Anaemia, prenatal iron use, and risk of adverse pregnancy outcomes: systematic review and meta-analysis

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Table 1: Characteristics of included randomised trials
High income countries

Author, country, publication year	Study participants	Intervention group	Control group	Supplementation initiation and duration	Trial quality
Barton et al, Ireland, 1994 [1]	Pregnant women during first trimester of pregnancy with Hb ≥140 g/L (n=97)	Iron and folic acid tablets, one tablet twice daily (each tablet contained elemental iron 60 mg and folic acid 0.5 mg)	Placebo	From the end of first trimester until delivery	High
Bloxam et al, UK, 1989 [2]	Pregnant women at 16 weeks of gestation (n=40)	Multivitamin capsules, twice daily (each containing iron (47 mg), folic acid (0.5 mg), thiamine (2 mg), riboflavin (2 mg), pyridoxine (1 mg), nicotinamide (10 mg), calcium pantothenate (2.17 mg), and vitamin C (50 mg), twice per day	Multivitamin capsules, twice daily (each containing folic acid (0.5 mg), thiamine (2 mg), riboflavin (2 mg), pyridoxine (1 mg), nicotinamide (10 mg), calcium pantothenate (2.17 mg), and vitamin C (50 mg))	From enrollment for 22 weeks	High
Butler et al, UK, 1968 [3]	Pregnant women less than 20 weeks of gestation with Hb >100 g/L (n=200)	Iron (122 mg); or iron (122 mg) and folic acid (3.4 mg), daily	No treatment	From 20th week until 40th week	-
Buytaert et al, Netherlands, 1983 [4]	Pregnant women between 8 and 14 weeks of gestation with Hb ≥ 112.8 g/L (n=45)	Iron (105 mg), daily	No iron supplement	From 16th week of gestation, until 6 weeks postpartum	-
Cantlie et al, Canada, 1971 [5]	Pregnant women between 1st and 5th month of gestation, with Hb ≥ 120 g/L in the 1st trimester, and ≥ 110 g/L in the 2nd trimester (n=27)	Iron tablet, twice daily (each tablet contained elemental iron 39 mg) and multivitamin tablet (each contained copper (2 mg), magnesium (6 mg), manganese (0.3 mg), vitamin A (1,000 IU), vitamin D (500 IU), bone flour (130 mg), vitamin B1 (1 mg), vitamin B2 (1 mg), brewer's yeast concentrate (50 mg), niacinamide (5 mg), vitamin C (25 mg), sodium iodide (0.2 mg) and folic acid (0.05 µg))	Multivitamin tablet (each contained copper (2 mg), magnesium (6 mg), manganese (0.3 mg), vitamin A (1,000 IU), vitamin D (500 IU), bone flour (130 mg), vitamin B1 (1 mg), vitamin B2 (1 mg), brewer's yeast concentrate (50 mg), niacinamide (5 mg), vitamin C (25 mg), sodium iodide (0.2 mg) and folic acid (0.05 µg))	Unclear	-
Chan et al, Hong Kong, 2009 [6]	Pregnant women less than 16 weeks of gestation with Hb between 80 to 140 g/L (n=1164)	Iron (60 mg), daily	Placebo	From enrollment until delivery	High
Chisholm et al, UK, 1966 [7]	Pregnant women less than 28 weeks of gestation with Hb ≥ 102 g/L or a normal serum iron reading (n=360)	Iron (900 mg); or iron (900 mg) and folic acid (500 µg); or iron (900 mg) and folic acid (5 mg), daily	Placebo	From 28th week until 40th week	-

