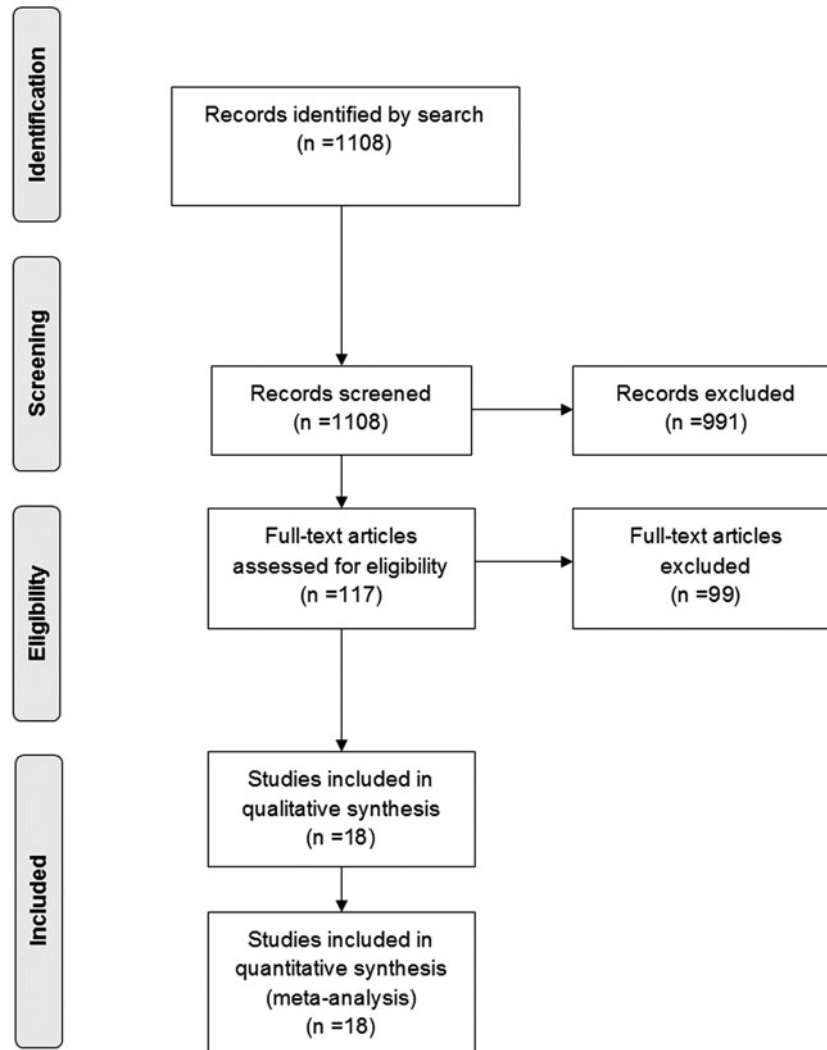


## Supplementary Data



**SUPPLEMENTARY FIG. S1.** PRISMA flow diagram (1).

SUPPLEMENTARY TABLE S1. POOLED RELATIVE RISK WITH 95% CONFIDENCE INTERVAL COMPARING PREGNANT WOMEN WITH SUBCLINICAL HYPOTHYROIDISM TO PREGNANT EUTHYROID WOMEN FOR ALL PREGNANCY OUTCOMES EXCLUDING THE STUDIES BY NEGRO 2010\* AND JACOB 2012\*\*

<i>Pregnancy outcome</i>	<i>Pooled RR [95% CI]</i>	<i>I<sup>2</sup> (%)</i>	<i>Studies used for meta-analysis</i>
Pregnancy loss	2.07 [1.59–2.69]	0	(4–11)
Preterm labor	0.93 [0.58–1.51]	0	(9,12,13)
Preterm delivery	1.19 [0.93–1.53]	30	(4,6,8–11,13,14,16,17)
Gestational hypertension	1.22 [0.84–1.78]	52	(6–9,11,12,17,18)
Preeclampsia	1.30 [1.00–1.68]	0	(7,9,13,15,17,18)
Gestational diabetes	1.24 [0.80–1.91]	51	(7–9,11–13,17,18)
Placental abruption	2.14 [1.23–3.70]	0	(7–9,12,13,15,18)
Placenta previa	0.78 [0.19–3.18]	0	(8,9,13)
PROM	1.50 [1.06–2.12]	10	(8,9,12–14)
Caesarean delivery	1.06 [0.94–1.19]	0	(7,10–12,15,16)
IUGR	2.29 [0.98–5.36]	16	(8,11,12)
Low birth weight	1.28 [0.83–1.96]	59	(4,6–10)
Low APGAR score	1.08 [0.71–1.65]	0	(6,10,13)
Small for gestational age	0.82 [0.43–1.56]	0	(4,10,13)
Neonatal death	2.85 [1.52–5.33]	0	(4,7,9,10,13)

\*Reference (2).

\*\*Reference (3).

RR, relative risk; CI, 95% confidence interval; PROM, premature rupture of membranes; IUGR, intrauterine growth restriction.

