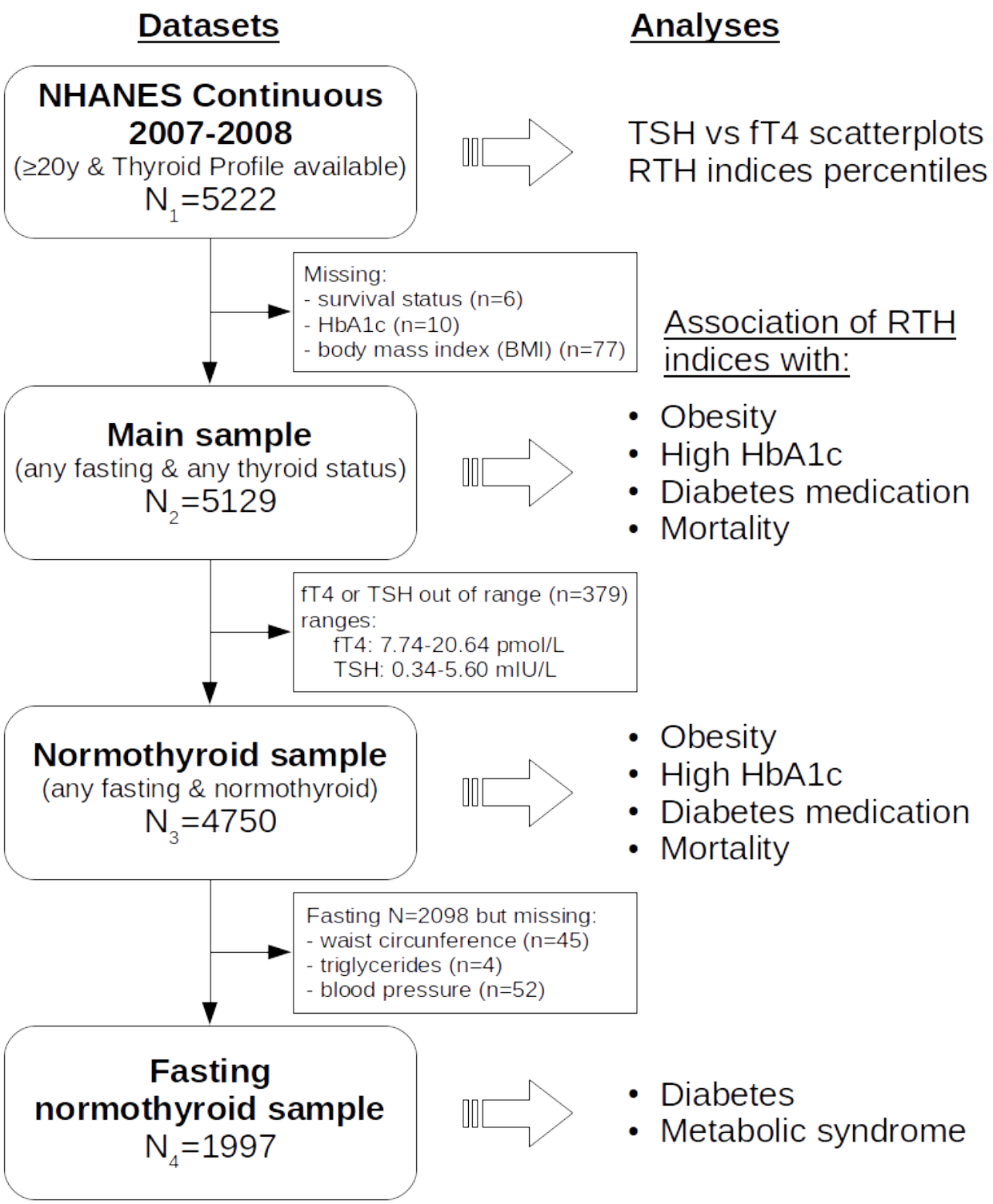
Supplementary material

SUPPLEMENTARY DATA

Supplementary material: Flow chart



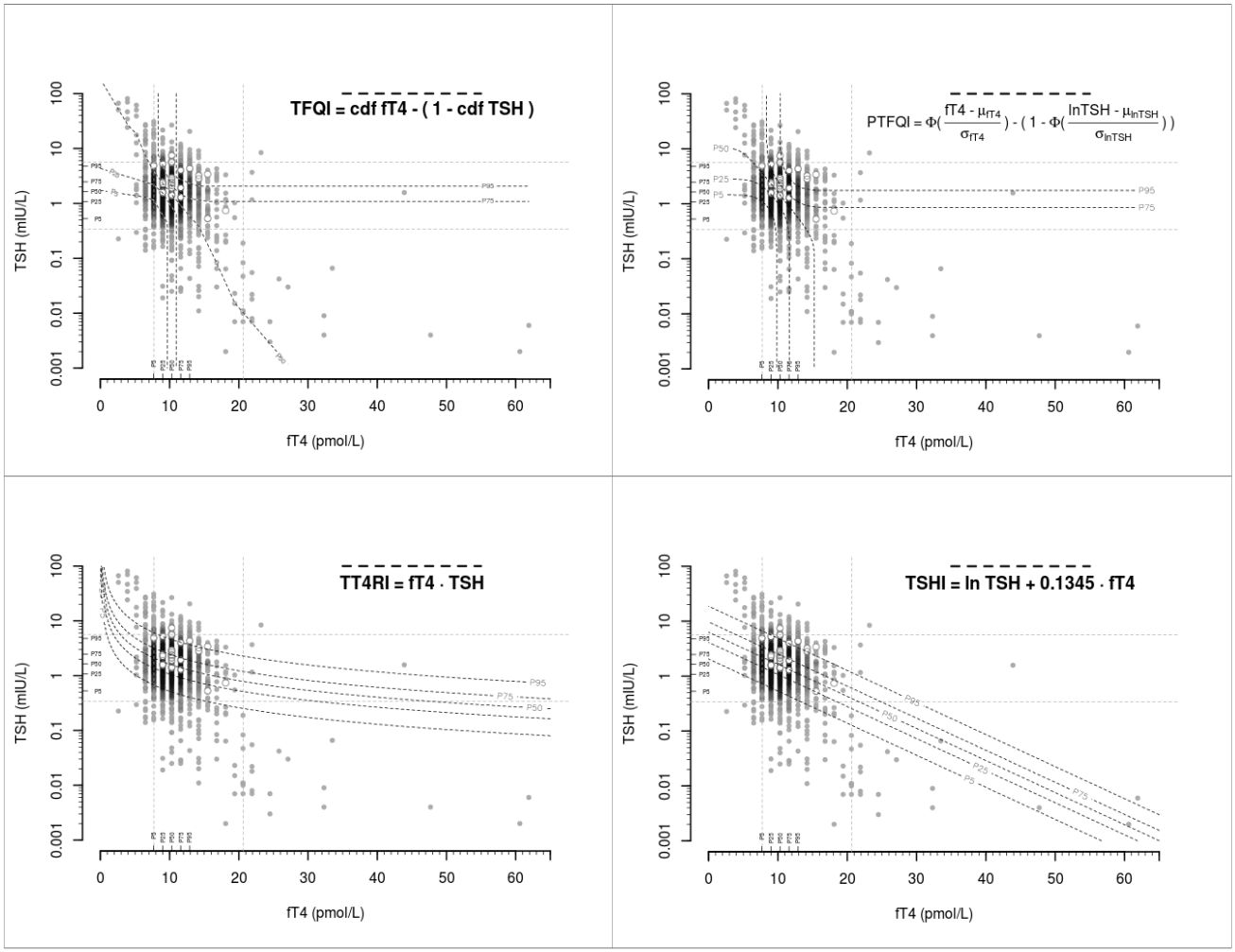
SUPPLEMENTARY DATA

Thyroid hormones and TSH were measured in serum in 5222 (N_1) adults 20y and older in the Continuous National Health And Nutrition Examinations Survey (NHANES) performed in 2007 and 2008. Data on mortality up to 2011 from the National Death Index is available for all but 6 of them. This NHANES dataset (N_1) was used for description of resistance to thyroid hormone indices and calculation of their population percentiles. A complete-case subset excluding participants with missing data in the variables of interest (main sample, N_2=5129) was used to analyze resistance to thyroid hormone indices cross-sectional association with glycohemoglobin>=6.5% (HbA1c), diabetes medication use, body mass index (BMI), and obesity, and longitudinal estimation of diabetes-related mortality rate. A subsequent subset of normothyroid subjects (Normothyroid sample, N_3=4750), i.e. who have thyroxine and TSH within their normal range (see limits in methods section), was used to confirm that the results were not dependent on overt thyroid illnesses. Finally, a fasting subset of the former normothyroid participants (Fasting normothyroid sample, N_4=1997), also excluding participants with missing data in the variables of interest, was used to analyze resistance to thyroid hormone indices cross-sectional association with glycemia-based diabetes and metabolic syndrome.