Author, country, publication year	Study participants	Intervention group	Control group	Supplementation initiation and duration	Trial quality
Cogswell et al, USA, 2003 [8]	Pregnant women less than 20 weeks of gestation with Hb ≥110 g/L and a ferritin concentration > 20 g/L (n=275)	Iron (30 mg), daily	Placebo	From enrollment until 28 week of gestation	High
Dawson et al, USA, 1989 [9]	Pregnant women between 8 to 17 weeks of gestation with Hb ≥ 110 g/L or hematocrit concentrations ≥ 0.33 (n=41)	Iron (18 mg) and multivitamin tablet (containing vitamin A (5000 IU), D (400 IU), C (60 mg), E (10 mg), folic acid (0.4 mg), thiamin (1.5 mg), riboflavin (1.7 mg), niacin (20 mg), pyridoxine (2 mg), vitamin B 12 (6 mg), pantothenic acid (10 mg)), daily	Multivitamin tablet (containing vitamin A (5000 IU), D (400 IU), C (60 mg), E (10 mg), folic acid (0.4 mg), thiamin (1.5 mg), riboflavin (1.7 mg), niacin (20 mg), pyridoxine (2 mg), vitamin B 12 (6 mg), pantothenic acid (10 mg)), daily	Throughout pregnancy	-
De Benaze et al, France, 1989 [10]	Pregnant women 3 months ± 3 weeks into pregnancy without anaemia (n=191)	Iron (45 mg), daily	Placebo	From enrollement for 6 months	-
Eskeland et al, Norway, 1997 [11]	Pregnant women less than 13 weeks of gestation with Hb between 110 and 148 g/L (n=60)	Iron and heme iron, three tablets daily (each containing elemental iron 8 mg and heme iron 1.2 mg)	Placebo	From the 20th week until delivery	High
Harvey et al, UK, 2007 [12]	Pregnant women less than 14 weeks of gestation with Hb ≥ 108 g/L (n=13)	Iron (100 mg), daily	Placebo	From 16 weeks until delivery	High
Holly et al, USA, 1955 [13]	Pregnant women less than 26 weeks of gestation with Hb > 100 g/L (n=207)	Iron salt (1 gm), daily	No treatment	From enrollment until delivery	-
Lee et al, South Korea, 2005 [14]	Pregnant women in their first trimester of pregnancy (n=154)	Iron (30 mg) and folic acid (175 µg) [early supplementation]; or iron (60 mg) and folic acid (350 µg) [early supplementation]; or iron (30 mg) and folic acid (175 µg) [late supplementation]; or iron (60 mg) and folic acid (350 µg) [late supplementation], daily	Placebo	From the first trimester until delivery (early supplementation); and from 20th week until delivery (late supplementation)	-
Makrides et al, Australia, 2003 [15]	Pregnant women with Hb ≥ 110 g/L (n=430)	Iron (20 mg), daily	Placebo	From 20th week of gestation until delivery	High
McKenna et al, UK, 2003 [16]	Pregnant women less than 20 weeks gestation and booking Hb>104 g/L (n=102)	Iron (10 mg) fortified water, daily	Non-fortified water	From 22nd week of gestation until 28th week	High

Author, country, publication year	Study participants	Intervention group	Control group	Supplementation initiation and duration	Trial quality
Meier et al, USA, 2003 [17]	Pregnant women at their first prenatal visit without iron deficiency (n=144)	Iron (60 mg), daily	Placebo	From enrollment till the end of pregnancy. Both groups received 1 mg of folic acid daily.	-
Milman et al, Denmark, 1991 [18-22]	Pregnant women between 9 to 18 weeks of gestation (n=248)	Iron (66 mg), daily	Placebo	From second trimester until delivery	-
Pritchard et al, USA, 1958 [23]	Pregnant women in the second trimester of pregnancy by date of last mentrual period (n=123)	Iron (112 mg), daily	Placebo	From second trimester until delivery	-
Puolakka et al, Finland, 1980 [24]	Pregnant women less than 16 weeks of gestation and no earlier haematological problems (n=32)	Iron (200 mg), daily	Placebo	From 16th week of gestation until one month postpartum	-
Romslo et al, Norway, 1983 [25]	Pregnant women less than 10 weeks of pregnancy (n=52)	Iron (200 mg), daily	Placebo	From 10 weeks of gestation onwards	-
Siega-Riz et al, USA, 2006 [26]	Pregnant women less than 20 weeks of gestation with Hb ≥ 110 g/L and serum ferritin > 40 mg/L (n=429)	Iron (30 mg) and multivitamin tablet (containing vitamin A (4000 IU), D (400 IU), C (70 mg), folic acid (0.5 mg), thiamine (1.5 mg), riboflavin (1.6 mg), niacin (17 mg), vitamin B6 (2.6 mg), B12 (2.5 µg), calcium (200 mg), magnesium (100 mg), copper (1.5 mg) and zinc (15 mg)), daily	Multivitamin tablet (each containing vitamin A (4000 IU), D (400 IU), C (70 mg), folic acid (0.5 mg), thiamine (1.5 mg), riboflavin (1.6 mg), niacin (17 mg), vitamin B6 (2.6 mg), B12 (2.5 µg), calcium (200 mg), magnesium (100 mg), copper (1.5 mg) and zinc (15 mg)), daily	From enrollment until 26-29 weeks of gestation	High
Svanberg et al, Sweden, 1975 [27]	Pregnant women less than 14 weeks of gestation and Hb > 120 g/L (n=60)	Iron (200 mg), daily	Placebo	From 12 weeks of gestation until 9 weeks postpartum	-
Taylor et al, UK, 1982 [28]	Pregnant women less than 12 weeks of gestation (n=48)	Iron (65 mg) and folic acid (350 µg), daily	No treatment	From 12 weeks of gestation until delivery	-

