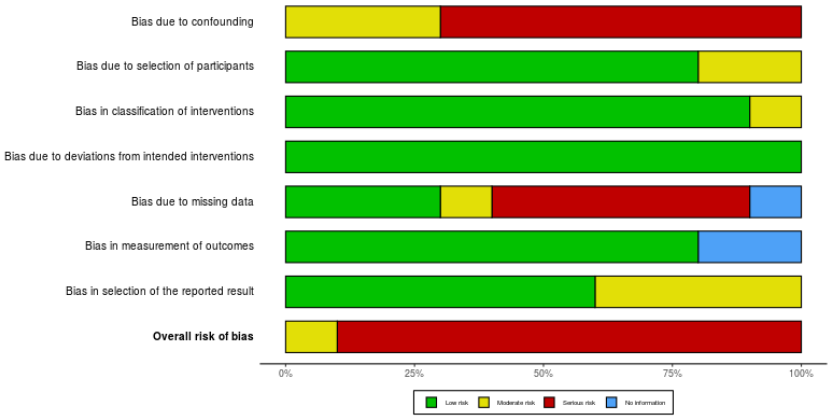
6.1C. Risk Of Bias In Non-randomized Studies – of Interventions (ROBINS-I) (v 01Aug2016)

Supplementary Figure 44. ROBINS assessment for studies assessing low birth weight and birth weight: traffic light plot.



Supplementary Figure 45. ROBINS assessment for studies assessing low birth weight and birth weight: summary plot.

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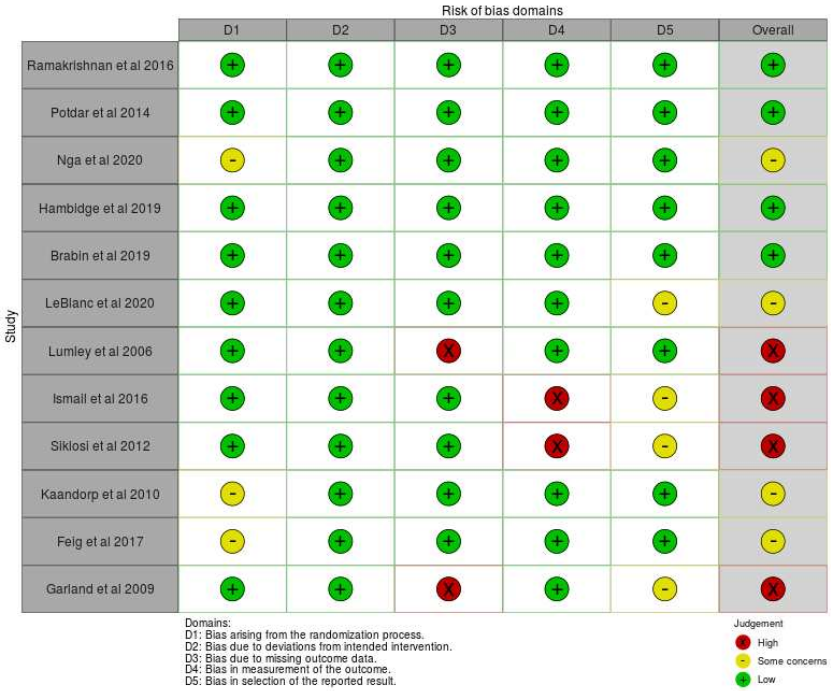
6.2. Small for gestational age and birth weight for gestational age

6.2A. Revised Cochrane risk-of-bias tool for randomized trials (RoB 2) (v 22Aug2019)



Supplementary Figure 46. RoB2 assessment for studies assessing small for gestational age and birth weight for gestational age: traffic light plot.

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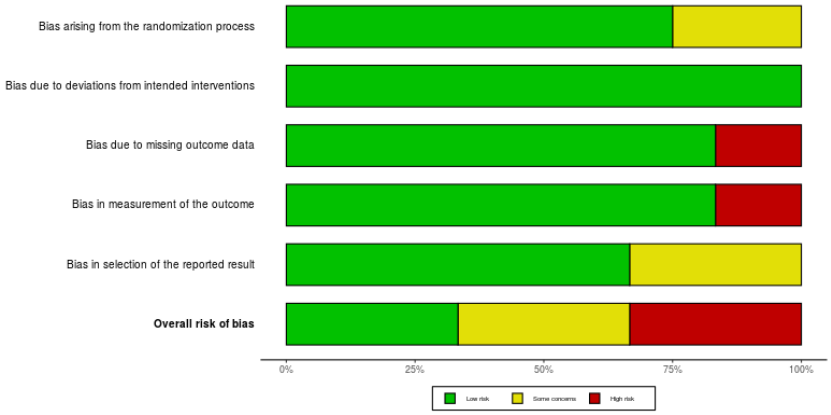

Supplementary Figure 47. RoB2 assessment for studies assessing small for gestational age and birth weight for gestational age: summary plot.

