Nepal 2003

Methods	Cluster RCT (also factorial design).
Participants	4926 pregnant women and 4130 liveborn infants in a rural community in Nepal = 426 sectors (communities of about 100-150 households) - only 2 of the 5 arms (total of 1659 infants) used in this review). Women who were currently pregnant, breastfeeding a baby less than 9 months old, menopausal, sterilised or widowed were excluded. Supplementation commenced before conception.
Interventions	Zinc: zinc + iron + folate (n = 858). No zinc: iron + folate (n = 801).
Outcomes	**Maternal** Preterm birth. **Neonatal** Stillbirth or neonatal death; birthweight; chest circumference; head circumference; length; low birthweight; small-for-gestational age.
Notes	Adherence: mean adherence was 88%. RRs adjusted for the cluster-design effects were presented for each of the 5 arms of the RCT

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Randomised sectors by "drawing numbered identical chips from a hat" (in blocks of 5 within each community)
Allocation concealment (selection bias)	Low risk	Supplements were of identical shape, size and colour and arrived in Nepal in opaque, sealed and labelled bottles coded 1-5. The code allocation was kept locked at the Johns Hopkins University, Baltimore
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Participants, investigators, field staff and statisticians were all blinded to the codes throughout the study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Investigators, field staff and statisticians were all blinded to the codes throughout the study

Nepal 2003 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Unclear risk	155/827 (19%) of infants in the zinc group and 167/872 (19%) in the non-zinc group were lost to follow-up or excluded from analysis (infant died, mother refused, home was inaccessible, birthweight was measured more than 72 hours after birth or missing data)
Selective reporting (reporting bias)	Low risk	Most expected outcomes were reported with some exceptions such as mode of birth and postpartum haemorrhage
Other bias	Low risk	No apparent evidence of other sources of bias apart from a small imbalance between groups in maternal weight (which was adjusted for in the analyses)

Pakistan 2005

Methods	RCT.
Participants	242 women from 2 urban hospitals and 1 rural community; 10-16 weeks' gestation. Women with known systemic disease were excluded. Serum zinc at enrolment was mean 71.51 µg/dl (SD 21) in the zinc group and 74.09 (SD 23.2) in the placebo group
Interventions	Zinc: 20 mg elemental zinc (zinc sulphate powder capsule) (n = 121). No zinc: placebo (n = 121) (capsule); in addition, all women had routine supplements of folic acid and iron
Outcomes	**Maternal** Preterm birth. **Neonatal** Occipitofrontal circumference; low birthweight; abortion/intrauterine death; birthweight; length.
Notes	Adherence: about 65% of women had good adherence, which was similar in both groups

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	"simple random sampling with preassigned code."

Pakistan 2005 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment not reported.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Women and health workers were blinded to content of medication
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Not reported but likely to have been done.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Losses to follow-up: 15% (actual figures not given, but paper notes that losses were non-differential)
Selective reporting (reporting bias)	Unclear risk	Only 1 of the maternal outcomes specified in the review were reported in the trial
Other bias	Low risk	No apparent risk of other bias.

Peru 1999

Methods	RCT.
Participants	1295 women with low zinc intakes from an urban shanty town in Lima, Peru; at 10 to 24 weeks' gestation
Interventions	Zinc: 15 mg zinc plus 60 mg iron plus 250 µg folate (n = 521). Non-zinc: 60 mg iron plus 250 µg folate (n = 495).
Outcomes	**Maternal** Duration of pregnancy; preterm birth (< 37 weeks); very preterm birth (< 33 weeks); post-term birth (> 42 completed weeks); serum and urinary zinc concentrations; haemoglobin; serum ferritin; fetal heart rate and movement measures. **Neonatal** Birthweight; low birthweight; high birthweight; cord vein zinc; cord vein haemoglobin; cord vein serum ferritin; crownheel length; head circumference; chest, calf and mid-upper arm circumference; biceps, subcapsular and calf skinfold thicknesses.