Author, country, publication year	Study participants	Intervention group	Control group	Supplementation initiation and duration	Trial quality
Tura et al, Itlay, 1989 [29]	Pregnant women, non-anaemic with normal iron balance at the beginning of their pregnancy (n= 245). 204 women who were iron-deficient and received two forms of iron preparation were not included.	Iron (40 mg) containing 250 g of ferritin, daily	Placebo	From 12-16 weeks of gestation until the end of puerperium	High
Van Eijk et al, Netherlands, 1978 [30]	Pregnant women with uncomplicated pregnancies and deliveries (n=30)	Iron (100 mg), daily	Placebo	From the third month of gestation until delivery	-
Wallenburg et al, Netherlands, 1984 [31]	Pregnant women between 8 to 14 weeks of gestation with Hb $\geq$ 112.8 g/L (n=44)	Iron (105 mg), daily	No iron supplementation	From 16th week of gestation until 6 weeks postpartum	High

Hb= Haemoglobin

Low or middle income countries

Author, country, publication year	Study participants	Intervention group	Control group	Supplementation initiation and duration	Trial quality
Batu et al, Burma, 1976 [32]	Pregnant women at their first prenatal visit (n=133)	Iron and placebo tablets, one tablet twice daily (each tablet contained elemental iron 60 mg); or iron and folic acid tablets, one tablet twice daily (each tablet contained elemental iron 60 mg and folic acid 0.5 mg)	Two placebo tablets, twice daily; or folic acid and placebo tablets, one tablet twice daily (each with folic acid 0.5 mg)	From 22-25 wks of pregnancy, for 16 wks	-
Charoenlarp et al, Thailand, 1988 [33]	Pregnant women with Hb >80 g/L (n=325)	Iron (120 mg) and folic acid (5 mg) (supervised); or iron (240 mg) and folic acid (5 mg) (supervised); or iron (240 mg) (supervised); or iron (120 mg) and folic acid (5 mg) (motivated but unsupervised); or iron (240 mg) and folic acid (5 mg) (motivated but unsupervised)	Placebo (unsupervised)	From 18-22 wks of gestation, throughout pregnancy	-
Christian et al, Nepal, 2003 [34-39]	Newly identified pregnant women (with positive pregnancy test) (n=2949)	Iron (60 mg), folic acid (400 µg) and vitamin A (1000 µg), daily	Vitamin A only (1000 µg); or folic acid (400 µg) and vitamin A (1000 µg), daily	From enrollment, upto 3 months postpartum	High
Falahi et al, Iran, 2011[40]	Pregnant women less than 20 weeks of gestation, with Hb>110 g/L and serum ferritin>20 µg/L (n=148)	Iron (60 mg), daily	Placebo	From enrolment until delivery	-
Fleming et al, Nigeria, 1986 [41]	Pregnant women less than 24 weeks of gestation (n=200)	Iron (60 mg), folic acid (1 mg), daily and malaria prophylaxis; or iron (60 mg), daily and malaria prophylaxis	Malaria prophylaxis; or folic acid (1 mg) dialy and malaria prophylaxis	From first antenatal attendance to 6 weeks postpartum	High
Freire et al, Ecuador, 1989 [42]	Pregnant women between 24-28th week of pregnancy (n=412)	Iron (78 mg), daily	Placebo	From enrollment for 2 months	-
Hoa et al, Vietnam, 2005 [43]	Pregnant women between 14th and 18th week of pregnancy; with Hb level >70 g/L (n=202)	Iron (60 mg) and folic acid (250 µg) tablet; or iron (15 mg), folic acid (200 µg) and vitamin C (17.5 g) as fortified milk, daily	Placebo (tablet); or folic acid (200 µg) and vitamin C (17.5 g) as fortified milk, daily	From enrollment, probably for 16 weeks	-
Liu et al, China, 1996 [44]	Pregnant women from 13 week of gestation (n=395)	Iron (60 mg) and folic acid (0.25 mg); or iron (120 mg) and folic acid (0.5 mg), daily	Placebo	From 13th week to 38th week of pregnancy	-

