

## **Web Appendix 1. Search Terms.**

The search terms were adapted to each service provider and database, and were composed of a combination of the following (or related) terms: B12 and pregnancy and birth weight or length of gestation. We added restriction terms excluding review articles, intervention studies and case reports, studies evaluating adults, children (other than infants), rodents, and patients with anemia. We used a combination of controlled vocabulary terms and free text words.

### **Pubmed**

("Vitamin B 12"[Mesh] OR B12[Text Word] OR "B 12"[Text Word] OR cobalamin\*[Text Word]) AND (pregnan\*[Text Word] OR Pregnancy[Mesh] OR gestation\*[Text Word] OR fetus[MeSH] OR fetus\*[Text Word] OR foetus\*[Text Word] OR foetal\* [Text Word] OR fetal\*[Text Word] OR "Fetal Development"[Mesh] OR "Infant, Newborn"[Mesh]) AND ("Infant, Low Birth Weight"[Mesh] OR "Birth Weight"[Mesh] OR birthweight[Text Word] OR "birth weight"[Text Word] OR SGA[Text Word] OR "fetal growth retardation"[MeSH] OR IUGR[Text Word] OR "growth restriction"[Text Word] OR "growth retardation"[Text Word] OR "small for gestational age"[Text Word] OR "small for date"[Text Word] OR "Infant, Premature"[Mesh] OR "Premature Birth"[Mesh] OR "Gestational Age"[Mesh] OR preterm[Text Word] OR prematur\*[Text Word] OR "gestational age"[Text Word] OR "length of gestation"[Text Word] OR "duration of pregnancy"[Text Word]) NOT ("Review"[Publication Type] OR "Child"[Mesh] OR "Aged"[Mesh] OR "Case Reports"[Publication Type] OR "Clinical Trial"[Publication Type] OR "Rodentia"[Mesh] OR "Anemia"[Mesh])

### **OvidSP Medline**

(exp Vitamin B 12/ or b12.tw or B 12.tw or cobalamin\*.tw) and (pregnan\*.tw or exp Pregnancy/ or gestation\*.tw or exp Fetus/ or fetus\*.tw or fetal\*.tw or foetus\*.tw or foetal\*.tw or exp Fetal Development/ or exp Infant, Newborn/) and (exp Infant, Low Birth Weight/ or exp Birth Weight/ or birth weight.tw or birthweight.tw or SGA.tw or exp Fetal Growth Retardation/ or IUGR.tw or growth restriction.tw or growth retardation.tw or small for gestational age.tw or small for date.tw or exp Infant, Premature/ or exp Premature Birth/ or exp Gestational Age/ or preterm.tw or prematur\*.tw or gestational age.tw or length of gestation.tw or duration of pregnancy.tw) not (review/ or exp child/ or exp aged/ or exp case report/ or exp clinical trial/ or exp rodentia/ or exp anemia/)

### **OvidSP Embase**

(exp cyanocobalamin/ or exp cyanocobalamin deficiency/ or exp cobalamin derivative/ or exp cobalamin/ or b12.tw or b 12.tw or cobalamin\*.tw) and (pregnan\*.tw or exp pregnancy/ or gestation\*.tw or exp fetus/ or fetus\*.tw or

fetal\*.tw or foetus\*.tw or foetal\*.tw or exp fetus growth/ or exp newborn/) and (exp birth weight/ or birthweight.tw or birth weight.tw or SGA.tw or exp intrauterine growth retardation/ or IUGR.tw or growth restriction.tw or growth retardation.tw or small for gestational age.tw or small for date.tw or exp prematurity/ or exp premature labor/ or exp gestational age/ or preterm.tw or premature.tw or gestational age.tw or length of gestation.tw or duration of pregnancy.tw) not (exp review/ or exp case report/ or exp aged/ or exp anemia/ or exp clinical trial/ or exp rodent/)

### **OvidSP Global Health**

(exp vitamin b12/ or b12.tw or b 12.tw or cobalamin\*.tw) and (pregnan\*.tw or exp pregnancy/ or gestation\*.tw or exp fetus/ or fetus\*.tw or fetal\*.tw or foetus\*.tw or foetal\*.tw or exp fetal development/ or exp neonates/) and (exp low birth weight infants/ or exp birth weight/ or birthweight.tw or birth weight.tw or sga.tw or exp growth retardation/ or iugr.tw or growth restriction.tw or growth retardation.tw or small for gestational age.tw or small for date.tw or exp prematurity/ or exp premature infants/ or exp gestation period/ or preterm.tw or prematur\*.tw or gestational age.tw or length of gestation.tw or duration of pregnancy.tw) not (exp reviews/ or exp elderly/ or exp case reports/ or exp clinical trials/ or exp rodents/ or anaemia.sh)