Peru 1999 *(Continued)*

Notes	Adherence: mean of about 85% of capsules consumed, which was similar across the groups. Adjustments for baseline differences in maternal age and in-home electricity were made by multiple regression

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Method of sequence generation not reported.
Allocation concealment (selection bias)	Low risk	Coded blister packages were prepared by a local pharmaceutical company, and allocation was thus concealed by use of this third party
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Investigators, other health personnel and women were blinded
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Not reported but likely to have been done due to use of placebo
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	21.5% (279/1295) women lost to follow-up by time of giving birth - 18 (1%) were found to live in another community and therefore not eligible to participate; 92 (7%) declined to participate; 71 (5%) moved out of the study area; 30 (2%) miscarried; 58 (4%) left the study for other reasons; 10 (1%) were subsequently found to have twin pregnancies or to have developed pregnancy complications
Selective reporting (reporting bias)	Unclear risk	Expected outcomes such as caesarean birth and perinatal death were not reported
Other bias	Low risk	No apparent risk of other bias.

Peru 2004

Methods	RCT.
Participants	242 low-income Peruvian women, with maternal dietary zinc intake approximately 8 mg/day; low-risk women with singleton pregnancy; supplementation commenced 10-16 weeks' gestation; exclusions made according to a protocol for fetal neurobehavioural assessment

Peru 2004 *(Continued)*

Interventions	Zinc: zinc + iron + folate (n = 109 [94]). No zinc: iron + folate (n = 113 [101]).
Outcomes	**Maternal** Preterm birth with complications; gestational age at birth. **Neonatal and infant** Fetal heart rate measures; birthweight; length; biparietal diameter; abdominal circumference; femur diaphysis length; infant feeding; infant growth; child development at 54 months; dietary and nutritional status at 54 months; mean arterial pressure at 54 months; BMI at 54 months; haemoglobin concentration at 54 months; plasma zinc concentration at 54 months; C-reactive protein concentration at 54 months; Home Observation for the Measurement of the Environment (HOME) Scale assessment at 54 months; heart rate measures at 54 months.
Notes	Adherence: mean adherence rate was 87% (86% in the zinc group and 88% in the no zinc group)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Women were randomly assigned in blocks of 2 using computer-generated lists from Johns Hopkins and sent to Peru
Allocation concealment (selection bias)	Low risk	The randomisation code was made by the pharmaceutical company and maintained in a sealed and secured envelope in Lima; supplements had the same appearance and taste
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Both study personnel and participants were blinded.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Not specifically stated, but we have assumed that outcome assessors were blinded and remained blinded for the longer-term analyses

Peru 2004 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	222/242 (90.1%) women completed the protocol and 195 (80.6%) were included in the analysis of birth outcomes - 94 (78%) zinc and 101 (84%) no zinc. The 47 lost were made up of 20 change of address, declining to continue in the study, or travel and 27 exclusions for significant obstetric or medical complications At 54-month follow-up, there were 205 eligible children (includes children of 10 mothers excluded from the initial analysis), and evaluations were completed for 184 (90%) of these children (86 (87%) from the zinc group and 98 (92%) from the non-zinc group
Selective reporting (reporting bias)	High risk	A number of birth outcomes such as postpartum haemorrhage, stillbirth or neonatal death, low birthweight or Apgar scores were not reported; and preterm birth was only reported as preterm birth with complications which were treated as study exclusions
Other bias	Low risk	No apparent source of other bias although the study was designed to primarily assess neonatal and infant outcomes (see selective reporting above)

S Africa 1985

Methods	RCT.
Participants	Black women before 20 weeks' gestation at antenatal clinic near Durban, South Africa. Women specifically selected on the basis of being at high risk for low zinc status. Dietary recall histories showed women to be deficient in energy, protein, B vitamins, calcium and iron. Women in the zinc group in this study had a significantly lower mean weight than the women in the placebo group
Interventions	Zinc: zinc gluconate 30-90 mg daily (n = 32). No zinc: placebo (n = 33).
Outcomes	Gestational age at birth; birthweight.
Notes	Adherence: figures for adherence were not given, but the authors commented that it was high, due to free transportation to the clinic where the supplements or placebo were consumed under supervision. Groups given dietary supplements are not included in the analysis

Risk of bias

Bias	Authors' judgement	Support for judgement

S Africa 1985 (*Continued*)

Random sequence generation (selection bias)	Unclear risk	Method of sequence generation not reported.
Allocation concealment (selection bias)	Low risk	Randomisation by numbered packets prepared at the pharmacy, code held by pharmacy until the end of the study
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Blinding by use of placebo until end of study.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Not reported but likely to have been blinded due to use of placebo
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Losses to follow-up: 10% (exact figures not given) of women before giving birth, principally due to moving out of the area
Selective reporting (reporting bias)	High risk	Only 2 of the outcomes specified in this review were reported in the trial
Other bias	Unclear risk	No apparent risk of other bias.

