

Risk of cancer in adults with primary immune thrombocytopenia: a binational population-based real-world cohort study from Denmark and France

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Received: January 14, 2025.
Accepted: May 14, 2025.
Early view: May 22, 2025.

<https://doi.org/10.3324/haematol.2025.287330>

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Supplementary Materials

Supplementary Methods

The Danish and French public health registries contain valid and continuously updated information, based on reporting from publicly financed health systems with full follow-up. Patients with hematological conditions are solely managed in public hospitals, and all hospital contacts in Denmark (DK) are assigned a diagnosis code by physicians using the International Classification of Diseases (ICD) and registered in the Danish National Patient Registry (DNPR).^{1,2} The DNPR contains information regarding hospitalizations since 1977, and have included outpatient and emergency room contracts since 1994. We used the DNPR to identify patients with ITP, and comorbidities for all individuals in the study.

The Danish Civil Registration System (DCRS) provided data on sex, date of birth, migration, and death.^{3,4} The DCRS was founded in 1968, and contains information on individual-linkage level on all inhabitants in DK through a unique ten-digit Civil Personal Register number. It is updated on a daily basis, and have a high degree of follow-up, completeness and accuracy.

From the Danish Cancer Registry, we retrieved information regarding cancer outcomes. This registry contains information on incident cancers since 1943, and has been continuously updated over time.⁵

We used the designated diagnosis codes for ITP in the ICD-8 (287.10) (1977-1993) and ICD-10 (D69.3) (1994-2018) for identification of patients with ITP in the DNPR (supplementary table S1). We defined ITP as secondary when a registration of at least one predefined qualifying diagnosis occurred any time before or up to 30 days after the first registration of ITP (table S3), and we therefore included a diagnostic run-in period with follow-up starting at index date +30 days. (supplementary table S2).²⁸⁻³¹ This approach was similar to other studies by our group.^{6,7} Individuals with a given prevalent solid cancer before the index date were excluded from the incidence analyses of that cancer, but remained in the parallel follow-up for other types of cancer. The follow-up period in DK ended on 31 December 2016, and 31 December 2018 in France. We identified prevalent comorbidities associated with an increased risk of cancer. In Denmark, we identified comorbidity the DNPR before or on index date (supplementary table S2). We based prevalent comorbidity at inclusion on diagnoses registered in the DNPR and DCR before or at the index date, and categorized into four groups. We did not have access to all cancer risk factors, but used the Quan 2011 updated Charlson Comorbidity to identify three comorbidity categories: liver disease, chronic pulmonary disease, and diabetes, while prevalent solid cancer was defined on registrations of specific ICD-codes in the DCR (table S2). This approach of classifying individual level comorbidity in longitudinal studies through the DNPR has been proven to be valid.⁸ Comorbidity covariates were included in the regressions as

dichotomous variables.⁹ All cancer registrations and outcomes were identified in the Danish Cancer Registry (DCR) (supplementary table S3).

In France, patients were identified in the French national health database (SNDS) using the hospital database (PMSI) and long-term diseases allowing full reimbursement registered by general practitioners between 2011 and 2018.^{10, 11} Comorbidities and cancers were identified using the same sources.

Supplementary Tables

Supplementary table S1. List of ICD-codes used for inclusion and exclusion of patients with immune thrombocytopenia

GROUP	ICD-8 (until 1993)	ICD-10 (1994 & onwards)
Included	287.10: thrombocytopenia essentialis	D69.3: purpura, idiopathic thrombocytopenia
Excluded	287.39: thrombocytopathia	D69.1: Platelet defect D69.1A: Bernard-Souliers syndrome D69.1B: Glanzmanns disease D69.1C: Thrombasthenia haemorrhagica hereditaria D82.0: Wiskott-Aldrich syndrome (WAS)

Supplementary table S1. ICD-codes used to identify patients. The date of the first registration of any of the included codes defined index date. Patients registered anytime with a minimum of one exclusionary code were excluded from the study.

Abbreviations: ICD: International Classification of Disease

Supplementary table S2. List of included ICD-codes applied to exclude secondary immune thrombocytopenia defined as one or more codes registered any time before or up to 30days after diagnosis of ITP

GROUP	ICD-8 (until 1993)	ICD-10 (1994 & onwards)
Immunodeficiency (non HIV)	275.09, 275.19	D80 – D84
Autoimmune disease	135.99, 275.09, 275.19, 712.09, 712.19, 712.39, 712.59, 716.09, 716.19, 734.00, 734.01, 734.02, 734.90	M32 – M35.1, M05, M06.2-M06.3, M06.8-M06.9, D86, D68.6
Systemic lupus erythematosus	734.19	M32
Systemic sclerosis	734.00, 734.01, 734.02	M34
Dermatopolymyositis	716.09, 716.19	M33
Sicca syndrome	734.90	M35.0
Mixed connective tissue disease	N/A	M35.1
Rheumatoid arthritis	712.09, 712.19, 712.39, 712.59	M05, M06.2-M06.3, M06.8-M06.9
Sarcoidosis	135.99	D86
Antiphospholipid syndrome	N/A	D68.6
Infection	070.02, 070.03, 070.04, 070.05, 570.00, 570.01, 570.08, 570.09, 571.93, 079.83	B16, B18.0-B18.2, B20 – B24
Hepatitis B & C	070.02, 070.03, 070.04, 070.05, 570.00, 570.01, 570.08, 570.09, 571.93	B16, B18.0-B18.1, B18.2
HIV & AIDS	079.83	B20 – B24
Hematological malignancies	196, 200.09, 200.19, 201.99, 202.09, 201.9, 202.29, 202.99, 203.99, 204.19, 204.99	C77, C81-C96, D46
Lymphoma	196, 200.09, 200.19, 202.09, 202.19, 202.29, 202.99	C77, C81-C86
Hodgkin's lymphoma	201.99	C81
Chronic lymphatic leukemia	204.19, 204.99	C91.1
Multiple myeloma and plasma cell neoplasms	203.99	C90
Waldenstroms macroglobulinemia	275.59, 287.90	C88.0
Myelodysplastic syndrome	N/A	D46

Supplementary table S2: ICD-codes used to exclude patients with secondary ITP. One or more of the listed diagnoses registered any time before or up to 30days after registration of ITP, defined patients as having secondary ITP. Abbreviations: N/A; not available, ICD: International Classification of Disease, ITP: immune thrombocytopenia

Supplementary table S3. List of included ICD-codes used to define cancer outcomes

Solid malignancies			
	Female cancer	174, 183	C50, C50.0, C50.1, C50.2, C50.3, C50.4, C50.5, C50.6, C50.8, C50.9, C51, C51.0, C51.1, C51.2, C51.8, C51.9, C52, C52.9, C53, C53.0, C53.1, C53.2, C53.3, C53.4, C53.8, C53.9, C54, C54.0, C54.1, C54.2, C54.3, C54.4, C54.5, C54.6, C54.8, C54.9, C55, C55.9, C56, C56.0, C56.1, C56.2, C56.3, C56.4, C56.7, C56.8, C56.9, C57, C57.0, C57.1, C57.2, C57.3, C57.4, C57.7, C57.8, C57.9, C58, C58.9, D05, D05.0, D05.1, D05.6, D05.7, D05.9, D06, D06.9, D07.1, D07.2, D07.3 D39, D39.0, D39.1, D39.2, D39.8
	Male cancer	185, 186	C60, C60.0, C60.1, C60.2, C60.8, C60.9, C61, C61.9, C62, C62.0, C62.1, C62.9, C63, C63.0, C63.1, C63.2, C63.7, C63.8, C63.9, D07.4, D07.5, D07.6, D40, D40.0, D40.1, D40.7, D40.9
	Thorax cancer	150, 162, 163	C33, C33.9, C34, C34.0, C34.1, C34.2, C34.3, C34.8, C34.9, C37, C37.9, C38, C38.0, C38.1, C38.2, C38.3, C38.4, C38.8, C39, C39.0, C39.8, C39.9, C45.0, C45.2, C76.1, D02.2, D38.0, D38.1, D38.2, D38.3, D38.4
	Urological cancer	188	C64, C64.9, C65, C65.9, C66, C66.9, C67, C67.0, C67.1, C67.2, C67.3, C67.4, C67.5, C67.6, C67.7, C67.8, C67.9, C68, C68.0, C68.1, C68.8, C68.9, D09.0, D09.1, D41, D41.0, D41.1, D41.2, D41.3, D41.4, D41.7, D41.9
	Upper gastrointestinal cancer	151, 152, 155, 156, 157, 158, 159	C15, C15.0, C15.1, C15.2, C15.3, C15.4, C15.5, C15.8, C15.9, C16, C16.0, C16.1, C16.2, C16.3, C16.4, C16.5, C16.6, C16.8, C16.9, C17, C17.0, C17.1, C17.2, C17.3, C17.8, C17.9, C22, C22.0, C22.1, C22.2, C22.3, C22.4, C22.7, C22.9, C23, C23.9, C24, C24.0, C24.1, C24.8, C24.9, C25, C25.0, C25.1, C25.2, C25.3, C25.4, C25.7, C25.8, C25.9, D00.1, D00.2, D01.4, D01.5,

			D37.1, D37.2
	Colorectal cancer	153, 154	C18, C18.0, C18.1, C18.2, C18.3, C18.4, C18.5, C18.6, C18.7, C18.8, C18.9, C19, C19.9, C20, C20.9, C21, C21.0, C21.1, C21.2, C21.8, D01.0, D01.1, D01.2, D01.3, D37.3, D37.4, D37.5
	Skin cancer	172, 173	C43, C43.0, C43.1, C43.2, C43.3, C43.4, C43.5, C43.6, C43.7, C43.8, C43.9, C44, C44.0, C44.1, C44.2, C44.3, C44.4, C44.5, C44.6, C44.7, C44.8, C44.9, C46.0, D03, D03.0, D03.1, D03.2, D03.3, D03.4, D03.5, D03.6, D03.7, D03.8, D03.9, D04, D04.0, D04.1, D04.2, D04.3, D04.4, D04.5, D04.6, D04.7, D04.8, D04.9
	Head-Neck cancer	140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 160, 161	C00, C00.0, C00.1, C00.2, C00.3, C00.4, C00.5, C00.6, C00.8, C00.9, C01, C01.9, C02, C02.0, C02.1, C02.2, C02.3, C02.4, C02.8, C02.9, C03, C03.0, C03.1, C03.9, C04, C04.0, C04.1, C04.8, C04.9, C05, C05.0, C05.1, C05.2, C05.8, C05.9, C06, C06.0, C06.1, C06.2, C06.8, C06.9, C07, C07.9, C08, C08.0, C08.1, C08.8, C08.9, C09, C09.0, C09.1, C09.2, C09.8, C09.9, C10, C10.0, C10.1, C10.2, C10.3, C10.4, C10.8, C10.9, C11, C11.0, C11.1, C11.2, C11.3, C11.8, C11.9, C12, C12.9, C12, C13.0, C13.1, C13.2, C13.8, C13.9, C14, C14.0, C14.1, C14.2, C14.8, C30, C30.0, C30.1, C31, C31.0, C31.1, C31.2, C31.3, C31.8, C31.9, C32, C32.0, C32.1, C32.2, C32.3, C32.8, C32.9, C73, C73.9, C76.0, D00.0, D02.0, D02.1, D02.3, D09.3, D44.0, D44.2, D44.3, D44.4, D44.5, D44.6, D44.7
	CNS cancer	190, 191, 192	C69, C69.0, C69.1, C69.2, C69.3, C69.4, C69.5, C69.6, C69.7, C69.8, C69.9, C70, C70.0, C70.1, C70.9, C71, C71.0, C71.1, C71.2, C71.3, C71.4, C71.5, C71.6, C71.7, C71.8, C71.9,

			C72, C72.0, C72.1, C72.2, C72.3, C72.4, C72.5, C72.8, C72.9, C75.0, C75.1, C75.2, C75.3, D09.2, D42, D42.0, D42.1, D42.9, D43, D43.0, D43.1, D43.2, D43.3, D43.4, D43.7, D43.9
	Other solid cancers	170, 171 198, 199	C26, C26.0, C26.1, C26.8, C26.9, C40, C40.0, C40.1, C40.2, C40.3, C40.8, C40.9, C41, C41.0, C41.1, C41.2, C41.3, C41.4, C41.5, C41.6, C41.7, C41.8, C41.9, C45.1, C45.7, C45.9, C46.1, C46.8, C47, C47.0, C47.2, C47.3, C47.4, C47.5, C47.6, C47.8, C47.9 C48, C48.0, C48.1, C48.2, C48.8, C49, C49.0, C49.1, C49.2, C49.3, C49.4, C49.5, C49.6, C49.8, C49.9, C74, C74.0, C74.1, C74.9, C76.2, C76.3, C76.4, C76.5, C76.7, C76.8, C76.9 C77, C77.0, C77.1, C77.2, C77.3, C77.4, C77.5, C77.8, C77.9, C78, C78.0, C78.1, C78.2, C78.3, C78.4, C78.5, C78.6, C78.7, C78.8, C79, C79.0, C79.1, C79.2, C79.3, C79.4, C79.5, C79.6, C79.7, C79.8, C80.0, C80.9, D37.7, D37.9, D44.1, D44.8, D44.9
Hematological malignancies			
	Leukemia	204, 205, 206, 207	C91, C91.0, C91.1, C91.2, C91.3, C91.4, C91.5, C91.6, C91.7, C91.8, C91.9, C92, C92.0, C92.1, C92.2, C92.3, C92.4, C92.5, C92.6, C92.7, C92.8, C92.9, C93, C93.0, C93.1, C93.2, C93.3, C93.7, C93.9, C94, C94.0, C94.1, C94.2, C94.3, C94.4, C94.5, C94.6, C94.7, C95, C95.0, CC95.9
	Lymphoma	201, 202	C81, C81.0, C81.1, C81.2, C81.3, C81.4, C81.7, C81.9, C82, C82.0, C82.1, C82.2, C82.5, C82.6, C82.7, C82.9, C83, C83.0, C83.1, C83.2, C83.3, C83.4, C83.5, C83.6, C83.7, C83.8, C83.9, C84, C84.0, C84.1, C84.2, C84.3, C84.4, C84.5, C84.6, C84.7, C84.8, C84.9, C85, C85.0, C85.1, C85.2, C85.7, C85.9, C86, C86.0, C86.1, C86.2, C86.3, C86.4, C86.5, C86.6
	Multiple myeloma	203	C90, C90.0, C90.1, C90.2, C90.3
	Other hematological cancers	208, 209	C88, C88.0, C88.1, C88.2, C88.3, C88.4, C88.7, C88.9, C96, C96.0, C96.1, C96.2, C96.3, C96.4, C96.5, C96.6, C96.7, C96.8, C96.9, D45, D45.9, D46, D46.0, D46.1, D46.2, D46.3, D46.4, D46.5, D46.6, D46.7, D46.9, D47, D47.0, D47.1, D47.3, D47.4, D47.7, D47.9