SUPPLEMENTARY DATA

Supplementary material: Figure S1

Figure S1. Scatterplots of thyrotropin (TSH) vs free thyroxine (fT4) and percentiles of resistance to thyroid hormone indices in the NHANES sample (N_1=5222)



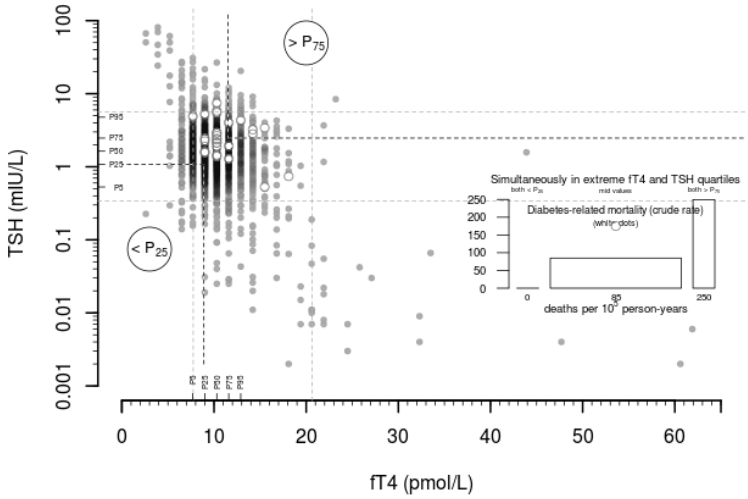
Dots represent observations. Grey dashed vertical and horizontal straight lines mark fT4 and TSH normality ranges. Inner marks in the axes represent the 5th, 25th, 50th, 75th, and 95th percentiles of fT4 and TSH. Black dashed curves represent the 5th, 25th, 50th, 75th, and 95th percentiles of the indices. White dots represent participants that suffered a diabetes-related death during follow-up.
N, number of participants; fT4, free Thyroxyne; TSH, Thyroid-Stimulating Hormone; TFQI, Thyroid Feedback Quantile-based Index; PTFQI, Parametric Thyroid Feedback Quantile-based Index; TT4RI, Thyrotroph T4 Resistance Index; TSHI, TSH Index; cdf, empirical cumulative distribution function; P5, P25, P50, P75, P95, Percentile 5-95.

Note: TT4RI and TSHI take values above their 95th percentile (suggesting resistance to thyroid hormones) for almost all clinical hypothyroidism patients (area beyond the upper-left corner of normality reference lines) and below their 5th percentile (suggesting high sensitivity to thyroid hormones) for almost all clinical hyperthyroidism patients (area beyond the lower-right corner of normality reference lines). In view of that probable inappropriateness of TT4RI and TSHI in primary thyroid diseases, it was pertinent to compare participants with both fT4 and TSH simultaneously high or low avoiding the influence of those clinical patients, which we achieved with a preliminary approach using extreme quartiles (Supplementary material: Preliminary analysis) and a subsequent study using the index TFQI, developed to that end. In contrast with the previous indices, TFQI takes values within the central 50% (between its 25th and 75th percentile) for patients with clinical thyroid-gland-caused (primary) disease.

SUPPLEMENTARY DATA

Supplementary material: Preliminary analysis comparing participants simultaneously in the extreme quartiles of fT4 and TSH

Figure Preliminary analysis. Scatterplot of thyrotropin (TSH) vs free thyroxine (fT4) in the NHANES sample (N_1=5222)



Scatterplot: Dots represent observations. White dots represent participants that suffered a diabetes-related death during follow-up. Grey dashed vertical and horizontal straight lines mark fT4 and TSH normality ranges. Inner marks in the axes represent the 5th, 25th, 50th, 75th, and 95th percentiles of fT4 and TSH. Black dashed angles delimit simultaneous extreme values of fT4 and TSH. Inner plot: The bars and the number at the base show crude death rates for each group.

Table Preliminary analysis. Association of simultaneous extreme fT4 and TSH values with obesity, high HbA1c, and use of diabetes medication in the main sample (N_2=5129).

	fT4 and TSH			
	Both <P_{25}	**Mid values**	**Both >P_{75}**	**P trend**
N (N_2=5129)	152	4662	315	
Obesity(%)	**27.3**	**33.0**	**37.9**	
Unadjusted (OR)	1.00	1.31	1.62	0.070
	(Reference)	(0.82,2.11)	(0.95,2.78)	
Model 1 (OR)	1.00	1.38	1.71	0.064
	(Reference)	(0.87,2.21)	(1.01,2.89)	
HbA1c>=6.5(%)	**4.0**	**7.4**	**12.0**	
Unadjusted (OR)	1.00	1.93	3.28	0.003
	(Reference)	(0.85,4.39)	(1.33,8.11)	
Model 1 (OR)	1.00	1.84	2.35	0.079
	(Reference)	(0.78,4.35)	(0.95,5.81)	
Diabetes Medication(%)	**3.9**	**7.5**	**13.7**	
Unadjusted (OR)	1.00	2.01	3.93	0.001
	(Reference)	(0.83,4.87)	(1.53,10.13)	
Model 1 (OR)	1.00	1.81	2.61	0.049
	(Reference)	(0.72,4.55)	(0.96,7.11)	

Odds ratios (OR) are estimated with generalized logistic regression models. Model 1 is adjusted for sex, age, and race. P trend is calculated with the group ordinal as a continuous variable

SUPPLEMENTARY DATA

Supplementary material: Tables for the association of PTFQI, TT4RI, and TSHI with BMI, obesity, high HbA1c, use of diabetes medication, and diabetes-related deaths in the main sample (N_2=5129).
(Equivalent to Table 2 in the manuscript, which shows the association of TFQI)

SUPPLEMENTARY DATA

Table Main sample - PTFQI. Association of parametric thyroid feedback quantile-based index (PTFQI) with BMI, obesity, high HbA1c, use of diabetes medication, and diabetes-related deaths in the main sample (N_2=5129).

