

SUPPLEMENTARY MATERIAL

Risk of cancer in patients with thyroid disease and venous thromboembolism

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Table S1: *International Classification of Diseases, Eighth Revision (ICD-8) and Tenth Revision (ICD-10) codes used in this study.*

Table S2: *Site-specific standardized incidence ratios of cancer in patients with venous thromboembolism and hypothyroidism, by follow-up interval, Denmark, 1978-2013.*

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Table S9: *Standardized incidence ratios of cancer in patients with venous thromboembolism and hypothyroidism, Denmark, 1978-2013, stratified by follow-up of 0-30 days vs. 31-90 days,*

restricted to patients with a maximum of 2 years between first hypothyroid disease diagnosis and first VTE diagnosis.

Table S10: 1-year standardized incidence ratios of cancer in patients with venous thromboembolism and hypothyroidism, excluding cancers detected within the first 30 days after VTE, Denmark, 1978-2013, *restricted to patients with a maximum of 2 years between first hypothyroid disease diagnosis and first VTE diagnosis.*

Table S11: Absolute one-year cancer risk and standardized incidence ratios of cancer in patients with venous thromboembolism and hyperthyroidism (N=637), by follow-up interval, Denmark, 1978-2013, *restricted to patients with a maximum of 2 years between first hyperthyroid disease diagnosis and first VTE diagnosis.*

Table S12: Standardized incidence ratios of cancer in patients with venous thromboembolism and hyperthyroidism, Denmark, 1978-2013, stratified by follow-up of 0-30 days vs. 31-90 days, *restricted to patients with a maximum of 2 years between first hyperthyroid disease diagnosis and first VTE diagnosis.*

Table S13: 1-year standardized incidence ratios of cancer in patients with venous thromboembolism and hyperthyroidism excluding cancers detected within the first 30 days after VTE, Denmark, 1978-2013, *restricted to patients with a maximum of 2 years between first hyperthyroid disease diagnosis and first VTE diagnosis.*

Table S1. *International Classification of Diseases, Eighth Revision (ICD-8) and Tenth Revision (ICD-10) codes used in this study.*

Venous thromboembolism	
Deep venous thrombosis	ICD-8: 451.00 ICD-10: I80.1-3
Pulmonary embolism	ICD-8: 450.99 ICD-10: I26
Thyroid disease	
Hypothyroidism	ICD-8: 244.00, 244.01-244.03, 244.08, 244.09, 245.03 ICD-10: E03.2-E03.9, E06.3, E06.5
Hyperthyroidism	ICD-8: 242.00-242.29 ICD-10: E05 (excluding E05.4), H052, H062
Cancer	
	ICD-10: DC00.x-DC97.x We grouped cancers as specified in the Annual Cancer Report published by the Danish National Board of Health (available at: http://sundhedsdatastyrelsen.dk/-/media/sds/filer/find-tal-og-analyser/sygdomme/cancerregisteret/cancerregisteret-2005-og-2006.pdf), excluding carcinoma in situ of the breast, dysplasia and carcinoma in situ of the uterine cervix, mola and neoplasma placenta, polycythemia vera, myelodysplastic syndromes, and other not-otherwise-specified neoplasms of lymphoid and hematopoietic tissue.
Charlson Comorbidity Index	
Score 1 (1 point)	
Myocardial infarction	ICD-8: 410 ICD-10: I21, I22, I23
Congestive heart failure	ICD-8: 427.09, 427.10, 427.11, 427.19, 428.99, 782.49 ICD-10: I50, I11.0, I13.0, I13.2
Peripheral vascular disease	ICD-8: 440, 441, 442, 443, 444, 445 ICD-10: I70, I71, I72, I73, I74, I77
Cerebrovascular disease	ICD-8: 430-438 ICD-10: I60-I69, G45, G46
Dementia	ICD-8: 290.09-290.19, 293.09 ICD-10: F00-F03, F05.1, G30
Chronic pulmonary disease	ICD-8: 490-493, 515-518 ICD-10: J40-J47, J60-J67, J68.4, J70.1, J70.3, J84.1, J92.0, J96.1, J98.2, J98.3
Connective tissue disease	ICD-8: 712, 716, 734, 446, 135.99 ICD-10: M05, M06, M08, M09, M30, M31, M32, M33, M34, M35, M36, D86
Ulcer disease	ICD-8: 530.91, 530.98, 531-534 ICD-10: K22.1, K25-K28
Mild liver disease	ICD-8: 571, 573.01, 573.04 ICD-10: B18, K70.0-K70.3, K70.9, K71, K73, K74, K76.0
Diabetes type 1 and 2	ICD-8: 249-250 ICD-10: E10-E14, O24 (except O24.4), H36.0
Score 2 (2 points)	
Hemiplegia	ICD-8: 344 ICD-10: G81, G82
Moderate to severe renal disease	ICD-8: 403, 404, 580-583, 584, 590.09, 593.19, 753.10-753.19, 792 ICD-10: 12, I13, N00-N05, N07, N11, N14, N17-N19, Q61
Diabetes mellitus with end-organ damage	ICD-8: 249.01-249.05, 249.08, 250.01-250.05, 250.08 ICD-10: E10.2-E10.8, E11.2-E11.8

Score 3 (3 points)

Moderate to severe liver disease

ICD-8: 070.00, 070.02, 070.04, 070.06, 070.08, 573.00, 456.00-456.09

ICD-10: B15.0, B16.0, B16.2, B19.0, K70.4, K72, K76.6, I85

Score 6 (6 points)

AIDS

ICD-8: 079.83

ICD-10: B21-B24

Classic provoking/risk factors for VTE

Pregnancy

ICD-8: 630-680

ICD-10: O00-O99

Fractures/trauma

ICD-8: 800-929, 950-959

ICD-10: S00-T14

Surgery

Danish Classification of Surgical Procedures: all codes (00000-99960)

NOMESCO Classification of surgical Procedures: All K-codes excluding minor procedures.