UK 1989

Methods	RCT.
Participants	500 women at first antenatal visit below 20 weeks' gestation. Median zinc concentrations at enrolment were 1.192 µmol/10 x 10 cells in the zinc group and 1.147 in the placebo group
Interventions	Zinc: 20 mg elemental zinc (n = 246). No zinc: placebo (n = 248).
Outcomes	**Maternal** Preterm delivery (< 37 weeks); post-term delivery (> 42 weeks); prelabour rupture of membranes; pregnancy hypertension; any maternal infection - (pre or postdelivery); caesarean section; postpartum haemorrhage; congenital malformations. **Neonatal** Low birthweight (< 2500 g); birthweight > 3500 g; small-for-gestational age (< 10th centile); Apgar score at 1 minute < 6; Apgar score at 5 minutes < 8;

UK 1989 *(Continued)*

	stillbirth/neonatal death.
Notes	Adherence: adherence levels were not reported, but non-adherers were included in study results. At 28 to 32 weeks' gestation, just over half the women claimed to be taking the supplement every day, and nearly 2 thirds were doing so by the time of giving birth. Although results were not presented separately for adherers and non-adherers, the authors state that no significant differences between them were found, apart from a significantly lower risk of postpartum infection among the adherers

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Computer generated randomisation tables.
Allocation concealment (selection bias)	Low risk	Bottles prepared by drug company and labelled A/B.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Use of placebo; code not broken until the end of the study.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Not reported but likely to have been done due to use of placebo
Incomplete outcome data (attrition bias) All outcomes	Low risk	Losses to follow-up: 6/500 (1%) - 4 women moved and 2 miscarried
Selective reporting (reporting bias)	Low risk	Most of the outcomes specified in the review were reported.
Other bias	Low risk	No apparent risk of other bias.

UK 1991a

Methods	RCT.
Participants	56 women with pre-pregnancy weight less than 95% of ideal or previous small-for-gestational age infant or Asian or primigravida smoking > 5 cigarettes per day, from last 15-25 weeks of pregnancy. Iron/folate as per doctor's instructions.
Interventions	Zinc: 22.5 mg elemental zinc (n = 30). No zinc: placebo (n = 26).
Outcomes	Pregnancy hypertension; preterm delivery; post-term labour;

UK 1991a *(Continued)*

	induction of labour; caesarean section; small-for-gestational age; low birthweight;. birthweight > 3500 g; congenital malformations; stillbirth/neonatal death.
Notes	Adherence was 43% in the zinc group and 67% in the placebo group - outcomes were presented separately for adherers and non-adherers

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random number table, no mention of how the numbers were generated but probably adequately done
Allocation concealment (selection bias)	Unclear risk	"coded placebo or non-placebo tablet or 22.5 mg effervescent zinc...was randomly prescribed."
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Described as double-blind, "all clinical decisions were made by staff in the labour and delivery wards who were unaware of the trial details"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Not reported, but probably done.
Incomplete outcome data (attrition bias) All outcomes	Low risk	4/60 (7%); 2 women moved home, 1 termination of pregnancy, 1 miscarriage (all in the placebo group)
Selective reporting (reporting bias)	Unclear risk	Trial did not report all of the primary outcomes expected or specified for this review
Other bias	Low risk	No apparent source of other bias.

UK 1991b

Methods	RCT.
Participants	134 women less than 18 weeks' gestation.
Interventions	Zinc: 62 mg elemental zinc (n = 72). No zinc: spansules without zinc (n = 62). All women were also given iron and folate.

UK 1991b *(Continued)*

Outcomes	Low birthweight < 2500 g; birthweight > 3500 g; congenital malformations; stillbirth/neonatal death.
Notes	Adherence was not reported.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	"double blind."
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Losses to follow-up: 18/152 (12%) due to GI effects, aborted or woman moved, leaving 72 in the zinc group and 62 in the control group
Selective reporting (reporting bias)	High risk	No maternal outcomes reported.
Other bias	Low risk	No apparent risk of other bias.