### **EBSCO-host CINAHL**

((MH "Vitamin B 12") OR (MH "Vitamin B12 Deficiency+") OR b12 OR "b 12" OR cobalamin\*) AND (pregnan\* OR (MH "Pregnancy+") OR gestation\* OR (MH "Fetus+") OR fetus\* OR foetus\* OR foetal\* OR fetal\* OR (MH "Infant, Newborn+")) AND ((MH "Infant, Low Birth Weight+") OR (MH "Birth Weight") OR birthweight OR "birth weight" OR SGA OR (MH "Fetal Growth Retardation") OR IUGR OR "growth restriction" OR "growth retardation" OR "small for gestational age" OR "small for date" OR (MH "Infant, Premature") OR (MH "Childbirth, Premature") OR (MH "Gestational Age") OR preterm OR prematur\* OR "gestational age" OR "length of gestation" OR "duration of pregnancy") NOT ((MH "Literature Review+") OR (MH "Child, Preschool") OR (MH "Aged+") OR (MH "Case Studies") OR (MH "Clinical Trials+") OR (MH "Rodents+") OR (MH "Anemia+"))

### **SCOPUS**

(TITLE-ABS-KEY(b12 OR "b 12" OR cobalamin\*)) AND (TITLE-ABS-KEY(pregnan\* OR gestation\* OR fetus\* OR fetal\* OR foetus\* OR foetal\* OR newborn\*)) AND (TITLE-ABS-KEY("birth weight" OR "birthweight" OR sga OR "growth retardation" OR "growth restriction" OR iugr OR "small for gestational age" OR "small for date" OR preterm OR prematur\* OR "gestational age" OR "length of gestation" OR "duration of pregnancy")) AND (EXCLUDE(DOCTYPE, "re")) AND NOT ((TITLE(anemi\* OR anaemi\*)) OR (TITLE-ABS-KEY(mouse OR mice OR rat OR rats OR rodent\*)))

## Web of Knowledge

#1: (TS=(b12 OR "b 12" OR cobalamin\*)) AND (TS=(pregnan\* OR gestation\* OR fetus\* OR fetal\* OR foetus\* OR foetal\* OR newborn\*)) AND (TS=("birth weight" OR "birthweight" OR sga OR "growth retardation" OR "growth restriction" OR iugr OR "small for gestational age" OR "small for date" OR preterm OR prematur\* OR "gestational age" OR "length of gestation" OR "duration of pregnancy")) NOT ((TI=(anemi\* OR anaemi\*)) OR (TS=(mouse OR mice OR ra OR rats OR rodent\*)))

#2: Restrict #1 to reviews

#3: #1 NOT #2

## **Web Appendix 2. Statistical Analyses.**

A multivariable model was applied adjusting for maternal age, BMI (or weight when BMI was unavailable) and parity. When IPD was not provided, we requested results from the following reanalyses of original studies: the association of B12 (SD score) with birth weight, gestational age at delivery, LBW and preterm birth; and the association of B12-deficiency with birth weight, LBW and preterm birth. Results were provided for both crude analyses, and two different multivariable analyses (adjusting for maternal age, BMI and parity; and adjusting for maternal age, BMI, parity and smoking habits). When neither IPD nor results from requested reanalyses were available, we extracted relevant results from the publications.

We stratified our analysis for the following *a priori* subgroup and sensitivity analyses: trimester of B12 measurement (four strata: 1<sup>st</sup>, 2<sup>nd</sup>, 3<sup>rd</sup> trimesters, and 1<sup>st</sup> and 2<sup>nd</sup> trimesters combined), country income category (high-income versus low- and middle-income countries, as defined by The World Bank),<sup>1</sup> risk of bias (high risk versus moderate or low risk of bias), and excluding each of the studies one by one. Additional sensitivity analyses that were carried out: overweight status (BMI  $\geq 25$  kg/m<sup>2</sup> versus BMI < 25 kg/m<sup>2</sup>), B12 assay technique (radioimmunoassay, electroluminescence, microbiological), alternative multivariable models (e.g. a more saturated model including maternal education and smoking habits in addition to the main model), fixed effects model, Poisson regression with non-robust error variance, logistic regression model (dichotomous outcomes), and by excluding studies that only evaluated newborns born at term.

### **References:**

1. The World Bank. The World Bank. (2016). at <<http://data.worldbank.org/country>>

**Web Table 1.** Study Characteristics of Eligible Studies Not Included in the Meta-Analysis<sup>a</sup>

Study	n	Country	Study years	B12	Week of B12	Main objectives
				analysis method	measurement, range, median	
Karakantza, 2008 (36)	392	Greece	2004-2006	NA	6-8	Studied three thrombophilic mutations in relation to pregnancy outcomes (including IUGR). Studied changes in iron status in pregnant adolescents, and iron status in relation to hepcidin and inflammatory markers.
Lee, 2014 (38)	T2: 83 T3: 42	USA	2006-2012	RIA	T2: 24.4 ± 2.2 <sup>b</sup> T3: 29.7 ± 1.8 <sup>b</sup>	Studied uterine artery Doppler velocimetry in relation to pregnancy outcomes and homocysteine, folate and B12.
López-Quesada, 2004 (37)	94	Spain	2000-2001	ECL	24-24, median 24	Studied B12 dietary intake during pregnancy and lactation in relation to pregnancy outcome, breast milk B12 concentration and infant growth and development.
Neumann, 2013 (39)	138	Kenya	1984-1986	NA	NA	

