Supplemental Table 1. Search strategy

Database	Search strategy
PubMed	#1. thyroidectomy[mesh] #2. Thyroidectomy[tiab] OR Thyroidectomies[tiab] OR strumectomy[tiab] #3. (thyroid[mesh] OR thyroid[tiab]) AND (resection[tiab] OR surgery[tw] OR removal[tiab] OR operation[tiab] OR remove[tiab]) #4. (#1 OR #2 OR #3) #5. osteoporosis[mesh] #6. Osteoporosis[tiab] OR Osteoporoses[tiab] OR Osteoporotic[tiab] OR "Female Athlete Triad"[tiab] OR "Bone Loss"[tiab] OR "Bone Losses"[tiab] #7. (Osteopenia[tiab] OR Osteopenias[tiab]) #8. Bone Density[mesh] #9. "Bone density"[tiab] OR "Bone densities"[tiab] OR "mineral density"[tiab] OR "mineral densities"[tiab] OR "osseous density"[tiab] OR "osseous densities"[tiab] OR "bone mineral content"[tiab] OR "bone mineral contents"[tiab] OR (BMD[tiab] AND bone[tiab]) #10. bone fractures[mesh] #11. fracture[tiab] OR fractures[tiab] OR "broken bone"[tiab] OR "broken bones"[tiab] #12. (#5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11) #13. (#4 AND #12) #14. (Prognosis/Broad[filter]) AND ((thyroidectomy OR thyroidectomies OR strumectomy OR "thyroid surgery" OR "thyroid resection" OR "thyroid removal") AND (osteoporosis OR osteopenia OR "bone density" OR fracture OR fractures)) #15. (#13 OR #14) #16. ((animals [mh:noexp] OR animal experimentation[mesh] OR animal models[mesh])) #17. animals[mesh] AND human[mesh] #18. (#16 NOT #17) #19. (#15 NOT #18) #20. (#13 OR #14) Filters: Humans #21. (#19 OR #20) #22. (#19 OR #20) Filters: English DATE OF SEARCH: April 10, 2020 NUMBER OF RESULTS: 421 UPDATED DATE OF SEARCH: February 24, 2021

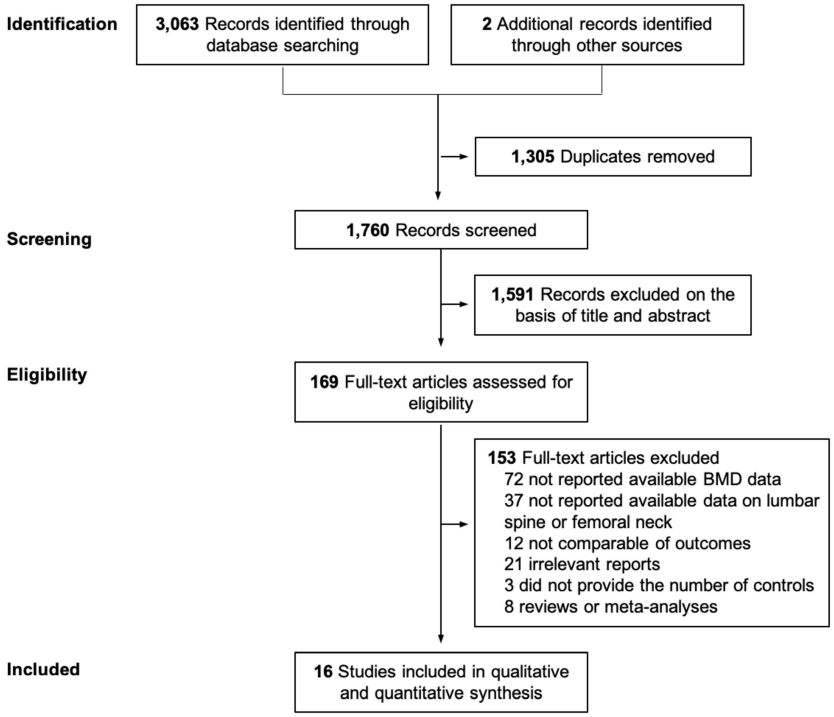
	NUMBER OF ADDITIONAL RESULTS: 20
EMBASE	#1. 'thyroid surgery'/exp #2. thyroidectomy:ti,ab OR thyroidectomies:ti,ab OR strumectomy:ti,ab OR thyroparathyroidectomy:ti,ab #3. 'thyroid gland'/de OR thyroid:ti,ab #4. resection:ti,ab,kw OR surgery:ti,ab,kw OR removal:ti,ab,kw OR operation:ti,ab,kw OR remove:ti,ab,kw #5. #3 AND #4 #6. #1 OR #2 OR #5 #7. 'osteoporosis'/exp #8. osteoporosis:ti,ab OR osteoporoses:ti,ab OR osteoporotic:ti,ab OR 'female athlete triad':ti,ab OR 'bone loss':ti,ab OR 'bone losses':ti,ab #9. 'osteopenia'/exp #10. osteopenia:ti,ab OR osteopenias:ti,ab #11. 'bone density'/exp #12. (bone NEAR/2 density) OR (bone NEAR/2 densities) OR 'mineral densit*' OR 'osseous densit*' OR 'bone mineral content*' OR (bmd:ti,ab AND bone:ti,ab) #13. 'fracture'/exp #14. fracture:ti,ab OR fractures:ti,ab OR 'broken bone*':ti,ab #15. #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 #16. #6 AND #15 #17. ('animal'/exp OR 'invertebrate'/exp OR 'animal experiment'/exp OR 'animal model'/exp OR 'animal tissue'/exp OR 'animal cell'/exp OR 'nonhuman'/exp) NOT ('human'/de OR 'normal human'/de OR 'human cell'/de) #18. #16 NOT #17 #19. #16 AND [humans]/lim #20. #18 OR #19 #21. (#18 OR #19) AND ([english]/lim) DATE OF SEARCH: April 10, 2020 NUMBER OF RESULTS: 1,010 UPDATED DATE OF SEARCH: February 24, 2021 NUMBER OF ADDITIONAL RESULTS: 60