6.2B. Revised Cochrane risk-of-bias tool for cluster-randomized trials (RoB 2 CRT) (v 10Nov2020)

No studies

6.2C. Risk Of Bias In Non-randomized Studies – of Interventions (ROBINS-I) (v 01Aug2016)

No studies

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6.3. Preterm birth and gestational age

6.3A. Revised Cochrane risk-of-bias tool for randomized trials (RoB 2) (v 22Aug2019)

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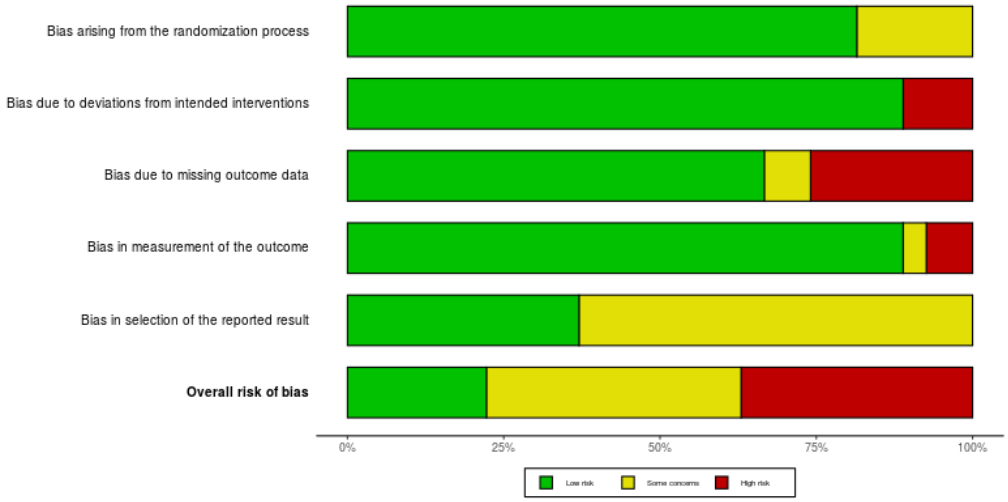
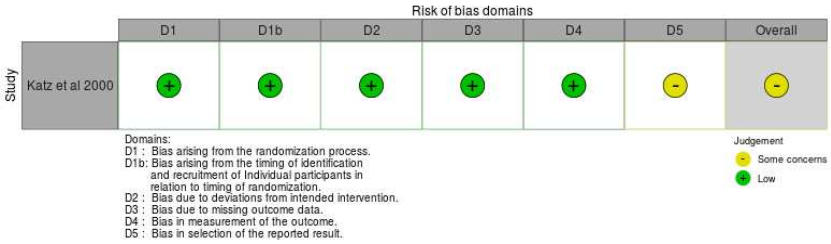
Supplementary Figure 48. RoB2 assessment for studies assessing preterm birth and gestational age: traffic light plot.



Supplementary Figure 49. RoB2 assessment for studies assessing preterm birth and gestational age: summary plot.

6.3B. Revised Cochrane risk-of-bias tool for cluster-randomized trials (RoB 2 CRT) (v 10Nov2020)



Supplementary Figure 50. RoB2 CRT assessment for studies assessing preterm birth and gestational age: traffic light plot.

