

## Supplemental Information

### Supplemental Figure 1(S1): Full Search Strategy – MEDLINE (Ovid)

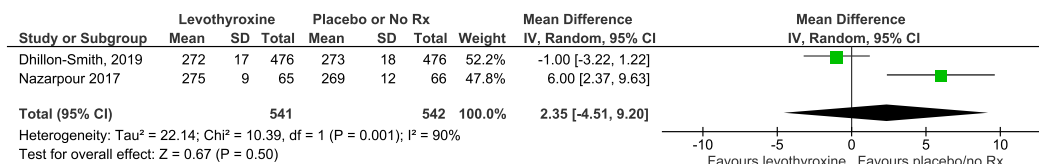
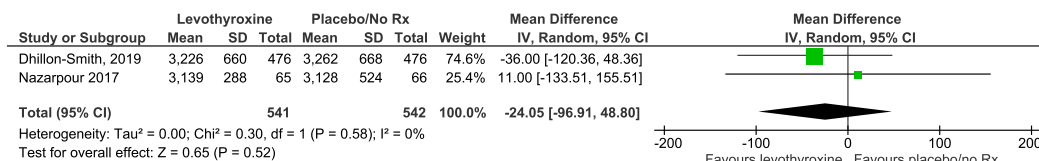
1. Hypothyroidism/
2. "hypothyroid\*".ab,ti,kf.
3. "hypothyroxinemia".ab,ti,kf.
4. (("thyroid-stimulating hormone\*" or "thyroid stimulating hormone\*" or TSH\*) adj2 deficien\*).ab,ti,kf.
5. (thyroid\* adj3 (autoimmun\* or "auto-immun\*" or antibod\*)).ab,ti,kf.
6. Thyroxine/
7. "levothyro\*".ab,ti,kf.
8. "thyrox\*".ab,ti,kf.
9. synthroid.ab,ti,kf.
10. lt4.ab,ti,kf.
11. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10
12. exp Pregnancy/
13. "pregnan\*".ab,ti,kf.
14. "gestat\*".ab,ti,kf.
15. Pregnant Women/
16. "maternal\*".ab,ti,kf.
17. "prenatal\*".ab,ti,kf.
18. 12 or 13 or 14 or 15 or 16 or 17
19. 11 and 18
20. randomized controlled trial.pt.
21. controlled clinical trial.pt.
22. random\*.ab.
23. placebo.ab.
24. drug therapy.fs.
25. trial.ab.
26. groups.ab.
27. 20 or 21 or 22 or 23 or 24 or 25 or 26
28. exp animals/ not humans.sh.
29. 27 not 28
30. 19 and 29
31. limit 30 to yr="1980 -Current"

Supplemental Table (S2). Baseline patient characteristics

Study Author (year)	Maternal Age (years)		Body Mass Index (kg/m <sup>2</sup> )		Baseline FT4 (pmol/L)		Duration of Treatment	LT4 dosing and titration	Funding source
	Intervention Arm (LT4)	Control Arm	Intervention Arm (LT4)	Control Arm	Intervention Arm (LT4)	Control Arm			
Dhillon-Smith <i>et al.</i> (2019)	32.5 ± 4.9	32.7 ± 4.9	26.4 ± 5.6	26.5 ± 5.5	14.6 ± 1.9	14.5 ± 2	From before conception until the end of pregnancy	LT4 was d/c if TFT were outside assay specific limits at 6-8 wks, 1-18wks and 28 wks	UK national institute for health research
Nazarpour <i>et al.</i> (2017)	26.6 ± 5.8	27 ± 4.7	24.9 ± 5.1	24.6 ± 3.6	N/A	N/A	From the first trimester until the end of pregnancy	If TSH < 1.0 mIU/mL: 0.5mcg/kg/d; If TSH 1.0-2.0, 0.75mcg/kg/d; If TSH > 2.0 or TPOAb > 1500IU/mL then 1mcg/kg/day	Did not receive any specific grant from any funding agency
Negro <i>et al.</i> (2005)	29.2 ± 4	30.1 ± 5	N/A	N/A	11.2 ± 1.8	11.7 ± 0.7	1 month before assisted reproductive technology until the end of pregnancy	1mg/kg/day	Unclear
Negro <i>et al.</i> (2006)	30 ± 5	30 ± 6	N/A	N/A	14.8 ± 4.2	14.6 ± 4.3	From the first trimester until the end of pregnancy	If TSH < 1.0 mIU/mL: 0.5mcg/kg/d; If TSH 1.0-2.0, 0.75mcg/kg/d; If TSH > 2.0 or TPOAb > 1500IU/mL then 1mcg/kg/day	Unclear
Negro <i>et al.</i> (2016)	28.9 ± 5.2	29.9 ± 5.1	N/A	N/A	N/A	N/A	From the first trimester	If TSH 0.5-1.5, LT4 0.5mcg/kg/d; TSH 1.5-2.5, LT4	Unclear

