Higher FT4 or TSH below the normal range are associated with increased risk of dementia: a meta-analysis of 11 studies

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Reference		Select	tion		Comparability		Outcome		
cohort study	Representative of cases	Selection of controls	Ascertainment of exposure	Outcomes present at start of study	Comparability the design or analysis	Assessment of outcome	Adequate follow-up time (≧ 5 year)	Adequacy of follow up (≧ 80%)	Overall Quality
de Jong 2006	*	*	*	*	**	*	*	*	9
Tan 2008	*	*	*	*	*	*	*	-	7
de Jong 2009	*	*	*	*	**	*	-	-	7
Annerbo 2009	*	*	*	*	*	*	*	-	7
Forti 2011	*	*	*	*	*	*	-	*	7
Vadiveloo 2011	*	*	*	-	**	*	*	-	7
Yeap 2012	*	*	*	*	**	*	*	*	9
Cappola 2015	*	*	*	_	**	*	*	_	7
case-control study	Case Definition	Representative of Cases	Selection of Control	<i>Definition of</i> <i>Control</i>	Comparability the design or analysis	Ascertainment of exposure	Same Method	Non - Response Rate	Overall Quality
Dobert 2003	*	*	-	*	**	*	*	-	7
van Osch 2004	*	-	*	*	**	*	*	-	7
Hu 2006	*	-	*	*	*	*	*	-	6

Supplementary Table 1 Quality assessment of included studies by Newcastle-Ottawa scale

Supplementary Figure legends

Supplementary Figure 1 Forest plot of high vs. middle category of TSH levels with dementia.

Supplementary Figure 2 Forest plot of low vs. middle category of TSH levels with dementia and

high vs. middle category of TSH levels with dementia in men.

Supplementary Figure 3 Sensitivity analysis of all models.

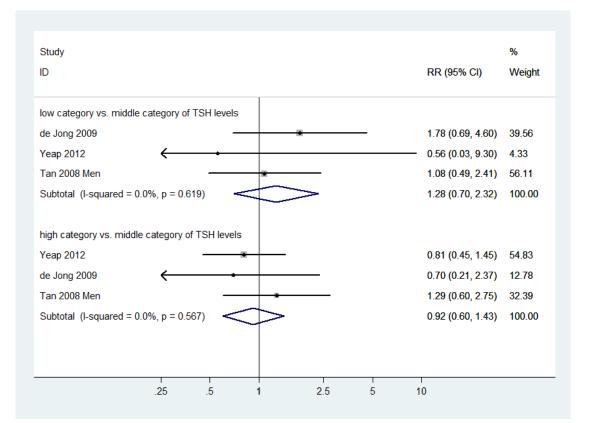
Supplementary Figure 4 Funnel plots to assess the risk of publication bias.

Supplementary Figure 5: MEDLINE search strategy

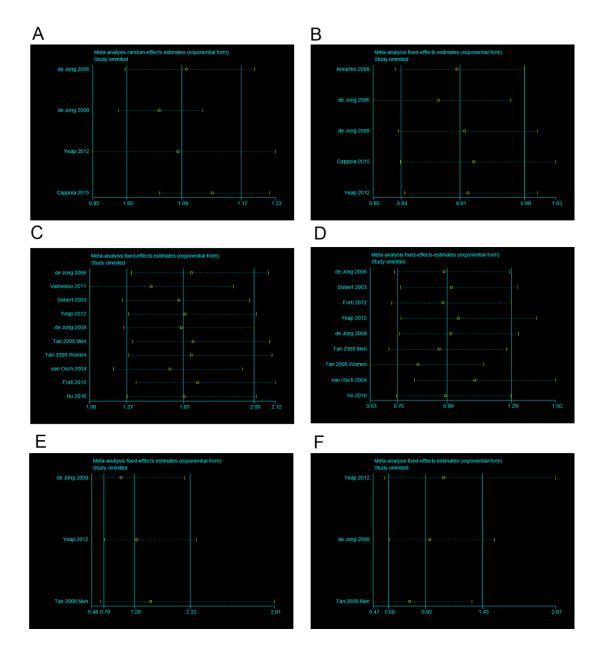
Supplementary Figure 1: Forest plot of high vs. middle category of TSH levels with dementia. Two subgroups were analyzed which were TSH above vs. within the normal range and upper vs. middle tertile of TSH within the normal range. The estimate of RRs and their 95% CIs are plotted with boxes and horizontal lines.