Studies are referred to according to their citation number in the text. ECL, electrochrominescence; IUGR, intrauterine growth restriction; n, number of pregnancies; NA, not available; RIA, radioimmunoassay; T2, 2<sup>nd</sup> trimester; T3, 3<sup>rd</sup> trimester.

a, Eligible studies were not included in the systematic review or the meta-analyses when individual participant data or results from requested reanalyses were not provided, appropriate data and results were not available in the original report, and when no association between B12 and birth weight or length of gestation was presented;

b, mean ± SD.

**Web Table 2. Risk of Bias of Studies Included in the Meta-Analysis**

Study	1	2	3	4	5	6	7	Total
Baker, 2009 (18)	1	1	1	0	1	1	0	5
Bergen, 2012 (19)	1	1	1	1	1	1	1	7
Bhate, 2012 (20)	1	1	1	1	1	1	1	7
Chen, 2015 (21)	1	1	1	1	1	1	1	7
Dayaldasani, 2014 (22)	1	1	1	1	1	?	1	6
Dwarkanath, 2013 (23)	1	1	1	1	1	1	0	6
Furness, 2013 (24)	1	1	1	0	1	1	1	6
Halicioğlu, 2012 (25)	1	0	0	1	1	1	1	5
Hay, 2010 (26)	1	1	1	0	1	1	0	5
Hogveen, 2010 (27)	1	0	1	1	1	1	0	5
Kaymaz, 2011 (28)	1	1	1	1	1	1	?	6
Krishnaveni, 2013 (29)	1	1	1	1	1	1	0	6
Mamabolo, 2006 (30)	1	0	0	1	1	1	1	5
Relton, 2005 (31)	1	0	0	1	?	1	0	3
Sukumar, 2011 (32)	1	1	1	1	1	1	0	6
Takimoto, 2007 (33)	1	1	1	1	1	1	0	6
Wu, 2013 (34)	1	0	0	?	1	1	?	3
Yajnik, 2008 (35)	1	1	1	1	1	1	1	7

Each item was scored “1” (i.e. “yes”), “0” (i.e. “no”) or “?” (i.e. “uncertain”), where only the answer “1” scored 1 point. The following questions were evaluated: 1: Was B12 ascertained irrespective of the risk of low birth weight birth or preterm birth, and otherwise not prone to selection bias?; 2: Was the study controlled for maternal body mass index or weight either by matching or by statistical methods?; 3: Was the study controlled for previous low birth weight birth or preterm birth, or maternal age, parity, socioeconomic status, smoking habits, ethnicity, vegetarian status or B12 supplement use (at least two of these) either by matching or by statistical methods? In addition, because of potential over-adjustment, if a study adjusted for levels of folate, homocysteine or methylmalonic acid, they earned no point on this item (even if they had adjusted for two or more of the mentioned confounders); 4: Was the exposed cohort truly or somewhat representative of the average pregnant population in the community?; 5: Did the women with B12-deficiency receive the same follow-up and interventions as the non-deficient women?; 6: Was the outcome assessed by independent or blind assessment, or by secure records or record linkage?; 7: Was follow-up >80% or was any description provided for those lost to follow-up? Studies are referred to according to their citation number in the text.