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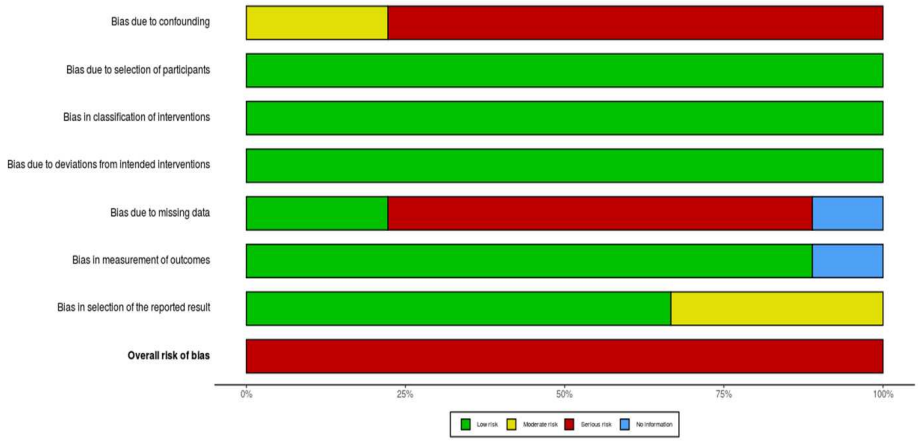
6.3C. Risk Of Bias In Non-randomized Studies – of Interventions (ROBINS-I) (v 01Aug2016)

Supplementary Figure 51. ROBINS assessment for studies assessing preterm birth and gestational age: traffic light plot.



Supplementary Figure 52. ROBINS assessment for studies assessing preterm birth and gestational age: summary plot.

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7. Preconception interventions to prevent low birth weight, preterm birth and small for gestational age: GRADE assessments

Notes

1. For all assessments, both available RCTs and qRCTS were assessed. Since only one option could be selected for study design, "randomised trials" was selected.

2. Studies in which the outcome of interest was part of a composite were not included. Based on this, one study was not included in analyses – de Jong-Potjer et al 2006 (comparison: pre- and periconception health interventions, outcome: composite including preterm birth).

3. Comparisons for which studies examining interventions that may affect low birth weight, small for gestational age and preterm birth were assessed separately to those examining interventions that may prevent these outcomes (signalled in the title).

4. Studies with no events of the outcome of interest were assessed separately, similarly to their treatment in meta-analyses (not included but reported separately).

5. GRADE assessments were performed and tables were generated using GRADEPro GDT (https://gradepro.org/)[74] .

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Supplementary Table 29. GRADE assessment: Any general population-based nutritional intervention in the pre- and periconception period compared to folic acid supplementation, supplementation with other micronutrients (not folic acid), placebo, standard or routine care or no intervention for preventing low birth weight, small for gestational age, or preterm birth.

Certainty assessment							№ of patients		Effect			
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**any general population-based nutritional intervention in the pre- and periconception period**	**folic acid supplementation, placebo or no intervention**	**Relative (95% CI)**	**Absolute (95% CI)**	**Certainty**	**Importance**
Low birth weight												
7	randomised trials	serious [a]	serious [b]	not serious	not serious	publication bias strongly suspected [c]	372/6949 (5.4%)	362/7024 (5.2%)	**RR 1.07** (0.93 to 1.23)	**4 more per 1,000** (from 4 fewer to 12 more)	⊕◯◯◯ VERY LOW	IMPORTANT
Small for gestational age												
2	randomised trials	not serious	not serious	serious	serious [d]	none	106/668 (15.9%)	116/693 (16.7%)	**RR 0.92** (0.73 to 1.15)	**13 fewer per 1,000** (from 45 fewer to 25 more)	⊕⊕◯◯ LOW	IMPORTANT
Preterm birth												
6	randomised trials	serious [e]	serious [f]	not serious	serious [g]	none	498/6856 (7.3%)	468/6827 (6.9%)	**RR 1.07** (0.79 to 1.43)	**5 more per 1,000** (from 14 fewer to 29 more)	⊕◯◯◯ VERY LOW	IMPORTANT

CI: Confidence interval; **RR:** Risk ratio

a. Out of 7 studies, 2 studies were high risk of bias, 3 were moderate/some concerns, and 2 were low risk.

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b. There was wide variation in effects between studies, and evidence of moderate heterogeneity (I^2 46.54%).
c. Egger's test P value <0.05.
d. Optimal information size criterion not met.
e. Out of 6 studies, 2 studies were high risk of bias, 2 had some concerns, and 2 were low risk.
f. There was wide variation in effects between studies, and evidence of substantial heterogeneity (I^2 78.51%).
g. Optimal information size criterion met but 95% CIs fail to exclude important harm.

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Supplementary Table 30. GRADE assessment: Any general population-based nutritional intervention from preconception throughout pregnancy compared to pregnancy-only intervention for preventing low birth weight, small for gestational age, or preterm birth.