	PTFQI				
	Q1	**Q2**	**Q3**	**Q4**	
	[-1,-0.23)	**[-0.23,-0.01)**	**[-0.01,0.21)**	**[0.21,1]**	**P trend**
N (N_2=5129)	1322	1249	1269	1289	
BMI (kg/m^2)	**28.1**	**28.0**	**29.1**	**28.8**	
Model 1 (dif.)	0.0	0.0	1.1	0.8	0.007
	(Reference)	(-0.6,0.7)	(0.7,1.5)	(0.1,1.5)	
Obesity(%)	**31.1**	**28.9**	**36.5**	**35.9**	
Model 1 (OR)	1.00	0.93	1.32	1.29	0.002
	(Reference)	(0.77,1.12)	(1.15,1.52)	(1.10,1.50)	
HbA1c>=6.5(%)	**5.0**	**6.0**	**9.4**	**10.0**	
Model 1 (OR)	1.00	1.21	1.84	1.70	0.005
	(Reference)	(0.93,1.58)	(1.47,2.30)	(1.24,2.33)	
Model 2 (OR)	1.00	1.11	1.49	1.43	0.041
	(Reference)	(0.86,1.43)	(1.16,1.91)	(1.04,1.98)	
Diabetes Medication(%)	**4.8**	**6.8**	**9.3**	**10.2**	
Model1 (OR)	1.00	1.40	1.78	1.68	0.002
	(Reference)	(0.92,2.13)	(1.30,2.42)	(1.26,2.25)	
Model2 (OR)	1.00	1.30	1.46	1.43	0.027
	(Reference)	(0.87,1.94)	(1.09,1.96)	(1.06,1.92)	
Diabetes-related deaths (n)	**0**	**4**	**8**	**15**	
Crude rate (per 100000 person-years)	**0.0**	**38.8**	**123.3**	**196.2**	
Crude rate (per 100000 person-years)	**19.5**		**159.3**		
Model 1 (RR)	1.00		4.65		0.013[#]
	(Reference)		(0.97,22.30)		
Model 2 (RR)	1.00		3.84		0.033[#]
	(Reference)		(0.86,17.19)		
Model 3 (RR)	1.00		3.42		0.103[#]
	(Reference)		(0.76,15.42)		

Differences, odds ratios (OR), and rate ratios (RR) are estimated with generalized linear, logistic, and Poisson regression models respectively. Model 1 is adjusted for sex, age, and race. Model 2 is further adjusted for BMI. Model 3 is further adjusted for initially presenting HbA1c>=6.5 and using diabetes medication. P trend is calculated with the PTFQI quartile ordinal as a continuous variable except in the models with only 2 categories[#] in which it is calculated with PTFQI as a continuous variable.

SUPPLEMENTARY DATA

Table Main sample - TT4RI. Association of thyrotroph T4 resistance index (TT4RI) with BMI, obesity, high HbA1c, use of diabetes medication, and diabetes-related deaths in the main sample (N_2=5129).

	TT4RI				
	Q1	**Q2**	**Q3**	**Q4**	
	[lo.,10.6)	**[10.6,16.2)**	**[16.2,24.6)**	**[24.6,hi.]**	**P trend**
N (N_2=5129)	1364	1262	1238	1265	
BMI (kg/m^2)	**27.9**	**28.1**	**28.7**	**29.2**	
Model 1 (dif.)	0.0	0.3	1.0	1.4	0.002
	(Reference)	(-0.5,1.2)	(0.3,1.6)	(0.6,2.2)	
Obesity(%)	**31.1**	**29.9**	**34.3**	**37.2**	
Model 1 (OR)	1.00	0.98	1.21	1.37	0.011
	(Reference)	(0.76,1.24)	(0.96,1.52)	(1.08,1.73)	
HbA1c>=6.5(%)	**6.0**	**6.8**	**8.3**	**9.2**	
Model 1 (OR)	1.00	1.13	1.34	1.33	0.090
	(Reference)	(0.82,1.57)	(1.03,1.75)	(0.93,1.91)	
Model 2 (OR)	1.00	1.02	1.14	1.07	0.609
	(Reference)	(0.73,1.43)	(0.86,1.52)	(0.73,1.58)	
Diabetes Medication(%)	**6.7**	**7.4**	**7.6**	**9.4**	
Model1 (OR)	1.00	1.08	1.02	1.13	0.491
	(Reference)	(0.82,1.42)	(0.81,1.29)	(0.87,1.47)	
Model2 (OR)	1.00	0.99	0.87	0.92	0.480
	(Reference)	(0.74,1.32)	(0.70,1.09)	(0.68,1.25)	
Diabetes-related deaths (n)	**1**	**6**	**6**	**14**	
Crude rate (per 100000 person-years)	**16.4**	**60.2**	**90.3**	**193.6**	
Crude rate (per 100000 person-years)	**38.5**		**141.7**		
Model 1 (RR)	1.00		2.52		0.012#
	(Reference)		(1.02,6.26)		
Model 2 (RR)	1.00		2.17		0.025#
	(Reference)		(0.92,5.10)		
Model 3 (RR)	1.00		1.89		0.018#
	(Reference)		(0.87,4.12)		