Cochrane Library	#1. [mh thyroidectomy] #2. (Thyroidectomy or Thyroidectomies or strumectomy):ti,ab #3. [mh thyroid] or thyroid:ti,ab #4. (resection or surgery or removal or operation or remove):ti,ab,kw #5. #3 and #4 #6. #1 or #2 or #5 #7. [mh osteoporosis] #8. (Osteoporosis or Osteoporoses or Osteoporotic or "Female Athlete Triad" or "Bone Loss" or "Bone Losses"):ti,ab #9. (Osteopenia or Osteopenias):ti,ab #10. [mh "Bone Density"] #11. ("Bone density" or "Bone densities" or "mineral density" or "mineral densities" or "osseous density" or "osseous densities" or "bone mineral content" or "bone mineral contents" or (BMD and bone)):ti,ab #12. [mh "bone fractures"] #13. (fracture or fractures or "broken bone" or "broken bones"):ti,ab #14. {or #7-#13} #15. #6 and #14 DATE OF SEARCH: April 10, 2020 NUMBER OF RESULTS: 39 UPDATED DATE OF SEARCH: February 24, 2021 NUMBER OF ADDITIONAL RESULTS: 2
Web Of Science	#1. TS=(thyroidectomy OR thyroidectomies OR strumectomy) #2. TS=(thyroid AND (resection OR surgery OR removal OR operation OR remove)) #3. #1 OR #2 #4. TS=(osteoporosis OR osteoporoses OR osteoporotic OR "female athlete triad" or "bone loss" OR "bone losses") #5. TS=(osteopenia OR osteopenias) #6. TS=("bone density" OR "bone densities" OR "mineral density" OR "mineral densities" OR "osseous density" OR "osseous densities" OR "bone mineral content" OR "bone mineral contents" OR (BMD AND bone))
	#7. TS=(fracture OR fractures OR "broken bone" OR "broken bones")