USA 1983

Methods	RCT.
Participants	213 Mexican women of Mexican descent, not adolescent (> 17 years age). Less than 27 weeks' gestation. No medical problems. Women specifically selected on the basis of being at high risk for low zinc status - at baseline, 81% of women had recalled dietary intakes providing < 2/3 RDA
Interventions	Zinc: 20 mg elemental zinc plus vitamins (n = 107). No zinc: placebo with vitamins (n = 106).
Outcomes	Pregnancy hypertension; low serum zinc before. birth (< 53.3 micrograms/dl); low hair zinc;

USA 1983 *(Continued)*

	smell dysfunction; taste dysfunction; preterm birth; low birthweight.
Notes	Adherence: defined as a woman who was in the study long enough to take supplements for more than 60 days and who returned to the pharmacy for 1 or more refills of 60 capsules. According to this definition, 82% overall (90% (81/90) in the control group and 75% (65/87) in the zinc group) were adherent in those 177 women who were not lost to follow-up

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Method of sequence generation not reported.
Allocation concealment (selection bias)	Low risk	"randomly assigned" - not definitively stated but likely to have been third party randomisation
Blinding of participants and personnel (performance bias) All outcomes	Low risk	"double-blind"; "capsules were indistinguishable."
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported but stated that "code was not broken until the study was completed"
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	36/213 (16.9%) lost to follow-up (3 spontaneous abortions < 20 weeks, 2 sets of twins, 31 records that could not be located). The breakdown was 20/107 (18.7%) lost from the zinc group and 16/106 (15.1%) from the placebo group. Breakdown of reasons was not reported except for spontaneous abortions - 1 in the zinc group and 2 in the control group
Selective reporting (reporting bias)	Unclear risk	A number of primary maternal, pregnancy and neonatal outcomes were not reported (e.g. caesarean section, postpartum haemorrhage, perinatal death)
Other bias	Low risk	No apparent source of other bias.

USA 1985

Methods	RCT.
Participants	138 Hispanic teenagers in Los Angeles; mean dietary zinc intakes were about 50% of the RDA. Under 17 years, were not over 27 weeks' gestation according to LMP, and did not have diabetes, heart, renal or thyroid disease
Interventions	Zinc (20 mg) versus no zinc (placebo): all women were also given a supplement of 8000 IU vitamin A, 400 IU vitamin D, 30 IU vitamin E, 2 mg thiamin mononitrate, 2 mg riboflavin, 20 mg niacinamide, 5 mg pyridoxine HCl, 1 mg folic acid, 10 µg vitamin B12 (cyanocobalamin), 10 mg pantothenic acid, 60 mg vitamin C, 100 mg calcium (as carbonate), 20 mg iron (as ferrous fumarate), 50 mg magnesium (as oxide), 1 mg manganese (as sulphate) and 150 µg iodine (as potassium iodide). In addition, 108 mg iron/day was prescribed routinely at 20 weeks' gestation
Outcomes	Infant weight; placental weight; pregnancy-induced hypertension; meconium-stained amniotic fluid; birthweight > 2500 g; Apgar scores; preterm birth; fetal death; plasma zinc; haemoglobin; haematocrit; ferritin levels; folacin levels.
Notes	Adherence: defined as those in study long enough to take supplements for more than 60 days and who then returned to the pharmacy for 1 or more refills of 60 capsules = 93% of teenagers who returned for a final interview. No significant difference in adherence rates between the groups, so results were not presented separately for adherers and non-adherers

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	"randomly assigned" - not further described.
Allocation concealment (selection bias)	Low risk	Third party (dispensed by clinic pharmacy).
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Capsules were identical in composition and indistinguishable in taste and appearance, and the code was not broken until the end of the study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Not reported but likely to have been blinded due to the use of a placebo

USA 1985 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Birthweight data not available for 31/138 (22%); due to 2 spontaneous abortions and 29 records that could not be located
Selective reporting (reporting bias)	High risk	Data for outcomes such as perinatal death and preterm birth were collected but not fully reported (only that no significant differences were found)
Other bias	Low risk	No apparent source of other bias.