Supplementary table S3. ICD–codes applied to identify solid and hematological cancers both prevalent as a covariate and as incident outcomes

Abbreviations: ICD: International Classification of Disease

Supplementary table S4. List of included ICD codes defining comorbidity covariates

CONDITION	ICD8	ICD10
Chronic pulmonary disease	490, 491, 492, 493, 515, 516, 517, 518	J40, J41, J42, J43, J44, J45, J46, J47, J60, J61, J62, J63, J64, J65, J66, J67, J684, J701, J703, J841, J920, J961, J982, J983
Diabetes	249, 250, 249.01, 249.02, 249.03, 249.04, 249.05, 249.08, 250.01, 250.02, 250.03, 250.04, 250.05, 250.08	E10, E11, E12, E13, E14, E102, E103, E104, E105, E106, E107, E108, E112, E113, E114, E115, E116, E117, E118, E122, E123, E124, E125, E126, E127, E128, E132, E133, E134, E135, E136, E137, E138, E142, E143, E144, E145, E146, E147, E148
Liver disease	571, 573.01, 57304, 070.00, 070.02, 070.04, 070.06, 070.08, 571.10, 456.00, 456.01, 456.09, 573.00	B18, K713, K714, K715, K717, K73, K74, K760, K7602, K7603, K7604, K7608, K7609, Z944, B150, B160, B162, B190, I85, I864, I982, K704, K711, K72, K765, K766, K767

Supplementary table S4. ICD-codes applied to assess comorbidity among patients and comparators

Abbreviations: ICD: International Classification of Disease

Supplementary table S5. Table with absolute number of five-year cumulative cancer events

Supplementary tables: Table with absolute number of five year cumulative cancer events

ICD-code & Category	Country	Primary ITP	General population comparators
	DK	n=4,768	n=189,662
	FR	n=7,688	n=29,309
FEMALE CANCER			
C50 (Breast)	DK	n=24	n=952
	FR	n=32	n=136
C51 (External genitals)	DK	n<5	n=16
	FR	n=0	n<5
C52	DK	n=0	n=8
	FR	n<5	n<5
C53 (Cervix uteri)	DK	n<5	n=78
	FR	n<5	n=9
C54 (Uterus)	DK	n<5	n=173
	FR	n=5	n=27
C55	DK	n=0	n=8
	FR	n<5	n=6
C56 (Ovarian)	DK	n<5	n=130
	FR	n<5	n=13
C57	DK	n=0	n=8
	FR	n=0	n<5
C58 (Placental)	DK	n=0	n=0
	FR	n=0	n=0
MALE CANCER			
C60 (Penis)	DK	n=0	n=19
	FR	n=0	n<5
C61 (Prostate)	DK	n=28	n=1,086
	FR	n=58	n=197
C62 (Testicular)	DK	n<5	n=28
	FR	n=0	n<5
C63	DK	n=0	n<5
	FR	n<5	n<5
THORAX CANCER			
C33	DK	n=0	n<5
	FR	n<5	n=0
C34 (Lung)	DK	n=32	n=1,030
	FR	n=55	n=166
C37	DK	n=0	n<5
	FR	n<5	n<5
C38	DK	n<5	n=13
	FR	n<5	n=7
C39	DK	n=0	n=0
	FR	n=0	n=5
C450 (Mesothelioma)	DK	n<5	n=18
	FR	n<5	n=8
C452	DK	n=0	n=0
	FR	n=0	n=0
C761	DK	n=0	n=0
	FR	n=0	n=0
UPPER GI CANCER			
C15 (Esophagus)	DK	n<5	n=116
	FR	n=5	n=20
C16 (Stomach)	DK	n<5	n=158
	FR	n=11	n=27
C17	DK	n=0	n=25
	FR	n<5	n=12
C22 (Liver)	DK	n=15	n=78
	FR	n=36	n=45
C23	DK	n=0	n=16

	FR	n=0	n<5
C24	DK	n=0	n=51
	FR	n=5	n=11
C25 (Pancreas)	DK	n=11	n=266
	FR	n=14	n=52
SKIN			
C43 (Melanoma)	DK	n=5	n=328
	FR	n=15	n=49
C44 (Skin)	DK	n=70	n=2,836
	FR	n=95	n=239
C46 (Kaposi's sarcoma)	DK	n=0	n=0
	FR	n=0	n=0
D03 (Melanoma IS)	DK	n=0	n=10
	FR	n<5	n<5
D04 (Skin carcinoma IS)	DK	n=0	n=21
	FR	n=14	n=18
OTHER SOLID			
C26	DK	n=0	n<5
	FR	n=7	n<5
C40	DK	n=0	n<5
	FR	n=0	n=5
C41	DK	n=0	n=5
	FR	n<5	n<5
C46	DK	n=0	n=0
	FR	n=0	n=0
C47	DK	n=0	n<5
	FR	n<5	n<5
C48	DK	n<5	n=10
	FR	n<5	n=14
C49	DK	n=0	n=27
	FR	n=0	n=12
C74	DK	n=0	n<5
	FR	n<5	n=0
C76	DK	n=0	n=25
	FR	n<5	n<5
C77 (Metastasis NOS)	DK	n=10	n=81
	FR	n=69	n=161
C78 (Metastasis)	DK	n<5	n=143
	FR	n=95	n=261
C79	DK	n<5	n=70
	FR	n=77	n=184
C451	DK	n=0	n<5
	FR	n=0	n=0
C457	DK	n=0	n=0
	FR	n=0	n=0
C459	DK	n=0	n=0
	FR	n=0	n<5
LEUKEMIAS			
C91	DK	n=7	n=145
	FR	n=43	n=32
- C911 (CLL)	DK	n=7	n=130
	FR	n=25	n=16
- C910 (ALL)	DK	n=0	n=6
	FR	n<5	n<5
	DK	n=25	n=74
C92	FR	n=43	n=19
	DK	n<5	n=15
- C921 (CML)	FR	n=5	n<5
	DK	n=10	n=8

C93	FR	n=22	n<5
	DK	n=0	n<5
C94	FR	n=14	n<5
	DK	n<5	n=5
C95	FR	n=9	n=8
LYMPHOMAS			
C81 (Hodgkins)	DK	n<5	n=15
	FR	n=11	n<5
C82 (Follicular)	DK	n<5	n=26
	FR	n=18	n=14
C83	DK	n=10	n=87
	FR	n=55	n=29
C84 (T-cell)	DK	n<5	n=16
	FR	n=14	n=6
C85	DK	n<5	n=53
	FR	n=63	n=20
C86 (T-cell)	DK	n=0	n=0
	FR	n=6	n=0
MYELOMA			
C90	DK	n<5	n=104
	FR	n=13	n=20
OTHER HEMATOLOGICAL			
C88	DK	n<5	n<5
	FR	n=18	n=11
C96	DK	n<5	n<5
	FR	n=9	n<5
D45 (PV)	DK	n<5	n=24
	FR	n=13	n=9
D46 (MDS)	DK	n=35	n=68
	FR	n=183	n=57
D47	DK	n=12	n=77
	FR	n=141	n=70

Supplementary table S5. Table with number of cancer diagnoses in selected groups of cancer in France and Denmark
Abbreviations: CLL: chronic lymphatic leukemia; ALL: acute lymphatic leukemia; AML: acute myeloid leukemia; CML: chronic myeloid leukemia; FL: follicular lymphoma; DLBCL: diffuse large B-cell lymphoma; TCL: T-cell lymphoma; PV: polycythemia vera; MDS: myelodysplastic syndrome; ITP: immune thrombocytopenia; NOS: not otherwise specified; IS: in situ

Supplementary table S6. One-year, ten-year (Denmark), and end of study cumulative incidences of cancers in patients with primary immune thrombocytopenia and age-sex matched general population comparators in Denmark (DK) and France (FR)

Cumulative incidence of cancers, % (95% CI)	Country	Primary ITP	General population comparators
	1 st year	1 st year	1 st year
Solid cancers			
Overall	DK	1.84 (1.46-2.29) (n=85)	1.18 (1.13-1.23) (n=1,968)
	FR	2.36 (2.01-2.76) (n=148)	1.26 (1.12-1.41) (n=284)
Female cancer	DK	0.59 (0.34-0.97) (n=15)	0.36 (0.32-0.40) (n=355)
	FR	0.35 (0.20-0.58) (n=13)	0.43 (0.33-0.55) (n=61)
Male	DK	0.57 (0.30-0.99) (n=11)	0.35 (0.31-0.39) (n=261)
	FR	0.62 (0.39-0.95) (n=19)	0.46 (0.35-0.61) (n=51)
Thorax	DK	0.26 (0.15-0.45) (n=18)	0.12 (0.10-0.13) (n=214)
	FR	0.40 (0.27-0.57) (n=29)	0.15 (0.11-0.20) (n=41)
Urological	DK	0.18 (0.09-0.34) (n=11)	0.08 (0.07-0.10) (n=152)
	FR	0.31 (0.20-0.46) (n=22)	0.17 (0.13-0.23) (n=46)
Upper GI	DK	0.24 (0.13-0.43) (n=12)	0.06 (0.05-0.08) (n=112)
	FR	0.30 (0.20-0.46) (n=22)	0.15 (0.11-0.21) (n=42)
Colorectal	DK	0.11 (0.04-0.25) (n=9)	0.17 (0.15-0.19) (n=314)
	FR	0.49 (0.35-0.68) (n=35)	0.27 (0.22-0.34) (n=74)
Skin	DK	0.51 (0.33-0.76) (n=19)	0.41 (0.39-0.45) (n=725)
	FR	0.44 (0.30-0.61) (n=31)	0.26 (0.21-0.33) (n=72)
Head-Neck	DK	<0.1 (n<5)	0.05 (0.04-0.06) (n=89)
	FR	0.21 (0.12-0.34) (n=15)	0.12 (0.08-0.16) (n=32)
CNS	DK	N/A (n=0)	0.02 (0.01-0.03) (n=34)
	FR	0.16 (0.09-0.28) (n=12)	0.03 (0.01-0.05) (n=7)
Other	DK	0.13 (0.06-0.28) (n=25)	0.05 (0.04-0.06) (n=81)
	FR	0.88 (0.68-1.12) (n=63)	0.44 (0.37-0.53) (n=119)
Hematological cancers			
Overall	DK	0.94 (0.69-1.26) (n=42)	0.08 (0.07-0.09) (n=136)
	FR	3.20 (2.81-3.62) (n=236)	0.19 (0.14-0.24) (n=52)
Leukemia	DK	0.29 (0.16-0.48) (n=12)	0.03 (0.02-0.03) (n=45)
	FR	0.50 (0.36-0.69) (n=37)	0.05 (0.03-0.08) (n=13)
Lymphoma	DK	0.11 (0.04-0.25) (n=5)	0.02 (0.01-0.03) (n=34)
	FR	0.78 (0.59-1.00) (n=57)	0.05 (0.03-0.08) (n=13)
Multiple myeloma	DK	. (-.) (n=0)	0.01 (0.01-0.02) (n=24)
	FR	0.04 (0.01-0.12) (n=3)	0.01 (0.00-0.03) (n=3)
Other	DK	0.57 (0.38-0.82) (n=25)	0.02 (0.01-0.03) (n=33)
	FR	2.15 (1.84-2.50) (n=159)	0.10 (0.07-0.14) (n=27)
	10 th YEAR	10 th YEAR	10 th YEAR
Solid cancers			
Overall	DK	10.92 (9.86-12.04) (n=374)	11.50 (11.33-11.68) (n=15,393)
	FR	N/A	N/A
Female cancer	DK	3.68 (2.85-4.67) (n=67)	3.82 (3.68-3.97) (n=2,774)
	FR	N/A	N/A
Male	DK	2.36 (1.69-3.20) (n=39)	3.18 (3.04-3.32) (n=1,916)
	FR	N/A	N/A

