

Supplementary Online Content

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eTable 1. Breakdown and *ICD-9* Codes for Different Types and Locations of Fractures (n=3,556)

eTable 2. Adjusted Hazard Ratios for Fracture Types by Categories of Thyroid Dysfunction at Baseline

eTable 3. Mortality Rate of Death by Categories of Thyroid Dysfunction at Baseline

eTable 4. Adjusted Subhazard Ratios for Fracture, Incorporating the Competing Risk of Death

eTable 5. Adjusted Hazard Ratios for Fracture by Categories of Thyroid Dysfunction at Baseline, Stratified by Race, Age, and Sex

eTable 6. Adjusted Hazard Ratios for Fracture by Categories of Thyroid Dysfunction and Thyroid Medication Users at Baseline

eTable 7. Adjusted Hazard Ratios for Inpatient Fracture by Categories of Thyroid Dysfunction at Baseline

eTable 8. Adjusted Hazard Ratios for Fracture, Excluding Pathologic Fractures (n=427)

eTable 9. Adjusted Hazard Ratios (95% CI) for Fracture by Categories of Thyroid Dysfunction at Baseline, Using Time-Varying Covariates

eTable 10. Adjusted Hazard Ratios for Fracture by Categories of Subclinical Thyroid Dysfunction at Baseline and Incident Clinical Thyroid Dysfunction

eFigure. Adjusted Cumulative Incidence of Fracture by Categories of Thyroid Dysfunction, Accounting for the Competing Risk of Death

This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Breakdown and *ICD-9* Codes for Different Types and Locations of Fractures (n=3,556)

Type	ICD-9 code	n (% of fractures)
Pathological	733.10-733.19	427 (12.0%)
Stress	733.93-733.98	36 (1.0%)
Injury	800-829	3,254 (91.5%)
Location	ICD-9 code	n (% of fractures)
Hip	820-820.9	502 (14.1%)
Spine	733.13; 805.2-805.5; 806.2-806.5	492 (13.8%)
Non-spine	Any fracture claims that do not contain the ICD-9 codes for spine	3,064 (86.2%)

eTable 2. Adjusted Hazard Ratios for Fracture Types by Categories of Thyroid Dysfunction at Baseline

	Subclinical Hypothyroidism	Euthyroidism	Subclinical Hyperthyroidism
N hip fractures	24	465	13
IR^a (95% CI) per 10,000 person-years	25.7 (17.2, 38.3)	23.4 (21.4, 25.7)	26.1 (15.2, 45.0)
Model 1^b	1.25 (0.83, 1.89)	1 (Reference)	1.97 (1.00, 3.88)
Model 2^c	1.28 (0.84, 1.93)	1 (Reference)	1.91 (0.96, 3.79)
N spine fractures	18	461	13
IR^a (95% CI) per 10,000 person-years	19.3 (12.1, 30.6)	23.2 (21.2, 25.5)	26.1 (15.2, 45.0)
Model 1^b	1.67 (1.04, 2.67)	1 (Reference)	2.64 (1.29, 5.42)
Model 2^c	1.59 (0.99, 2.56)	1 (Reference)	2.18 (1.06, 4.49)
N non-spine fractures	151	2,830	83
IR^a (95% CI) per 10,000 person-years	161.6 (137.7, 189.5)	142.6 (137.5, 148.0)	166.6 (134.4, 206.6)
Model 1^b	1.09 (0.92, 1.28)	1 (Reference)	1.52 (1.16, 2.00)
Model 2^c	1.06 (0.90, 1.25)	1 (Reference)	1.42 (1.08, 1.86)