**Web Table 3.** Pooled Results From Subgroup and Sensitivity Analyses of B12 SD Score on Birth Weight

Analysis	Number of studies	Number of pregnancies	Birth weight (g) per 1 SD increase in B12 (95% CI)		I <sup>2</sup>
<b>Alternative models</b>					
Crude	12 <sup>18-23,26-29,32,35</sup>	9,819	-4.9 (-15.7, 5.8)		0
Adjusting for BMI or weight <sup>a</sup>	9 <sup>18,19,21-23,26,28,29,32</sup>	8,505	7.8 (-9.0, 24.6)		28
Adjusting for maternal age, <sup>b</sup> parity, <sup>c</sup> and BMI or weight <sup>a</sup> (“main model”)	12 <sup>18-23,26,28,29,32,33,35</sup>	9,406	5.1 (-10.9, 21.0)		30
Adjusting for maternal age, <sup>b</sup> parity, <sup>c</sup> BMI or weight, <sup>a</sup> and smoking <sup>d</sup>	10 <sup>18-22,26,28,29,32,35</sup>	8,420	0.7 (-15.5, 16.9)		29
Adjusting for maternal age, <sup>b</sup> parity, <sup>c</sup> BMI or weight, <sup>a</sup> smoking <sup>d</sup> and education <sup>e</sup> (“extended model”)	4 <sup>18,19,26,29</sup>	5,948	-1.9 (-40.5, 36.6)		76
Adjusted main model among those with data on smoking	10 <sup>18-22,26,28,29,32,35</sup>	8,420	2.4 (-8.8, 13.6)		0
Adjusted main model among those with data on the extended model	4 <sup>18,19,26,29</sup>	5,948	4.1 (-27.8, 35.9)		65
Adjusting for BMI <sup>b</sup> among those with weight	4 <sup>19,21,22,29</sup>	7,416	6.3 (-10.5, 23.1)		26
Adjusting for weight <sup>b</sup> among those with BMI	4 <sup>19,21,22,29</sup>	7,416	8.2 (-6.2, 22.5)		13
Fixed effects model	12 <sup>18-23,26,28,29,32,33,35</sup>	9,406	3.4 (-7.4, 14.1)		30
<b>Trimester of B12 measurement</b>					
1 <sup>st</sup> trimester	4 <sup>19,22,23,32</sup>	1,461	19.1 (-13.1, 51.4)		0
2 <sup>nd</sup> trimester	8 <sup>19,21-23,26,28,29,32</sup>	6,217	11.5 (-11.4, 34.5)		34
1 <sup>st</sup> and 2 <sup>nd</sup> trimester	10 <sup>19,21-23,26,28,29,32,33,35</sup>	8,325	12.1 (-9.7, 33.8)		47
3 <sup>rd</sup> trimester	6 <sup>18,21,23,29,32,33</sup>	1,140	-0.1 (-31.0, 30.8)		14
<b>Measurement technique<sup>f</sup></b>					
Radioimmunoassay	2 <sup>18,32</sup>	459	-16.1 (-84.9, 52.7)		61
Electroluminescence assay	7 <sup>19,21-23,28,32,33</sup>	7,256	0.0 (-18.3, 18.4)		14
Microbiologic assay	4 <sup>20,26,29,35</sup>	1,691	20.4 (-0.9, 41.7)		0
<b>Country income category</b>					
High income	7 <sup>18,19,21,22,26,32,33</sup>	7,411	-5.5 (-24.8, 13.7)		23
Middle or low income	5 <sup>20,23,28,29,35</sup>	1,995	22.2 (2.1, 42.4)		0

(continued)

**Web Table 3. Continued**

<b>Maternal BMI</b>				
BMI <25 kg/m <sup>2</sup>	6 <sup>19,21,22,28,29,32</sup>	4,728	-1.9 (-16.4, 12.5)	0
BMI ≥25 kg/m <sup>2</sup>	6 <sup>19,21,22,28,29,32</sup>	2,945	17.5 (-17.6, 52.5)	41

Pooled results of the mean difference (95% CI) in birth weight (g) per 1 SD increase in maternal BMI. All analyses are linear regression analyses with random effects, and adjusted for the main model (i.e. maternal age, BMI (weight if missing BMI), and parity (nulliparous yes/no)) unless otherwise specified. Studies included in the analyses are referred to according to their citation number in the text. BMI, body mass index; CI, confidence interval; SD, standard deviation.

- a. BMI and weight (if missing BMI) as continuous covariates;
- b. continuous covariate;
- c. nulliparous (yes/no);
- d. smoking during pregnancy (yes/no);
- e. completed high school (yes/no);
- f. Sukumar 2011<sup>32</sup> measured n=182 by radioimmunoassay and n=27 by electroimmunesence assay.



**Web Table 4. B12-Deficiency and B12 Tertiles in Relation to Birth Weight**

<b>Analysis</b>	<b>Number of studies</b>	<b>Number of pregnancies</b>	<b>Number of exposed</b>	<b>Mean difference in birth weight (g) in exposed versus non-exposed (95% CI)</b>	<b>I<sup>2</sup></b>
<b>B12-deficiency</b>					
IPD, crude	9 <sup>18,19,21,23,26-29,32</sup>	8,735	3,006	9.3 (-14.9, 33.5)	0
IPD, main model <sup>a</sup>	8 <sup>18,19,21,23,26,28,29,32</sup>	8,279	2,846	-14.5 (-39.1, 10.2)	0
Aggregate, crude <sup>b</sup>	4 <sup>20,25,34,35</sup>	1,323	695	63.8 (-32.6, 159.9)	69
Aggregate, main model <sup>a</sup>	2 <sup>20,35</sup>	894	542	-1.36 (-53.5, 50.8)	0
IPD + aggregate, crude	13 <sup>18-21,23,25-29,32,34,35</sup>	10,058	3,701	23.3 (-6.7, 53.4)	24
IPD + aggregate, main model <sup>a</sup>	10 <sup>18-21,23,26,28,29,32,35</sup>	9,173	3,388	-14.0 (-36.3, 8.3)	0
<b>B12 tertiles<sup>c</sup></b>					
IPD, crude	10 <sup>18,19,21-23,26-29,32</sup>	5,942	3,179	18.9 (-15.8, 53.8)	8
IPD, main model <sup>a</sup>	9 <sup>18,19,21-23,26,28,29,32</sup>	5,633	2,997	-16.6 (-54.5, 21.2)	11