Thorax	DK	1.58 (1.21-2.03) (n=64)	1.40 (1.34-1.46) (n=1,987)
	FR	N/A	N/A
Urological	DK	0.81 (0.56-1.15) (n=33)	0.82 (0.78-0.87) (n=1,190)
	FR	N/A	N/A
Upper GI	DK	1.25 (0.92-1.66) (n=49)	0.83 (0.79-0.88) (n=1,197)
	FR	N/A	N/A
Colorectal	DK	1.18 (0.85-1.59) (n=46)	1.54 (1.48-1.61) (n=2,224)
	FR	N/A	N/A
Skin	DK	3.47 (2.89-4.14) (n=118)	3.77 (3.67-3.87) (n=5,314)
	FR	N/A	N/A
Head-Neck	DK	0.63 (0.41-0.95) (n=23)	0.51 (0.48-0.55) (n=732)
	FR	N/A	N/A
CNS	DK	0.16 (0.07-0.33) (n=6)	0.19 (0.17-0.22) (n=273)
	FR	N/A	N/A
Other	DK	0.60 (0.39-0.90) (n=24)	0.54 (0.50-0.58) (n=773)
	FR	N/A	N/A
Hematological cancers			
Overall	DK	3.90 (3.30-4.56) (n=146)	0.85 (0.80-0.90) (n=1,225)
	FR	N/A	N/A
Leukemia	DK	1.60 (1.23-2.06) (n=59)	0.26 (0.23-0.29) (n=379)
	FR	N/A	N/A
Lymphoma	DK	0.67 (0.44-0.98) (n=23)	0.22 (0.20-0.25) (n=319)
	FR	N/A	N/A
Multiple myeloma	DK	<0.1 (n<5)	0.12 (0.10-0.14) (n=176)
	FR	N/A	N/A
Other	DK	1.71 (1.33-2.16) (n=67)	0.26 (0.23-0.28) (n=364)
	FR	N/A	N/A
Solid cancers			
Overall	DK	30.98 (26.69-35.35) (n=536)	30.94 (29.99-31.90) (n=22,932)
	FR	10.89 (9.79-12.07) (n=461)	8.94 (8.24-9.67) (n=1,155)
Female cancer	DK	12.03 (7.67-17.44) (n=89)	14.60 (13.69-15.53) (n=4,328)
	FR	1.93 (1.45-2.53) (n=53)	2.47 (2.11-2.86) (n=211)
Male	DK	6.27 (4.42-8.54) (n=58)	8.47 (7.81-9.16) (n=2,739)
	FR	2.80 (2.09-3.66) (n=59)	3.46 (2.90-4.09) (n=211)
Thorax	DK	6.80 (3.99-10.62) (n=86)	4.08 (3.76-4.42) (n=2,966)
	FR	1.68 (1.17-2.33) (n=69)	1.36 (0.99-1.83) (n=195)
Urological	DK	1.85 (1.23-2.69) (n=47)	2.01 (1.87-2.15) (n=1,739)
	FR	1.21 (0.90-1.59) (n=59)	0.99 (0.82-1.18) (n=166)
Upper GI	DK	2.44 (1.80-3.24) (n=67)	2.27 (2.08-2.46) (n=1,777)
	FR	1.77 (1.14-2.63) (n=74)	1.13 (0.93-1.35) (n=165)
Colorectal	DK	2.74 (1.53-4.51) (n=59)	4.06 (3.68-4.48) (n=3,222)
	FR	2.29 (1.88-2.77) (n=117)	1.82 (1.59-2.08) (n=296)
Skin	DK	11.00 (8.53-13.81) (n=187)	11.47 (10.70-12.26) (n=8,152)
	FR	2.22 (1.79-2.73) (n=111)	1.94 (1.68-2.24) (n=294)
Head-Neck	DK	1.64 (0.84-2.91) (n=29)	1.35 (1.23-1.49) (n=1,100)
		1.13 (0.79-1.57) (n=49)	0.67 (0.51-0.85) (n=107)

	FR		
CNS	DK	0.83 (0.26-2.10) (n=9)	0.52 (0.44-0.61) (n=402)
	FR	0.56 (0.38-0.80) (n=31)	0.13 (0.09-0.19) (n=27)
Other	DK	2.14 (1.20-3.56) (n=39)	1.31 (1.13-1.51) (n=1,107)
	FR	4.09 (3.33-4.95) (n=182)	3.20 (2.86-3.56) (n=490)
Hematological cancers			
Overall	DK	6.83 (5.48-8.38) (n=183)	2.35 (2.18-2.54) (n=1,837)
	FR	9.79 (8.65-11.02) (n=506)	1.63 (1.36-1.94) (n=242)
Leukemia	DK	2.25 (1.44-3.36) (n=65)	0.69 (0.60-0.80) (n=554)
	FR	2.70 (1.89-3.73) (n=107)	0.48 (0.29-0.76) (n=58)
Lymphoma	DK	1.91 (1.14-3.01) (n=37)	0.69 (0.60-0.79) (n=503)
	FR	2.07 (1.70-2.50) (n=116)	0.37 (0.24-0.56) (n=51)
Multiple myeloma	DK	0.36 (0.15-0.78) (n=7)	0.37 (0.30-0.46) (n=257)
	FR	0.30 (0.17-0.50) (n=15)	0.12 (0.07-0.18) (n=21)
Other	DK	2.50 (1.92-3.18) (n=79)	0.63 (0.56-0.71) (n=546)
	FR	6.84 (5.81-7.97) (n=344)	0.93 (0.76-1.12) (n=144)

Supplementary table S6. Cumulative incidence of cancers at 1st year, 10th year and end of study time in Denmark and France. Competing events were death or emigration. Please note that no ten-year estimates are provided from the French cohorts since maximum follow-up time was 10 years in France.

Abbreviations: ITP: immune thrombocytopenia; CI: confidence interval; GI: Gastrointestinal; CNS: central nervous system; N/A: not available, DK: Denmark; FR: France

Supplementary table S7. 1st-year, 2-5th year, 5th-year, and combined meta-analysis Cox cause-specific hazard and Fine-Gray subdistribution hazard ratios for risk of cancer in patients with primary ITP compared with general population comparators in Denmark (DK) and France (FR)

Groups and cancers	Country	Cox model (adjusted / crude)	Fine-Gray model (adjusted / crude)
		<u>5-year</u>	<u>5-year</u>
SOLID			
Overall	DK	1.29 (1.13-1.46) / 1.18 (1.04-1.34)	1.12 (0.98-1.27) / 1.11 (0.97-1.26)
	FR	1.34 (1.18-1.52) / 1.38 (1.22-1.55)	1.30 (1.17-1.44) / 1.31 (1.19-1.45)
	META	1.32 (1.20-1.44) / 1.28 (1.10-1.49) (pQ : 0.68 / 0.08)	1.21 (1.05-1.40) / 1.28 (1.03-1.43) (pQ : 0.08 / 0.05)
	DK 1980-1989	1.14 (0.70-1.84) / 1.05 (0.65-1.71)	NE
	DK 1990-1999	1.33 (1.02-1.74) / 1.20 (0.91-1.56)	NE
	DK 2000-2009	1.38 (1.14-1.68) / 1.26 (1.04-1.53)	NE
	DK 2010-2016	1.16 (0.90-1.49) / 1.09 (0.85-1.40)	NE
	DK FU +6M	1.24 (1.09-1.41) / 1.13 (0.99-1.29)	NE
	DK FU +12M	1.21 (1.06-1.39) / 1.10 (0.96-1.26)	NE
Age groups			
18-59 years	DK	1.49 (1.16-1.91) / 1.47 (1.15-1.89)	1.43 (1.11-1.83) / 1.44 (1.12-1.84)
	FR	1.64 (1.26-2.13) / 1.74 (1.36-2.24)	1.65 (1.32-2.05) / 1.76 (1.43-2.16)
	META	1.56 (1.30-1.87) / 1.60 (1.34-1.91) (pQ : 0.60 / 0.35)	1.55 (1.31-1.83) / 1.60 (1.33-1.96) (pQ : 0.40 / 0.22)
≥60 years	DK	1.21 (1.04-1.41) / 1.22 (1.05-1.42)	1.04 (0.89-1.21) / 1.06 (0.91-1.23)
	FR	1.26 (1.10-1.46) / 1.29 (1.13-1.48)	1.22 (1.08-1.37) / 1.22 (1.09-1.37)
	META	1.24 (1.11-1.37) / 1.26 (1.14-1.39) (pQ : 0.70 / 0.59)	1.14 (0.97-1.33) / 1.26 (1.00-1.32) (pQ : 0.11 / 0.15)
Sex			
Women	DK	1.40 (1.18-1.67) / 1.28 (1.08-1.53)	1.25 (1.05-1.49) / 1.21 (1.02-1.45)
	FR	1.40 (1.16-1.69) / 1.44 (1.20-1.72)	1.37 (1.17-1.61) / 1.39 (1.20-1.62)
	META	1.40 (1.23-1.59) / 1.36 (1.20-1.54) (pQ : 1.00 / 0.36)	1.31 (1.17-1.48) / 1.36 (1.14-1.50) (pQ : 0.07 / 0.06)
Men	DK	1.19 (0.99-1.43) / 1.09 (0.91-1.32)	1.00 (0.83-1.21) / 1.01 (0.84-1.21)
	FR	1.29 (1.10-1.53) / 1.33 (1.13-1.56)	1.24 (1.08-1.43) / 1.25 (1.10-1.43)
	META	1.24 (1.10-1.41) / 1.21 (1.00-1.47) (pQ : 0.52 / 0.11)	1.12 (0.91-1.39) / 1.21 (0.92-1.40) (pQ : 0.45 / 0.24)
Cancer subgroups			
Female	DK	1.41 (1.07-1.87) / 1.35 (1.02-1.79)	1.28 (0.96-1.69) / 1.27 (0.96-1.68)
	FR	1.05 (0.75-1.47) / 1.05 (0.76-1.45)	0.98 (0.73-1.31) / 0.98 (0.74-1.29)
Male	DK	1.24 (0.86-1.80) / 1.12 (0.77-1.61)	1.04 (0.72-1.50) / 1.01 (0.70-1.46)
	FR	1.08 (0.78-1.49) / 1.00 (0.73-1.38)	1.00 (0.76-1.30) / 0.90 (0.70-1.18)
Thorax	DK	1.58 (1.15-2.18) / 1.50 (1.09-2.07)	1.35 (0.98-1.86) / 1.39 (1.01-1.91)
	FR	1.18 (0.86-1.62) / 1.27 (0.94-1.72)	1.09 (0.83-1.44) / 1.18 (0.91-1.54)
Urological	DK	1.30 (0.83-2.03) / 1.21 (0.77-1.88)	1.09 (0.70-1.71) / 1.12 (0.72-1.74)
	FR	1.28 (0.92-1.78) / 1.33 (0.97-1.84)	1.16 (0.87-1.54) / 1.18 (0.90-1.56)
Upper GI	DK	2.01 (1.41-2.87) / 1.93 (1.35-2.75)	2.01 (1.41-2.85) / 1.78 (1.25-2.54)
	FR	1.25 (0.89-1.77) / 1.77 (1.31-2.40)	1.25 (0.93-1.66) / 1.68 (1.30-2.17)
Colorectal	DK	0.88 (0.59-1.32) / 0.78 (0.52-1.18)	0.75 (0.50-1.12) / 0.72 (0.48-1.08)
	FR	1.33 (1.04-1.69) / 1.39 (1.10-1.76)	1.30 (1.06-1.61) / 1.35 (1.11-1.64)
Skin	DK	1.15 (0.91-1.44) / 1.05 (0.84-1.32)	0.98 (0.78-1.24) / 0.97 (0.77-1.22)
	FR	1.43 (1.13-1.83) / 1.40 (1.10-1.78)	1.37 (1.12-1.69) / 1.33 (1.09-1.62)
Head-Neck	DK	1.37 (0.78-2.38) / 1.37 (0.79-2.39)	1.19 (0.68-2.06) / 1.27 (0.73-2.20)
	FR	1.60 (1.10-2.34) / 1.70 (1.18-2.45)	1.62 (1.19-2.20) / 1.69 (1.25-2.28)
CNS	DK	1.52 (0.62-3.71) / 1.46 (0.60-3.56)	1.33 (0.54-3.28) / 1.35 (0.55-3.28)
	FR	2.98 (1.69-5.24) / 3.51 (2.05-6.02)	3.01 (1.89-4.79) / 3.57 (2.30-5.53)
Other	DK	1.88 (1.17-3.01) / 1.75 (1.09-2.80)	1.59 (0.99-2.55) / 1.61 (1.01-2.58)
	FR	1.24 (1.01-1.52) / 1.38 (1.14-1.67)	1.15 (0.96-1.38) / 1.28 (1.09-1.50)
HEMATOLOGICAL			
Overall	DK	7.41 (6.07-9.06) / 6.69 (5.48-8.17)	6.44 (5.25-7.90) / 6.21 (5.08-7.58)