Differences, odds ratios (OR), and rate ratios (RR) are estimated with generalized linear, logistic, and Poisson regression models respectively. Model 1 is adjusted for sex, age, and race. Model 2 is further adjusted for BMI. Model 3 is further adjusted for initially presenting HbA1c>=6.5 and using diabetes medication. P trend is calculated with the TT4RI quartile ordinal as a continuous variable except in the models with only 2 categories# in which it is calculated with ln TT4RI as a continuous variable.

SUPPLEMENTARY DATA

Table Main sample - TSHI. Association of TSH index (TSHI) with BMI, obesity, high HbA1c, use of diabetes medication, and diabetes-related deaths in the main sample (N_2=5129).

	TSHI				
	Q1	**Q2**	**Q3**	**Q4**	
	[lo.,1.41)	**[1.41,1.84)**	**[1.84,2.27)**	**[2.27, hi.]**	**P trend**
N (N_2=5129)	1359	1263	1240	1267	
BMI (kg/m^2)	**27.8**	**28.3**	**28.8**	**29.1**	
Model 1 (dif.)	0.0	0.6	1.2	1.5	0.002
	(Reference)	(-0.2,1.4)	(0.5,1.8)	(0.7,2.3)	
Obesity(%)	**30.1**	**30.7**	**34.2**	**37.5**	
Model 1 (OR)	1.00	1.06	1.26	1.45	0.005
	(Reference)	(0.84,1.33)	(1.00,1.58)	(1.15,1.83)	
HbA1c>=6.5(%)	**5.7**	**6.8**	**8.2**	**9.6**	
Model 1 (OR)	1.00	1.19	1.41	1.44	0.049
	(Reference)	(0.81,1.75)	(1.06,1.89)	(1.01,2.07)	
Model 2 (OR)	1.00	1.03	1.17	1.15	0.391
	(Reference)	(0.71,1.48)	(0.88,1.56)	(0.78,1.69)	
Diabetes Medication(%)	**6.2**	**7.6**	**7.1**	**10.1**	
Model1 (OR)	1.00	1.21	1.03	1.29	0.201
	(Reference)	(0.85,1.71)	(0.83,1.28)	(1.00,1.65)	
Model2 (OR)	1.00	1.06	0.85	1.04	0.893
	(Reference)	(0.76,1.48)	(0.70,1.03)	(0.80,1.35)	
Diabetes-related deaths (n)	**0**	**6**	**7**	**14**	
Crude rate (per 100000 person-years)	**0.0**	**57.1**	**109.3**	**194.0**	
Crude rate (per 100000 person-years)	**28.8**		**151.3**		
Model 1 (RR)	1.00		3.41		0.004[#]
	(Reference)		(1.49,7.80)		
Model 2 (RR)	1.00		2.95		0.010[#]
	(Reference)		(1.35,6.43)		
Model 3 (RR)	1.00		2.72		0.007[#]
	(Reference)		(1.29,5.75)		

Differences, odds ratios (OR), and rate ratios (RR) are estimated with generalized linear, logistic, and Poisson regression models respectively. Model 1 is adjusted for sex, age, and race. Model 2 is further adjusted for BMI. Model 3 is further adjusted for initially presenting HbA1c>=6.5 and using diabetes medication. P trend is calculated with the TSHI quartile ordinal as a continuous variable except in the models with only 2 categories[#] in which it is calculated with TSHI as a continuous variable.

SUPPLEMENTARY DATA

Supplementary material: Tables for the association IN NORMOTHYROID SUBJECTS of TFQI, PTFQI, TT4RI, and TSHI with BMI, obesity, high HbA1c, use of diabetes medication, and diabetes-related deaths.