Obesity

ICD-8: 277.99

ICD-10: E65, E66.0, E66.1, E66.2, E66.8, E66.9

Abbreviations: ICD = International Classification of Diseases, AIDS = Acute immunodeficiency syndrome

Supplementary Table S2. Site-specific standardized incidence ratios of cancer in patients with venous thromboembolism and hypothyroidism, by follow-up interval, Denmark, 1978-2013.

Cancer site	N - cancers	0-90 days		91-365 days		0-1 year		1+ year	
		O/E	SIR (95% CI)	O/E	SIR (95% CI)	O/E	SIR (95% CI)	O/E	SIR (95% CI)
Large intestine including rectosigmoid colon	12	3/0.5	5.68 (1.17; 16.57)	1/1.4	0.70 (0.02; 3.91)	4/2.0	2.05 (0.56; 5.24)	8/9.3	0.86 (0.37; 1.69)
Lung, bronchi and trachea	18	0	-	2/1.5	1.30 (0.16; 4.69)	2/2.1	0.95 (0.11; 3.41)	16/10.0	1.60 (0.92; 2.60)
Other skin cancer (excluding basal cell carcinoma)	7	1/0.3	3.64 (0.09; 20.28)	1/0.7	1.35 (0.03; 7.50)	2/1.0	1.97 (0.24; 7.10)	5/4.9	1.03 (0.33; 2.39)
Breast	20	0	-	4/2.3	1.76 (0.48; 4.50)	4/3.1	1.83 (0.35; 3.29)	16/15.5	1.04 (0.59; 1.68)
Ovary	5	2/0.1	14.80 (1.79; 53.44)	0	-	2/0.5	4.00 (0.48; 14.42)	3/2.4	1.26 (0.26; 3.68)
Urinary bladder	11	0	-	1/0.6	1.78 (0.04; 9.90)	1/0.8	1.30 (0.03; 7.24)	10/3.5	2.84 (1.36; 5.22)
Non-Hodgkin malignant lymphoma	14	2/0.2	10.60 (1.28; 38.25)	6/0.5	11.81 (4.34; 25.76)	8/0.7	11.48 (4.95; 22.62)	6/3.3	1.84 (0.67; 4.00)
Basal cell carcinoma	31	1/1.2	0.83 (0.02; 4.64)	1/3.2	0.31 (0.01; 1.72)	2/4.4	0.45 (0.05; 1.63)	29/21.4	1.36 (0.91; 1.95)

Abbreviations: O/E = observed number/expected number; SIR = standardized incidence ratio; CI = confidence interval

Note: Only cancer sites with a minimum of 5 observed cases overall are shown.

Supplementary Table S3. Site-specific standardized incidence ratios of cancer in patients with venous thromboembolism and hyperthyroidism, by follow-up interval, Denmark, 1978-2013.

Cancer site	N - cancers	0-90 days		91-365 days		0-1 year		1+ year	
		O/E	SIR (95% CI)	O/E	SIR (95% CI)	O/E	SIR (95% CI)	O/E	SIR (95% CI)
Large intestine including rectosigmoid colon	25	4/0.6	6.46 (1.76; 16.53)	4/1.6	2.43 (0.66; 6.23)	8/2.3	3.53 (1.52; 6.96)	17/11.6	1.46 (0.85; 2.34)
Rectum	8	0	-	0	-	0	-	8/4.8	1.68 (0.73; 3.32)
Pancreas	10	3/0.2	16.20 (3.34; 47.32)	1/0.5	2.01 (0.05; 11.22)	4/0.7	5.87 (1.60; 15.02)	6/3.5	1.70 (0.63; 3.72)
Lung, bronchi and trachea	26	4/0.7	5.88 (1.60; 15.04)	2/1.8	1.10 (0.13; 3.97)	6/2.5	2.40 (0.88; 5.23)	20/13.2	1.52 (0.93; 2.34)
Malignant melanoma	5	0	-	0	-	0	-	5/3.0	1.67 (0.54; 3.89)
Other skin cancer (excluding basal cell carcinoma)	12	0	-	2/0.8	2.45 (0.30; 8.86)	2/1.1	1.77 (0.21; 6.40)	10/6.3	1.58 (0.75; 2.90)
Breast	33	0	-	5/2.6	1.95 (0.63; 4.55)	5/3.5	1.42 (0.46; 3.31)	28/18.6	1.50 (1.00; 2.17)
Cervix of uterus	7	2/0.1	28.24 (3.42; 101.95)	0	-	2/0.3	7.76 (0.94; 28.02)	5/1.3	3.99 (1.29; 9.29)
Uterus	6	3/0.2	14.47 (2.98; 42.24)	1/0.6	1.81 (0.05; 10.10)	4/0.8	5.27 (1.43; 13.49)	2/3.9	0.52 (0.06; 1.88)
Ovary	6	3/0.2	19.60 (4.04; 57.22)	1/0.4	2.45 (0.06; 13.66)	4/0.6	7.13 (1.94; 18.26)	2/2.8	0.71 (0.09; 2.57)
Prostate	13	2/0.3	7.29 (0.88; 26.32)	2/0.7	2.73 (0.33; 9.86)	4/1.0	3.98 (1.08; 10.18)	9/6.2	1.46 (0.67; 2.78)
Urinary bladder	6	2/0.3	7.77 (0.94; 28.05)	1/0.7	1.45 (0.04; 8.08)	3/1.0	3.17 (0.65; 9.25)	3/5.1	0.59 (0.12; 1.73)
Non-Hodgkin malignant lymphoma	7	1/0.2	4.60 (0.12; 25.62)	0	-	1/0.8	1.26 (0.03; 7.00)	6/4.2	1.43 (0.52; 3.12)
Metastases and non-specified cancer in lymph nodes	7	1/0.2	5.83 (0.15; 32.50)	1/0.5	2.21 (0.06; 12.32)	2/0.6	3.21 (0.39; 11.58)	5/3.2	1.55 (0.50; 3.62)
Other cancers with poorly specified localization and non-specified cancer	7	3/0.1	37.35 (7.69; 109.06)	2/0.2	9.69 (1.17; 34.97)	5/0.3	17.44 (5.65; 40.63)	2/1.5	1.37 (0.17; 4.96)
Basal cell carcinoma	33	1/1.4	0.73 (0.02; 4.08)	3/3.6	0.82 (0.17; 2.40)	4/5.0	0.80 (0.22; 2.04)	29/27.7	1.05 (0.70; 1.51)