Author, country, publication year	Study participants	Intervention group	Control group	Supplementation initiation and duration	Trial quality
Ma et al, China, 2010 [45]	Pregnant women with Hb between 80 and 110g/L at 12-24 weeks of gestation (n=164)	Iron (60 mg), or iron (60 mg) and folic acid (400 µg), daily	Placebo	From enrollment, for 2 months	-
Menendez et al, Gambia, 1994 [46,47]	Pregnant women <34 wks of gestation (n=550)	Iron (60 mg), daily	Placebo	From enrollment until delivery. All women received a weekly dose of 5 mg folic acid	-
Ndyomugyenyi et al, Uganda, 2000 [48]	Pregnant women in the first or second trimester with Hb >80 g/L (n=576)	Iron (120 mg), daily, folic acid (5 mg) weekly and placebo chloroquine	Placebo	From enrollment for less than 8 weeks to more than 12 weeks	-
Ouladsahebmadarek et al, Iran, 2011[49]	Pregnant women in the first trimester with Hb>120 g/L (n= 960)	Iron (30 mg) and multivitamins (details not provided in the paper), daily	Placebo and multivitamins	From 13 weeks of gestation, until delivery	-
Preziosi et al, Niger, 1997 [50]	Pregnant women between 25 to 31 weeks of pregnancy (n=197)	Iron (100 mg), daily	Placebo	From enrollment until delivery	High
Simmons et al, Jamaica, 1993 [51]	Pregnant women, 14-22 weeks of gestation and Hb between 80 and 110 g/L (n=244)	Iron (100 mg), daily	Placebo	From enrollment for 12 weeks	-
Sood et al, India, 1975 [52]	Pregnant women at 20-24 weeks of gestation with Hb >50 g/L (n=151)	Iron (120 mg); or iron (30 mg), folic acid (5 mg) and vitamin B12 (100 µg injection every two weeks); or iron (60 mg), folic acid (5 mg) and vitamin B12 (100 µg injection every two weeks); or iron (120 mg), folic acid (5 mg) and vitamin B12 (100 µg injection every two weeks); or iron (240 mg), folic acid (5 mg) and vitamin B12 (100 µg injection every two weeks)	Placebo; or folic acid (5 mg) and vitamin B12 (100 µg injection every two weeks)	From 24-28 weeks till the end of trial	-
Suharno et al, Indonesia, 1993 [53]	Pregnant women between 16-24 weeks of gestation with Hb between 80 and 109 g/L (n=251)	Iron (60 mg), or Iron (60 mg) and vitamin A (2.4 mg), daily	Placebo, or vitamin A (2.4 mg), daily	From 16-24 weeks for 8 weeks	High