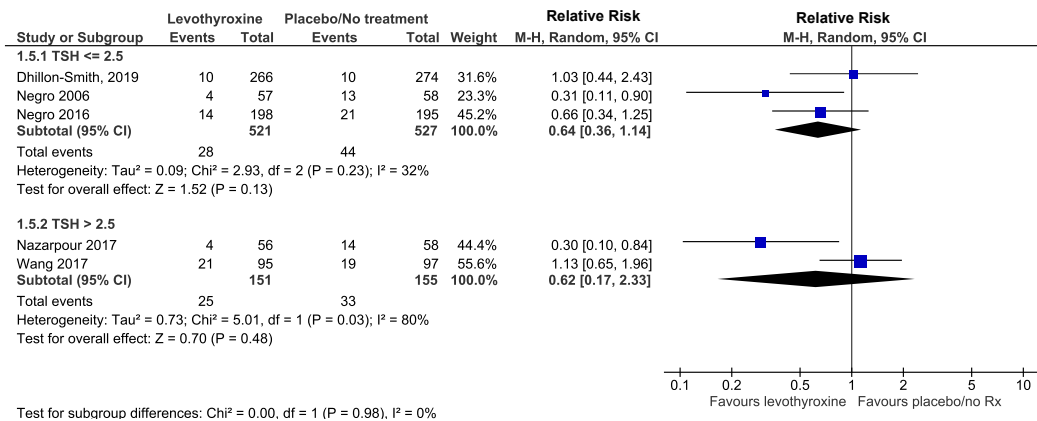
							until the end of pregnancy	1mcg/kg/d. Titration: If TSH > 3.0 in 2nd or 3rd trimester, LT4 dose increased by 12.5mcg/d; If TSH <0.5 in 2nd or 3rd trimester, then decrease by 12.5mcg/d	
Wang <i>et al.</i> (2017)	31.3 ± 3.9	31.7 ± 3.8	22.7 ± 3.3	22.8 ± 3.2	N/A	N/A	2-4 weeks before controlled ovarian hyperstimulation until the end of pregnancy	STARTING Dose: TSH ≥ 2.5mIU/L: starting dose is 50mcg/d; TSH <2.5mIU/L, starting dose is 25mcg/d. If body weight <50kg, then starting dosing decreased by 50%  Titration: TSH in first trimester 0.1-2.5mIU/L, 0.2-3.0mIU/L in second trimester, 0.3-3.0mIU/L in third trimester	National Key Technology R and D program and Chinese National 973 program (Both form the Ministry of Science and Technology of China)

Table S2: N/A specifies that information was not available. FT4 denotes free thyroxine. LT4 denotes levothyroxine.