Abbreviations: O/E = observed number/expected number; SIR = standardized incidence ratio; CI = confidence interval

Note: Only cancer sites with a minimum of 5 observed cases overall are shown.

Supplementary Table S4. Standardized incidence ratios of cancer in patients with venous thromboembolism and hypothyroidism, Denmark, 1978-2013, stratified by follow-up of 0-30 days vs. 31-90 days.

	0-30 days		31-90 days	
	O/E	SIR (95% CI)	O/E	SIR (95% CI)
Hypothyroidism	8/2.0	3.91 (1.69; 7.70)	6/3.9	1.55 (0.57; 3.37)
Female	6/1.7	3.56 (1.31; 7.75)	6/3.2	1.87 (0.69; 4.09)
Male	2/0.4	5.58 (0.67; 20.13)	0	-
Age at venous thromboembolism diagnosis < 60	0	-	0	-
Age at venous thromboembolism diagnosis 60-74	6/0.7	9.20 (3.38; 20.05)	3/1.3	2.39 (0.49; 6.98)
Age at venous thromboembolism diagnosis ≥ 75	2/1.3	1.59 (0.19; 5.73)	3/2.4	1.27 (0.26; 3.71)
Comorbidity burden, ¹ normal	3/0.7	4.52 (0.93; 13.19)	2/1.3	1.56 (0.19; 5.64)
Comorbidity burden, moderate	4/1.0.	4.20 (1.14; 10.75)	4/1.8	2.22 (0.60; 5.69)
Comorbidity burden, high	1/0.4	2.33 (0.06; 12.98)	0	-
Obesity -	7/1.8	3.82 (1.53; 7.87)	5/3.5	1.44 (0.47; 3.36)
Obesity +	1/0.2	4.68 (0.12; 26.04)	1/0.4	2.42 (0.06; 13.50)
Year of venous thromboembolism diagnosis 1978-1993	1/0.3	3.76 (0.10; 20.93)	0	-
Year of venous thromboembolism diagnosis 1994-2013	7/1.8	3.93 (1.58; 8.10)	6/3.4	1.78 (0.65; 3.88)
Classic provoking factors, ² Overall -	8/1.6	5.15 (2.22; 10.14)	5/3.0	1.69 (0.55; 3.95)
Classic provoking factors, Overall +	0	-	1/0.9	1.08 (0.03; 6.01)
Recent pregnancy -	8/2.0	3.91 (1.69; 7.71)	6/3.9	1.55 (0.57; 3.38)
Recent pregnancy +	0	-	0	-
Recent fracture/trauma -	8/1.9	4.32 (1.86; 8.52)	6/3.5	1.71 (0.63; 3.73)
Recent fracture/trauma +	0	-	0	-
Recent surgery -	8/1.7	4.83 (2.08; 9.52)	5/3.2	1.59 (0.51; 3.70)
Recent surgery +	0	-	1/0.7	1.37 (0.03; 7.65)

Abbreviations: O/E = observed number/expected number; SIR = standardized incidence ratio; CI = confidence interval

¹3 categories of comorbidity burden based on the Charlson Comorbidity Index; normal = 0 points, moderate = 1-2 points, and high = 3 or more points. Cancer was excluded from the comorbidity index.

²Within the 3 months prior to a venous thromboembolism diagnosis.

Supplementary Table S5. Standardized incidence ratios of cancer in patients with venous thromboembolism and hyperthyroidism, Denmark, 1978-2013, stratified by follow-up of 0-30 days vs. 31-90 days.