SUPPLEMENTARY DATA

Table Normothyroid sample - TFQI. Association of thyroid feedback quantile-based index (TFQI) with BMI, obesity, high HbA1c, use of diabetes medication, and diabetes-related deaths in the normothyroid sample (N_3=4750)

	TFQI				
	Q1	**Q2**	**Q3**	**Q4**	
	[-1,-0.25)	**[-0.25,0)**	**[0,0.25)**	**[0.25,1]**	**P trend**
N (N_3=4750)	1208	1173	1188	1181	
BMI (kg/m^2)	**28.1**	**27.9**	**29.0**	**28.8**	
Model 1 (dif.)	0.0	-0.1	1.1	0.8	0.005
	(Reference)	(-0.7,0.6)	(0.7,1.4)	(0.1,1.6)	
Obesity(%)	**30.7**	**28.3**	**36.5**	**35.7**	
Model 1 (OR)	1.00	0.91	1.34	1.28	0.001
	(Reference)	(0.73,1.14)	(1.16,1.54)	(1.11,1.48)	
HbA1c>=6.5(%)	**4.9**	**6.6**	**8.9**	**10.3**	
Model 1 (OR)	1.00	1.31	1.67	1.75	0.002
	(Reference)	(0.97,1.78)	(1.36,2.06)	(1.33,2.31)	
Model 2 (OR)	1.00	1.24	1.37	1.47	0.027
	(Reference)	(0.92,1.65)	(1.07,1.74)	(1.11,1.94)	
Diabetes Medication(%)	**4.7**	**7.4**	**8.5**	**10.2**	
Model1 (OR)	1.00	1.53	1.61	1.72	0.001
	(Reference)	(1.03,2.26)	(1.10,2.35)	(1.37,2.15)	
Model2 (OR)	1.00	1.45	1.32	1.44	0.021
	(Reference)	(1.00,2.12)	(0.92,1.89)	(1.17,1.79)	
Diabetes-related deaths (n)	**0**	**4**	**7**	**14**	
Crude rate (per 100000 person-years)	**0.0**	**41.6**	**115.3**	**192.7**	
Crude rate (per 100000 person-years)	**20.9**		**153.0**		
Model 1 (RR)	1.00		4.29		0.054[#]
	(Reference)		(0.94,19.55)		
Model 2 (RR)	1.00		3.56		0.107[#]
	(Reference)		(0.84,14.94)		
Model 3 (RR)	1.00		3.49		0.312[#]
	(Reference)		(0.82,14.81)		

Differences, odds ratios (OR), and rate ratios (RR) are estimated with generalized linear, logistic, and Poisson regression models respectively. Model 1 is adjusted for sex, age, and race. Model 2 is further adjusted for BMI. Model 3 is further adjusted for initially presenting HbA1c>=6.5 and using diabetes medication. P trend is calculated with the TFQI quartile ordinal as a continuous variable except in the models with only 2 categories[#] in which it is calculated with TFQI as a continuous variable.

SUPPLEMENTARY DATA

Table Normothyroid sample - PTFQI. Association of parametric thyroid feedback quantile-based index (PTFQI) with BMI, obesity, high HbA1c, use of diabetes medication, and diabetes-related deaths in the normothyroid sample (N_3=4750)

	PTFQI				
	Q1	**Q2**	**Q3**	**Q4**	
	[-1,-0.23)	**[-0.23,-0.01)**	**[-0.01,0.21)**	**[0.21,1]**	**P trend**
N (N_3=4750)	1195	1194	1172	1189	
BMI (kg/m^2)	**28.1**	**27.9**	**29.1**	**28.7**	
Model 1 (dif.)	0.0	0.0	1.1	0.7	0.006
	(Reference)	(-0.7,0.7)	(0.7,1.5)	(0.1,1.4)	
Obesity(%)	**30.6**	**28.5**	**36.4**	**35.8**	
Model 1 (OR)	1.00	0.93	1.35	1.30	0.001
	(Reference)	(0.74,1.16)	(1.17,1.55)	(1.12,1.50)	
HbA1c>=6.5(%)	**4.9**	**6.1**	**9.4**	**10.3**	
Model 1 (OR)	1.00	1.23	1.81	1.72	0.008
	(Reference)	(0.92,1.64)	(1.47,2.24)	(1.22,2.41)	
Model 2 (OR)	1.00	1.14	1.48	1.46	0.047
	(Reference)	(0.87,1.50)	(1.18,1.86)	(1.05,2.03)	
Diabetes Medication(%)	**4.6**	**7.1**	**8.7**	**10.4**	
Model1 (OR)	1.00	1.51	1.72	1.79	0.001
	(Reference)	(0.99,2.28)	(1.22,2.43)	(1.36,2.35)	
Model2 (OR)	1.00	1.41	1.41	1.52	0.016
	(Reference)	(0.94,2.11)	(1.02,1.94)	(1.17,1.99)	
Diabetes-related deaths (n)	**0**	**4**	**8**	**13**	
Crude rate (per 100000 person-years)	**0.0**	**40.6**	**132.0**	**176.5**	
Crude rate (per 100000 person-years)	**20.8**		**153.9**		
Model 1 (RR)	1.00		4.26		0.051[#]
	(Reference)		(0.92,19.62)		
Model 2 (RR)	1.00		3.59		0.108[#]
	(Reference)		(0.85,15.15)		
Model 3 (RR)	1.00		3.42		0.321[#]
	(Reference)		(0.81,14.53)		

Differences, odds ratios (OR), and rate ratios (RR) are estimated with generalized linear, logistic, and Poisson regression models respectively. Model 1 is adjusted for sex, age, and race. Model 2 is further adjusted for BMI. Model 3 is further adjusted for initially presenting HbA1c>=6.5 and using diabetes medication. P trend is calculated with the PTFQI quartile ordinal as a continuous variable except in the models with only 2 categories[#] in which it is calculated with PTFQI as a continuous variable.