	#8. #4 OR #5 OR #6 OR #7 #9. #3 AND #8 #10. (#3 AND #8) AND LANGUAGE: (English) DATE OF SEARCH: February 24, 2021 NUMBER OF RESULTS: 370
Scopus	#1. TITLE-ABS-KEY(thyroidectomy OR thyroidectomies OR strumectomy) #2. TITLE-ABS-KEY(thyroid AND (resection OR surgery OR removal OR operation OR remove)) #3. #1 OR #2 #4. TITLE-ABS-KEY(osteoporosis OR osteoporoses OR osteoporotic OR "female athlete triad" or "bone loss" OR "bone losses") #5. TITLE-ABS-KEY(osteopenia OR osteopenias) #6. TITLE-ABS-KEY("bone density" OR "bone densities" OR "mineral density" OR "mineral densities" OR "osseous density" OR "osseous densities" OR "bone mineral content" OR "bone mineral contents" OR (BMD AND bone)) #7. TITLE-ABS-KEY(fracture OR fractures OR "broken bone" OR "broken bones") #8. #4 OR #5 OR #6 OR #7 #9. #3 AND #8 #10. (#3 AND #8) AND LANGUAGE(English) DATE OF SEARCH: February 24, 2021 NUMBER OF RESULTS: 1,141
Related article search	Related articles searched according to the following references: 1) Quan ML, Pasieka JL, Rorstad O. Bone mineral density in well-differentiated thyroid cancer patients treated with suppressive thyroxine: a systematic overview of the literature. *J Surg Oncol.* 2002;79(1):62-69; discussion 69-70. 2) Heemstra KA, Hamdy NA, Romijn JA, Smit JW. The effects of thyrotropin-suppressive therapy on bone metabolism in patients with well-differentiated thyroid carcinoma. *Thyroid.* 2006;16(6):583-591. 3) Parker WA, Edafe O, Balasubramanian SP. Long-term treatment-related morbidity in differentiated thyroid cancer: a systematic review of the literature. *Pragmat Obs Res.* 2017;8:57-67. 4) Uzzan B, Campos J, Cucherat M, Nony P, Boissel JP, Perret GY. Effects on bone mass of long term treatment with thyroid hormones: a meta-analysis. *J Clin*

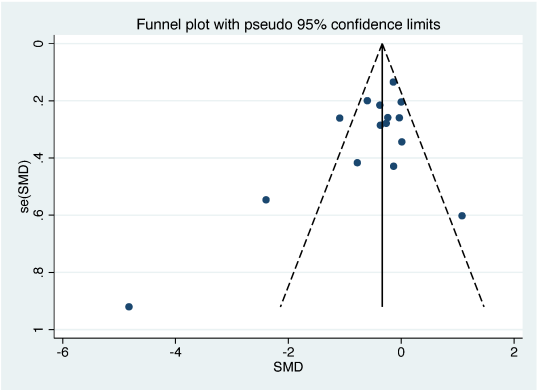
	Endocrinol Metab. 1996;81(12):4278-4289. 5) Yoon B-H, Lee Y, Oh HJ, Kim SH, Lee Y-K. Influence of thyroid-stimulating hormone suppression therapy on bone mineral density in patients with differentiated thyroid cancer: a meta-analysis DATE OF SEARCH FOR RELATED ARTICLES: April 20, 2020 TOTAL: 332 NUMBER OF RESULTS: 2

Supplemental Figure 1. Flow diagram of reference selection process

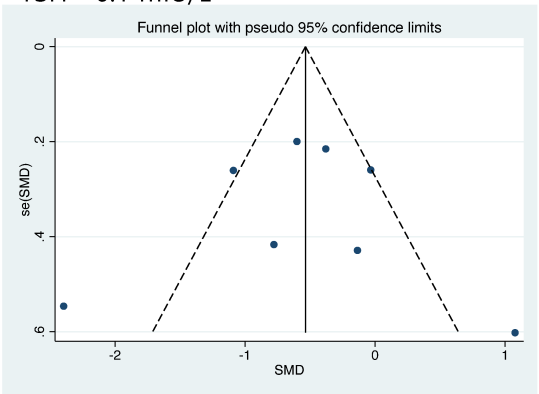


Supplemental Figure 2a. Funnel plots for evaluation of publication bias (Lumbar spine)