	0-30 days		31-90 days	
	O/E	SIR (95% CI)	O/E	SIR (95% CI)
Hyperthyroidism	27/2.4	11.10 (7.32; 16.16)	10/4.5	2.21 (1.06; 4.07)
Female	21/1.9	10.91 (6.75; 16.68)	6/3.6	1.68 (0.62; 3.66)
Male	6/0.5	11.83 (4.34; 25.78)	4/1.0	4.20 (1.14; 10.75)
Age at venous thromboembolism diagnosis < 60	2/0.2	11.79 (1.43; 42.57)	0	-
Age at venous thromboembolism diagnosis 60-74	12/0.8	15.11 (7.80; 26.39)	4/1.5	2.64 (0.72; 6.75)
Age at venous thromboembolism diagnosis ≥ 75	13/1.5	8.86 (4.71; 15.15)	6/2.7	2.24 (0.82; 4.89)
Comorbidity burden, ¹ normal	10/1.0	10.26 (4.91; 18.87)	5/1.9	2.69 (0.87; 6.28)
Comorbidity burden, moderate	13/1.1	12.12 (6.45; 20.73)	3/2.0	1.53 (0.31; 4.46)
Comorbidity burden, high	4/0.4	10.40 (2.83; 26.62)	2/0.7	2.85 (0.34; 10.29)
Obesity -	26/2.3	11.35 (7.41; 16.63)	9/4.3	2.12 (0.97; 4.02)
Obesity +	1/0.1	7.10 (0.18; 39.53)	1/0.3	3.69 (0.09; 20.56)
Year of venous thromboembolism diagnosis 1978-1993	1/0.3	3.08 (0.08; 17.18)	0	-
Year of venous thromboembolism diagnosis 1994-2013	26/2.1	12.34 (8.06; 18.08)	10/3.9	2.55 (1.22; 4.70)
Classic provoking factors, ² Overall -	20/1.9	10.56 (6.45; 16.31)	9/3.5	2.56 (1.17; 4.87)
Classic provoking factors, Overall +	7/0.5	13.03 (5.23; 26.85)	1/1.0	0.99 (0.03; 5.51)
Recent pregnancy -	27/2.4	11.11 (7.32; 16.16)	10/4.5	2.21 (1.06; 4.07)
Recent pregnancy +	0	-	0	-
Recent fracture/trauma -	23/2.2	10.47 (6.63; 15.71)	10/4.1	2.44 (1.17; 4.50)
Recent fracture/trauma +	4/0.2	17.08 (4.64; 43.72)	0	-
Recent surgery -	21/2.0	10.46 (6.47; 15.99)	27/15.2	1.78 (1.17; 2.58)
Recent surgery +	6/0.4	14.16 (5.20; 30.88)	4/3.3	1.21 (0.33; 3.10)

Abbreviations: O/E = observed number/expected number; SIR = standardized incidence ratio; CI = confidence interval

¹3 categories of comorbidity burden based on the Charlson Comorbidity Index; normal = 0 points, moderate = 1-2 points, and high = 3 or more points. Cancer was excluded from the comorbidity index.

²Within the 3 months prior to a venous thromboembolism diagnosis.

Supplementary Table S6. 1-year standardized incidence ratios of cancer in patients with venous thromboembolism and hypothyroidism, excluding cancers detected within the first 30 days after VTE, Denmark, 1978-2013.

	0-1 year minus 30 days	
	O/E	SIR (95% CI)
Hypothyroidism	35/19.9	1.76 (1.23; 2.45)
Female	31/16.4	1.89 (1.29; 2.69)
Male	4/3.5	1.14 (0.31; 2.91)
Age at venous thromboembolism diagnosis < 60	6/1.4	4.21 (1.55; 9.18)
Age at venous thromboembolism diagnosis 60-74	12/6.6	1.82 (0.94; 3.17)
Age at venous thromboembolism diagnosis ≥ 75	17/11.9	1.43 (0.83; 2.30)
Comorbidity burden, ¹ normal	13/6.8	1.90 (1.01; 3.25)
Comorbidity burden, moderate	16/9.2	1.74 (1.00; 2.83)
Comorbidity burden, high	6/3.9	1.56 (0.57; 3.39)
Obesity -	31/17.8	1.75 (1.19; 2.48)
Obesity +	4/2.1	1.88 (0.51; 4.80)
Year of venous thromboembolism diagnosis 1978-1993	6/2.7	2.23 (0.82; 4.87)
Year of venous thromboembolism diagnosis 1994-2013	29/17.2	1.69 (1.13; 2.42)
Classic provoking factors, ² Overall -	30/15.0	1.99 (1.34-2.85)
Classic provoking factors, Overall +	5/4.8	1.03 (0.33; 2.41)
Recent pregnancy -	35/19.86	1.76 (1.23; 2.45)
Recent pregnancy +	0	-
Recent fracture/trauma -	34/18.0	1.89 (1.31; 2.65)
Recent fracture/trauma +	1/2.0	0.52 (0.01; 2.88)
Recent surgery -	30/16.1	1.87 (1.26; 2.66)
Recent surgery +	5/3.8	1.32 (0.43; 3.07)

Abbreviations: O/E = observed number/expected number; SIR = standardized incidence ratio; CI = confidence interval

¹3 categories of comorbidity burden based on the Charlson Comorbidity Index; normal = 0 points, moderate = 1-2 points, and high = 3 or more points. Cancer was excluded from the comorbidity index.

²Within the 3 months prior to a venous thromboembolism diagnosis.

Supplementary Table S7. 1-year standardized incidence ratios of cancer in patients with venous thromboembolism and hyperthyroidism, excluding cancers detected within the first 30 days after VTE, Denmark, 1978-2013.

	0-1 year minus 30 days	
	O/E	SIR (95% CI)
Hyperthyroidism	41/23.0	1.78 (1.28; 2.42)
Female	28/18.2	1.54 (1.02; 2.23)
Male	13/4.8	2.68 (1.43; 4.59)
Age at venous thromboembolism diagnosis < 60	2/1.8	1.09 (0.13; 3.92)
Age at venous thromboembolism diagnosis 60-74	17/8.1	2.11 (1.23; 3.38)
Age at venous thromboembolism diagnosis ≥ 75	22/13.1	1.68 (1.05; 2.54)
Comorbidity burden, ¹ normal	17/9.9	1.72 (1.00; 2.76)
Comorbidity burden, moderate	22/9.8	2.25 (1.41; 3.41)
Comorbidity burden, high	2/3.4	0.59 (0.07; 2.14)
Obesity -	37/21.6	1.71 (1.20; 2.36)
Obesity +	4/1.4	2.88 (0.78; 7.37)
Year of venous thromboembolism diagnosis 1978-1993	5/3.2	1.57 (0.51; 3.67)
Year of venous thromboembolism diagnosis 1994-2013	36/19.8	1.81 (1.27; 2.51)
Classic provoking factors, ² Overall -	36/17.8	2.02 (1.42; 2.80)
Classic provoking factors, Overall +	5/5.2	0.95 (0.31; 2.22)
Recent pregnancy -	41/23.0	1.78 (1.28; 2.42)
Recent pregnancy +	0	-
Recent fracture/trauma -	39/20.8	1.88 (1.33; 2.57)
Recent fracture/trauma +	2/2.2	0.89 (0.11; 3.22)
Recent surgery -	36/18.9	1.90 (1.33; 2.63)