Author, country, publication year	Study participants	Intervention group	Control group	Supplementation initiation and duration	Trial quality
Torlesse et al, Sierra Leone, 2000 [54,55]	Women with Hb ≥80g/L and gestational age <14 weeks at baseline (n=125)	Iron (36 mg), folic acid (5 mg), daily and a single dose of albendazole (400 mg); or iron (36 mg), folic acid (5 mg), daily and albendazole control (calcium and vitamin D)	Calciferol tablets (1.25 mg calciferol equivalent), daily and a single dose of albendazole (400 mg); or calciferol tablets (1.25 mg calciferol equivalent), daily and albendazole control (calcium and vitamin D)	From the first antenatal visit in the second trimester until delivery	High
Tanumihardjo et al, Indonesia, 2002 [56]	Pregnant women in the second or early third trimester (n=27)	Iron (60 mg); or iron (60 mg) and vitamin A (8.4 µmol), daily	Placebo; or vitamin A (8.4 µmol), daily	From enrollment, for 8 weeks	-
Zeng et al, China, 2008 [57]	Pregnant women <28 wk of gestation (n=3929)	Iron (60 mg) and folic acid (400 µg), daily	Folic acid (400 µg), daily	From enrollment until delivery	-
Ziaei et al, Iran, 2008 [58-59]	Pregnant women between 13th and 18th week of pregnancy, Hb level ≥132g/L and serum ferritin levels ≥15 µg/L (n=244)	Iron (50 mg), daily	Placebo	From enrollment until delivery	High
Ziaei et al, Iran, 2007 [60]	Pregnant women with Hb ≥ 13.2 g/dl in the early stage of the second trimester (n=750)	Iron (50 mg), daily	Placebo	From enrollment until delivery. All participants received 1mg of folic acid daily.	High

Hb= Haemoglobin

Table 2: Characteristics of included cohort studies
High income countries

Author, country, publication year	Period of data collection	Selection criteria of participants	Definition and time of anaemia assessment
Arbuckle et al, Canada, 1989 [61]	1970-1973	Women with singleton pregnancies (n=806)	Anaemia during pregnancy (Hb cutoff used is unclear)
Banhidy et al, Hungary, 2010 [62]	1980-1996	Mothers and their newborn infants without any congenital abnormality. This is the control group of a case-control study where controls were selected from the National Birth Registry, Hungary (n=38151)	Anaemia defined as Hb <110 g/L in first and third trimesters, and Hb <105 g/L in the second trimester
Baraka et al, Belgium, 2012[63]	2009	Pregnant women in third trimester of pregnancy (n=341)	Anaemia defined as Hb <110 g/L in first and third trimesters, and Hb <105 g/L in the second trimester
Chang et al, USA, 2003 [64]	1990-2000	African-American adolescents with singleton pregnancies, who had received prenatal care at an inner-city maternity clinic affiliated with Johns Hopkins Hospital and delivered at Johns Hopkins Hospital (n=918)	Anaemia defined as Hb <105 g/L in the second or third trimester
El Guindi et al, French Guiana, 2004 [65]	1999	Pregnant women attending antenatal clinic at the hospital center of Saint-Laurent of Maroni (n=222)	Anaemia defined as Hb <80 g/L during the period of study (time of assessment is unclear)
Fareh et al, UAE, 2005 [66]	Not specified	Women with singleton pregnancies who received antenatal care at the hospital and delivered vaginally (n=202)	Anaemia defined as Hb <110 g/L during pregnancy, irrespective of the period of gestation
Hamalainen et al, Finland, 2003 [67]	1990-2000	Women with singleton pregnancies who gave birth at Kuopio University Hospital between 1990 and 2000 (n=22799)	Anaemia defined as Hb <100 g/L during pregnancy (women having anaemia in more than one trimester were allocated to the trimester in which their anaemia was first recognised)
Hwang et al, Korea, 2010 [68]	2000-2006	Women with singleton pregnancies delivered at the institution (n=3560)	Anemia defined as Hb <100 g/L in the third trimester
Klebanoff et al, USA, 1989 [69]	1959-1966	Pregnant women with one or more hematocrit values between 25 and 42 weeks of gestation, registered at 12 hospitals (n=35423) (The Collaborative Perinatal Project)	Anaemia defined as haematocrit ≤ 0.34 in the second trimester
Knottnerus et al, Netherlands, 1990 [70]	1985-1986	Women with singleton pregnancies, attending routine antenatal care in the 31st or 32nd week of gestation at the obstetric outpatient department of Maastricht University Hospital, or one of two midwife practices in Maastricht (n=796)	Anaemia defined as Hb ≤111.1 g/L at 31-32 weeks of gestation