Study		%
D	RR (95% CI)	Weight
TSH above vs. within the normal range		
de Jong 2006	1.28 (0.39, 4.23)	5.04
Dobert 2003	0.22 (0.02, 2.16)	1.31
Forti 2012	1.13 (0.53, 2.38)	12.70
Yeap 2012	0.81 (0.45, 1.45)	20.93
de Jong 2009 🗲 🔹	0.70 (0.21, 2.37)	4.88
Hu 2016 🗲 🔹	> 1.29 (0.24, 6.70)	2.59
Subtotal (I-squared = 0.0%, p = 0.769)	0.91 (0.61, 1.34)	47.45
upper vs. middle tertile of TSH within the normal range		
Tan 2008 Men	1.29 (0.60, 2.75)	12.36
Tan 2008 Women	1.56 (0.91, 2.69)	24.39
van Osch 2004 🛛 🔳	0.51 (0.26, 1.00)	15.79
Subtotal (I-squared = 70.3%, p = 0.034)	1.07 (0.74, 1.54)	52.55
Heterogeneity between groups: p = 0.552		
Overall (I-squared = 17.0%, p = 0.291)	0.99 (0.76, 1.29)	100.00

Supplementary Figure 2: Forest plot of low vs. middle category of TSH levels with dementia and high vs. middle category of TSH levels with dementia in men. The estimate of RRs and their 95% CIs are plotted with boxes and horizontal lines.

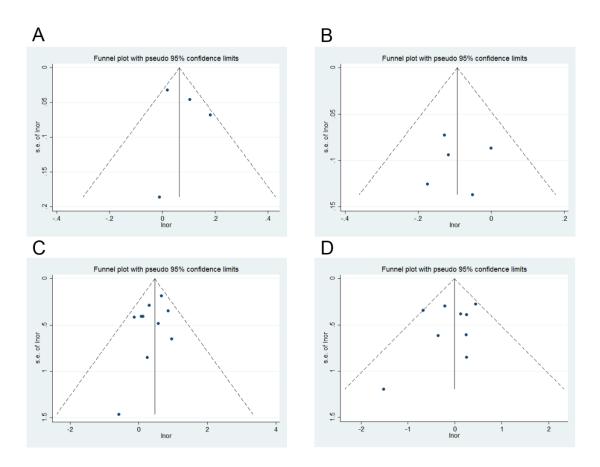


Supplementary Figure 3: Sensitivity analysis of all models. A: per SD increment of FT4 and dementia B: per SD increment of TSH and dementia C: low vs. middle categories of TSH levels and dementia D: high vs. middle categories of TSH levels and dementia E: low vs. middle categories of TSH levels and dementia in men F: high vs. middle categories of TSH levels and dementia in men.



Supplementary Figure 4: Funnel plots to assess the risk of publication bias.

A: per SD increment of FT4 and dementia B: per SD increment of TSH and dementia C: low vs. middle categories of TSH levels and dementia D: high vs. middle categories of TSH levels and dementia



Supplementary Figure 5: MEDLINE search strategy

1 exp Cognition Disorders/ or exp Alzheimer Disease/ or exp Mild Cognitive

Impairment/ or exp Dementia/ or exp Memory Disorders/

2 (mci or ad).ti,ab,kw.

3 (dementia or "alzheimer* disease" or "cognitive dysfunction" or "cognitive decline" or "cognitive impairment" or "cognitive defect" or "cognitive disorder*" or "memory disorder*").mp.

4 or/1-3

5 exp Hypothyroidism/ or exp Thyroxine/ or exp Triiodothyronine/ or exp

Hyperthyroidism/ or exp Thyrotropin/

6 ("Thyroid Stimulating Hormone*" or thyrotropin or triiodothyronine or "thyroid hormone*" or "subclinical hypothyroidism" or hypothyroidism or "subclinical hyperthyroidism" or hyperthyroidism or euthyroid).mp.

7 (tsh or ft3 or ft4 or tt4 or tt3 or "total T3" or "total T4").ab,kw,ti.

8 or/5-7

94 and 8

10 exp cohort studies/

11 cohort\$.tw.

12 controlled clinical trial.pt.

13 epidemiologic methods/

14 limit 13 to yr=1966-1989

15 exp case-control studies/

16 (case\$ and control\$).tw.

17 or/10-12,14-16

18 9 and 17