^a IR: Incidence rate

^b Model 1: age, sex, race/center

^c Model 2: Model 1 + diabetes, HDL cholesterol, antihypertensive treatment, heart rate, BMI, smoking status, alcohol consumption, physical activity, menopause, and Vitamin D level

eTable 3. Mortality Rate of Death by Categories of Thyroid Dysfunction at Baseline

	n deaths/N	Mortality rate (95% CI) per 1,000 person-years
Subclinical Hypothyroidism	235/484	20.8 (18.3, 23.7)
Euthyroidism	5,193 /10,177	22.2 (21.6, 22.8)
Subclinical Hyperthyroidism	165/285	27.3 (23.4, 31.8)

eTable 4. Adjusted^a Subhazard Ratios for Fracture, Incorporating the Competing Risk of Death

	sHR (95% CI)
Subclinical Hypothyroidism	1.09 (0.93, 1.28)
Euthyroidism	1 (Reference)
Subclinical Hyperthyroidism	1.33 (1.02, 1.73)

^aAdjusted for age, sex, race/center, diabetes, HDL cholesterol, antihypertensive treatment, heart rate, BMI, smoking status, alcohol consumption, physical activity, menopause, and Vitamin D level

eTable 5. Adjusted Hazard Ratios for Fracture by Categories of Thyroid Dysfunction at Baseline, Stratified by Race, Age, and Sex

Black individuals	Subclinical Hypothyroidism	Euthyroidism	Subclinical Hyperthyroidism
n/N	11/52	546/2,441	45/133
IR (95% CI) per 10,000 person-years ^a	132.7 (73.5, 239.7)	117.7 (108.3, 128.0)	201.9 (150.7, 270.4)
Model 1 ^b	0.87 (0.48, 1.58)	1 (Reference)	1.83 (1.35, 2.49)
Model 2 ^c	0.91 (0.50, 1.66)	1 (Reference)	1.73 (1.27, 2.36)
White individuals^d	Subclinical Hypothyroidism	Euthyroidism	Subclinical Hyperthyroidism
n/N	158/432	2,745/7,736	51/152
IR (95% CI) per 10,000 person-years ^a	186.8 (159.9, 218.3)	181.4 (174.8, 188.3)	185.4 (140.9, 243.9)
Model 1 ^b	0.86 (0.73, 1.01)	1 (Reference)	1.20 (0.91, 1.58)
Model 2 ^c	0.88 (0.75, 1.04)	1 (Reference)	1.12 (0.85, 1.48)
60 years +	Subclinical Hypothyroidism	Euthyroidism	Subclinical Hyperthyroidism
n/N	91/215	1,447/3,502	43/90
IR (95% CI) per 10,000 person-years ^a	261.9 (213.3, 321.7)	264.2 (250.9, 278.2)	379.9 (281.8, 512.3)
Model 1 ^b	0.88 (0.71, 1.09)	1 (Reference)	1.73 (1.27, 2.35)
Model 2 ^c	0.88 (0.71, 1.10)	1 (Reference)	1.63 (1.19, 2.21)
Less than 60 years^e	Subclinical Hypothyroidism	Euthyroidism	Subclinical Hyperthyroidism
n/N	78/269	1,844/6,675	53/195
IR (95% CI) per 10,000 person-years ^a	132.8 (106.4, 165.9)	128.3 (122.6, 134.3)	137.7 (105.2, 180.3)
Model 1 ^b	0.86 (0.69, 1.09)	1 (Reference)	1.25 (0.95, 1.64)
Model 2 ^c	0.89 (0.71, 1.12)	1 (Reference)	1.18 (0.89, 1.55)
Female	Subclinical Hypothyroidism	Euthyroidism	Subclinical Hyperthyroidism
n/N	123/305	2,069/5,476	64/158
IR (95% CI) per 10,000 person-years ^a	206.0 (172.7, 245.9)	191.5 (183.4, 199.9)	223.2 (174.7, 285.2)
Model 1 ^b	0.89 (0.74, 1.07)	1 (Reference)	1.49 (1.16, 1.92)
Model 2 ^c	0.90 (0.75, 1.09)	1 (Reference)	1.38 (1.07, 1.77)
Male^f	Subclinical Hypothyroidism	Euthyroidism	Subclinical Hyperthyroidism
n/N	46/179	1,222/4,701	32/127
IR (95% CI) per 10,000 person-years ^a	136.3 (102.1, 181.9)	135.2 (127.8, 143.0)	151.4 (107.1, 214.1)