Recent surgery +

5/4.1

1.22 (0.40; 2.85)

Abbreviations: O/E = observed number/expected number; SIR = standardized incidence ratio; CI = confidence interval

¹3 categories of comorbidity burden based on the Charlson Comorbidity Index; normal = 0 points, moderate = 1-2 points, and high = 3 or more points. Cancer was excluded from the comorbidity index.

²Within the 3 months prior to a venous thromboembolism diagnosis.

Supplementary Table S8. Absolute one-year cancer risk and standardized incidence ratios of cancer in patients with venous thromboembolism and hypothyroidism (N=575), by follow-up interval, Denmark, 1978-2013, restricted to patients with a maximum of 2 years between first hypothyroid disease diagnosis and first VTE diagnosis.

	Absolute risk	0-90 days		91-365 days		0-1 year		1+ year	
	1 year AR (%) (95% CI)	O/E	SIR (95% CI)	O/E	SIR (95% CI)	O/E	SIR (95% CI)	O/E	SIR (95% CI)
Hypothyroidism	2.85 (1.70-4.47)	5/2.0	2.39 (0.77-5.56)	11/5.7	1.93 (0.96-3.45)	16/7.8	2.05 (1.17-3.33)	53/44.6	1.19 (0.89-1.55)
Female	-	5/1.7	2.97 (0.96-6.91)	10/4.6	2.17 (1.04-4.00)	15/6.3	2.39 (1.33-3.94)	45/37.0	1.22 (0.89-1.63)
Male	-	0	-	1/1.1	0.90 (0.02-5.01)	1/1.5	0.66 (0.02-3.67)	8/7.6	1.05 (0.45-2.06)
Age at venous thromboembolism diagnosis < 60	-	0	-	5/0.4	11.76 (3.81-27.41)	5/0.6	8.73 (2.83-20.35)	13/8.9	1.46 (0.78-2.49)
Age at venous thromboembolism diagnosis 60-74	-	5/0.7	7.32 (2.37-17.05)	4/1.9	2.06 (0.56-5.27)	9/2.6	3.43 (1.57-6.51)	13/20.6	0.63 (0.34-1.08)
Age at venous thromboembolism diagnosis ≥ 75	-	0	-	2/3.3	0.60 (0.07-2.16)	2/4.6	0.43 (0.05-1.57)	27/15.2	1.78 (1.17-2.59)
Comorbidity burden, ¹ low	-	2/0.9	2.36 (0.29-8.50)	6/2.5	2.44 (0.90-5.33)	8/3.3	2.42 (1.04-4.77)	25/26.9	0.93 (0.60-1.37)
Comorbidity burden, moderate	-	2/0.9	2.23 (0.27-8.03)	2/2.4	0.84 (0.10-3.02)	4/3.3	1.22 (0.33-3.11)	24/14.9	1.62 (1.03-2.40)
Comorbidity burden, high	-	1/0.3	2.89 (0.07-16.09)	3/0.9	3.46 (0.71-10.10)	4/1.2	3.30 (0.90-8.44)	4/2.9	1.37 (0.37-3.51)
Obesity -	-	4/1.9	2.07 (0.56-5.31)	9/5.3	1.71 (0.78-3.25)	13/7.2	1.81 (0.96-3.09)	49/42.0	1.17 (0.86-1.54)
Obesity +	-	1/0.2	6.03 (0.15-33.60)	2/0.5	4.38 (0.53-15.81)	3/0.6	4.82 (0.99-14.07)	4/2.6	1.52 (0.41-3.89)
Year of venous thromboembolism diagnosis 1978-1993	-	1/0.4	2.32 (0.06-12.93)	4/1.2	3.29 (0.89-8.41)	5/1.6	3.03 (0.98-7.07)	18/15.9	1.13 (0.67-1.79)
Year of venous thromboembolism diagnosis 1994-2013	-	4/1.7	2.41 (0.65-6.16)	7/4.5	1.56 (0.62-3.21)	11/6.2	1.79 (0.89-3.20)	35/28.7	1.22 (0.85-1.69)
Classic provoking factors, ²	-	5/1.5	3.26 (1.06-7.60)	11/4.1	2.65 (1.32-4.75)	16/5.7	2.82 (1.61-4.58)	42/33.9	1.24 (0.89-1.68)
Overall - Classic provoking factors,	-	0	.	0	-	0	-	11/10.8	1.02 (0.51-1.83)

Overall +

Recent pregnancy -	-	5/2.0	2.39 (0.77-5.57)	11/5.7	1.93 (0.96-3.45)	16/7.8	2.05 (1.17-3.33)	53/44.1	1.20 (0.90-1.57)
Recent pregnancy +	-	0	-	0	-	0	-	0	-
Recent fracture/trauma -	-	51.9	2.65 (0.86-6.18)	11/5.1	2.14 (1.07-3.83)	16/7.0	2.28 (1.30-3.70)	52/41.8	1.25 (0.93-1.63)
Recent fracture/trauma +	-	0	-	0	-	0	0.00 (-.)	1	0.35 (0.01-1.94)
Recent surgery -	-	5/1.6	3.08 (1.00-7.18)	11/4.4	2.50 (1.25-4.48)	16/6.1	2.66 (1.52-4.32)	43/35.1	1.23 (0.89-1.65)
Recent surgery +	-	0	-	0	-	0	-	10/9.5	1.05 (0.50-1.93)

Abbreviations: AR = absolute risk; O/E = observed number/expected number; SIR = standardized incidence ratio; CI = confidence interval

¹3 categories of comorbidity burden based on the Charlson Comorbidity Index; low = 0 points, moderate = 1-2 points, and high = 3 or more points. Cancer was excluded from the comorbidity index.