USA 1989

Methods	RCT.
Participants	652 low-income adolescents (average age 17.6 years; range 13.5 to 19.6); less than 25 weeks' gestation; women thought be at risk for zinc deficiency.
Interventions	Zinc: 30 mg zinc (n = 268). No zinc: placebo (n = 288).
Outcomes	**Maternal** Preterm birth; weight. **Neonatal** Birthweight; respiratory assistance.
Notes	Reported compliance was good - 87% consumed 6 or 7 tablets per week

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	"randomly assigned."
Allocation concealment (selection bias)	Unclear risk	"randomly assigned."
Blinding of participants and personnel (performance bias) All outcomes	Low risk	"double-blind"; "identical-appearing tablets".
Blinding of outcome assessment (detection bias) All outcomes	Low risk	"Neither the subjects nor the investigators were informed of tablet identity until after completion of the data collection."

USA 1989 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Losses to follow-up: 10.9% (71/652) at entry and 14.7% (96/652) [cumulative] at birth. Breakdown of losses by group was not reported, nor were reasons for losses
Selective reporting (reporting bias)	Unclear risk	A number of primary maternal, pregnancy and neonatal outcomes were not reported (e.g. caesarean, postpartum haemorrhage, perinatal death)
Other bias	Low risk	No apparent source of other bias.

USA 1995

Methods	RCT.
Participants	589 Afro American women. At 19 weeks' gestation. Plasma zinc level less than median gestation specific for the population. No medical problems.
Interventions	Zinc: 25 mg elemental zinc per day (n = 286). No zinc: placebo (n = 294). All women also received multivitamins.
Outcomes	Preterm birth; pregnancy hypertension; low birthweight; small-for-gestational age; stillbirth/neonatal death; neonatal sepsis; child mental and psychomotor development at 5 years.
Notes	Adherence: mean was 78% of days for both groups. Adherence was defined as the percentage of zinc tablets consumed compared with the number of days enrolled in the project prior to birth

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Computer-generated random numbers.
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment not described.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	"both caregivers and subjects were blind regarding the content of the supplement."

USA 1995 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Low risk	Not reported but likely to have been done due to the use of a placebo
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Losses to follow-up: samples unavailable from 24.7% (143/580 women; 63/294 (21.4%) in the zinc group and 80/286 (28%) in the placebo group At 5 years of age, results were available for 355/580 children (61%)
Selective reporting (reporting bias)	Unclear risk	Not all outcomes specified in the review, or expected, were reported in the trial
Other bias	Low risk	No apparent source of other bias.

BMI: body mass index
dl: decilitre
g: gram
GI: gastrointestinal
IU: international units
kJ: kilojoule
L: litre
LMP: last menstrual period
mg: milligram
RCT: randomised controlled trial
RDA: recommended daily allowance
RR: risk ratio
SD: standard deviation
µg: micrograms
µmol: micromoles

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
An 2001	Not truly randomised - allocation was by order of hospital visits
Appelbaum 1979	Only outcome is zinc level in amniotic fluid.
Christian 2001	Women had night blindness; no prespecified outcomes reported
Fawzi 2005	Population was not women in a normal state of health (women with HIV)
France 2004	Compared micronutrients (including zinc) with placebo.

(*Continued*)

Hambidge 1983	No mention of randomisation, or method of allocating women to zinc or no-zinc groups
India 1993	Large discrepancies in numbers of participants and losses to follow-up
Kynast 1986	Not truly randomised - allocation was by a form of alternation
Mahmoudian 2005	Different population and not relevant outcomes.
Makola 2003	Some women with gestation greater than 26 weeks; micronutrients versus placebo
Nishiyama 1999	Not a randomised controlled trial - mothers chose 1 of 3 intervention groups
Nogueira 2003	No mention of randomisation; serum zinc levels only outcome.
Van Vliet 2001	Different intervention.
Villamor 2006	Different population.
Yalda 2010	Different population and not relevant outcomes.