	FR	8.98 (7.47-10.80) / 8.99 (7.53-10.73)	8.17 (6.99-9.54) / 8.17 (7.06-9.46)
	META	8.19 (6.79-9.89) / 7.78 (5.83-10.40) (pQ : 0.17 / 0.03)	7.32 (5.80-9.24) / 7.78 (5.50-9.40) (pQ : 0.07 / 0.03)
	DK 1980-1989	8.43 (2.88-24.67) / 7.80 (2.70-22.55)	NE
	DK 1990-1999	3.50 (1.70-7.20) / 3.14 (1.54-6.44)	NE
	DK 2000-2009	9.03 (6.89-11.86) / 8.03 (6.13-10.52)	NE
	DK 2010-2016	6.87 (4.86-9.71) / 6.38 (4.52-9.01)	NE
	Index date +6M	6.12 (4.90-7.63) / 5.46 (4.38-6.80)	NE
	Index date +12M	5.81 (4.62-7.30) / 5.18 (4.12-6.50)	NE
Age groups			
18-59 years	DK	11.27 (7.50-16.94) / 11.21 (7.49-16.78)	10.92 (7.16-16.64) / 10.92 (7.29-16.34)
	FR	28.13 (15.95-49.61) / 27.83 (16.16-47.91)	28.25 (15.81-50.49) / 28.01 (16.88-46.49)
	META	17.41 (7.11-42.63) / 17.33 (7.11-42.22) (pQ : 0.01 / 0.01)	17.18 (6.78-43.58) / 17.33 (6.86-43.44) (pQ : 0.01 / 0.00)
≥60 years	DK	6.45 (5.11-8.14) / 6.32 (5.02-7.97)	5.56 (4.39-7.04) / 5.46 (4.33-6.89)
	FR	7.31 (5.98-8.92) / 7.25 (5.99-8.77)	6.64 (5.64-7.81) / 6.58 (5.64-7.69)
	META	6.93 (5.96-8.07) / 6.86 (5.92-7.94) (pQ : 0.42 / 0.37)	6.21 (5.24-7.35) / 6.86 (5.12-7.31) (pQ : 0.23 / 0.19)
Sex			
Women	DK	8.03 (5.90-10.92) / 7.43 (5.47-10.09)	7.12 (5.21-9.71) / 6.99 (5.15-9.50)
	FR	11.13 (8.27-14.98) / 11.24 (8.49-14.88)	9.84 (7.64-12.67) / 9.91 (7.85-12.50)
	META	9.48 (6.88-13.05) / 9.18 (6.12-13.77) (pQ : 0.62 / 0.29)	6.72 (5.72-7.89) / 7.02 (5.30-7.99) (pQ : 0.32 / 0.20)
Men	DK	7.01 (5.38-9.13) / 6.32 (4.85-8.22)	6.02 (4.59-7.88) / 5.73 (4.40-7.47)
	FR	7.67 (6.04-9.74) / 7.63 (6.06-9.60)	7.13 (5.84-8.69) / 7.09 (5.86-8.57)
	META	7.37 (6.17-8.79) / 7.02 (5.85-8.44) (pQ : 0.13 / 0.05)	8.48 (6.18-11.63) / 9.18 (6.01-11.88) (pQ : 0.11 / 0.08)
Cancer subgroups			
Leukemia	DK	9.53 (6.94-13.10) / 8.65 (6.30-11.86)	8.20 (5.92-11.35) / 8.00 (5.83-10.98)
	FR	6.60 (4.50-9.68) / 6.49 (4.52-9.32)	6.44 (4.68-8.86) / 6.44 (4.79-8.67)
Lymphoma	DK	4.15 (2.52-6.82) / 3.80 (2.32-6.24)	3.57 (-.) / 3.50 (2.13-5.74)
	FR	9.73 (6.53-14.49) / 9.70 (6.69-14.06)	9.34 (6.57-13.28) / 9.34 (6.78-12.86)
Multiple myeloma	DK	0.47 (0.07-3.36) / 0.41 (0.06-2.97)	0.40 (0.06-2.89) / 0.38 (0.05-2.75)
	FR	3.57 (1.62-7.87) / 2.94 (1.42-6.08)	3.08 (1.67-5.65) / 2.51 (1.40-4.48)
Other	DK	12.35 (9.07-16.83) / 11.16 (8.21-15.17)	10.73 (7.84-14.67) / 10.34 (7.60-14.06)
	FR	10.18 (8.03-12.89) / 10.17 (8.10-12.79)	8.92 (7.32-10.87) / 8.96 (7.43-10.81)
		1-year	1-year
SOLID			
Overall	DK	1.69 (1.34-2.13) / 1.62 (1.28-2.13)	1.57 (1.24-1.98) / 1.57 (1.24-1.98)
	FR	1.82 (1.47-2.53) / 1.77 (1.45-2.18)	1.75 (1.47-2.09) / 1.70 (1.43-2.01)
Age groups			
18-59 years	DK	1.65 (0.97-2.82) / 1.63 (0.96-2.78)	1.63 (0.96-2.77) / 1.62 (0.95-2.77)
	FR	1.77 (1.05-2.98) / 1.72 (1.06-2.81)	1.77 (1.14-2.74) / 1.73 (1.14-2.62)
≥60 years	DK	1.68 (1.30-2.17) / 1.72 (1.33-2.22)	1.55 (1.20-2.01) / 1.61 (1.24-2.08)
	FR	1.88 (1.49-2.37) / 1.82 (1.46-2.29)	1.78 (1.47-2.16) / 1.72 (1.43-2.08)
Sex			
Women	DK	1.97 (1.44-2.69) / 1.86 (1.36-2.54)	1.86 (1.36-2.54) / 1.81 (1.33-2.48)
	FR	1.79 (1.29-2.47) / 1.73 (1.26-2.36)	1.77 (1.35-2.31) / 1.70 (1.31-2.19)
Men	DK	1.44 (1.02-2.04) / 1.39 (0.99-1.97)	1.32 (0.93-1.87) / 1.34 (0.95-1.90)
	FR	1.89 (1.43-2.51) / 1.81 (1.38-2.37)	1.77 (1.40-2.24) / 1.70 (1.35-2.13)
HEMATOLOGICAL			
Overall	DK	13.11 (9.32-18.44) / 12.18 (8.68-18.44)	12.29 (8.74-17.29) / 11.77 (8.38-17.29)
	FR	17.94 (12.93-24.88) / 17.23 (12.62-23.52)	17.77 (13.21-23.89) / 16.98 (12.80-22.53)
Age groups			
18-59 years	DK	29.18 (15.34-55.49) / 28.16 (14.88-53.31)	28.94 (15.08-55.52) / 27.95 (14.76-52.90)
	FR	75.40 (21.78-260.99) / 47.30 (18.88-118.51)	75.40 (25.37-224.06) / 47.30 (19.69-113.63)
≥60 years	DK	9.89 (6.52-15.02) / 9.51 (6.28-14.41)	9.15 (6.04-13.88) / 8.89 (5.86-13.47)
	FR	14.38 (10.12-20.45) / 13.88 (9.93-19.38)	14.24 (10.45-19.41) / 13.68 (10.15-18.44)
Sex			

Women	DK	18.39 (11.00-30.74) / 17.61 (10.58-29.32)	17.47 (10.44-29.22) / 17.13 (10.29-28.52)
	FR	29.46 (15.68-55.37) / 26.66 (15.20-46.75)	29.72 (16.51-53.50) / 26.93 (15.95-45.46)
Men	DK	10.34 (6.51-16.44) / 9.45 (5.96-15.01)	9.63 (6.06-15.32) / 9.06 (5.71-14.39)
	FR	13.82 (9.35-20.42) / 13.43 (9.20-19.61)	13.55 (9.56-19.20) / 13.09 (9.33-18.37)
		2-5 year	2-5 year
SOLID CANCERS			
Overall	DK	1.17 (1.00-1.36) / 1.06 (0.91-1.36)	1.11 (0.95-1.29) / 1.03 (0.88-1.29)
	FR	1.16 (1.00-1.35) / 1.21 (1.04-1.41)	1.14 (1.00-1.29) / 1.16 (1.02-1.31)
Age groups			
18-59 years	DK	1.44 (1.09-1.91) / 1.43 (1.08-1.90)	1.40 (1.06-1.86) / 1.41 (1.06-1.86)
	FR	1.60 (1.18-2.18) / 1.75 (1.31-2.34)	1.62 (1.26-2.09) / 1.77 (1.39-2.25)
≥60 years	DK	1.06 (0.89-1.28) / 1.07 (0.89-1.28)	1.00 (0.83-1.20) / 1.01 (0.84-1.21)
	FR	1.03 (0.86-1.24) / 1.07 (0.90-1.28)	1.01 (0.87-1.17) / 1.02 (0.88-1.17)
Sex			
Women	DK	1.24 (1.00-1.53) / 1.12 (0.91-1.38)	1.18 (0.95-1.45) / 1.09 (0.88-1.35)
	FR	1.24 (0.99-1.56) / 1.32 (1.06-1.64)	1.22 (1.00-1.48) / 1.27 (1.06-1.53)
Men	DK	1.11 (0.89-1.38) / 1.01 (0.81-1.25)	1.05 (0.84-1.31) / 0.97 (0.78-1.21)
	FR	1.10 (0.89-1.35) / 1.13 (0.93-1.38)	1.07 (0.90-1.27) / 1.08 (0.91-1.27)
HEMATOLOGICAL			
Overall	DK	5.84 (4.54-7.52) / 5.22 (4.06-7.52)	5.56 (4.31-7.19) / 5.06 (3.94-7.19)
	FR	5.79 (4.57-7.34) / 5.85 (4.68-7.30)	5.20 (4.29-6.30) / 5.27 (4.41-6.29)
Age groups			
18-59 years	DK	6.68 (3.78-11.80) / 6.66 (3.79-11.71)	6.52 (3.62-11.74) / 6.53 (3.71-11.47)
	FR	19.19 (9.00-40.90) / 18.31 (9.26-36.21)	19.34 (9.59-39.01) / 18.57 (10.01-34.43)
≥60 years	DK	5.56 (4.19-7.37) / 5.42 (4.10-7.18)	5.25 (3.95-6.99) / 5.12 (3.87-6.79)
	FR	4.88 (3.77-6.31) / 4.77 (3.75-6.07)	4.37 (3.57-5.36) / 4.31 (3.57-5.21)
Sex			
Women	DK	5.62 (3.76-8.38) / 5.13 (3.45-7.65)	5.43 (3.62-8.13) / 5.02 (3.37-7.48)
	FR	6.91 (4.84-9.88) / 7.09 (5.06-9.93)	6.00 (4.46-8.06) / 6.12 (4.67-8.01)
Men	DK	5.98 (4.32-8.28) / 5.37 (3.89-7.42)	5.66 (4.06-7.88) / 5.15 (3.72-7.11)
	FR	5.13 (3.72-7.08) / 4.99 (3.71-6.72)	4.74 (3.66-6.13) / 4.66 (3.68-5.89)

Supplementary table S7. Risk of cancer in patients with primary ITP compared with age-sex matched general population comparators. Estimates are presented as Cox cause-specific hazard ratios (csHR) and Fine-Gray subdistribution hazard ratios (subHR), the latter taking death and emigration into account as competing events. Both adjusted (left) and crude (right) estimates are provided. Time-split estimates are only provided for the larger groups due to few events in the remaining subgroups. Combined meta-analysis results were estimated using a random effects model with two-decimal precision.

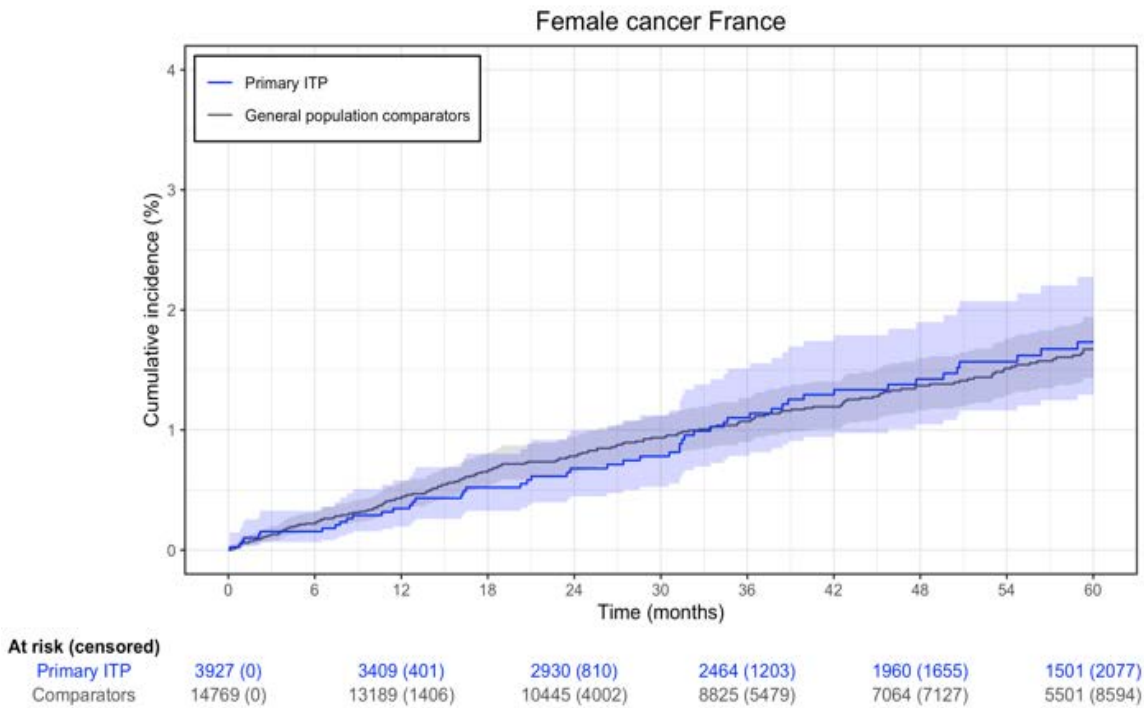
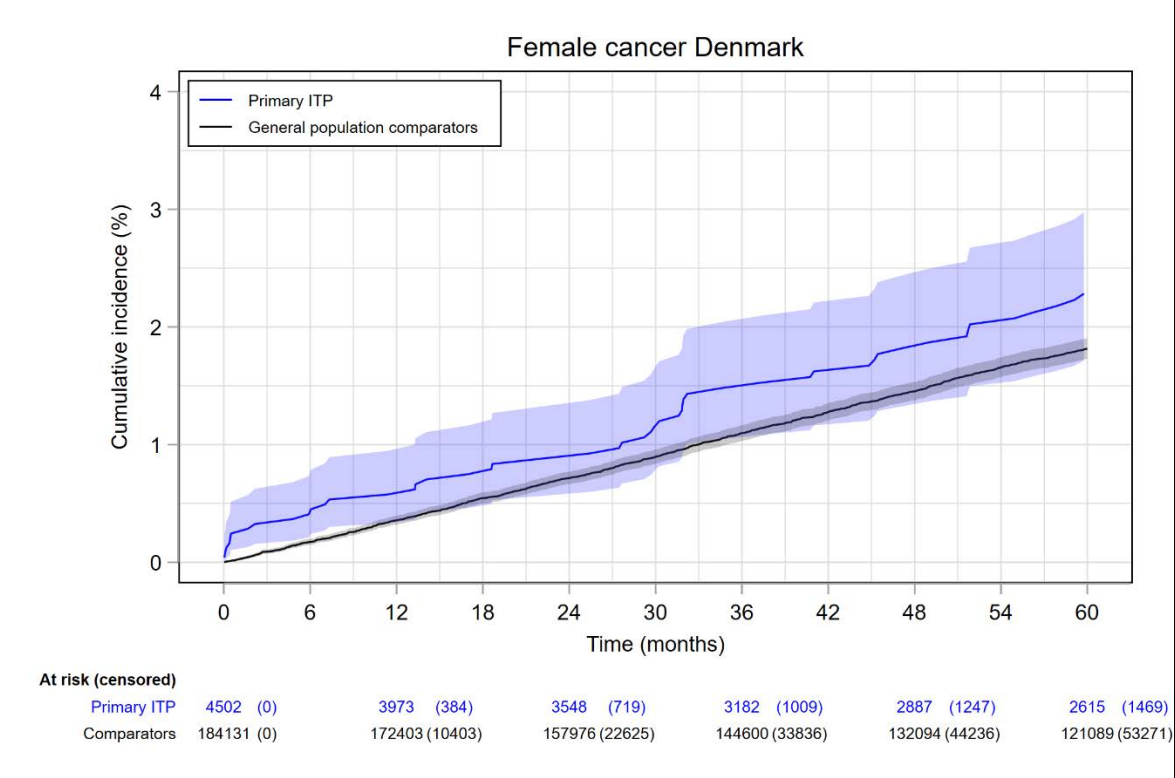
Abbreviations: CI: confidence interval; ITP: immune thrombocytopenia; NE: not estimated; FU +6/12M: follow-up and incidence analyses starting at index date +6 and +12 months respectively