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**any nutritional intervention from preconception throughout pregnancy**	**pregnancy-only intervention**	**Relative (95% CI)**	**Absolute (95% CI)**		
Low birth weight												
3	randomised trials	serious [a]	serious [b]	serious	serious [c]	publication bias strongly suspected [d]	125/662 (18.9%)	135/672 (20.1%)	**RR 0.68** (0.33 to 1.43)	**64 fewer per 1,000** (from 135 fewer to 86 more)	⊕◯◯◯ VERY LOW	IMPORTANT
Small for gestational age												
0									not estimable		-	
Preterm birth												
0									not estimable		-	

CI: Confidence interval; **RR:** Risk ratio

a. Out of 3 studies, 1 study was low risk of bias, 1 had some concerns and one was high risk.

b. There was variation in effect estimates, and evidence of moderate heterogeneity (I^2 54.12%).

c. Optimal information size criterion not met.

d. Egger's test P value <0.05.

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Supplementary Table 31. GRADE assessment: Pre- and periconception multiple micronutrient supplementation containing iron and folic acid compared to pre- and periconception folic acid supplementation, supplementation with other micronutrients (not folic acid), placebo or no intervention for preventing low birth weight, small for gestational age, or preterm birth.

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**pre- and periconception multiple micronutrient supplementation containing iron and folic acid**	**pre- and periconception folic acid supplementation, placebo or no intervention**	**Relative (95% CI)**	**Absolute (95% CI)**		
Low birth weight												
4	randomised trials	serious [a]	serious [b]	not serious	not serious	none	290/6044 (4.8%)	271/6010 (4.5%)	**RR 1.06** (0.90 to 1.25)	**3 more per 1,000** (from 5 fewer to 11 more)	⊕⊕◯◯ LOW	IMPORTANT
Small for gestational age												
1	randomised trials	not serious	serious [c]	serious	serious [d]	none	65/525 (12.4%)	68/559 (12.2%)	**RR 1.02** (0.74 to 1.40)	**2 more per 1,000** (from 32 fewer to 49 more)	⊕◯◯◯ VERY LOW	IMPORTANT
Preterm birth												
4	randomised trials	serious [a]	serious [b]	not serious	not serious	none	413/6125 (6.7%)	402/6110 (6.6%)	**RR 1.03** (0.90 to 1.18)	**2 more per 1,000** (from 7 fewer to 12 more)	⊕⊕◯◯ LOW	IMPORTANT

CI: Confidence interval; **RR:** Risk ratio

a. Out of 4 studies, 1 study was low risk of bias, 1 had some concerns, and 2 were high risk of bias.

b. There was notable variation in effect size point estimates, though heterogeneity was low.

c. Single study.

d. Optimal information size criterion not met.

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Supplementary Table 32. GRADE assessment: Pre- and periconception iron and folic acid supplementation compared to pre- and periconception folic acid supplementation or no intervention for preventing low birth weight, small for gestational age, or preterm birth.

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**pre- and periconception iron and folic acid supplementation**	**pre- and periconception folic acid supplementation or no intervention**	**Relative (95% CI)**	**Absolute (95% CI)**		
Low birth weight												
3	randomised trials	serious [a]	serious [b]	serious	serious [c]	publication bias strongly suspected [d]	80/838 (9.5%)	95/993 (9.6%)	**RR 0.74** (0.34 to 1.61)	**25 fewer per 1,000** (from 63 fewer to 58 more)	⊕◯◯◯ VERY LOW	IMPORTANT
Small for gestational age												
2	randomised trials	not serious	not serious	serious	serious [c]	none	94/658 (14.3%)	116/693 (16.7%)	**RR 0.83** (0.66 to 1.05)	**28 fewer per 1,000** (from 57 fewer to 8 more)	⊕⊕◯◯ LOW	IMPORTANT
Preterm birth												
2	randomised trials	not serious	serious [e]	serious	serious [c]	none	89/664 (13.4%)	75/696 (10.8%)	**RR 1.42** (0.60 to 3.37)	**45 more per 1,000** (from 43 fewer to 255 more)	⊕◯◯◯ VERY LOW	IMPORTANT

CI: Confidence interval; **RR:** Risk ratio

a. Out of 3 studies, 1 was moderate risk of bias, while 2 were low risk.

b. There was wide variation in effect estimates, with high heterogeneity (I^2 83.10%).

c. Optimal information size criterion not met.

d. Egger's test P value <0.05.

e. There was wide variation in effect estimates, with high heterogeneity (I^2 87.79%).