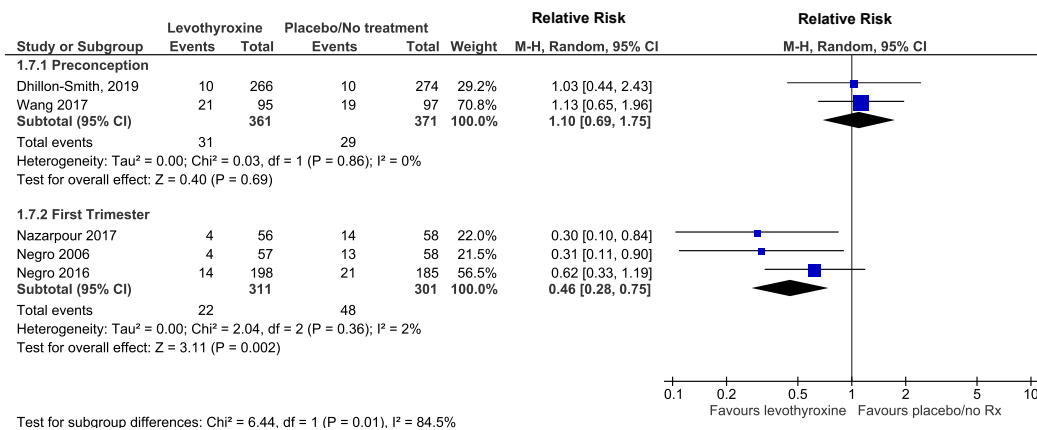
**Supplemental Figure (S3):****A. Weighted mean difference for gestational age at time of delivery (days)****B. Weighted mean difference for birth weight (g)**

## Supplemental Figure (S4): Stratified meta-analysis for preterm delivery subgroups.

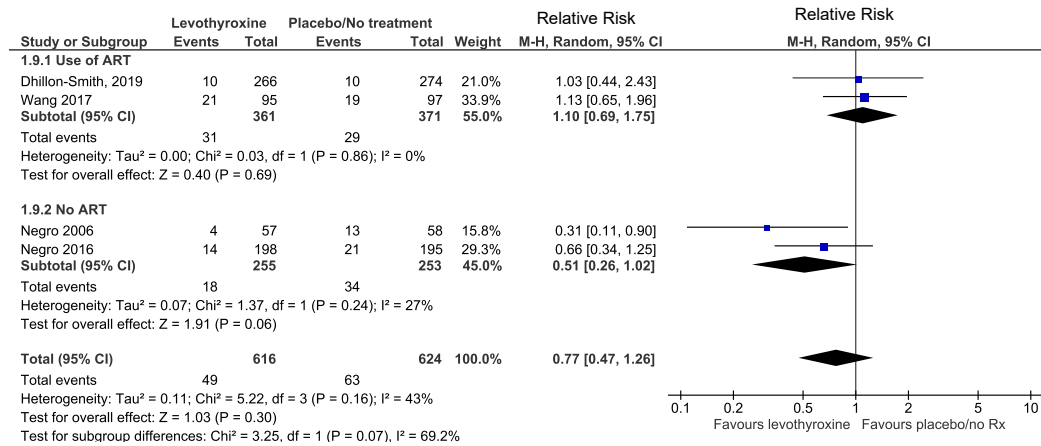
## A. Stratified by TSH levels at baseline



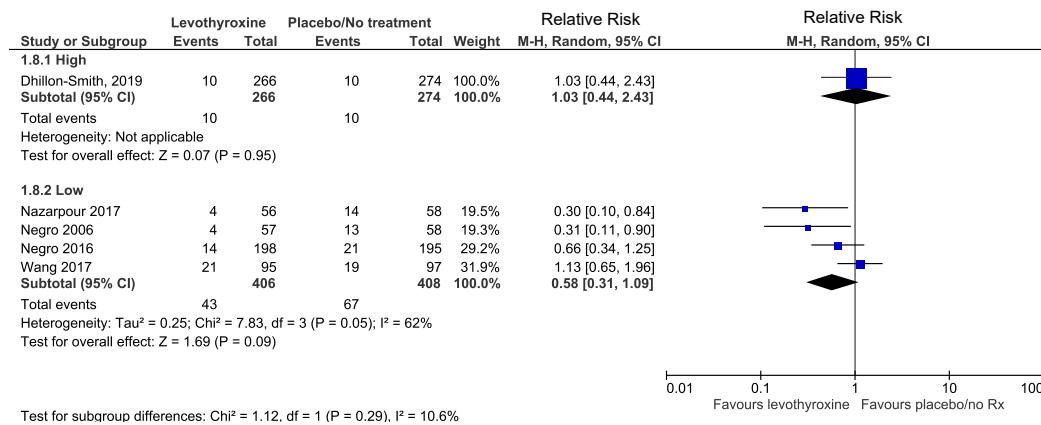
## B. Stratified by timing of levothyroxine initiation.