Supplementary table S8. Sensitivity analysis with adjusted and unadjusted five-year Cox cause-specific estimates of risk of solid and hematological cancers in primary ITP in Denmark and France

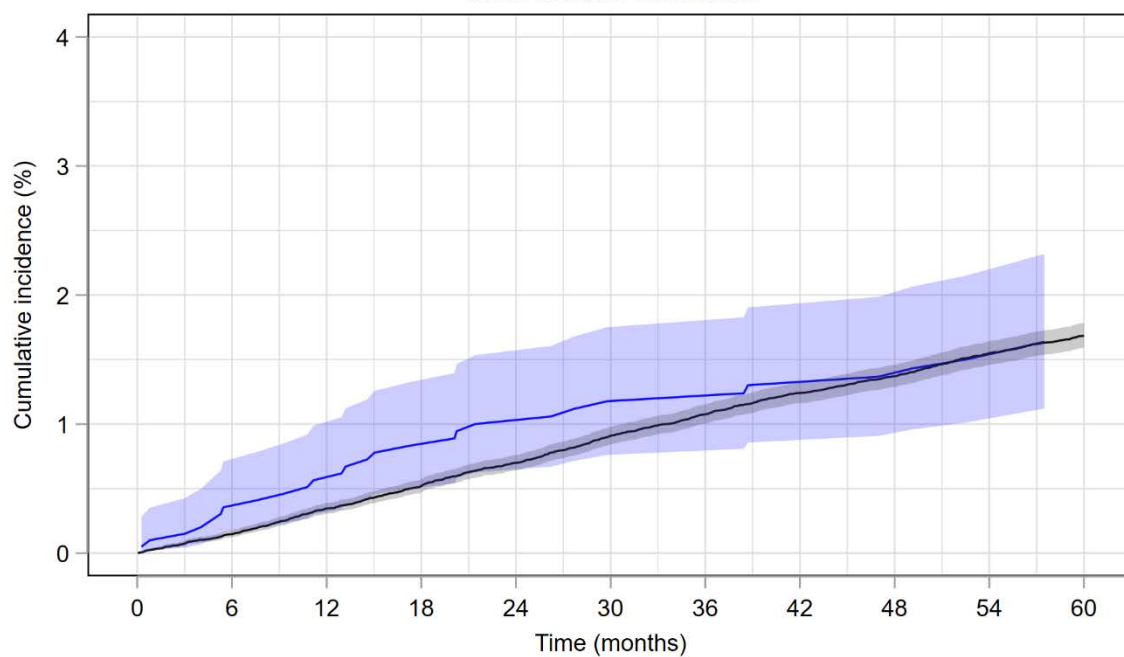
Cancer category	Country	Primary ITP SENSITIVITY	PRIMARY ITP MAIN
SOLID			
Female	DK	1.43 [1.08-1.91] / 1.37 [1.03-1.82]	1.41 [1.07-1.87] / 1.35 [1.02-1.79]
	FR	1.07 [0.75-1.52] / 1.01 [0.72-1.41]	1.05 [0.75-1.47] / 1.05 [0.76-1.45]
Male	DK	1.16 [0.78-1.73] / 1.03 [0.69-1.53]	1.24 [0.86-1.80] / 1.12 [0.77-1.61]
	FR	1.00 [0.69-1.45] / 0.90 [0.63-1.29]	1.08 [0.78-1.49] / 1.00 [0.73-1.38]
Thorax	DK	1.37 [0.97-1.96] / 1.31 [0.92-1.86]	1.58 [1.15-2.18] / 1.50 [1.09-2.07]
	FR	1.29 [0.88-1.89] / 1.30 [0.91-1.88]	1.18 [0.86-1.62] / 1.27 [0.94-1.72]
Urological	DK	1.42 [0.91-2.21] / 1.30 [0.84-2.03]	1.30 [0.83-2.03] / 1.21 [0.77-1.88]
	FR	1.47 [1.01-2.13] / 1.52 [1.05-2.19]	1.28 [0.92-1.78] / 1.33 [0.97-1.84]
Upper GI	DK	1.88 [1.28-2.74] / 1.78 [1.22-2.60]	2.01 [1.41-2.87] / 1.93 [1.35-2.75]
	FR	1.09 [0.72-1.66] / 1.76 [1.24-2.51]	1.25 [0.89-1.77] / 1.77 [1.31-2.40]
Colorectal	DK	0.86 [0.57-1.32] / 0.76 [0.50-1.16]	0.88 [0.59-1.32] / 0.78 [0.52-1.18]
	FR	1.34 [1.01-1.78] / 1.39 [1.06-1.82]	1.33 [1.04-1.69] / 1.39 [1.10-1.76]
Skin	DK	1.17 [0.93-1.47] / 1.06 [0.84-1.33]	1.15 [0.91-1.44] / 1.05 [0.84-1.32]
	FR	1.53 [1.15-2.03] / 1.44 [1.10-1.90]	1.43 [1.13-1.83] / 1.40 [1.10-1.78]
Head-Neck	DK	1.42 [0.81-2.47] / 1.43 [0.83-2.49]	1.37 [0.78-2.38] / 1.37 [0.79-2.39]
	FR	1.48 [0.96-2.27] / 1.57 [1.04-2.38]	1.60 [1.10-2.34] / 1.70 [1.18-2.45]
CNS	DK	1.63 [0.67-3.98] / 1.56 [0.64-3.80]	1.52 [0.62-3.71] / 1.46 [0.60-3.56]
	FR	3.29 [1.66-6.53] / 3.38 [1.75-6.55]	2.98 [1.69-5.24] / 3.51 [2.05-6.02]
Other solid	DK	1.83 [1.11-3.02] / 1.69 [1.03-2.79]	1.88 [1.17-3.01] / 1.75 [1.09-2.80]
	FR	1.13 [0.87-1.47] / 1.17 [0.90-1.51]	1.24 [1.01-1.52] / 1.38 [1.14-1.67]
HEMATOLOGICAL			
Leukemia	DK	10.32 [7.49-14.21] / 9.34 [6.80-12.83]	9.53 [6.94-13.10] / 8.65 [6.30-11.86]
	FR	5.29 [3.44-8.15] / 5.15 [3.44-7.71]	6.60 [4.50-9.68] / 6.49 [4.52-9.32]
Lymphoma	DK	4.41 [2.68-7.26] / 4.05 [2.46-6.65]	4.15 [2.52-6.82] / 3.80 [2.32-6.24]
	FR	13.62 [8.28-22.41] / 14.35 [8.88-23.19]	9.73 [6.53-14.49] / 9.70 [6.69-14.06]
Myeloma	DK	0.51 [0.07-3.63] / 0.45 [0.06-3.19]	0.47 [0.07-3.36] / 0.41 [0.06-2.97]
	FR	4.38 [1.87-10.25] / 4.07 [1.81-9.16]	3.57 [1.62-7.87] / 2.94 [1.42-6.08]
Other hematological	DK	13.03 [9.53-17.83] / 11.70 [8.57-15.98]	12.35 [9.07-16.83] / 11.16 [8.21-15.17]
	FR	13.32 [9.85-18.01] / 12.70 [9.55-16.89]	10.18 [8.03-12.89] / 10.17 [8.10-12.79]

Supplementary table S8. Sensitivity analysis with five-year Cox cause-specific hazard ratios estimated *after exclusion of all patients and comparators with a prevalent solid cancer <5 year before diagnosis of ITP* (left column). We present corresponding estimates from the text main model analysis in the right column for comparison.
Abbreviations: ITP: immune thrombocytopenia; GI = gastrointestinal

Supplementary figures S1. Five-year cumulative incidences of solidsubgroup cancers in primary ITP and general population comparators in Denmark (top) and France (bottom)



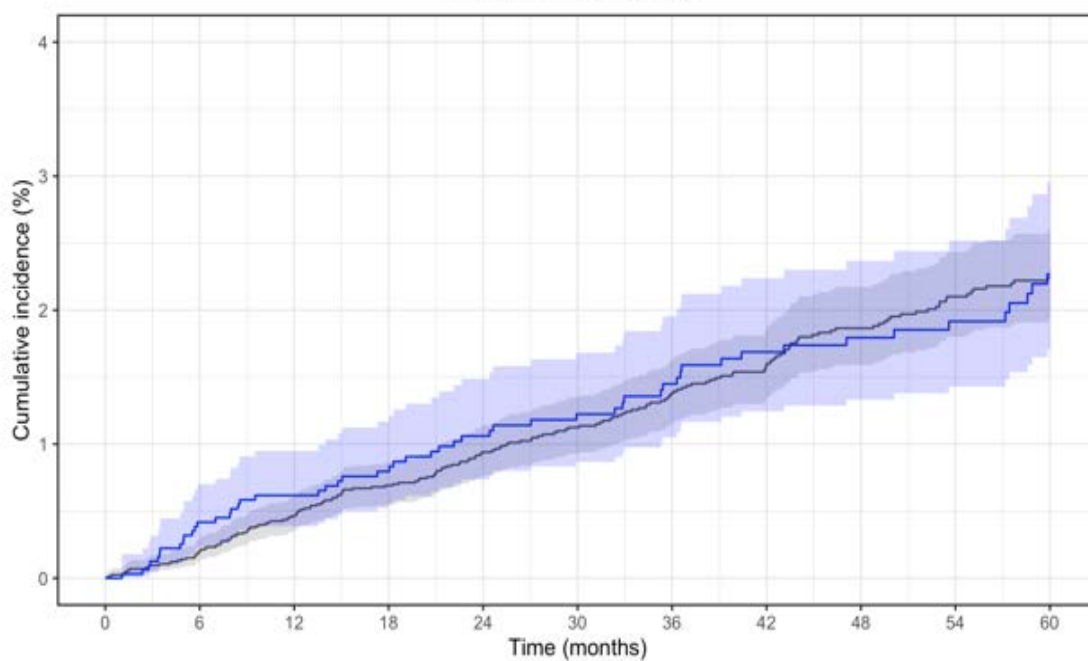
Male cancer Denmark



At risk (censored)

Primary ITP	4611 (0)	4082 (360)	3642 (696)	3274 (977)	2968 (1231)	2687 (1453)
Comparators	187076 (0)	175328 (10376)	160832 (22521)	147403 (33726)	134814 (44337)	123727 (53519)