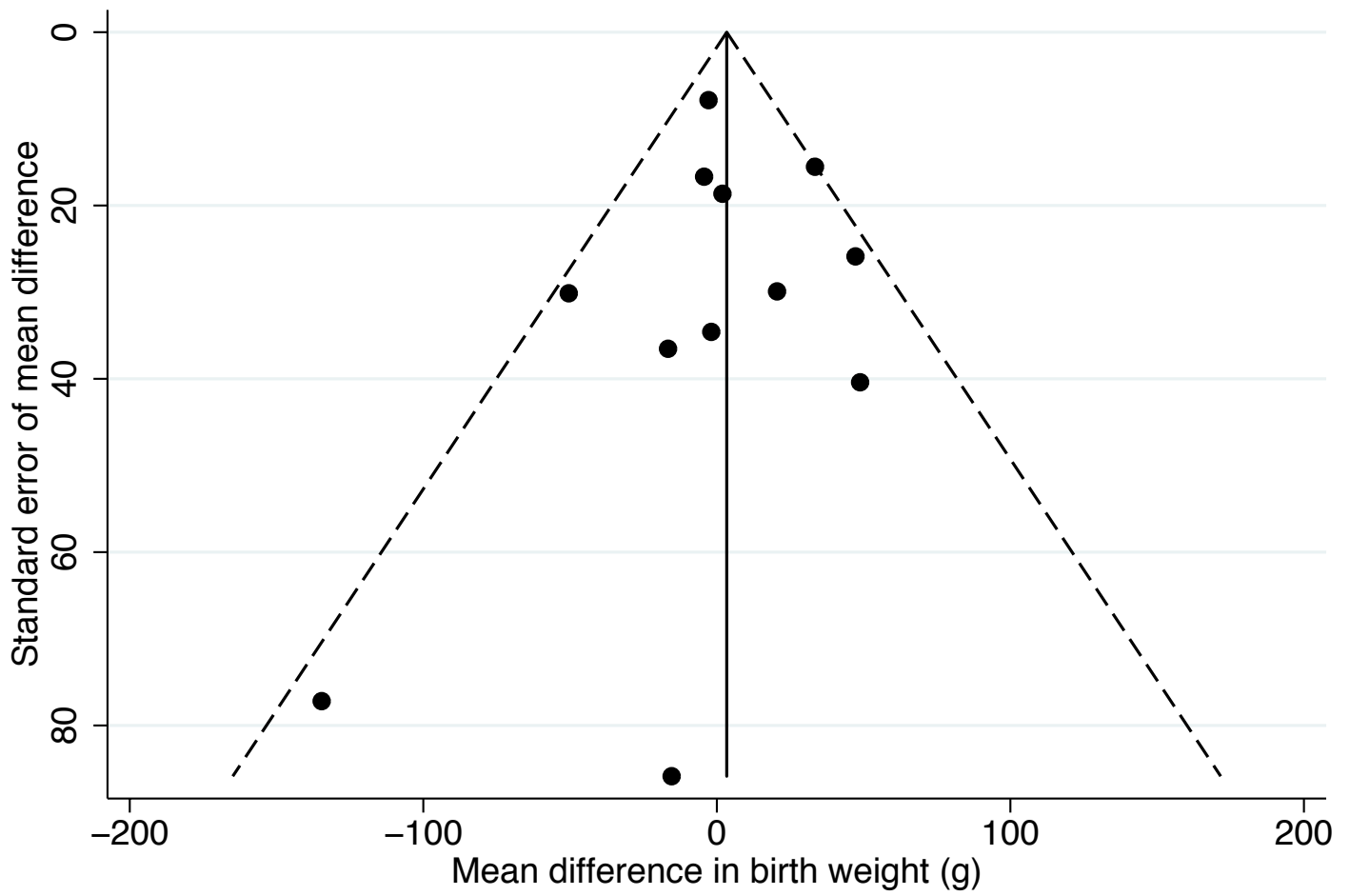
Pooled results of the mean difference in birth weight (g) in exposed versus non-exposed pregnancies. All analyses are random effects models and crude, unless otherwise specified. Studies included in the analyses are referred to according to their citation number in the text. CI, confidence interval; IPD, individual participant data.

a, adjusted for maternal age, body mass index (weight if missing body mass index), and parity (nulliparous yes/no);

b, B12-deficiency defined as <148 pmol/L except for Halicioğlu 2012<sup>25</sup> (<118 pmol/L);