Characteristics of ongoing studies *[ordered by study ID]*

Zahiri 2010

Trial name or title	Assessment of the effect of zinc supplementation on adverse outcomes of pregnancy
Methods	Randomised controlled trial.
Participants	Inclusion criteria: gestational age of 12-16 weeks based on reliable LMP or first trimester ultrasound, lack of history of high-risk pregnancy, lack of chronic underlying diseases (such as heart disease, HTN, DM). Exclusion criteria: lack of complete treatment or lack of follow-up
Interventions	Zinc 30 mg from 12th week of gestation every other day in the intervention group and no zinc is supplemented in the control group
Outcomes	Gestation, birthweight and other pregnancy and neonatal clinical outcomes
Starting date	March 2009.
Contact information	Dr Ziba Zahiri (drzibazahiri@gums.ac.ir).
Notes	

DM: diabetes mellitus
HTN: hypertension

LMP: last menstrual period

DATA AND ANALYSES

Comparison 1. Zinc supplementation versus no zinc (with or without placebo)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Preterm birth	16	7637	Risk Ratio (M-H, Fixed, 95% CI)	0.86 [0.76, 0.97]
1.1 Low zinc or nutrition	14	7099	Risk Ratio (M-H, Fixed, 95% CI)	0.87 [0.77, 0.98]
1.2 Normal zinc or nutrition	2	538	Risk Ratio (M-H, Fixed, 95% CI)	0.64 [0.31, 1.32]
2 Stillbirth or neonatal death	8		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
2.1 Low zinc or nutrition: stillbirth or neonatal death	4	1364	Risk Ratio (M-H, Fixed, 95% CI)	1.57 [0.83, 2.98]
2.2 Low zinc or nutrition: stillbirth or deaths in first 7 days	1	1555	Risk Ratio (M-H, Fixed, 95% CI)	1.03 [0.71, 1.51]
2.3 Low zinc or nutrition: deaths from 0 to 28 days	1	1498	Risk Ratio (M-H, Fixed, 95% CI)	1.08 [0.68, 1.71]
2.4 Normal zinc or nutrition: stillbirth or neonatal death	3	683	Risk Ratio (M-H, Fixed, 95% CI)	0.93 [0.24, 3.65]
3 Birthweight	16	5780	Mean Difference (IV, Fixed, 95% CI)	-9.48 [-34.28, 15.33]
3.1 Low zinc or nutrition	13	5103	Mean Difference (IV, Fixed, 95% CI)	-9.87 [-35.70, 15.96]
3.2 Normal zinc or nutrition	3	677	Mean Difference (IV, Fixed, 95% CI)	-4.78 [-93.67, 84.11]
4 Small-for-gestational age	8	4252	Risk Ratio (M-H, Fixed, 95% CI)	1.02 [0.94, 1.11]
4.1 Low zinc or nutrition	7	4200	Risk Ratio (M-H, Fixed, 95% CI)	1.03 [0.95, 1.12]
4.2 Normal zinc or nutrition	1	52	Risk Ratio (M-H, Fixed, 95% CI)	0.24 [0.05, 1.10]
5 Low birthweight	14	5643	Risk Ratio (M-H, Random, 95% CI)	0.93 [0.78, 1.12]
5.1 Low zinc or nutrition	11	4964	Risk Ratio (M-H, Random, 95% CI)	0.93 [0.75, 1.14]
5.2 Normal zinc or nutrition	3	679	Risk Ratio (M-H, Random, 95% CI)	0.88 [0.58, 1.36]
6 Antepartum haemorrhage	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
6.1 Second trimester	1	1206	Risk Ratio (M-H, Fixed, 95% CI)	1.59 [0.57, 4.45]
6.2 Third trimester	1	1206	Risk Ratio (M-H, Fixed, 95% CI)	0.96 [0.39, 2.33]
7 Pregnancy hypertension or pre-eclampsia	7	2975	Risk Ratio (M-H, Fixed, 95% CI)	0.83 [0.64, 1.08]
8 Prelabour rupture of membranes	2	1691	Risk Ratio (M-H, Fixed, 95% CI)	0.93 [0.78, 1.11]
9 Post-term birth	3	1554	Risk Ratio (M-H, Fixed, 95% CI)	1.09 [0.74, 1.60]
10 Induction of labour	1	52	Risk Ratio (M-H, Fixed, 95% CI)	0.27 [0.10, 0.73]
11 Any maternal infection	3	1185	Risk Ratio (M-H, Fixed, 95% CI)	1.06 [0.74, 1.53]
12 Meconium in liquor	2	1385	Risk Ratio (M-H, Fixed, 95% CI)	1.16 [0.86, 1.56]
13 Caesarean section	6	2164	Risk Ratio (M-H, Random, 95% CI)	0.95 [0.58, 1.53]
14 Instrumental vaginal birth	1	1206	Risk Ratio (M-H, Fixed, 95% CI)	1.12 [0.79, 1.59]
15 Retention of placenta	1	179	Risk Ratio (M-H, Fixed, 95% CI)	6.62 [0.83, 52.71]
16 Postpartum haemorrhage	3	718	Risk Ratio (M-H, Fixed, 95% CI)	1.33 [0.78, 2.26]
17 Smell dysfunction	1	170	Risk Ratio (M-H, Fixed, 95% CI)	1.01 [0.55, 1.86]
18 Taste dysfunction	1	170	Risk Ratio (M-H, Fixed, 95% CI)	0.74 [0.36, 1.50]
19 Fetal heart rate (beats/minute)	1	176	Mean Difference (IV, Fixed, 95% CI)	-1.20 [-3.31, 0.91]