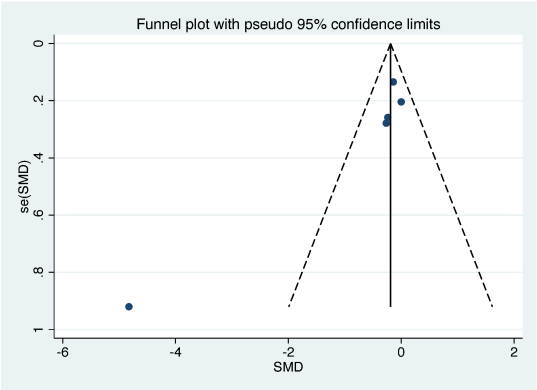
Overall



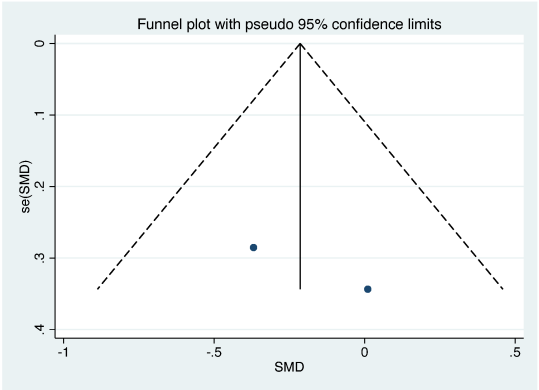
TSH <0.1 mIU/L



TSH 0.1-0.49 mIU/L

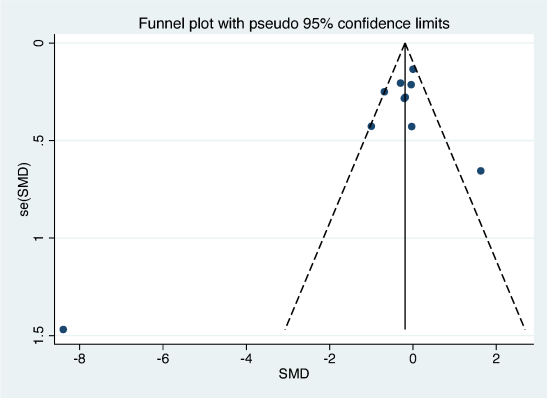


TSH ≥0.50 mIU/L

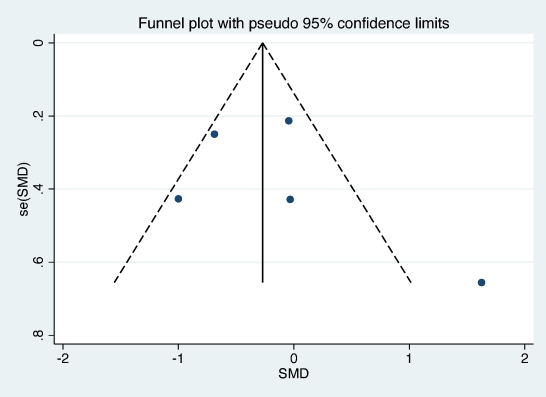


Supplemental Figure 2b. Funnel plots for evaluation of publication bias (Femoral neck)