²Within the 3 months prior to a venous thromboembolism diagnosis.

Supplementary Table S9. Standardized incidence ratios of cancer in patients with venous thromboembolism and hypothyroidism, Denmark, 1978-2013, stratified by follow-up of 0-30 days vs. 31-90 days, restricted to patients with a maximum of 2 years between first hypothyroid disease diagnosis and first VTE diagnosis.

	0-30 days		31-90 days	
	O/E	SIR (95% CI)	O/E	SIR (95% CI)
Hypothyroidism	3/0.7	4.16 (0.86-12.16)	2/1.4	1.46 (0.18-5.26)
Female	3/0.6	5.17 (1.06-15.09)	2/1.1	1.81 (0.22-6.53)
Male	0	-	0	-
Age at venous thromboembolism diagnosis < 60	0	-	0	-
Age at venous thromboembolism diagnosis 60-74	3/0.2	12.92 (2.66-37.74)	2/0.5	4.43 (0.54-16.00)
Age at venous thromboembolism diagnosis ≥ 75	0	-	0	-
Comorbidity burden, ¹ low	1/0.3	3.45 (0.09-19.20)	1/0.6	1.79 (0.05-9.96)
Comorbidity burden, moderate	1/0.3	3.22 (0.08-17.95)	1/0.6	1.70 (0.04-9.47)
Comorbidity burden, high	1/0.1	8.32 (0.21-46.37)	0	-
Obesity -	2/0.7	3.01 (0.36-10.87)	2/1.3	1.58 (0.19-5.71)
Obesity +	1/0.1	17.82 (0.45-99.23)	0	-
Year of venous thromboembolism diagnosis 1978-1993	1/0.1	6.71 (0.17-37.39)	0	-
Year of venous thromboembolism diagnosis 1994-2013	2/0.6	3.50 (0.42-12.63)	2/1.1	1.83 (0.22-6.61)
Classic provoking factors, ² Overall -	3/0.5	5.68 (1.17-16.58)	2/1.0	1.99 (0.24-7.19)
Classic provoking factors, Overall +	0	-	0	-
Recent pregnancy -	3/0.7	4.17 (0.86-12.16)	2/1.4	1.46 (0.18-5.26)
Recent pregnancy +	0	-	0	-
Recent fracture/trauma -	3/0.6	4.62 (0.95-13.50)	2/1.2	1.62 (0.20-5.85)
Recent fracture/trauma +	0	-	0	-
Recent surgery -	3/0.6	5.37 (1.11-15.68)	2/1.1	1.88 (0.23-6.79)
Recent surgery +	0	-	0	-

Abbreviations: O/E = observed number/expected number; SIR = standardized incidence ratio; CI = confidence interval

¹3 categories of comorbidity burden based on the Charlson Comorbidity Index; low = 0 points, moderate = 1-2 points, and high = 3 or more points. Cancer was excluded from the comorbidity index.

²Within the 3 months prior to a venous thromboembolism diagnosis.

Supplementary Table S10. 1-year standardized incidence ratios of cancer in patients with venous thromboembolism and hypothyroidism, excluding cancers detected within the first 30 days after VTE, Denmark, 1978-2013, **restricted to patients with a maximum of 2 years between first hypothyroid disease diagnosis and first VTE diagnosis.**

	0-1 year minus 30 days	
	O/E	SIR (95% CI)
Hypothyroidism	13/7.1	1.83 (0.98-3.14)
Female	12/5.7	2.10 (1.09-3.67)
Male	1/1.4	0.73 (0.02-4.04)
Age at venous thromboembolism diagnosis < 60	5/0.5	9.56 (3.10-22.27)
Age at venous thromboembolism diagnosis 60-74	6/2.4	2.51 (0.92-5.46)
Age at venous thromboembolism diagnosis ≥ 75	2/4.2	0.48 (0.06-1.73)
Comorbidity burden, ¹ low	7/3.0	2.32 (0.93-4.78)
Comorbidity burden, moderate	3/3.0	1.01 (0.21-2.94)
Comorbidity burden, high	3/1.1	2.74 (0.57-8.01)
Obesity -	11/6.5	1.69 (0.84-3.02)
Obesity +	2/0.6	3.53 (0.43-12.75)
Year of venous thromboembolism diagnosis 1978-1993	4/1.5	2.67 (0.73-6.83)
Year of venous thromboembolism diagnosis 1994-2013	9/5.6	1.61 (0.74-3.06)
Classic provoking factors, ² Overall -	13/5.2	2.52 (1.34-4.32)
Classic provoking factors, Overall +	0	-
Recent pregnancy -	13/7.1	1.84 (0.98-3.14)
Recent pregnancy +	0	-
Recent fracture/trauma -	13/6.4	2.04 (1.09-3.49)
Recent fracture/trauma +	0	-
Recent surgery -	13/5.5	2.38 (1.27-4.07)
Recent surgery +	0	-

Abbreviations: O/E = observed number/expected number; SIR = standardized incidence ratio; CI = confidence interval

¹3 categories of comorbidity burden based on the Charlson Comorbidity Index; normal = 0 points, moderate = 1-2 points, and high = 3 or more points. Cancer was excluded from the comorbidity index.