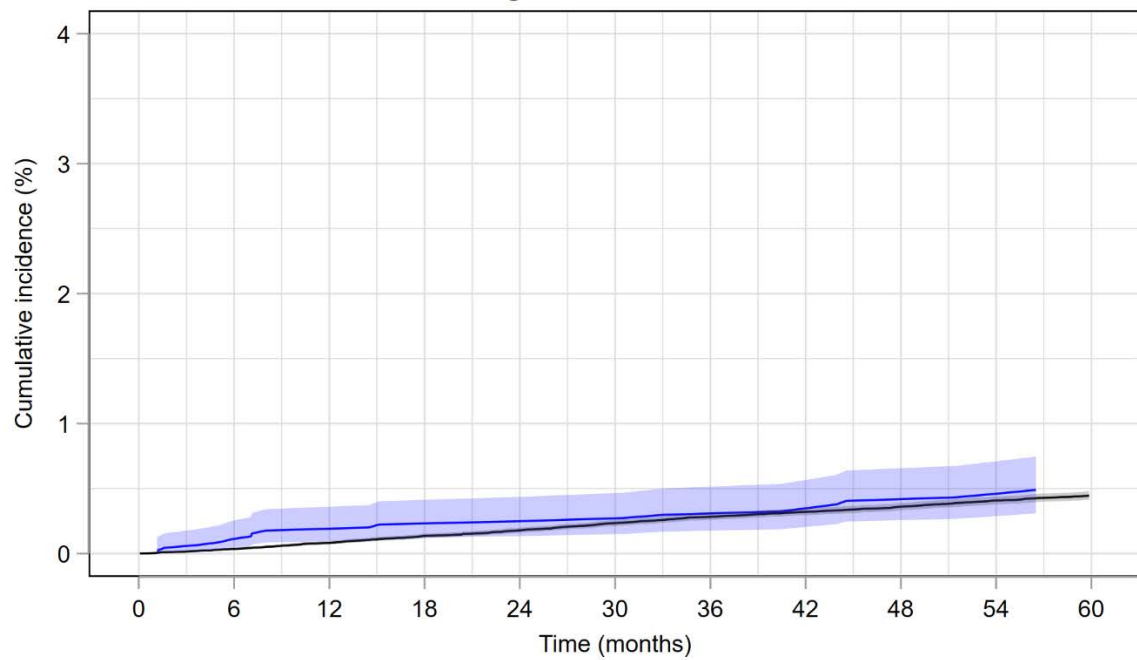
Male cancer France



At risk (censored)

Primary ITP	3213 (0)	2691 (328)	2278 (649)	1851 (976)	1463 (1295)	1086 (1617)
Comparators	11533 (0)	10221 (1121)	8065 (3056)	6719 (4264)	5409 (5414)	4064 (6651)

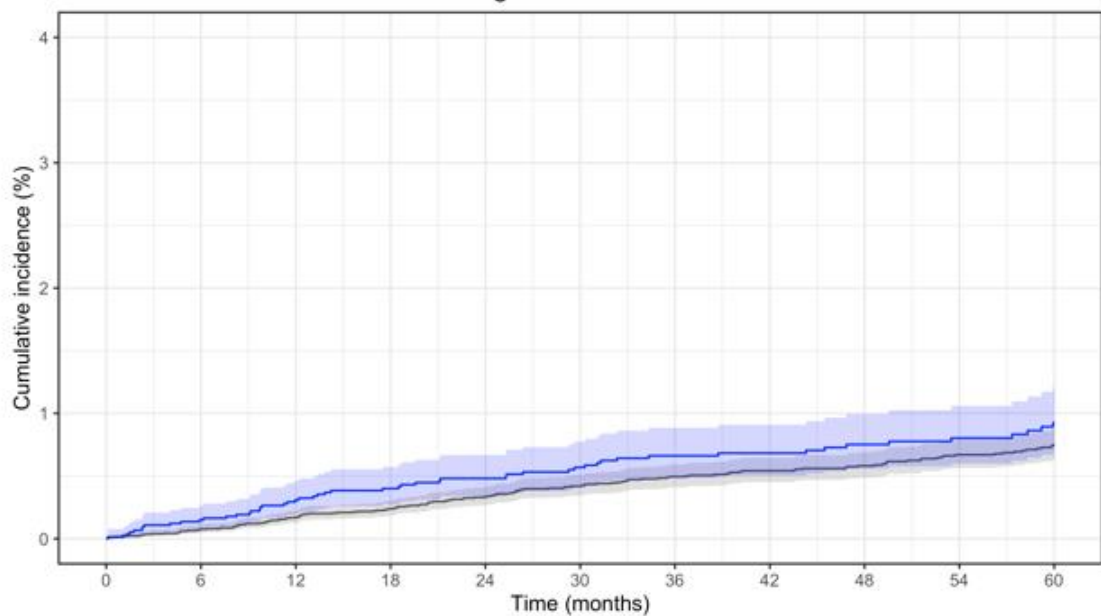
Urological cancer Denmark



At risk (censored)

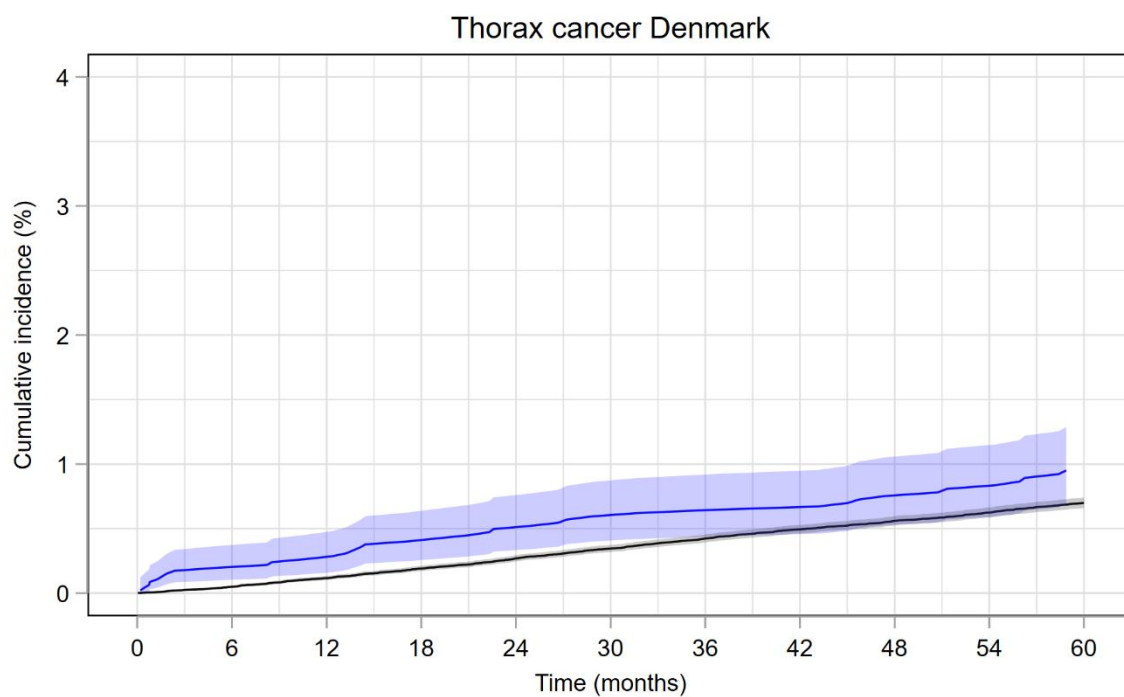
Primary ITP	4609 (0)	4081 (520)	3652 (946)	3284 (1312)	2978 (1614)	2697 (1892)
Comparators	187523 (0)	175779 (11594)	161257 (25949)	147813 (39223)	135167 (51750)	124045 (62747)

Urological cancer France



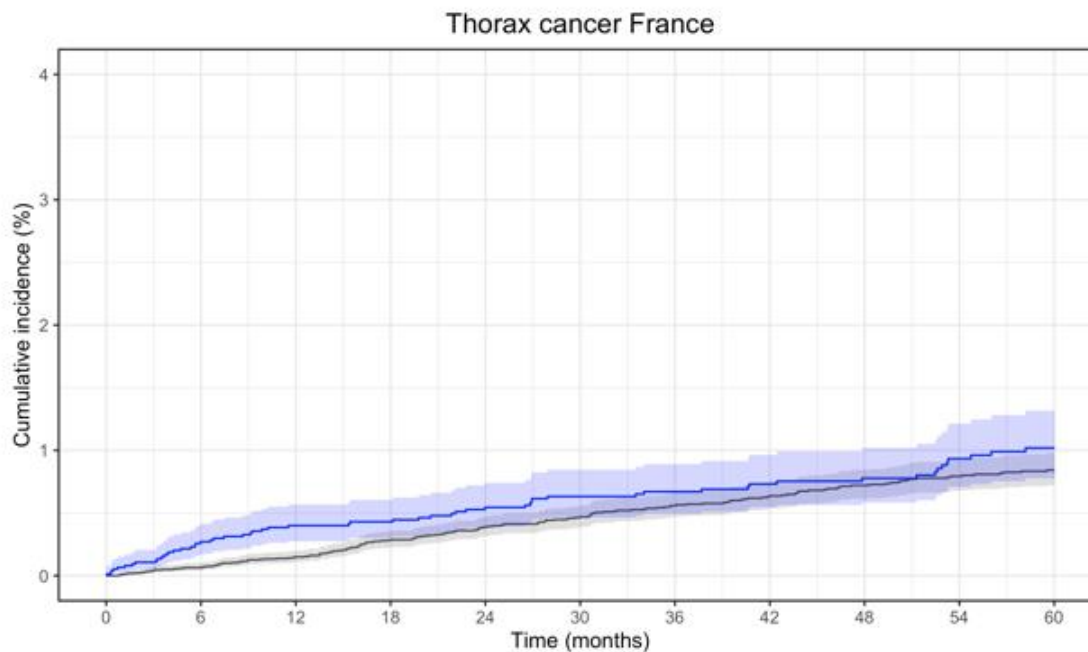
At risk (censored)

Primary ITP	7507 (0)	6397 (767)	5450 (1539)	4509 (2305)	3579 (3116)	2695 (3908)
Comparators	28463 (0)	25368 (2739)	20012 (7707)	16770 (10636)	13477 (13667)	10267 (16655)



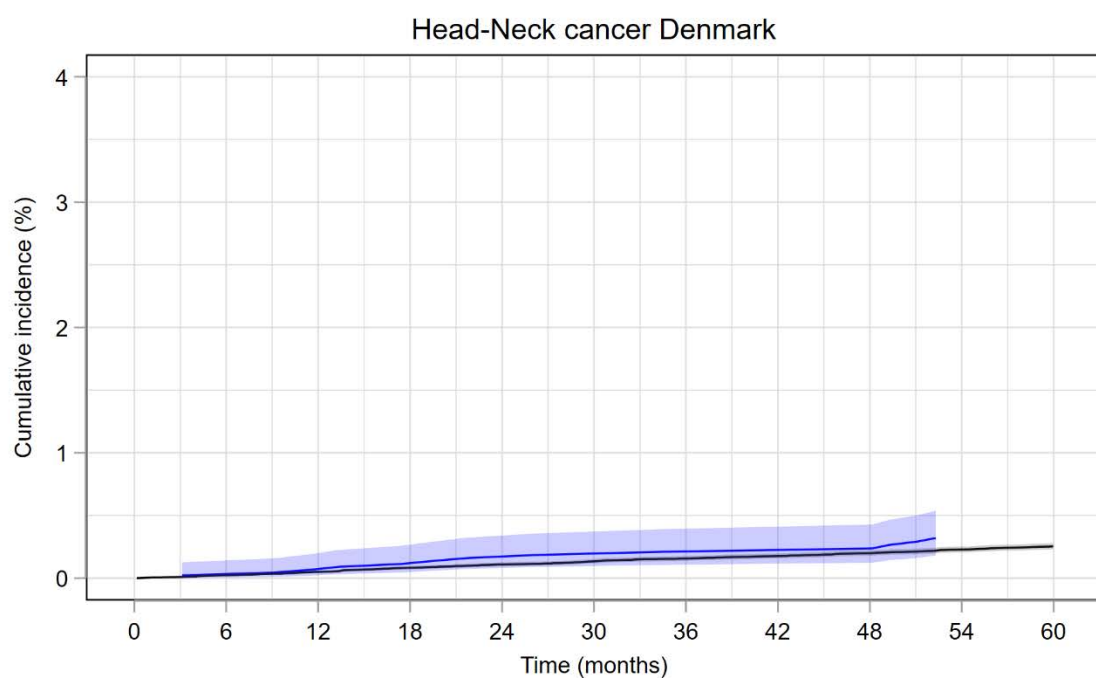
At risk (censored)

Primary ITP	4621 (0)	4100 (509)	3661 (938)	3298 (1296)	2987 (1602)	2702 (1880)
Comparators	188450 (0)	176644 (11592)	162047 (25923)	148525 (39193)	135833 (51673)	124622 (62680)



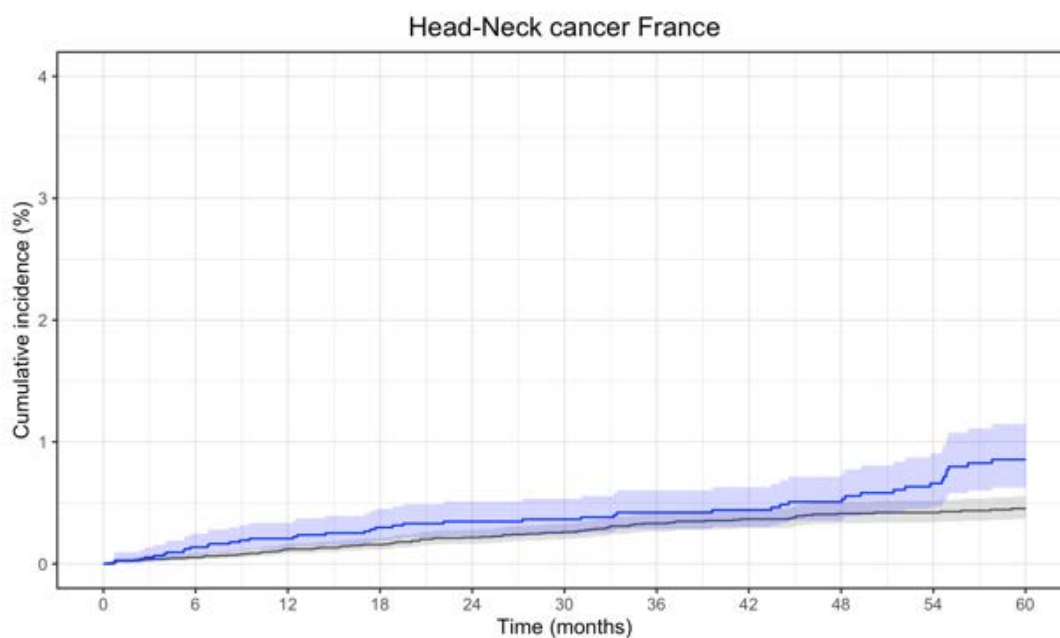
At risk (censored)