Author, country, publication year	Period of data collection	Selection criteria of participants	Definition and time of anaemia assessment
Lao et al, Hong Kong, 2002 [71,72]	4 month period	Women with singleton pregnancies, who had normal hemoglobin and mean corpuscular volume at the initial antenatal visit at or before 14 weeks of gestation, and who attended one of the antenatal clinics at 28-30 weeks (n=762)	Anaemia defined as Hb ≤115 g/L at 28-30 weeks gestation
Lee et al, South Korea, 2006 [73]	Not specified	Pregnant women between 24 and 28 weeks of gestation (n=248)	Anaemia defined as Hb <108 g/L between 24 to 28 weeks of gestation
Levy et al, Israel, 2005 [74]	1988-2002	Women with singleton pregnancies (n=153, 396)	Anemia defined as Hb <100 g/L in the first trimester
Mau et al, Germany, 1977 [75]	Not specified	Women with singleton pregnancies in the first trimester (n=4690)	Anaemia defined as Hb <112 g/L in the first trimester and Hb <105 g/L in the third trimester
Murphy et al, Wales, 1986 [76]	1970-1982	All singleton births to South Glamorgan residents between 1970-1979 anb 1980-1982 (n=54382) (Cardiff Births Survey)	Anaemia defined as Hb <104 g/L at first antenatal visit before 24 weeks of gestation
Nordenvall et al, Sweden, 1990 [77]	1983	Women with singleton pregnancies at Danderyd hospital (n=330)	Anaemia defined as Hb <110 g/L at 20 weeks of gestation
Scanlon et al, USA, 2000 [78]	1990-1993	Pregnant women who delivered a liveborn infant between 26 and 42 weeks of gestation (attended publicly funded health programs in ten states; CDC Pregnancy Nutrition Surveillance System) (n= 173, 031)	Various categories of anaemia measured in the first trimester were used (very low Hb <95 g/L)
Scholl et al, USA, 1992 [79,80,81]	1985-1995	Pregnant women attending two prenatal clinics (n=779)	Anaemia defined as Hb <110 g/L in the first and third trimester, and Hb <105 g/L in the second trimester, measured at entry into prenatal care
Siega-Riz et al, USA, 1998 [82]	1983-1986	Pregnant women at first antenatal visit and between 28 to 32 weeks of gestation (n=7589)	Anaemia defined as haematocrit <0.33 at first antenatal visit and in third trimester
Steer et al, UK, 2005 [83-84]	1988-2000	Pregnant women with first live or stillbirth pregnancy with complete information, attending 17 maternity units in Northwest Thames region (n=144, 209)	Anaemia defined as Hb <105 g/L at the first prenatal visit and/or irrespective of the period of gestation
von Tempelhoff et al, West Germany, 2008 [85,86]	1990-1996	Women with singleton pregnancies who delivered in the Obstetric department of the hospital (n=4985)	Anaemia defined using mean hemoglobin levels between 14 and 30 weeks of gestation (Hb cut off used is unclear)
Williams et al, Australia, 1997 [87,88]	1989	Women with singleton pregnancies who delivered after 37 completed weeks of gestation (n=2507)	Anaemia defined as Hb <110 g/L, irrespective of the period of gestation