SUPPLEMENTARY DATA

Table Normothyroid sample - TT4RI. Association of thyrotroph T4 resistance index (TT4RI) with BMI, obesity, high HbA1c, use of diabetes medication, and diabetes-related deaths in the normothyroid sample (N_3=4750)

	TT4RI				
	Q1	**Q2**	**Q3**	**Q4**	
	[lo.,10.6)	**[10.6,16.2)**	**[16.2,24.6)**	**[24.6,hi.]**	**P trend**
N (N_3=4750)	1186	1240	1223	1101	
BMI (kg/m^2)	**27.9**	**28.1**	**28.7**	**29.1**	
Model 1 (dif.)	0.0	0.3	0.9	1.4	0.002
	(Reference)	(-0.5,1.2)	(0.3,1.6)	(0.6,2.2)	
Obesity(%)	**30.8**	**29.5**	**34.3**	**36.9**	
Model 1 (OR)	1.00	0.97	1.21	1.35	0.009
	(Reference)	(0.75,1.24)	(0.97,1.51)	(1.07,1.72)	
HbA1c>=6.5(%)	**5.9**	**6.8**	**8.4**	**9.6**	
Model 1 (OR)	1.00	1.11	1.31	1.34	0.105
	(Reference)	(0.78,1.59)	(0.98,1.73)	(0.91,1.98)	
Model 2 (OR)	1.00	1.02	1.13	1.09	0.551
	(Reference)	(0.70,1.48)	(0.83,1.54)	(0.73,1.63)	
Diabetes Medication(%)	**6.5**	**7.4**	**7.6**	**9.3**	
Model1 (OR)	1.00	1.07	0.99	1.08	0.734
	(Reference)	(0.79,1.43)	(0.78,1.26)	(0.83,1.40)	
Model2 (OR)	1.00	0.98	0.85	0.88	0.301
	(Reference)	(0.71,1.35)	(0.66,1.11)	(0.64,1.20)	
Diabetes-related deaths (n)	**1**	**6**	**6**	**12**	
Crude rate (per 100000 person-years)	**18.6**	**61.0**	**91.3**	**183.4**	
Crude rate (per 100000 person-years)	**41.2**		**134.4**		
Model 1 (RR)	1.00		2.11		0.081[#]
	(Reference)		(0.80,5.57)		
Model 2 (RR)	1.00		1.84		0.116[#]
	(Reference)		(0.73,4.64)		
Model 3 (RR)	1.00		1.49		0.193[#]
	(Reference)		(0.58,3.83)		

Differences, odds ratios (OR), and rate ratios (RR) are estimated with generalized linear, logistic, and Poisson regression models respectively. Model 1 is adjusted for sex, age, and race. Model 2 is further adjusted for BMI. Model 3 is further adjusted for initially presenting HbA1c>=6.5 and using diabetes medication. P trend is calculated with the TT4RI quartile ordinal as a continuous variable except in the models with only 2 categories[#] in which it is calculated with ln TT4RI as a continuous variable.

SUPPLEMENTARY DATA

Table Normothyroid sample - TSHI. Association of TSH index (TSHI) with BMI, obesity, high HbA1c, use of diabetes medication, and diabetes-related deaths in the normothyroid sample (N_3=4750).