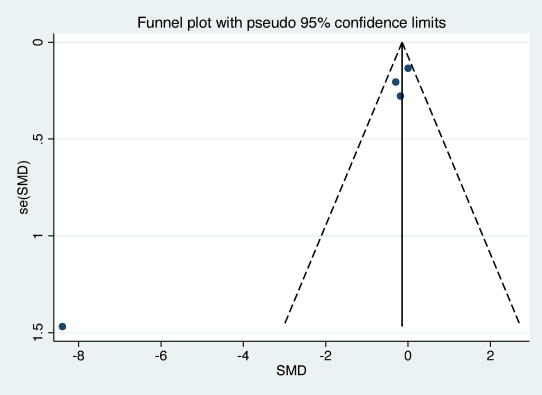
Overall



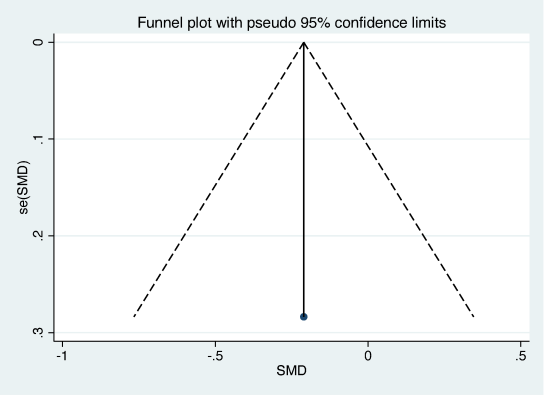
TSH <0.1 mIU/L



TSH 0.1-0.49 mIU/L



TSH ≥0.50 mIU/L



Supplemental Table 2. Additional information on the included studies

First author (year)	Postoperative levothyroxine dose, mean	TSH level at follow-up period, mean	Lists of exclusion criteria for medications*	Lists of exclusion criteria for medical conditions†
Recker (1989)	Range, 0.15-0.20 mg/day	Patients, 1.8 (SD, 0.9) mIU/L; Controls, 3.2 (SD, 1.6) mIU/L	Estrogens, corticosteroids, calcium	Metastatic thyroid cancer, diabetes, post-oophorectomy, post-hysterectomy
Diamond (1991)	Cumulative dose of levothyroxine, mg: 337 (SE, 72)	‡ Patients, 0.3 (SE, 0.1) mIU/L; Controls, 1.2 (SE, 0.2) mIU/L	Estrogens, calcium, vitamin D	(Stated without the list of medical conditions)
Franklyn (1992)	175 (range, 100-200) μg/day	Patients, 0.26 (SD, 0.54) mIU/L; Controls, 1.94 (SD, 1.32) mIU/L	Estrogens, calcium, vitamin D, tamoxifen, thiazide diuretics	Recurrent or metastatic thyroid cancer, osteoporotic fracture, rheumatoid arthritis, diabetes, hypoparathyroidism, alcohol abuse, chronic amenorrhea, late menarche, early menopause, post-oophorectomy
Abugassa (1993)	0.23 (SE, 0.02) mg/day	<0.1 mIU/L	Estrogens	Osteoporotic fracture, endocrinological (apart from hyperparathyroidism), hepatic, intestinal, or renal abnormalities
Kung (1993)	179 (SD, 60) μg/day	Patients, <0.05 mIU/L; Controls, 2.2 (SD, 0.8) mIU/L	Calcium, hormonal contraceptive agents	Recurrent thyroid cancer, late menopause, early menarche, post-oophorectomy, history of other thyroid disorder, family history of osteoporosis
Giannini (1994)	144.2 (SE, 4.15) μg/day	<0.1 mIU/L	(Stated without the list of drugs)	Metastatic thyroid cancer, hypoparathyroidism
Hawkins (1994)	158.3 (SD, 43.7) μg/day	0.3 (SD, 0.4) mIU/L	Estrogens, calcium, vitamin D, thiazide diuretics	(Stated without the list of medical conditions)
Frusciante (1998)	133.6 (SE, 8.4) μg/day	0.04 (SE, 0.016) mIU/L	(Stated without the list of drugs)	(Stated without the list of medical conditions)
Toivonen	215 (SD, 53) μg/day	Patients, <0.05	(Stated without the list of drugs)	(Stated without the list of medical conditions)

(1998)		mIU/L; Controls, 2.4 (range, 0.06-4.1) mIU/L		
Goerres (1998)	NR ††	0.019 (SD, 0.056) mIU/L	Calcitonin, calcium, vitamin D compounds	NR
Chen (2004)	Starting dose: young patients, 2.0 μg/kg/day; elderly patients, 1.5 μg/kg/day **	1.76 (SD, 0.41) mIU/L	Hormone replacement therapy, corticosteroids, tamoxifen, anticonvulsants, heparin, lithium	Metastatic or recurrent thyroid cancer, hyperparathyroidism, hypoparathyroidism, gonadal insufficiency, diabetes, Cushing's syndrome, severe liver or kidney disorder, chronic obstructive pulmonary disease, rheumatoid arthritis.
Reverter (2005)	NR	Patients, 0.04 (SD, 0.03) mIU/L; Controls, 1.8 (SD, 1.0) mIU/L	Hormonal replacement therapy, corticosteroids, calcium, vitamin D, bisphosphonates, raloxifene, tamoxifen, thiazide diuretics,	Prolonged immobilization, recent bone fracture, inflammatory osteoarticular disease, diabetes, serum creatinine levels >1.3 mg/dL, increased alkaline phosphatase
Eftekhari (2008)	168.33 (SD, 24.3) μg/day	< 0.3 mIU/L	Estrogens, corticosteroids, calcium, vitamin D, bisphosphonates, tamoxifen, thiazide diuretics, anticonvulsants, heparin,	< 45 years, osteoporotic fracture, diabetes, alcohol abuse, rheumatoid arthritis, chronic amenorrhea (> 3 months), late menarche, early menopause, post oophorectomy
Tournis (2015)	122.9 (SD, 21.8) μg/day	Patients, 0.11 (SD, 0.2) mIU/L; Controls, 2.28 (SD, 1.2) mIU/L	Hormonal replacement therapy, corticosteroids, calcium, vitamin D, vitamin D analogues, bisphosphonates, SERMS, denosumab, teriparatide, strontium ranelate, oral contraceptives, diuretics, lithium	Liver or renal disease, prior hyperthyroidism, hyperparathyroidism, hypoparathyroidism, malabsorption syndrome and rheumatic diseases, previous osteoporotic fracture
Moon (2016)	133.5 (SD, 33.5) μg/day	0.09 (SD, 0.13) mIU/L	Bisphosphonate, oral contraceptives, menopausal hormone therapy, SERMS, diuretics, lithium, corticosteroids	Liver or renal diseases, hyperthyroidism, hyper- or hypoparathyroidism, malabsorption syndrome, rheumatic diseases
Kim (2019)	135 (SD, 3.06) μg/day	Patients, 0.000 (IQR 0.00 to 0.242); Controls, 2.450 (IQR 1.263 to 3.813)	Glucocorticoids, anti-osteoporotic drugs	Renal or hepatic impairment