Model 1 ^b	0.81 (0.60, 1.09)	1 (Reference)	1.29 (0.91, 1.84)
Model 2 ^c	0.86 (0.64, 1.16)	1 (Reference)	1.26 (0.88, 1.79)

^aIR: Incidence rate

^b Model 1: age, race/center, sex

^c Model 2: Model 1 + diabetes, HDL cholesterol, antihypertensive treatment, heart rate, BMI, smoking status, alcohol consumption, physical activity, menopause, and Vitamin D level

^d p-value for interaction between thyroid category and race = 0.117

^e p-value for interaction between thyroid category and age = 0.178

^f p-value for interaction between thyroid category and sex = 0.773

eTable 6. Adjusted Hazard Ratios for Fracture by Categories of Thyroid Dysfunction and Thyroid Medication Users at Baseline

	Subclinical Hypothyroidism	Euthyroidism	Subclinical Hyperthyroidism	Thyroid Medication Users
n/N	169/484	3,291/10,177	96/285	281/662
IR (95% CI) per 10,000 person-years ^a	182.0 (156.5, 211.6)	166.5 (160.9, 172.3)	192.8 (157.8, 235.4)	230.6 (205.2, 259.2)
Model 1 ^b	0.88 (0.75, 1.02)	1 (Reference)	1.41 (1.15, 1.73)	1.13 (1.00, 1.28)
Model 2 ^c	0.90 (0.77, 1.05)	1 (Reference)	1.33 (1.08, 1.63)	1.12 (0.99, 1.27)

^aIR: Incidence rate

^bModel 1: age, race/center, sex

^cModel 2: Model 1 + diabetes, HDL cholesterol, antihypertensive treatment, heart rate, BMI, smoking status, alcohol consumption, physical activity, menopause, and Vitamin D level

eTable 7. Adjusted Hazard Ratios for Inpatient Fracture^a by Categories of Thyroid Dysfunction at Baseline

Overall (n=10,965)	Subclinical Hypothyroidism	Euthyroidism	Subclinical Hyperthyroidism
n/N	77/488	1,680/10,191	54/286
Model 1 ^b	0.73 (0.58, 0.92)	1 (Reference)	1.66 (1.26, 2.18)
Model 2 ^c	0.76 (0.60, 0.95)	1 (Reference)	1.54 (1.17, 2.03)

^a Hospitalized Inpatient Fracture using ARIC Data and CMS Data, n=1,809 fractures

^b Model 1: age, race/center, sex

^c Model 2: Model 1 + diabetes, HDL cholesterol, antihypertensive treatment, heart rate, BMI, smoking status, alcohol consumption, physical activity, menopause, and Vitamin D level

eTable 8. Adjusted Hazard Ratios for Fracture, Excluding Pathologic Fractures (n=427)

Overall (n=10,519)	Subclinical Hypothyroidism	Euthyroidism	Subclinical Hyperthyroidism
n/N	151/466	2,893/9,779	85/274
Model 1 ^a	0.88 (0.74, 1.03)	1 (Reference)	1.43 (1.15, 1.77)
Model 2 ^b	0.90 (0.76, 1.06)	1 (Reference)	1.36 (1.10, 1.69)

^aModel 1: age, race/center, sex

^bModel 2: Model 1 + diabetes, HDL cholesterol, antihypertensive treatment, heart rate, BMI, smoking status, alcohol consumption, physical activity, menopause, and Vitamin D level

eTable 9. Adjusted Hazard Ratios (95% CI) for Fracture by Categories of Thyroid Dysfunction at Baseline, Using Time-Varying Covariates