Primary ITP	7548 (0)	6428 (772)	5481 (1548)	4546 (2312)	3619 (3117)	2722 (3920)
Comparators	28671 (0)	25570 (2760)	20150 (7774)	16911 (10711)	13619 (13733)	10392 (16739)



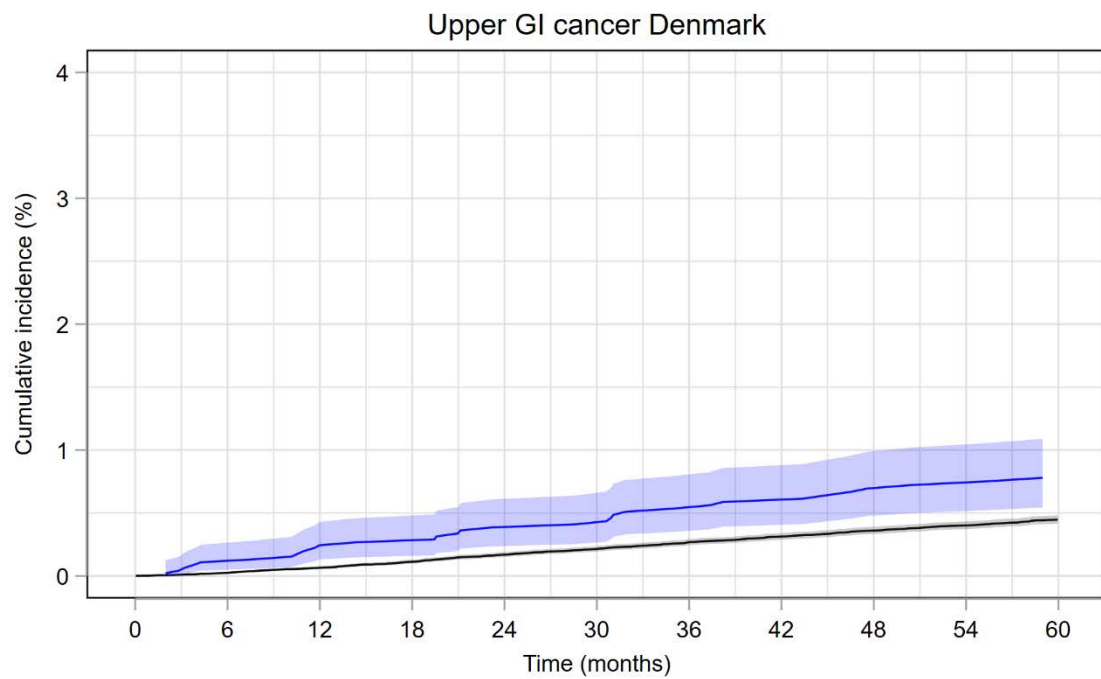
At risk (censored)

Primary ITP	4635 (0)	4103 (529)	3662 (966)	3294 (1332)	2986 (1640)	2704 (1918)
Comparators	188112 (0)	176366 (11656)	161799 (26120)	148298 (39541)	135605 (52170)	124414 (63281)



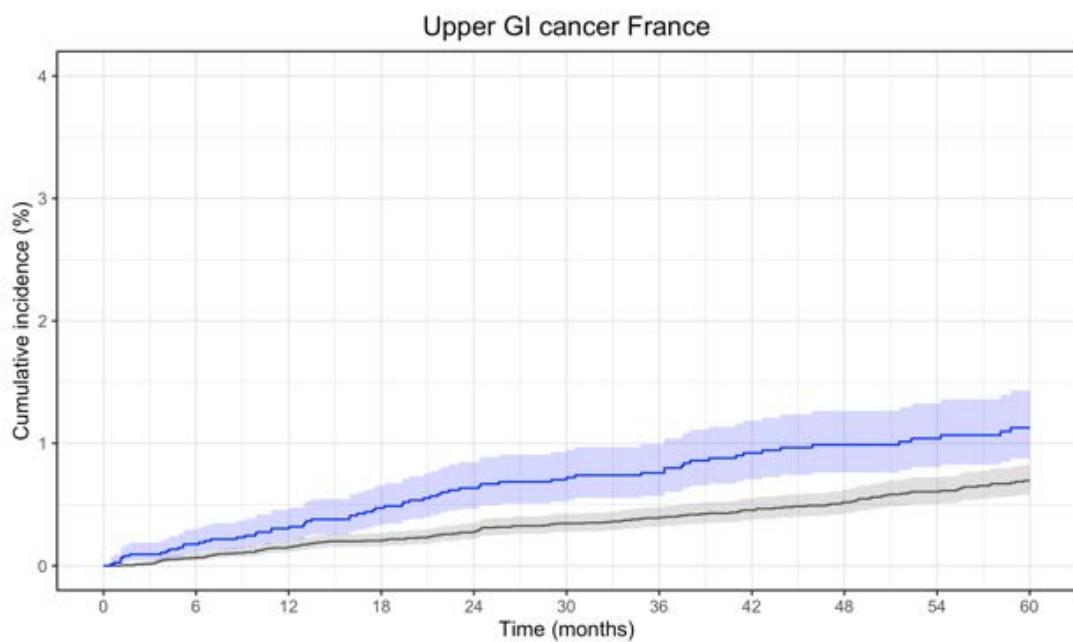
At risk (censored)

Primary ITP	7542 (0)	6421 (773)	5467 (1552)	4525 (2317)	3595 (3128)	2705 (3920)
Comparators	28584 (0)	25452 (2770)	20051 (7783)	16825 (10710)	13510 (13759)	10307 (16738)



At risk (censored)

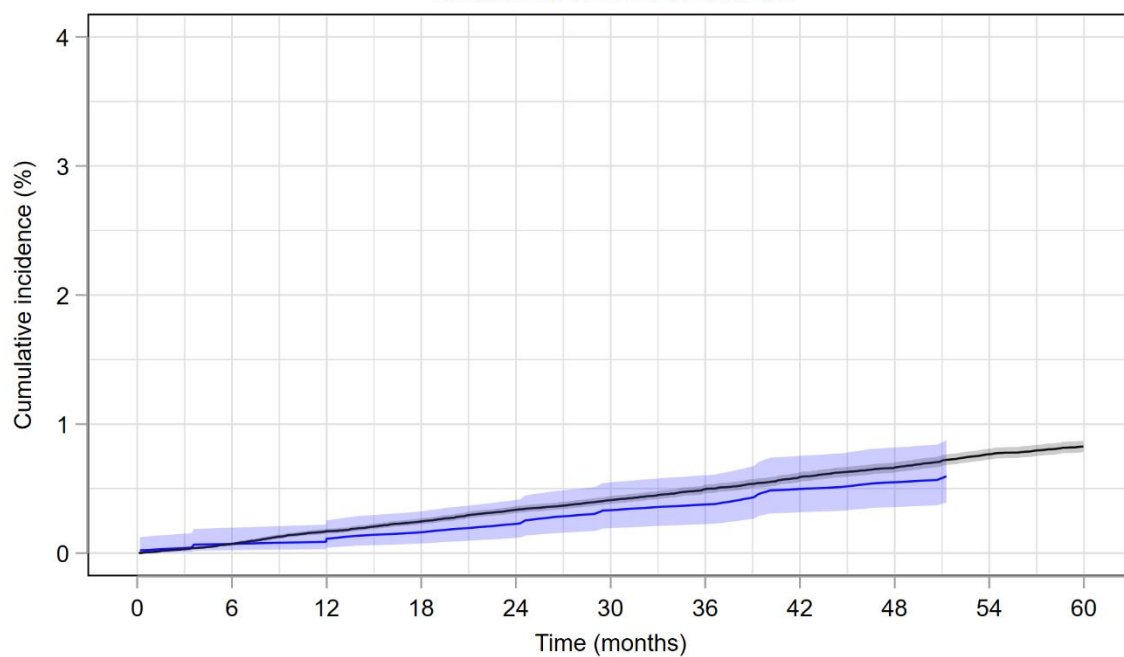
Primary ITP	4634 (0)	4103 (520)	3671 (946)	3298 (1313)	2985 (1620)	2708 (1894)
Comparators	188628 (0)	176835 (11674)	162206 (26120)	148678 (39487)	135956 (52066)	124749 (63144)



At risk (censored)

Primary ITP	7557 (0)	6443 (774)	5490 (1553)	4552 (2323)	3612 (3140)	2720 (3941)
Comparators	28759 (0)	25631 (2774)	20231 (7789)	16984 (10739)	13644 (13813)	10401 (16828)

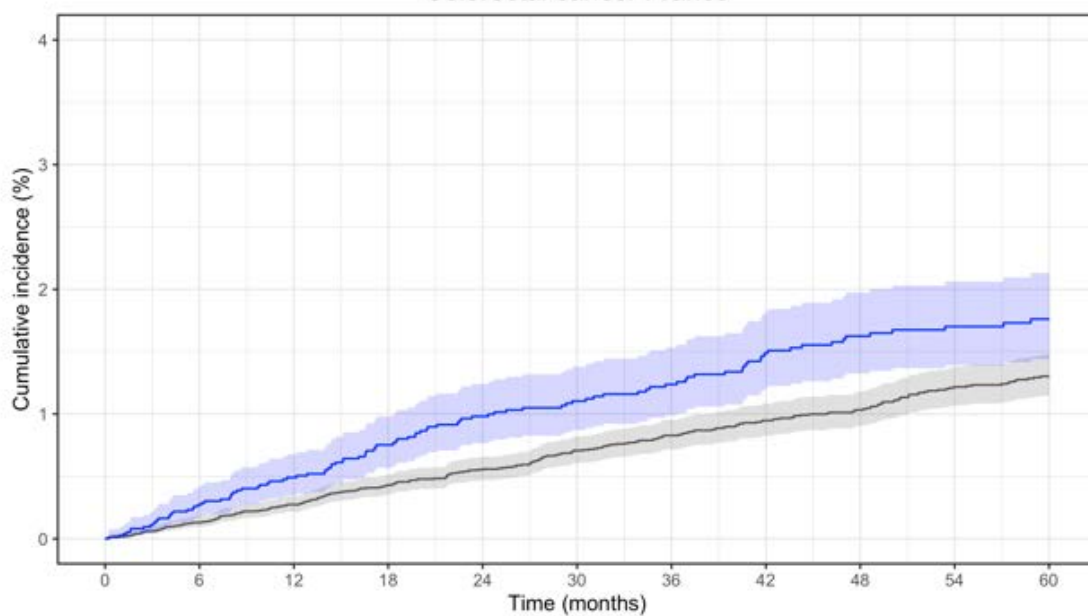
Colorectal cancer Denmark



At risk (censored)

Primary ITP	4593 (0)	4070 (518)	3634 (950)	3266 (1312)	2958 (1613)	2681 (1888)
Comparators	187065 (0)	175260 (11495)	160767 (25700)	147331 (38878)	134681 (51272)	123589 (62124)

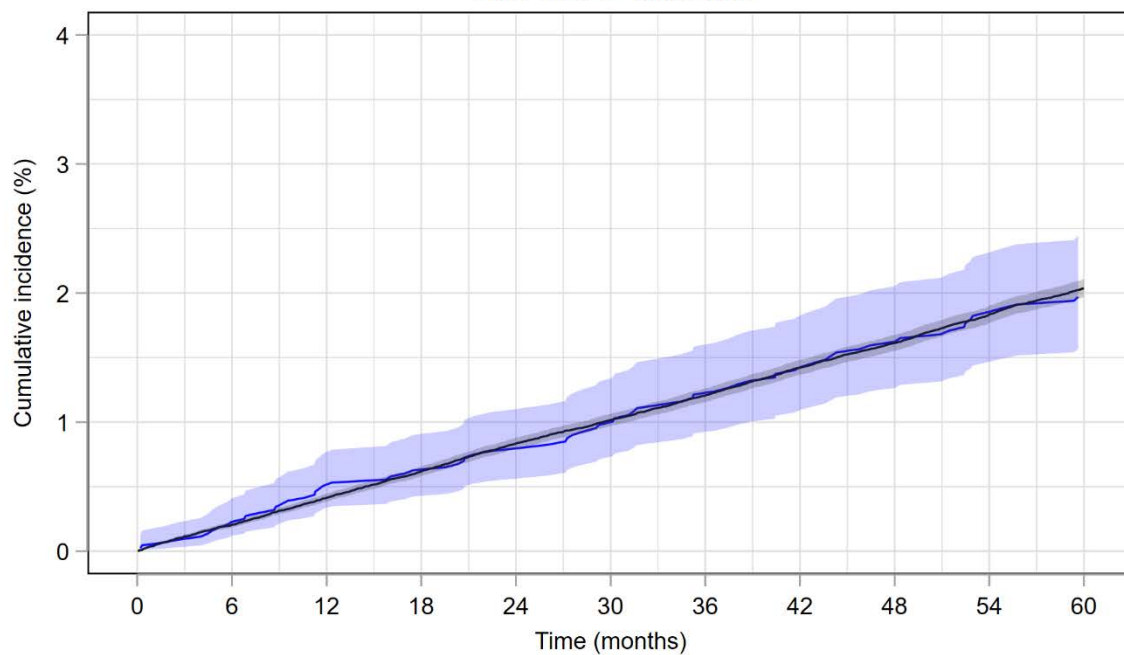
Colorectal cancer France



At risk (censored)