20 Fetal heart rate variability (beats/minute)	1	176	Mean Difference (IV, Fixed, 95% CI)	0.60 [0.04, 1.16]
21 Number of fetal accelerations	1	176	Mean Difference (IV, Fixed, 95% CI)	1.9 [0.91, 2.89]
22 Number of fetal movement bouts	1	176	Mean Difference (IV, Fixed, 95% CI)	1.70 [-2.53, 5.93]
23 Fetal activity level	1	176	Mean Difference (IV, Fixed, 95% CI)	-0.30 [-2.66, 2.06]
24 Fetal movement amplitude	1	176	Mean Difference (IV, Fixed, 95% CI)	0.20 [-0.79, 1.19]
25 Gestational age at birth	7	2857	Mean Difference (IV, Fixed, 95% CI)	0.08 [-0.07, 0.22]
26 High birthweight	5	2837	Risk Ratio (M-H, Fixed, 95% CI)	1.00 [0.84, 1.18]
27 Five-minute Apgar score less than 5	2	1692	Risk Ratio (M-H, Fixed, 95% CI)	1.02 [0.26, 4.03]
28 Infant head circumference (cm)	7	3991	Mean Difference (IV, Random, 95% CI)	-0.03 [-0.17, 0.11]
29 Blue or floppy (neonatal hypoxia)	1	179	Risk Ratio (M-H, Fixed, 95% CI)	5.67 [0.70, 46.18]
30 Neonatal sepsis	2	736	Risk Ratio (M-H, Fixed, 95% CI)	0.17 [0.03, 1.01]
31 Neonatal jaundice	1	179	Risk Ratio (M-H, Fixed, 95% CI)	0.95 [0.20, 4.56]
32 Respiratory distress syndrome	2	1136	Risk Ratio (M-H, Fixed, 95% CI)	0.68 [0.40, 1.14]
33 Neonatal intraventricular haemorrhage	1	580	Risk Ratio (M-H, Fixed, 95% CI)	0.97 [0.14, 6.86]
34 Necrotising enterocolitis	1	580	Risk Ratio (M-H, Fixed, 95% CI)	1.95 [0.18, 21.34]
35 Neonatal hospital stay	1	580	Mean Difference (IV, Fixed, 95% CI)	-1.1 [-2.39, 0.19]
36 Congenital malformation	6	1240	Risk Ratio (M-H, Fixed, 95% CI)	0.67 [0.33, 1.34]
37 Diarrhoea (episodes/infant over 6 months)	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
37.1 Acute diarrhoea	1	410	Mean Difference (IV, Fixed, 95% CI)	-0.40 [-0.79, -0.01]
37.2 Persistent diarrhoea	1	410	Mean Difference (IV, Fixed, 95% CI)	0.0 [-0.13, 0.13]
38 Dysentery (episodes/infant over 6 months)	1	410	Mean Difference (IV, Fixed, 95% CI)	-0.06 [-0.12, 4.66]
39 Cough (episodes/infant over 6 months)	1	410	Mean Difference (IV, Fixed, 95% CI)	-0.20 [-0.56, 0.16]
40 Acute lower respiratory infection (episodes/infant over 6 months)	1	410	Mean Difference (IV, Fixed, 95% CI)	-0.10 [-0.34, 0.14]
41 Impetigo (episodes/infant over 6 months)	1	410	Mean Difference (IV, Fixed, 95% CI)	-0.30 [-0.44, -0.16]
42 Infant weight-for-age (Z-score)	2		Mean Difference (IV, Random, 95% CI)	Subtotals only
42.1 Z-score at 6 months	2	304	Mean Difference (IV, Random, 95% CI)	0.20 [-0.19, 0.59]
42.2 Z-score at 13 months	1	168	Mean Difference (IV, Random, 95% CI)	-0.40 [-0.70, -0.10]
43 Infant weight-for-height (Z-score)	1	136	Mean Difference (IV, Fixed, 95% CI)	-0.05 [-0.33, 0.23]
44 Infant mid-upper arm circumference (mm)	3	1844	Mean Difference (IV, Fixed, 95% CI)	0.74 [-0.17, 1.65]
45 Infant mental development index	1	168	Mean Difference (IV, Fixed, 95% CI)	-3.30 [-6.51, -0.09]
46 Infant psychomotor development index	1	168	Mean Difference (IV, Fixed, 95% CI)	-7.0 [-11.92, -2.08]
47 Infant approach	1	168	Mean Difference (IV, Fixed, 95% CI)	0.10 [-0.38, 0.58]
48 Infant emotional tone	1	168	Mean Difference (IV, Fixed, 95% CI)	-0.65 [-1.13, -0.17]
49 Infant activity	1	168	Mean Difference (IV, Fixed, 95% CI)	-0.10 [-0.43, 0.23]
50 Infant co-operation	1	168	Mean Difference (IV, Fixed, 95% CI)	-0.60 [-1.16, -0.04]
51 Infant vocalisation	1	168	Mean Difference (IV, Fixed, 95% CI)	-0.08 [-0.54, 0.38]