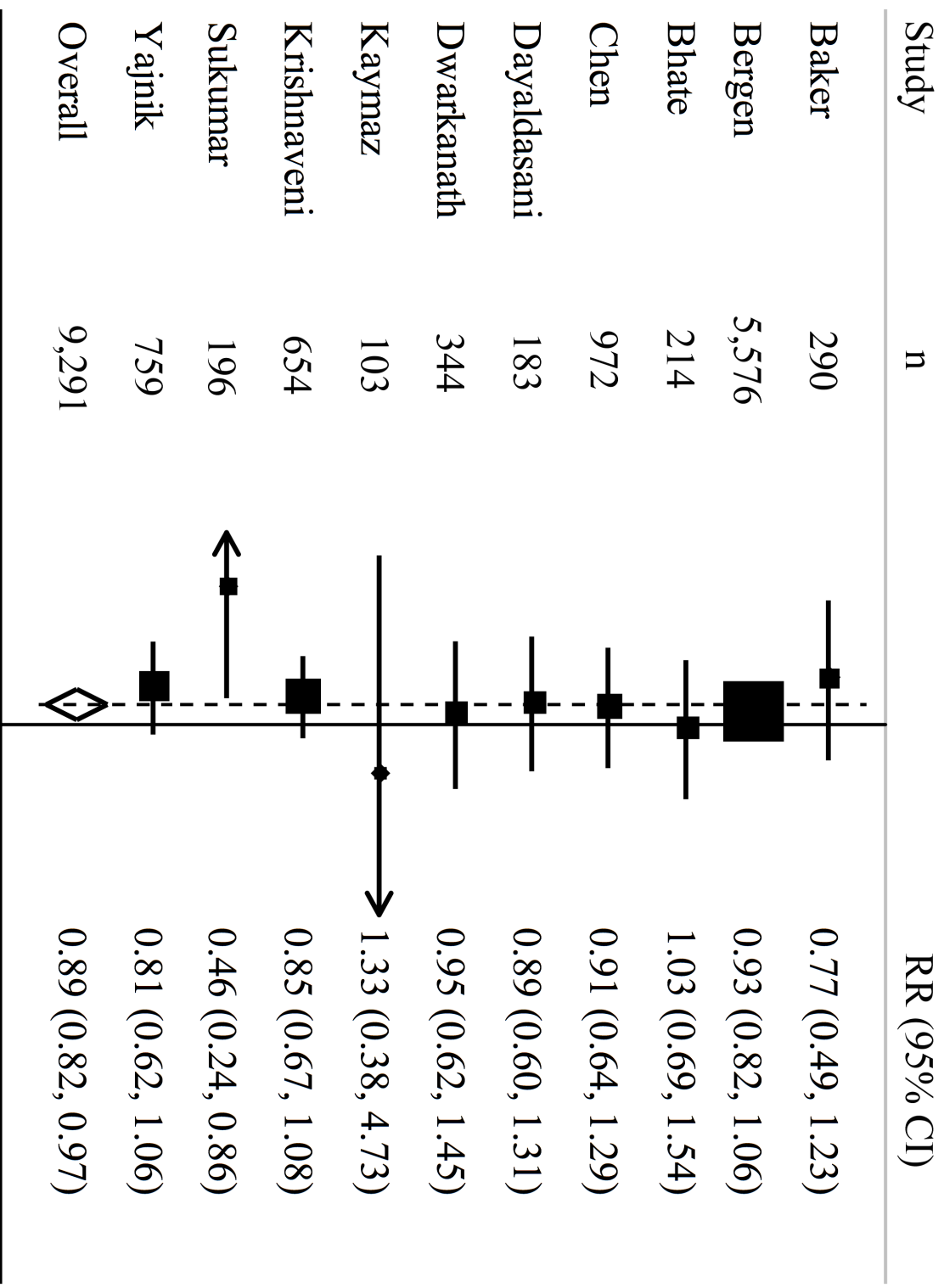
c, lowest tertile (i.e. exposed) versus highest tertile.

Web Figure 1. Funnel plot of studies evaluating the association between B12 and birth weight



Funnel plot of studies evaluating the association between vitamin B12 and birth weight after adjustment for maternal age, parity and body mass index or weight. Individual studies are represented by solid dots, and the pseudo-95% confidence interval by broken lines.

Web Figure 2. Forest plot presenting the association between B12 and the risk of preterm birth



Test for heterogeneity:  $I^2 = 0\%$

Meta-analysis of studies of the association between vitamin B12 and the risk of preterm birth after adjustment for maternal age, parity and body mass index or weight. Effect estimates are expressed as risk ratios of preterm birth per one standard deviation increase of vitamin B12. CI, confidence interval; n, number pregnancies; RR, risk ratio.