TSH = thyroid stimulating hormone; NR = not reported; NA = not applicable; SD = standard deviation; SE = standard error; SERMS = selective estrogen receptor modulators; hypoPT = patients with hypoparathyroidism; DTC = differentiated thyroid carcinoma; IQR = interquartile range; NTG = non-toxic goiter

[*] Sixteen studies presented the list of excluded medications, and 6 studies stated that patients who had taken any medication influencing bone density were excluded from the study.

[†] Sixteen studies presented the list of excluded comorbidities, and 6 studies stated that patients who had any medical condition influencing bone density were excluded from the study.

[‡] Lower limit of detection for TSH in this assay was 0.3 mIU/L.

[§] Lower limit of detection for TSH in this assay was 0.15 mIU/L.

[‖] Among 50 participants, 12 were treated with dihydrotachysterol and another 2 with calcitriol, besides calcium tablets. Two patients had well-controlled type 2 diabetes. Three women had been taking hormonal contraceptives for 1 or 3 years, and another had a received low-dose post-menopausal estrogen substitution.

[¶] Lower limit of detection for TSH in this study was 0.2 mIU/L.

[††] Mean cumulated T4 dose of patients was reported as 8527.3 (6102.6) μg/kg body weight.

[**] The dose was adjusted at an increment/decrement of 12.5 to 25 μg/day according to the TSH value at 8- to 12-week intervals.

[‡‡] Levothyroxine dose was adjusted to keep the TSH level under or equal to 0.1 mIU/L.

Supplemental Table 3. Quality Assessment of Included Studies in the Meta-analysis Using the Newcastle-Ottawa Quality Assessment Scale

First author (year)	Patient selection				Comparability	Exposure			Sum of score
	Adequate case definition	Representativeness of the cases	Selection of controls	Definition of controls		Assessment of Exposure	Same method of ascertainment	Non-Response rate	
Recker (1989)	*	*	*	*	*	-	-	*	6
Diamond (1991)	*	*	*	*	*	-	-	*	6
Franklyn (1992)	*	*	*	*	*	-	-	*	6
Abugassa (1993)	*	*	*	*	**	-	-	*	7
Kung (1993)	*	*	*	*	*	-	-	*	6
Giannini (1994)	*	*	*	*	*	*	-	*	7
Hawkins (1994)	*	*	*	*	*	-	-	*	6
Frusciante (1998)	*	*	*	*	*	*	-	*	7
Toivonen (1998)	*	*	*	*	*	*	-	*	7
Goerres (1998)	*	*	*	*	*	*	-	*	7
Chen (2004)	*	*	*	*	*	*	-	*	7
Reverter (2005)	*	*	*	*	**	*	*	*	9
Eftekhari (2008)	*	*	*	*	**	*	*	*	9
Tournis (2015)	*	*	*	*	**	*	*	*	9
Moon (2016)	*	*	*	*	**	*	*	*	9
Kim (2019)	*	*	*	*	**	*	*	*	9