²Within the 3 months prior to a venous thromboembolism diagnosis.

Supplementary Table S11. Absolute one-year cancer risk and standardized incidence ratios of cancer in patients with venous thromboembolism and hyperthyroidism (N=637), by follow-up interval, Denmark, 1978-2013, restricted to patients with a maximum of 2 years between first hyperthyroid disease diagnosis and first VTE diagnosis.

	Absolute risk	0-90 days		91-365 days		0-1 year		1+ year	
	1 year AR (%) (95% CI)	O/E	SIR (95% CI)	O/E	SIR (95% CI)	O/E	SIR (95% CI)	O/E	SIR (95% CI)
Hyperthyroidism	4.12 (2.76-5.87)	18/2.2	8.27 (4.90-13.08)	8/5.9	1.36 (0.59-2.68)	26/8.1	3.22 (2.11-4.72)	82/53.3	1.54 (1.22-1.91)
Female	-	15/1.6	9.18 (5.13-15.14)	4/4.5	0.89 (0.24-2.28)	19/6.1	3.10 (1.87-4.84)	65/40.7	1.60 (1.23-2.03)
Male	-	3/0.5	5.55 (1.14-16.20)	4/1.4	2.87 (0.78-7.34)	7/1.9	3.62 (1.45-7.45)	17/12.6	1.35 (0.79-2.16)
Age at venous thromboembolism diagnosis < 60	-	0	0.00 (-.)	0	0.00 (-.)	0	0.00 (-.)	18/11.2	1.60 (0.95-2.54)
Age at venous thromboembolism diagnosis 60-74	-	6/0.8	7.59 (2.79-16.55)	4/2.2	1.78 (0.48-4.56)	10/3.0	3.29 (1.58-6.05)	42/26.7	1.57 (1.13-2.12)
Age at venous thromboembolism diagnosis ≥ 75	-	12/1.2	9.80 (5.06-17.13)	4/3.2	1.27 (0.34-3.25)	16/4.4	3.65 (2.09-5.94)	22/15.4	1.43 (0.90-2.17)
Comorbidity burden, ¹ low	-	9/1.0	8.78 (4.02-16.69)	3/3.0	1.01 (0.21-2.94)	12/4.0	2.99 (1.54-5.23)	57/39.4	1.45 (1.10-1.88)
Comorbidity burden, moderate	-	7/0.8	8.61 (3.45-17.75)	5/2.1	2.39 (0.77-5.56)	12/2.9	4.13 (2.13-7.21)	21/11.5	1.83 (1.13-2.80)
Comorbidity burden, high	-	2/0.3	5.92 (0.72-21.36)	0	-	2/1.1	1.74 (0.21-6.30)	4/2.4	1.63 (0.44-4.18)
Obesity -	-	17/2.1	8.16 (4.75-13.07)	7/5.7	1.24 (0.50-2.55)	24/7.7	3.10 (1.99-4.61)	79/52.2	1.51 (1.20-1.88)
Obesity +	-	1/0.1	10.72 (0.27-59.72)	1/0.2	4.36 (0.11-24.26)	2/0.3	6.20 (0.75-22.37)	3/1.1	2.81 (0.58-8.21)
Year of venous thromboembolism diagnosis 1978-1993	-	1/0.5	1.90 (0.05-10.59)	3/1.5	2.04 (0.42-5.95)	4/2.0	2.00 (0.54-5.12)	32/21.8	1.46 (1.00-2.07)
Year of venous thromboembolism diagnosis 1994-2013	-	17/1.6	10.31 (6.00-16.50)	5/4.4	1.13 (0.37-2.64)	22/6.1	3.63 (2.27-5.49)	50/31.4	1.59 (1.18-2.09)
Classic provoking factors, ²	-	15/1.7	8.78 (4.91-14.49)	7/4.5	1.54 (0.62-3.17)	22/6.2	3.52 (2.21-5.33)	60/39.5	1.52 (1.16-1.96)
Overall -	-	3/0.5	6.41 (1.32-18.73)	1/1.3	0.74 (0.02-4.14)	4/1.8	2.20 (0.60-5.64)	22/13.8	1.59 (1.00-2.41)

Overall +									
Recent pregnancy -	-	182.2	8.28 (4.90-13.08)	8/5.9	1.36 (0.59-2.68)	26/8.1	3.22 (2.11-4.73)	8253.3	1.54 (1.22-1.91)
Recent pregnancy +	-	0	-	0	-	0	-	0	-
Recent fracture/trauma -	-	17/2.0	8.55 (4.98-13.70)	8/5.3	1.50 (0.65-2.95)	25/7.3	3.41 (2.21-5.04)	76/48.7	1.56 (1.23-1.95)
Recent fracture/trauma +	-	1/0.2	5.32 (0.13-29.64)	0	-	1/0.7	1.35 (0.03-7.53)	6/4.6	1.30 (0.48-2.84)
Recent surgery -	-	16/1.8	8.89 (5.08-14.44)	7/4.8	1.46 (0.58-3.00)	23/6.6	3.48 (2.21-5.23)	63/41.7	1.51 (1.16-1.94)
Recent surgery +	-	2/0.4	5.31 (0.64-19.18)	1/1.1	0.92 (0.02-5.14)	3/1.5	2.06 (0.42-6.00)	119/11.	1.63 (0.98-2.54)
								7	

Abbreviations: AR = absolute risk; O/E = observed number/expected number; SIR = standardized incidence ratio; CI = confidence interval

¹3 categories of comorbidity burden based on the Charlson Comorbidity Index; low = 0 points, moderate = 1-2 points, and high = 3 or more points. Cancer was excluded from the comorbidity index.