**Web Table 5.** Pooled Results From Subgroup and Sensitivity Analyses of B12 SD Score and the Risk of Preterm Birth

Analysis	Number of studies	Number of pregnancies	Number of preterm births	Risk ratio of preterm birth per 1 SD increase in B12 (95% CI)		I <sup>2</sup>
<b>Alternative models</b>						
Crude	11 <sup>18,23,27-29,32,35</sup>	9,747	643	0.90 (0.81, 1.00)		15
Adjusting for BMI or weight <sup>a</sup>	8 <sup>18,19,21-23,28,29,32</sup>	8,362	510	0.89 (0.81, 0.98)		0
Adjusting for maternal age, <sup>b</sup> parity, <sup>c</sup> and BMI or weight <sup>a</sup> (“main model”)	10 <sup>18-23,28,29,32,35</sup>	9,291	615	0.89 (0.82, 0.97)		0
Adjusting for maternal age, <sup>b</sup> parity, <sup>c</sup> BMI or weight, <sup>a</sup> and smoking <sup>d</sup>	9 <sup>18-22,28,29,32,35</sup>	8,365	531	0.90 (0.82, 0.99)		0
Adjusting for maternal age, <sup>b</sup> parity, <sup>c</sup> BMI or weight, <sup>a</sup> smoking <sup>d</sup> and education <sup>e</sup> (“extended model”)	3 <sup>18,19,29</sup>	5,813	304	0.92 (0.82, 1.03)		0
Adjusted main model among those with data on smoking	9 <sup>18-22,28,29,32,35</sup>	8,365	531	0.89 (0.81, 0.98)		0
Adjusted main model among those with data on the extended model	3 <sup>18,19,29</sup>	5,813	304	0.91 (0.81, 1.02)		0
Adjusting for BMI <sup>b</sup> among those with data on weight	4 <sup>19-22,29</sup>	7,416	424	0.91 (0.82, 1.01)		0
Adjusting for weight <sup>b</sup> among those with data on BMI	4 <sup>19-22,29</sup>	7,416	424	0.90 (0.81, 1.00)		0
Fixed effects model	10 <sup>18-23,28,29,32,35</sup>	9,291	615	0.89 (0.82, 0.97)		0
Non-robust error variance	10 <sup>18-23,28,29,32,35</sup>	9,291	615	0.90 (0.82, 0.99)		0
Logistic regression	10 <sup>18-23,28,29,32,35</sup>	9,285	615	0.88 (0.80, 0.97) <sup>f</sup>		0
<b>Trimester of B12 measurement</b>						
1 <sup>st</sup> trimester	3 <sup>19,22,23</sup>	1,453	107	1.01 (0.84, 1.20)		0
2 <sup>nd</sup> trimester	6 <sup>19,21,23,28,29,32</sup>	6,061	344	0.85 (0.67, 1.07)		57
1 <sup>st</sup> and 2 <sup>nd</sup> trimesters	8 <sup>19,21-23,28,29,32,35</sup>	8,190	522	0.86 (0.71, 1.05)		45
3 <sup>rd</sup> trimester	5 <sup>18,21,23,29,32</sup>	1,058	86	0.86 (0.70, 1.06)		4
<b>Measurement technique</b>						
Radioimmunoassay	2 <sup>18,32</sup>	459	29	0.60 (0.33, 1.07)		56
Electroluminescence assay	5 <sup>19,21-23,28</sup>	7,178	418	0.93 (0.83, 1.04)		0
Microbiologic assay	3 <sup>20,29,35</sup>	1,627	168	0.86 (0.73, 1.02)		0
<b>Country income category</b>						
High income	5 <sup>18,19,21,22,32</sup>	7,217	391	0.87 (0.74, 1.02)		19
Middle or low income	5 <sup>20,23,28,29,35</sup>	2,074	224	0.88 (0.76, 1.02)		0

(continued)

**Web Table 5. Continued**

<b>Maternal BMI</b>					
BMI <25 kg/m <sup>2</sup>	6 <sup>19,21,22,28,29,32</sup>	4,728	241	0.90 (0.81, 1.01)	0
BMI ≥25 kg/m <sup>2</sup>	5 <sup>19,21,22,29,32</sup>	2,913	200	0.81 (0.63, 1.05)	44

Pooled results of the risk ratio (95% CI) of preterm birth per 1 SD increase in maternal BMI. All analyses are Poisson regression analyses with random effects, robust error variance and adjusted for the main model (maternal age, BMI (weight if missing BMI), and parity (nulliparous yes/no)) unless otherwise specified. Studies included in the analyses are referred to according to their citation number in the text. BMI, body mass index; CI, confidence interval; SD, standard deviation.

a, BMI and weight (if missing BMI) as continuous covariates;

b, continuous covariate;