## C. Stratified by use of assisted reproductive technologies

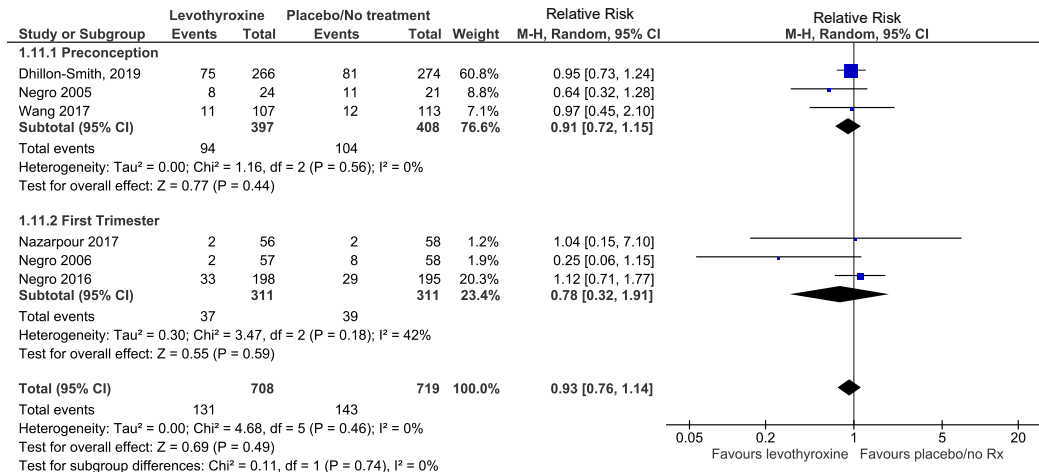


## D. Stratified by study quality

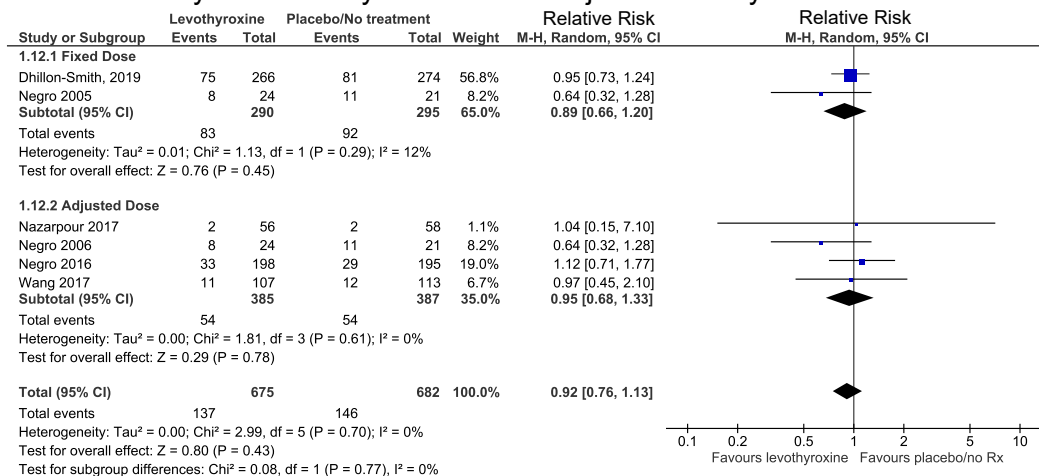


## Supplemental Figure (S5): Stratified meta-analysis for miscarriage subgroups.

## A. Stratified by timing of levothyroxine initiation.



## B. Stratified by fixed levothyroxine versus adjusted levothyroxine dose.



Supplemental Figure (S6): Funnel plot for preterm delivery