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Supplementary Table 33. GRADE assessment: Preconception and pregnancy iron and folic acid supplementation compared to pregnancy-only iron and folic acid supplementation for preventing low birth weight, small for gestational age, or preterm birth.

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**preconception and pregnancy iron and folic acid supplementation**	**Pregnancy-only iron and folic acid supplementation**	**Relative (95% CI)**	**Absolute (95% CI)**		
Low birth weight												
1	randomised trials	serious [a]	serious [b]	serious	serious [c]	all plausible residual confounding would reduce the demonstrated effect	3/144 (2.1%)	8/86 (9.3%)	**RR 0.28** (0.08 to 1.03)	**67 fewer per 1,000** (from 86 fewer to 3 more)	⊕◯◯◯ VERY LOW	IMPORTANT
Small for gestational age												
0									not estimable		-	
Preterm birth												
0									not estimable		-	

CI: Confidence interval; **RR:** Risk ratio

a. The single identified study was rated as high risk of bias.

b. Single study.

c. Optimal information size criterion not met.

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Supplementary Table 34. GRADE assessment: Pre- and periconception food supplementation longer duration compared to shorter duration of food supplementation for preventing low birth weight, small for gestational age, or preterm birth.

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**pre- and periconception food supplementation longer duration**	**shorter duration of food supplementation**	**Relative (95% CI)**	**Absolute (95% CI)**		
Low birth weight												
1	randomised trials	serious [a]	serious [b]	serious	serious [c]	none	-/273	-/256	**OR 0.40** (0.14 to 1.12)	**0 fewer per 1,000** (from 0 fewer to 0 fewer)	⊕◯◯◯ VERY LOW	IMPORTANT
Small for gestational age												
0									not estimable		-	
Preterm birth												
0									not estimable		-	

CI: Confidence interval; **OR:** Odds ratio

a. The single identified study was rated as high risk of bias.

b. Single study.

c. Optimal information size criterion not met.

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Supplementary Table 35. GRADE assessment: Preconception and pregnancy food supplementation compared to pregnancy-only food supplementation for preventing low birth weight, small for gestational age, or preterm birth.

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**preconception and pregnancy food supplementation**	**pregnancy-only food supplementation**	**Relative (95% CI)**	**Absolute (95% CI)**		
Low birth weight												
2	randomised trials	not serious	serious [a]	serious	serious [b]	none	122/548 (22.3%)	127/586 (21.7%)	**RR 1.00** (0.79 to 1.26)	**0 fewer per 1,000** (from 46 fewer to 56 more)	⊕◯◯◯ VERY LOW	IMPORTANT
Small for gestational age												
2	randomised trials	not serious	not serious	serious	serious [b]	none	171/562 (30.4%)	202/599 (33.7%)	**RR 0.89** (0.78 to 1.02)	**37 fewer per 1,000** (from 74 fewer to 7 more)	⊕⊕◯◯ LOW	IMPORTANT
Preterm birth												
2	randomised trials	not serious	serious [a]	serious	serious [b]	none	73/563 (13.0%)	57/600 (9.5%)	**RR 1.38** (1.06 to 1.79)	**36 more per 1,000** (from 6 more to 75 more)	⊕◯◯◯ VERY LOW	IMPORTANT

CI: Confidence interval; **RR:** Risk ratio

a. There was notable variation in effect size estimates, although there was no evidence of heterogeneity.

b. Optimal information size criterion not met.

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Supplementary Table 36. GRADE assessment: Pre- and periconception general health interventions compared to standard or routine care for preventing low birth weight, small for gestational age, or preterm birth.