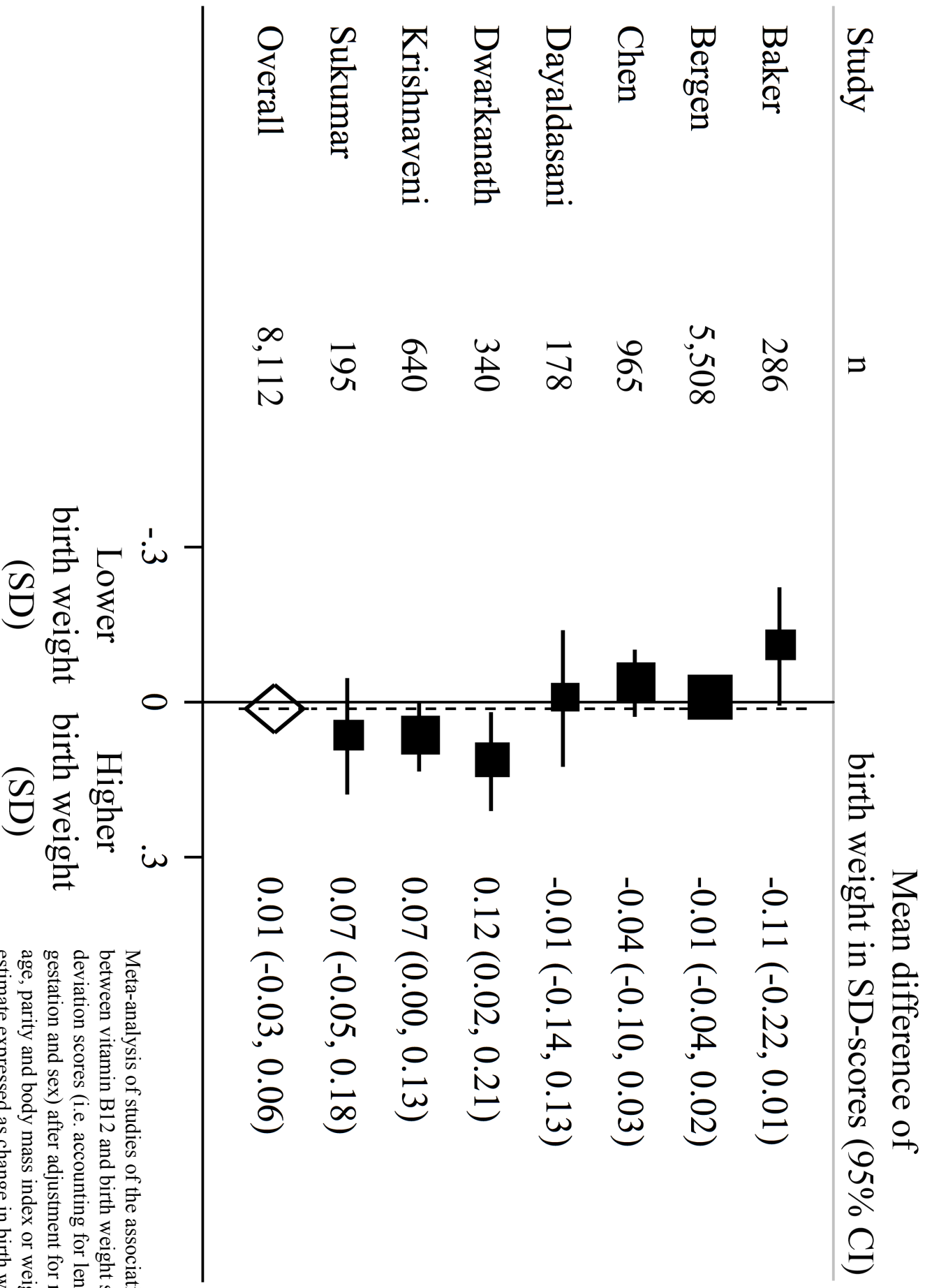
c, nulliparous (yes/no);

d, smoking during pregnancy (yes/no);

e, completed high school (yes/no);

f, odds ratio.

Web Figure 3. Forest plot presenting the association between B12 and birth weight SD score



Test for heterogeneity:  $I^2 = 62\%$

Meta-analysis of studies of the association between vitamin B12 and birth weight standard deviation scores (i.e. accounting for length of gestation and sex) after adjustment for maternal age, parity and body mass index or weight. Effect estimate expressed as change in birth weight standard deviation score per one standard deviation increase of vitamin B12. CI, confidence interval; n, number pregnancies.

**Web Table 6.** Level of B12 in Small-for-Gestational-Age and Non-Small-for-Gestational-Age Pregnancies

<b>Analysis</b>	<b>Number of studies</b>	<b>Number of pregnancies</b>	<b>Number of SGA<sup>a</sup> births</b>	<b>Mean difference in B12 (pmol/L) in SGA versus non-SGA (95% CI)</b>	<b>I<sup>2</sup></b>
IPD	8 <sup>18,19,21-23,27,29,32</sup>	8,561	882	3.3 (-3.4, 9.9)	0
Aggregate	2 <sup>24,30</sup>	303	87	-11.7 (-47.4, 24.1)	49
IPD + aggregate	10 <sup>18,19,21-24,27,29,30,32</sup>	8,864	969	2.4 (-3.9, 8.7)	0

Pooled results of the mean difference in maternal B12 (pmol/L) in SGA versus non-SGA pregnancies. All analyses are random effects models and crude. Studies included in the analyses are referred to according to their citation number in the text. CI, confidence interval; IPD, individual participant data; SGA, small-for-gestational-age.

a. SGA defined as birth weight <10th centile after taking sex and length of gestation into account, with the following exceptions: In Furness 2013,<sup>24</sup> SGA was defined as “serial tapering of growth in abdominal circumference and of estimated fetal weight below the 10th centile of population-based growth charts”, and in Mamabolo 2006,<sup>30</sup> SGA was defined as birth weight in the 1<sup>st</sup> tertile (mean 2,940 g).