### Supplementary References

- Moher D, Liberati A, Tetzlaff J, Altman DG 2009 Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *J Clin Epidemiol* **62**: 1006–1012.
- Negro R, Schwartz A, Gismondi R, Tinelli A, Mangieri T, Stagnaro-Green A 2010 Increased pregnancy loss rate in thyroid antibody negative women with TSH levels between 2.5 and 5.0 in the first trimester of pregnancy. *J Clin Endocrinol Metab* **95**:E44–48.
- Jacob JJ, Aditya K, Achint S, Dhar T, Avasti K 2012 Increased pregnancy losses and poor neonatal outcomes in women with first-trimester TSH levels between 2.5 and 4 mIU/L compared to euthyroid women with TSH less than or equal to 2.5. *Endocr Rev* **33**:OR04-01.
- Su PY, Huang K, Hao JH, Xu YQ, Yan SQ, Li T, Xu YH, Tao FB 2011 Maternal thyroid function in the first twenty weeks of pregnancy and subsequent fetal and infant development: a prospective population-based cohort study in China. *J Clin Endocrinol Metab* **96**:3234–3241.
- Liu HX, Shan ZY, Li CY, Mao JY, Xie XC, Wang WW, Fan CL, Wang H, Zhang HM, Han C, Wang XY, Liu X, Fan YX, Bao SQ, Teng WP 2014 Maternal subclinical hypothyroidism, thyroid autoimmunity, and the risk of miscarriage: a prospective cohort study. *Thyroid* **24**: 1642–1649.
- Wang S, Teng WP, Li JX, Wang WW, Shan ZY 2012 Effects of maternal subclinical hypothyroidism on obstetrical outcomes during early pregnancy. *J Endocrinol Invest* **35**:322–325.
- Casey BM, Dashe JS, Spong CY, McIntire DD, Leveno KJ, Cunningham GF 2007 Perinatal significance of isolated maternal hypothyroxinemia identified in the first half of pregnancy. *Obstet Gynecol* **109**:1129–1135.
- Chen LM, Du WJ, Dai J, Zhang Q, Si GX, Yang H, Ye EL, Chen QS, Yu LC, Zhang C, Lu XM 2014 Effects of subclinical hypothyroidism on maternal and perinatal outcomes during pregnancy: a single-center cohort study of a chinese population. *PLoS One* **9**:e109364.
- Cleary-Goldman J, Malone FD, Lambert-Messerlian G, Sullivan L, Canick J, Porter TF, Luthy D, Gross S, Bianchi DW, D'Alton ME 2008 Maternal thyroid hypofunction and pregnancy outcome. *Obstet Gynecol* **112**: 85–92.
- Männistö T, Väärämäki M, Pouta A, Hartikainen AL, Ruokonen A, Surcel HM, Bloigu A, Järvelin MR, Suvanto-Luukkonen E 2009 Perinatal outcome of children born to mothers with thyroid dysfunction or antibodies: a prospective population-based cohort study. *J Clin Endocrinol Metab* **94**:772–779.
- Sahu MT, Das V, Mittal S, Agarwal A, Sahu M 2010 Overt and subclinical thyroid dysfunction among Indian pregnant women and its effect on maternal and fetal outcome. *Arch Gynecol Obstet* **281**:215–220.
- Breathnach FM, Donnelly J, Cooley SM, Geary M, Malone FD 2013 Subclinical hypothyroidism as a risk factor for placental abruption: evidence from a low-risk primigravid population. *Aust N Z J Obstet Gynaecol* **53**: 553–560.
- Ong GS, Hadlow NC, Brown SJ, Lim EM, Walsh JP 2014 Does the thyroid-stimulating hormone measured concurrently with first trimester biochemical screening tests predict adverse pregnancy outcomes occurring after 20 weeks gestation? *J Clin Endocrinol Metab* **99**: E2668–E2672.
- Korevaar TI, Schalekamp-Timmermans S, de Rijke YB, Visser WE, Visser W, de Muinck Keizer-Schrama SM, Hofman A, Ross HA, Hooijkaas H, Tiemeier H, Bongers-Schokking JJ, Jaddoe VW, Visser TJ, Steegers EA, Medici M, Peeters RP 2013 Hypothyroxinemia and TPO-antibody positivity are risk factors for premature delivery: the generation R study. *J Clin Endocrinol Metab* **98**:4382–4390.
- Feldthusen AD, Larsen J, Pedersen PL, Kristensen TT, Kvetny J 2014 Pregnancy-induced alterations in mito-

- chondrial function in euthyroid pregnant women and pregnant women with subclinical hypothyroidism; relation to adverse outcome. *J Clin Transl Endocrinol* **1**: e13–e17.
16. Kumar A, Agarwal K, Gupta RK, Kar P 2009 Obstetric outcome in women with hepatitis C virus infection and thyroid dysfunction. *Acta Obstet Gynecol Scand* **88**: 1133–1137.
  17. Yuan P, Wang Q, Huang R, Cao F, Zhu Z, Sun D, Zhou H, Yu B 2013 Clinical evaluation with self-sequential longitudinal reference intervals: pregnancy outcome and neonatal thyroid stimulating hormone level associated with maternal thyroid diseases. *West Indian Med J* **62**: 28–34.
  18. Männistö T, Vääräsmäki M, Pouta A, Hartikainen AL, Ruokonen A, Surcel HM, Bloigu A, Järvelin MR, Suvanto E 2010 Thyroid dysfunction and autoantibodies during pregnancy as predictive factors of pregnancy complications and maternal morbidity in later life. *J Clin Endocrinol Metab* **95**:1084–1094.