52 Differential abilities score at 5 years	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
52.1 Non-verbal ability	1	355	Mean Difference (IV, Fixed, 95% CI)	-2.40 [-5.70, 0.90]
52.2 Verbal ability	1	355	Mean Difference (IV, Fixed, 95% CI)	-0.30 [-2.56, 1.96]
52.3 General conceptual ability, IQ	1	355	Mean Difference (IV, Fixed, 95% CI)	-1.10 [-3.74, 1.54]
53 Visual sequential memory score	1	355	Mean Difference (IV, Fixed, 95% CI)	-0.80 [-2.24, 0.64]
54 Auditory sequential memory score	1	355	Mean Difference (IV, Fixed, 95% CI)	0.60 [-0.65, 1.85]
55 Knox cube score	1	355	Mean Difference (IV, Fixed, 95% CI)	0.10 [-0.19, 0.39]
56 Gross motor scale score	1	355	Mean Difference (IV, Fixed, 95% CI)	-2.0 [-4.79, 0.79]
57 Grooved pegboard score	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
57.1 Dominant hand	1	355	Mean Difference (IV, Fixed, 95% CI)	2.5 [-1.26, 6.26]
57.2 Non-dominant hand	1	355	Mean Difference (IV, Fixed, 95% CI)	1.20 [-2.71, 5.11]
58 Intelligence quotient of infants at 54 months	1	181	Mean Difference (IV, Fixed, 95% CI)	-0.40 [-3.33, 2.53]

WHAT'S NEW

Last assessed as up-to-date: 1 March 2012.

Date	Event	Description
9 November 2011	New search has been performed	Search updated. Three new trials included (China 2001; Ghana 2009; Iran 2010) and four new trials excluded (Mahmoudian 2005; Van Vliet 2001; Villamor 2006; Yalda 2010).
9 November 2011	New citation required but conclusions have not changed	New authors helped to update this review.

HISTORY

Protocol first published: Issue 3, 1997

Review first published: Issue 3, 1997

Date	Event	Description
1 July 2011	Amended	Search updated. Thirteen trial reports added to Studies awaiting classification
6 November 2008	Amended	Converted to new review format.