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**pre- and periconception general health interventions**	**standard or routine care or no intervention**	**Relative (95% CI)**	**Absolute (95% CI)**		
Low birth weight												
2	randomised trials	very serious [a]	not serious	serious	serious [b]	none	39/476 (8.2%)	66/712 (9.3%)	**RR 1.27** (0.83 to 1.94)	**25 more per 1,000** (from 16 fewer to 87 more)	⊕◯◯◯ VERY LOW	IMPORTANT
Small for gestational age												
1	randomised trials	very serious [c]	serious [d]	serious	serious [b]	none	40/378 (10.6%)	31/382 (8.1%)	**RR 1.13** (0.57 to 2.14)	**11 more per 1,000** (from 35 fewer to 93 more)	⊕◯◯◯ VERY LOW	IMPORTANT
Preterm birth												
1	randomised trials	very serious [c]	serious [d]	serious	serious [b]	none	24/392 (6.1%)	17/394 (4.3%)	**RR 1.41** (0.74 to 2.69)	**18 more per 1,000** (from 11 fewer to 73 more)	⊕◯◯◯ VERY LOW	IMPORTANT

CI: Confidence interval; **RR:** Risk ratio

a. Both studies identified were high risk of bias.

b. Optimal information size criterion not met.

c. The single study identified was assessed as high risk of bias.

d. Single study.

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Supplementary Table 37. GRADE assessment: Pre- and periconception interventions to prevent early adverse pregnancy outcomes compared to placebo or no intervention for preventing low birth weight, small for gestational age, or preterm birth, among women with one or more previous miscarriages.

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**pre- and periconception interventions to prevent early adverse pregnancy outcomes**	**placebo or no intervention**	**Relative (95% CI)**	**Absolute (95% CI)**		
Low birth weight												
1	randomised trials	very serious [a]	serious [b]	serious	serious [c]	strong association	7/52 (13.5%)	17/30 (56.7%)	**RR 0.23** (0.11 to 0.51)	**436 fewer per 1,000** (from 504 fewer to 278 fewer)	⊕◯◯◯ VERY LOW	IMPORTANT
Small for gestational age												
2	randomised trials	very serious [d]	not serious	not serious	serious [c]	strong association	11/119 (9.2%)	24/89 (27.0%)	**RR 0.35** (0.18 to 0.68)	**175 fewer per 1,000** (from 221 fewer to 86 fewer)	⊕⊕◯◯ LOW	IMPORTANT
Preterm birth												
5	randomised trials	very serious [e]	serious [f]	not serious	serious [c]	strong association	21/219 (9.6%)	50/163 (30.7%)	**RR 0.32** (0.20 to 0.51)	**209 fewer per 1,000** (from 245 fewer to 150 fewer)	⊕◯◯◯ VERY LOW	IMPORTANT

CI: Confidence interval; **RR:** Risk ratio

a. The single identified study was assessed as high risk of bias.

b. Single study.

c. Optimal information size criterion not met.

d. Both identified studies were assessed as high risk of bias.

e. Out of 5 studies, 3 studies were high risk of bias and 2 had some concerns.

f. There was notable variation in effect size point estimates, though heterogeneity was low.

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Supplementary GRADE assessment: Preconception and pregnancy interventions to prevent or manage non-communicable diseases compared to pregnancy-only intervention that may affect low birth weight, small for gestational age, or preterm birth.

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**preconception and pregnancy interventions to prevent or manage non-communicable diseases**	**pregnancy-only intervention**	**Relative (95% CI)**	**Absolute (95% CI)**		
Low birth weight												
1	randomised trials	very serious [a]	serious [b]	serious	serious [c]	all plausible residual confounding would suggest spurious effect, while no effect was observed	7/92 (7.6%)	1/57 (1.8%)	**RR 4.34** (0.55 to 34.34)	**59 more per 1,000** (from 8 fewer to 585 more)	⊕◯◯◯ VERY LOW	IMPORTANT
Small for gestational age												
0									not estimable		-	
Preterm birth												
0									not estimable		-	

CI: Confidence interval; **RR:** Risk ratio

a. The single study identified was assessed as high risk of bias.

b. Single study.

c. Optimal information size criterion not met.

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Supplementary Table 39. GRADE assessment: Pre- and periconception interventions to prevent or manage infectious diseases compared to placebo or no intervention for preventing low birth weight, small for gestational age, or preterm birth.

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**pre- and periconception interventions to prevent or manage infectious diseases**	**placebo or no intervention**	**Relative (95% CI)**	**Absolute (95% CI)**		
Low birth weight												
0									not estimable		-	
Small for gestational age												
0									not estimable		-	
Preterm birth												
2	randomised trials	very serious [a]	serious [b]	serious	serious [c]	none	131/2009 (6.5%)	62/266 (23.3%)	**RR 0.62** (0.20 to 1.93)	**89 fewer per 1,000** (from 186 fewer to 217 more)	⊕◯◯◯ VERY LOW	IMPORTANT

CI: Confidence interval; **RR:** Risk ratio

a. Both identified studies were high risk of bias.

b. There was wide variation in effects between studies, and evidence of substantial heterogeneity (I^2 95.34%).

c. Optimal information size criterion not met.