Hb= Haemoglobin

Low or middle income countries

Author, country, publication year	Study year	Selection criteria of participants	Definition and time of anaemia assessment
Abeysena et al, Sri Lanka, 2010[89]	2001-2002	Women with singleton pregnancies on or before 16 weeks of gestation (n= 817)	Anaemia defined as Hb <110 g/L at first antenatal visit on or before 16 weeks of gestation
Agarwal et al, India, 1998 [90,91]	1987-1993	Eligible (married, reproductive age) women contacted by female village workers every month for weight record and last menstrual period (n=1954)	Anaemia defined as Hb <100 g/L in the third trimester
Bhalerao et al, India, 2011[92]	2009	Women with singleton pregnancies attending outpatient clinics before 20 weeks of gestation (n= 1200)	Anaemia defined as Hb <110 g/L on two occasions during pregnancy and labour
Bodeau-Livinec et al, Benin, 2011[93]	2005-2008	Pregnant women in second trimester of pregnancy (n= 1601)	Anaemia defined as Hb <110 g/L
Bondevik et al, Nepal, 2001 [94]	1994-1996	Pregnant women attending hospital for antenatal care and delivery (n=1400)	Anaemia defined as Hb <113 g/L at the first antenatal visit
Conde-Agudelo et al, Latin America, 2000 [95]	1985-1997	Women with singleton births from Latin American countries (n=837,232, birth records in SIP database)	Anemia defined using ICD-10 (coded O99.0)
Feresu et al, Zimbabwe, 2004 [96]	March - June, 1999	Women delivering singleton infants who survived the first hour of life (n=3103)	Anaemia (no definition provided)
Gonzales et al, Peru, 2009 [97]	2003-2006	Women with singleton pregnancies after 22 weeks of gestation in the database of all deliveries in seven hospitals (n=35449)	Anaemia defined as Hb <110 g/L during pregnancy
Harrison et al, Nigeria, 1985 [98]	1976-1979	Pregnant women in Zaria area (n=18140)	Anaemia defined as Hb <100 g/L at the first antenatal visit (either to book for antenatal care or seek emergency care)
Jehan et al, Pakistan, 2007 [99]	2003-2005	Pregnant women who were permanent residents of and planned to deliver in the catchment area, returned to the clinic after the initial lady home worker visit, and between 20 and 26 weeks of gestation (n=1369)	Anaemia defined as Hb <110 g/L between 20 and 26 weeks of gestation
Kumar et al, India, 2010[100]	2005-2006	Women with singleton pregnancies registered at the antenatal clinic before 8 weeks of gestation (n= 2027)	Anaemia defined as Hb <100 g/L at less than 8 weeks of gestation
Lone et al, Pakistan, 2004 [101,102]	2001-2002	Women with singleton pregnancies, attending the outpatient clinic before 16 weeks of gestation, and with complete medical record (n=629)	Anaemia defined as Hb <110 g/L in labour and on 2 previous occasions in the current pregnancy

Author, country, publication year	Study year	Selection criteria of participants	Definition and time of anaemia assessment
Malhotra et al, India, 2002 [103]	2001	Pregnant women attending the antenatal out-patient department of the institution (n=447)	Anaemia defined as Hb <110 g/L during pregnancy, irrespective of the period of gestation
Mamun et al, Bangladesh, 2006 [104]	1994-1997	Pregnant women with Hb ≥90 g/L and less than 21 weeks of gestation (n=1584)	Anaemia defined as Hb 90-109 g/L between 18 and 24 weeks of gestation
Marhatta et al, Nepal, 2007 [105]	1996-2006	Pregnant women attending Nepal Medical College Teaching Hospital for antenatal care and delivered at the same hospital, with complete records (n=863)	Anaemia defined as Hb <110 g/L probably at the first antenatal visit
Mola et al, Papua New Guinea, 1999 [106]	1987-1992	Pregnant women booked at antenatal clinics in or around Port Moresby and delivered in Port Moresby hospital, with haemoglobin records (n=22405)	Anaemia defined as Hb <110g/L during pregnancy, irrepective of the period of gestation. Lowest Hb concentration from multiple values.
Ren et al, China, 2007 [107]	1995-2000	Women with liveborn singleton infants of at least 28 weeks of gestation, and with Hb measured at the first prenatal visit in first trimester (n=88149)	Anemia defined as Hb <110 g/L at the first antenatal visit
Shobeiri et al, India, 2006 [108]	Not specified	Pregnant women, 15 to 20 days postconception, attending outpatient prenatal clinics (n=500)	Anaemia defined as Hb <110 g/L in the first and third trimesters, and Hb <105 g/L in the second trimester (group A); or anaemia defined as Hb <110 g/L in the second trimester and Hb >110 g/L in the first and third trimesters (group C)
Vijayalaxmi et al, India, 2009 [109]	Not specified	Pregnant women attending antenatal care at private and government hospitals (n=255)	Anaemia, probably in the first trimester (Hb cutoff used is unclear)
Xiong et al, China, 2003 [110]	1989-1990	Pregnant women with singleton births in the Suzhou perinatal care records (n=16936)	Anaemia defined as Hb <100 g/L at first antenatal visit or in third trimester
Zhang et al, China, 2009 [111]	1993-1996	Women with singleton live births and stillbirths between 20 and 44 weeks of gestation, with at least one haemoglobin measurement during pregnancy (n= 164667)	Anaemia defined as Hb <100g/L during pregnancy
Zhou et al, China, 1998 [112]	1991-1992	Women with singleton pregnancies, reporting a pregnancy at the local family planning office (n=829)	Anaemia defined as Hb <110 g/L between 4 and 8 weeks of gestation