Overall (n=10,946)	Subclinical Hypothyroidism	Euthyroidism	Subclinical Hyperthyroidism
n/N	169/484	3,291/10,177	96/285
Model 2 ^a	0.90 (0.77, 1.05)	1 (Reference)	1.34 (1.09, 1.65)
Model 2b ^b	0.88 (0.75, 1.02)	1 (Reference)	1.37 (1.12, 1.68)

^a Model 2: age, sex, race/center diabetes, HDL cholesterol, antihypertensive treatment, heart rate, BMI, smoking status, alcohol consumption, physical activity, menopause, and Vitamin D level

^a Model 2b: age, sex, race/center, heart rate, menopause, and Vitamin D level; **time-varying:** diabetes, HDL cholesterol, antihypertensive treatment, BMI, smoking status, alcohol consumption, and physical activity

eTable 10. Adjusted Hazard Ratios for Fracture by Categories of Subclinical Thyroid Dysfunction at Baseline and Incident Clinical Thyroid Dysfunction

	Subclinical Hypothyroidism	Euthyroidism	Subclinical Hyperthyroidism	Incident clinical thyroid dysfunction^a
n fractures	118	3,074	79	285
IR (95% CI) per 10,000 person-years^b	168.5 (140.7, 201.8)	162.9 (157.3, 168.8)	175.1 (140.5, 218.3)	226.6 (201.8, 254.5)
Model 1^c	0.89 (0.74, 1.07)	1 (Reference)	1.36 (1.09, 1.70)	0.94 (0.83, 1.06)
Model 2^d	0.92 (0.76, 1.11)	1 (Reference)	1.29 (1.03, 1.61)	0.93 (0.82, 1.05)

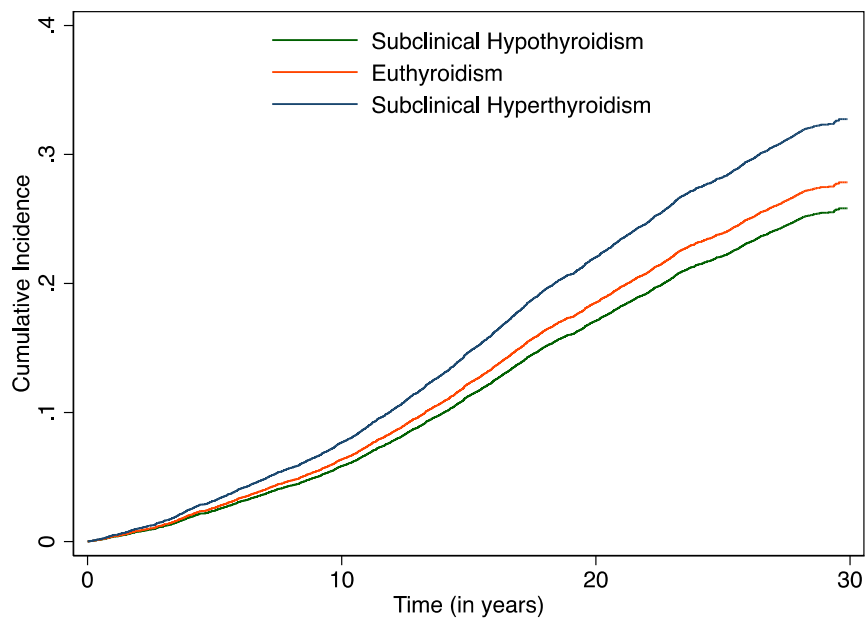
^a Modeled as a time-varying exposure

^b IR: Incidence rate

^c Model 1: age, sex, race/center

^d Model 2: Model 1 + diabetes, HDL cholesterol, antihypertensive treatment, heart rate, BMI, smoking status, alcohol consumption, physical activity, menopause, and Vitamin D level

eFigure. Adjusted^a Cumulative Incidence of Fracture by Categories of Thyroid Dysfunction, Accounting for the Competing Risk of Death



^aAdjusted for age, sex, race/center, diabetes, HDL cholesterol, antihypertensive treatment, heart rate, BMI, smoking status, alcohol consumption, physical activity, menopause, and Vitamin D level