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Supplementary Table 40. GRADE assessment: Pre- and periconception interventions to prevent or manage infectious diseases compared to placebo or alternative intervention, or no intervention that may affect low birth weight, small for gestational age, or preterm birth.

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**pre- and periconception interventions to prevent or manage infectious diseases**	**placebo or no intervention**	**Relative (95% CI)**	**Absolute (95% CI)**		
Low birth weight												
1	randomised trials	very serious [a]	serious [b]	serious	serious [c]	none	3/23 (13.0%)	0/16 (0.0%)	**RR 4.96** (0.27 to 89.87)	**0 fewer per 1,000** (from 0 fewer to 0 fewer)	⊕◯◯◯ VERY LOW	IMPORTANT
Small for gestational age												
1	randomised trials	very serious [a]	serious [b]	serious	serious [d]	none	5/1447 (0.3%)	4/1424 (0.3%)	**RR 1.23** (0.33 to 4.57)	**1 more per 1,000** (from 2 fewer to 13 more)	⊕◯◯◯ VERY LOW	IMPORTANT
Preterm birth												
3	randomised trials	very serious [e]	not serious	not serious	serious [c]	none	49/1872 (2.6%)	43/1794 (2.4%)	**RR 1.05** (0.71 to 1.57)	**1 more per 1,000** (from 7 fewer to 14 more)	⊕◯◯◯ VERY LOW	IMPORTANT
Preterm birth (single study no events intervention group)												
1	randomised trials	serious [f]	serious [b]	serious	serious [c]	strong association	0/87 (0.0%)	9/94 (9.6%)	**RR 0.06** (0.00 to 0.96)	**90 fewer per 1,000** (from 4 fewer to --)	⊕◯◯◯ VERY LOW	IMPORTANT

CI: Confidence interval; **RR:** Risk ratio

a. The single study identified was assessed as high risk of bias.

b. Single study.

c. Optimal information size criterion not met.

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d. Optimal information size criterion met but 95% CIs fail to exclude important benefit or harm.
e. Out of 3 studies, 2 were high risk of bias and one had some concerns.
f. The identified study had some concerns for risk of bias.

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Supplementary Table 41. GRADE assessment: Preconception and pregnancy interventions to prevent or manage infectious diseases compared to pregnancy-only intervention that may affect low birth weight, small for gestational age, or preterm birth.

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**preconception and pregnancy interventions to prevent or manage infectious diseases**	**pregnancy-only intervention**	**Relative (95% CI)**	**Absolute (95% CI)**		
Low birth weight												
1	randomised trials	serious [a]	serious [b]	serious	serious [c]	strong association	19/90 (21.1%)	9/96 (9.4%)	**RR 2.65** (1.20 to 5.81)	**155 more per 1,000** (from 19 more to 451 more)	⊕◯◯◯ VERY LOW	IMPORTANT
Small for gestational age												
0									not estimable		-	
Preterm birth												
0									not estimable		-	

CI: Confidence interval; **RR:** Risk ratio

a. The single study identified was assessed to have some concerns for risk of bias.

b. Single study.

c. Optimal information size criterion not met.

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Supplementary Table 42. GRADE assessment: Pre- and periconception interventions to promote reproductive planning compared to standard or routine care for preventing low birth weight, small for gestational age, or preterm birth.

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**pre- and periconception interventions to promote reproductive planning**	**standard or routine care**	**Relative (95% CI)**	**Absolute (95% CI)**		
Low birth weight												
0									not estimable		-	
Small for gestational age												
0									not estimable		-	
Preterm birth												
1	randomised trials	very serious [a]	serious [b]	serious	serious [c]	none	122/603 (20.2%)	140/537 (26.1%)	**RR 0.79** (0.63 to 0.99)	**55 fewer per 1,000** (from 96 fewer to 3 fewer)	⊕◯◯◯ VERY LOW	IMPORTANT

CI: Confidence interval; **RR:** Risk ratio

a. The single identified study was high risk of bias.

b. Single study.

c. Optimal information size criterion not met.

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