Hb= Haemoglobin

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Table 3. Subgroup analysis and meta-regression of association between maternal anaemia and preterm birth

Characteristic	No. of studies	Crude OR[£] (95% CI)	Significance of effect (p value)	Test for heterogeneity (p value)	I^2 (%)	Interaction test p value	No. of studies	Adjusted OR [£] (95% CI)	Significance of effect (p value)	Test for heterogeneity (p value)	I^2 (%)	Interaction test p values
Trimester of pregnancy						0.008						0.71
First second trimester (<27 wks)	12	1.43* (1.20, 1.69)	<0.001	<0.001	77		7	1.21* (1.13, 1.30)	<0.001	0.47	0	
Third trimester (≥27 wks)	6	0.71*(0.60, 0.82)	<0.001	0.21	34		6	1.20 (0.80, 1.79)	<0.001	<0.001	90	
Country						0.14						0.83
Low or middle income	14	1.50* (1.23, 1.83)	<0.001	<0.001	81		5	1.30* (1.05, 1.61)	0.018	0.002	77	
High income	12	1.10 (0.90, 1.34)	0.70	<0.001	92		9	1.26* (1.02, 1.57)	<0.001	<0.001	87	
Malaria endemic						-						-
Endemic	3	-	-	-	-		1					
Non-endemic	23	1.20* (1.05, 1.37)	0.001	<0.001	89		13	1.25* (1.08, 1.43)	<0.001	<0.001	83	

[£] OR= Odds ratio

Table 4. Subgroup analysis and meta-regression for association between anaemia and low birth weight

[£] OR= Odds ratio

Characteristic	No. of studies	Crude OR[£] (95% CI)	Significance of effect (p value)	Test for heterogeneity (p value)	I^2 (%)	Interaction test p value	No. of studies	Adjusted OR[£] (95% CI)	Significance of effect (p value)	Test for heterogeneity (p value)	I^2 (%)	Interaction test p value
Trimester of pregnancy						-						-
First second trimester (<27 wks)	13	1.40 (1.16, 1.69)	<0.001	<0.001	76		6	1.29 (1.09, 1.53)	0.004	<0.001	82	
Third trimester (≥27 wks)	4	-	-	-	-		4	-	-	-	-	
Country						0.83						-
Low or middle income	13	1.25 (1.08, 1.46)	0.004	<0.001	72		3	-	-	-	-	
High income	11	1.23 (0.96, 1.58)	0.10	<0.001	94		6	1.21 (0.95, 1.53)	0.12	<0.001	90	
Malaria endemic						0.52						-
Endemic	6	1.50 (1.00, 2.23)	0.049	<0.001	81		0	-	-	-	-	
Non-endemic	23	1.22 (1.03, 1.45)	0.022	<0.001	91		9	1.13 (0.94, 1.35)	0.19	<0.001	86	

Table 5. Summary of exposure-response relationships of haemoglobin difference (1g/L) in the prenatal period with birth outcomes (cohort studies)*

Outcomes	No. of studies	WMD or RR[£]	P-value linear trend
Low birth weight	25	0.99 (0.98, 0.99)	<0.001
Birth weight	9	3.19 (-17.88, 24.26)	0.77
Preterm birth	12	0.98 (0.98, 0.99)	<0.001

*Haemoglobin difference is the difference in mean haemoglobin concentration between the anaemic and non-anaemic groups in included studies, [£] WMD= Weighted mean difference, and RR= Relative risk