	TSHI				
	Q1	**Q2**	**Q3**	**Q4**	
	[lo.,1.41)	**[1.41,1.84)**	**[1.84,2.27)**	**[2.27, hi.)**	**P trend**
N (N_3=4750)	1181	1242	1225	1102	
BMI (kg/m^2)	**27.8**	**28.2**	**28.8**	**29.0**	
Model 1 (dif.)	0.0	0.6	1.1	1.4	0.002
	(Reference)	(-0.2,1.3)	(0.5,1.8)	(0.6,2.2)	
Obesity(%)	**29.8**	**30.2**	**34.2**	**37.2**	
Model 1 (OR)	1.00	1.05	1.27	1.44	0.004
	(Reference)	(0.83,1.32)	(1.02,1.57)	(1.14,1.82)	
HbA1c>=6.5(%)	**5.5**	**6.8**	**8.3**	**10.1**	
Model 1 (OR)	1.00	1.18	1.38	1.46	0.061
	(Reference)	(0.78,1.76)	(1.00,1.91)	(0.99,2.15)	
Model 2 (OR)	1.00	1.03	1.16	1.18	0.351
	(Reference)	(0.69,1.53)	(0.83,1.61)	(0.79,1.76)	
Diabetes Medication(%)	**6.0**	**7.6**	**7.2**	**10.1**	
Model1 (OR)	1.00	1.19	1.02	1.25	0.273
	(Reference)	(0.83,1.70)	(0.80,1.29)	(0.99,1.58)	
Model2 (OR)	1.00	1.05	0.85	1.01	0.706
	(Reference)	(0.73,1.51)	(0.66,1.08)	(0.78,1.31)	
Diabetes-related deaths (n)	**0**	**6**	**7**	**12**	
Crude rate (per 100000 person-years)	**0.0**	**57.8**	**110.5**	**184.0**	
Crude rate (per 100000 person-years)	**30.8**		**144.7**		
Model 1 (RR)	1.00		2.83		0.038[#]
	(Reference)		(1.14,7.05)		
Model 2 (RR)	1.00		2.48		0.055[#]
	(Reference)		(1.04,5.96)		
Model 3 (RR)	1.00		2.14		0.113[#]
	(Reference)		(0.85,5.39)		

Differences, odds ratios (OR), and rate ratios (RR) are estimated with generalized linear, logistic, and Poisson regression models respectively. Model 1 is adjusted for sex, age, and race. Model 2 is further adjusted for BMI. Model 3 is further adjusted for initially presenting HbA1c>=6.5 and using diabetes medication. P trend is calculated with the TSHI quartile ordinal as a continuous variable except in the models with only 2 categories[#] in which it is calculated with TSHI as a continuous variable.

SUPPLEMENTARY DATA

Supplementary material: Sensitivity analysis: manuscript's Table 2 with further adjustments.

SUPPLEMENTARY DATA

Adjusted Table 2: adjusted for education, physical activity, and sedentary time. Association of thyroid feedback quantile-based index (TFQI) with BMI, obesity, high HbA1c, use of diabetes medication, and diabetes-related deaths in the main sample ($N_{2'}$=5105).

	TFQI				
	Q1	**Q2**	**Q3**	**Q4**	
	[-1,-0.25)	**[-0.25,0)**	**[0,0.25)**	**[0.25,1]**	**P trend**
N ($N_{2'}$=5105)	1315	1255	1263	1272	
BMI (kg/m2)	**28.1**	**28.0**	**29.1**	**28.8**	
Model 1 (dif.)	0.0	0.0	1.0	0.8	0.021
	(Reference)	(-0.6,0.6)	(0.6,1.4)	(0.0,1.5)	
Obesity(%)	**31.0**	**28.9**	**36.7**	**35.9**	
Model 1 (OR)	1.00	0.91	1.32	1.26	0.009
	(Reference)	(0.74,1.12)	(1.13,1.53)	(1.07,1.48)	
HbA1c>=6.5%(%)	**5.0**	**6.3**	**8.9**	**10.0**	
Model 1 (OR)	1.00	1.28	1.74	1.73	0.006
	(Reference)	(0.96,1.69)	(1.38,2.20)	(1.32,2.27)	
Model 2 (OR)	1.00	1.19	1.41	1.45	0.047
	(Reference)	(0.91,1.55)	(1.09,1.84)	(1.09,1.92)	
Diabetes Medication(%)	**4.8**	**7.1**	**9.2**	**9.9**	
Model1 (OR)	1.00	1.44	1.71	1.63	0.006
	(Reference)	(0.99,2.07)	(1.19,2.47)	(1.29,2.06)	
Model2 (OR)	1.00	1.35	1.42	1.38	0.053
	(Reference)	(0.96,1.91)	(0.99,2.02)	(1.10,1.74)	
Diabetes-related deaths (n)	**0**	**4**	**7**	**15**	
Crude rate (per 100000 person-years)	**0.0**	**39.1**	**109.3**	**208.2**	
Crude rate (per 100000 person-years)	**19.5**		**157.9**		
Model 1 (RR)	1.00		4.66		0.027[#]
	(Reference)		(1.01,21.54)		
Model 2 (RR)	1.00		3.89		0.075[#]
	(Reference)		(0.87,17.32)		
Model 3 (RR)	1.00		3.35		0.205[#]
	(Reference)		(0.76,14.73)		

Differences, odds ratios (OR), and rate ratios (RR) are estimated with generalized linear, logistic, and Poisson regression models respectively. Model 1 is adjusted for sex, age, race, education (less, equal, or more than high school graduate), physical activity (less than moderate, moderate, vigorous), and sedentary time/day. Model 2 is further adjusted for BMI. Model 3 is further adjusted for initially presenting HbA1c>=6.5% and using diabetes medication. P trend is calculated with the TFQI quartile ordinal as a continuous variable except in the models with only 2 categories[#] in which it is calculated with TFQI as a continuous variable.