²Within the 3 months prior to a venous thromboembolism diagnosis.

Supplementary Table S12. Standardized incidence ratios of cancer in patients with venous thromboembolism and hyperthyroidism, Denmark, 1978-2013, stratified by follow-up of 0-30 days vs. 31-90 days, restricted to patients with a maximum of 2 years between first hyperthyroid disease diagnosis and first VTE diagnosis.

	0-30 days		31-90 days	
	O/E	SIR (95% CI)	O/E	SIR (95% CI)
Hyperthyroidism	12/0.7	15.77 (8.14-27.55)	6/1.4	4.24 (1.56-9.25)
Female	11/0.6	19.23 (9.59-34.41)	4/1.1	3.76 (1.02-9.64)
Male	1/0.2	5.30 (0.13-29.50)	2/0.4	5.68 (0.69-20.52)
Age at venous thromboembolism diagnosis < 60	0	0.00 (-.)	0	0.00 (-.)
Age at venous thromboembolism diagnosis 60-74	4/0.3	14.60 (3.97-37.38)	2/0.5	3.87 (0.47-13.98)
Age at venous thromboembolism diagnosis ≥ 75	8/0.4	18.45 (7.95-36.35)	4/0.8	5.06 (1.38-12.96)
Comorbidity burden, ¹ low	5/0.4	14.24 (4.61-33.17)	4/0.7	5.94 (1.62-15.20)
Comorbidity burden, moderate	6/0.3	20.78 (7.63-45.30)	1/0.5	1.91 (0.05-10.63)
Comorbidity burden, high	1/0.1	8.27 (0.21-46.09)	1/0.2	4.60 (0.12-25.65)
Obesity -	12/0.7	16.48 (8.51-28.79)	5/1.4	3.69 (1.20-8.60)
Obesity +	0	0.00 (-.)	1/0.1	16.51 (0.42-91.95)
Year of venous thromboembolism diagnosis 1978-1993	1/0.2	5.57 (0.14-31.00)	0	0.00 (-.)
Year of venous thromboembolism diagnosis 1994-2013	11/0.6	18.93 (9.44-33.87)	6/1.1	5.62 (2.06-12.24)
Classic provoking factors, ² Overall -	9/0.6	14.93 (6.84-28.36)	6/1.1	5.43 (1.99-11.84)
Classic provoking factors, Overall +	3/0.2	19.00 (3.91-55.49)	0	-
Recent pregnancy -	12/0.8	15.77 (8.14-27.56)	6/1.4	4.24 (1.56-9.25)
Recent pregnancy +	0	-	0	-
Recent fracture/trauma -	11/0.7	15.77 (7.86-28.22)	6/1.3	4.65 (1.71-10.14)
Recent fracture/trauma +	1/0.1	15.77 (0.40-87.85)	0	0.00 (-.)
Recent surgery -	10/0.6	15.78 (7.56-29.03)	6/1.2	5.15 (1.89-11.22)
Recent surgery +	2/0.1	15.72 (1.90-56.75)	0	-

Abbreviations: O/E = observed number/expected number; SIR = standardized incidence ratio; CI = confidence interval

¹3 categories of comorbidity burden based on the Charlson Comorbidity Index; low = 0 points, moderate = 1-2 points, and high = 3 or more points. Cancer was excluded from the comorbidity index.

²Within the 3 months prior to a venous thromboembolism diagnosis.

Supplementary Table S13. 1-year standardized incidence ratios of cancer in patients with venous thromboembolism and hyperthyroidism excluding cancers detected within the first 30 days after VTE, Denmark, 1978-2013, **restricted to patients with a maximum of 2 years between first hyperthyroid disease diagnosis and first VTE diagnosis.**

	0-1 year minus 30 days	
	O/E	SIR (95% CI)
Hyperthyroidism	14/7.3	1.92 (1.05-3.22)
Female	8/5.6	1.44 (0.62-2.84)
Male	6/1.7	3.43 (1.26-7.49)
Age at venous thromboembolism diagnosis < 60	0	0.00 (-.)
Age at venous thromboembolism diagnosis 60-74	6/2.8	2.17 (0.80-4.73)
Age at venous thromboembolism diagnosis ≥ 75	8/3.9	2.03 (0.87-4.00)
Comorbidity burden, ¹ low	7/3.7	1.91 (0.77-3.94)
Comorbidity burden, moderate	6/2.6	2.29 (0.84-4.99)
Comorbidity burden, high	1/1.0	0.98 (0.02-5.43)
Obesity -	12/7.0	1.71 (0.88-2.99)
Obesity +	2/0.3	6.89 (0.83-24.88)
Year of venous thromboembolism diagnosis 1978-1993	3/1.8	1.65 (0.34-4.82)
Year of venous thromboembolism diagnosis 1994-2013	11/5.5	2.01 (1.00-3.59)
Classic provoking factors, ² Overall -	13/5.2	2.52 (1.34-4.32)
Classic provoking factors, Overall +	0	-
Recent pregnancy -	14/7.3	1.92 (1.05-3.22)
Recent pregnancy +	0	-
Recent fracture/trauma -	14/6.6	2.11 (1.15-3.55)
Recent fracture/trauma +	0	0.00 (-.)
Recent surgery -	13/5.5	2.38 (1.27-4.07)
Recent surgery +	0	-

Abbreviations: O/E = observed number/expected number; SIR = standardized incidence ratio; CI = confidence interval

¹3 categories of comorbidity burden based on the Charlson Comorbidity Index; normal = 0 points, moderate = 1-2 points, and high = 3 or more points. Cancer was excluded from the comorbidity index.

²Within the 3 months prior to a venous thromboembolism diagnosis.