Primary ITP	7472 (0)	6361 (754)	5408 (1520)	4475 (2271)	3548 (3073)	2674 (3859)
Comparators	28151 (0)	25083 (2695)	19782 (7585)	16607 (10440)	13347 (13426)	10166 (16380)

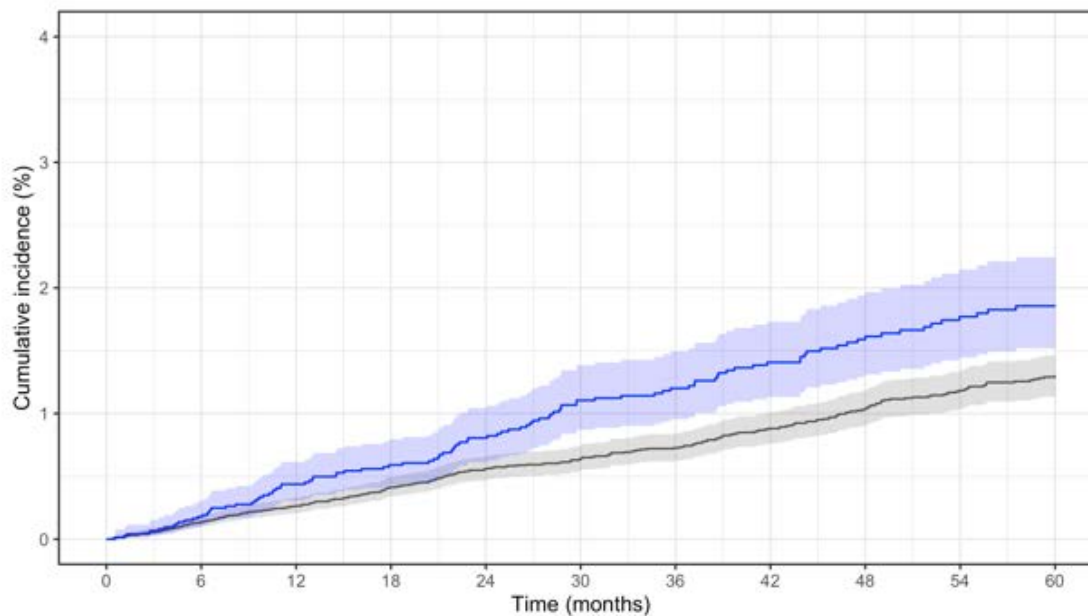
Skin cancer Denmark



At risk (censored)

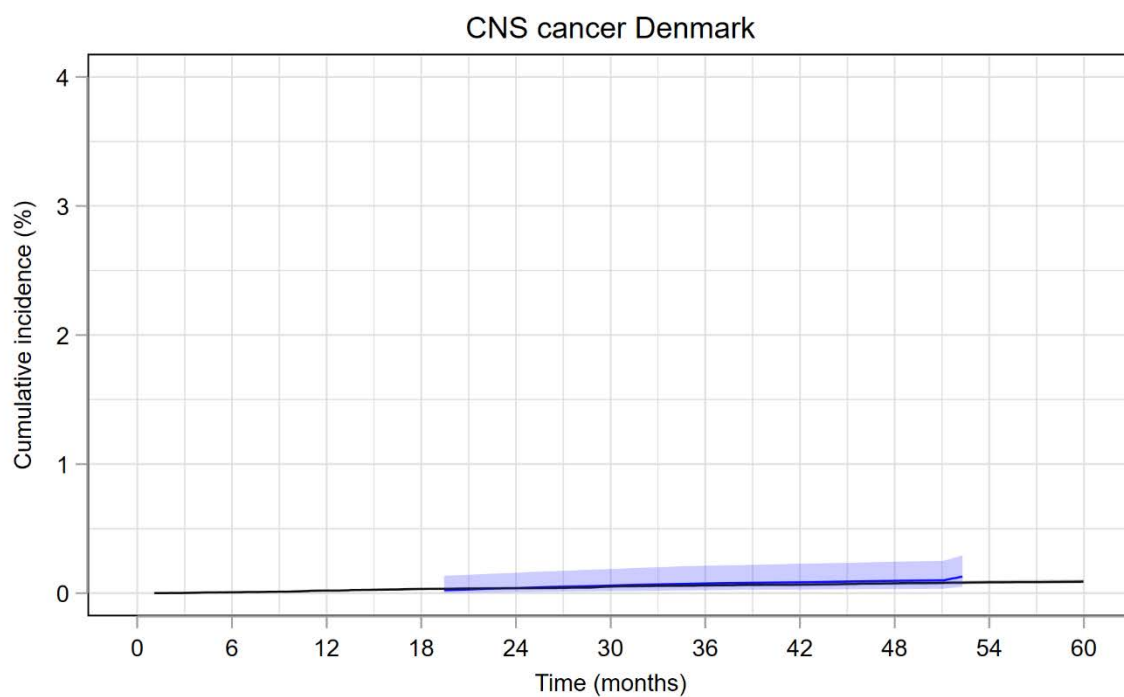
Primary ITP	4456 (0)	3939 (495)	3512 (911)	3160 (1246)	2860 (1532)	2590 (1789)
Comparators	181918 (0)	170184 (10998)	155864 (24611)	142767 (37117)	130403 (48870)	119574 (59097)

Skin cancer France



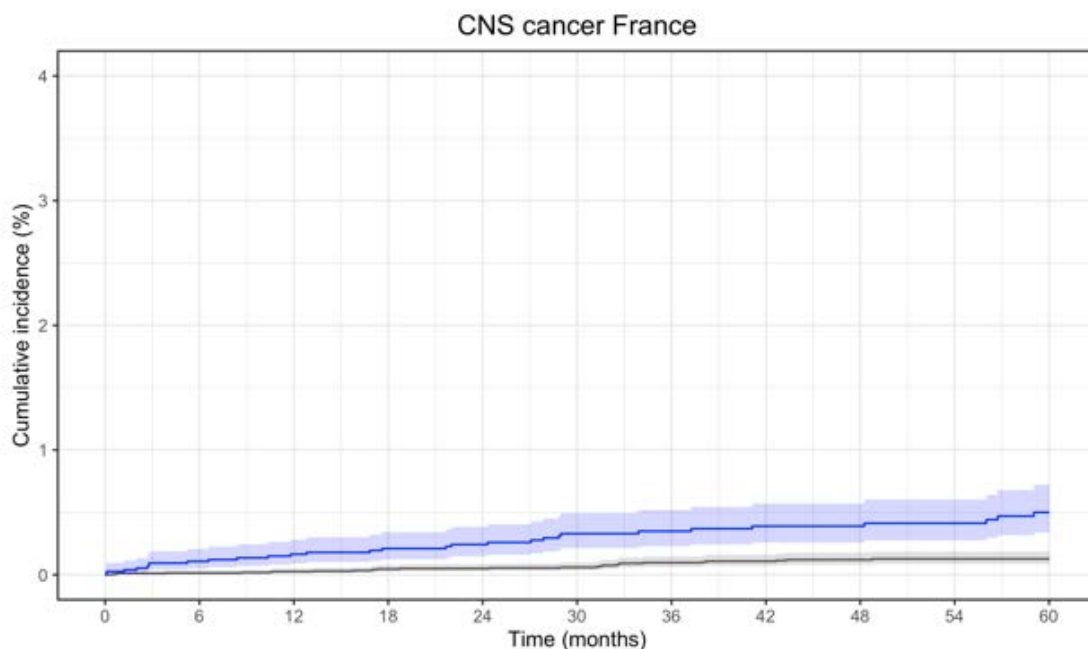
At risk (censored)

Primary ITP	7500 (0)	6382 (767)	5426 (1541)	4477 (2302)	3550 (3100)	2676 (3888)
Comparators	28423 (0)	25306 (2737)	19933 (7692)	16716 (10600)	13419 (13608)	10225 (16570)



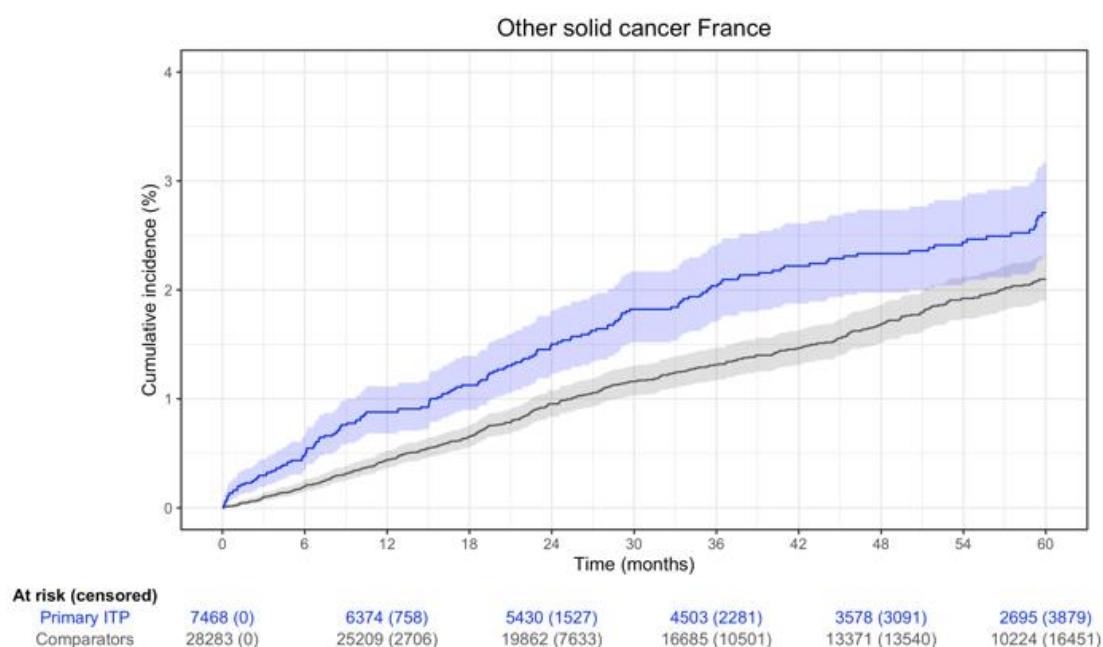
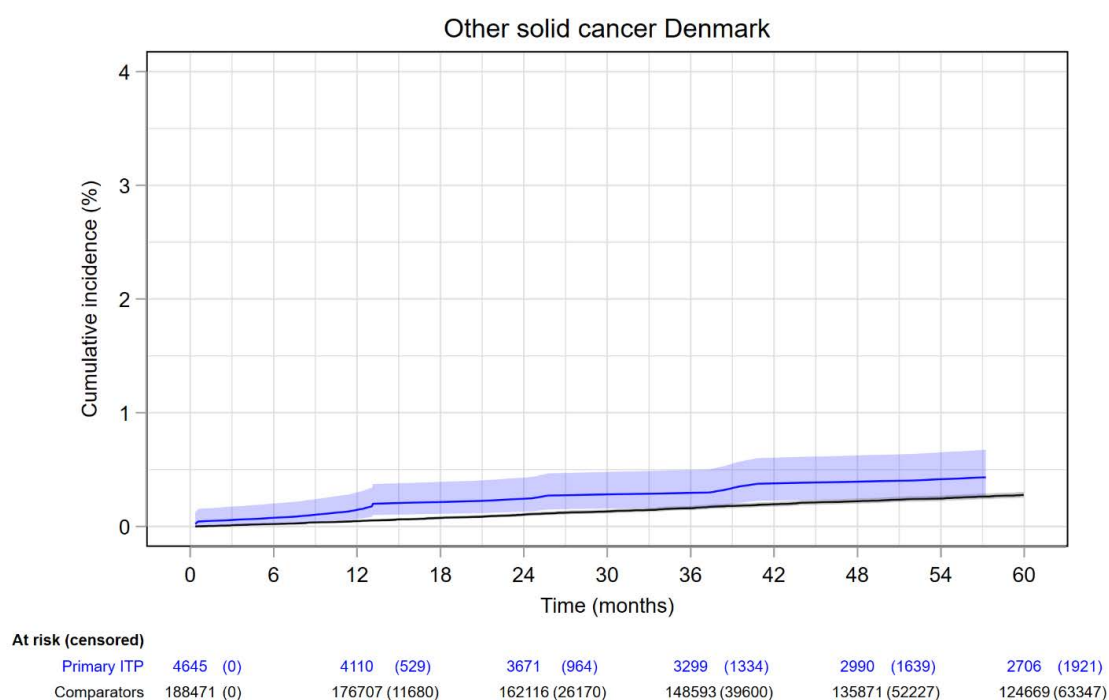
At risk (censored)

Primary ITP	4648 (0)	4116 (532)	3676 (971)	3303 (1342)	2994 (1651)	2711 (1932)
Comparators	188707 (0)	176944 (11727)	162340 (26297)	148790 (39812)	136048 (52530)	124828 (63728)



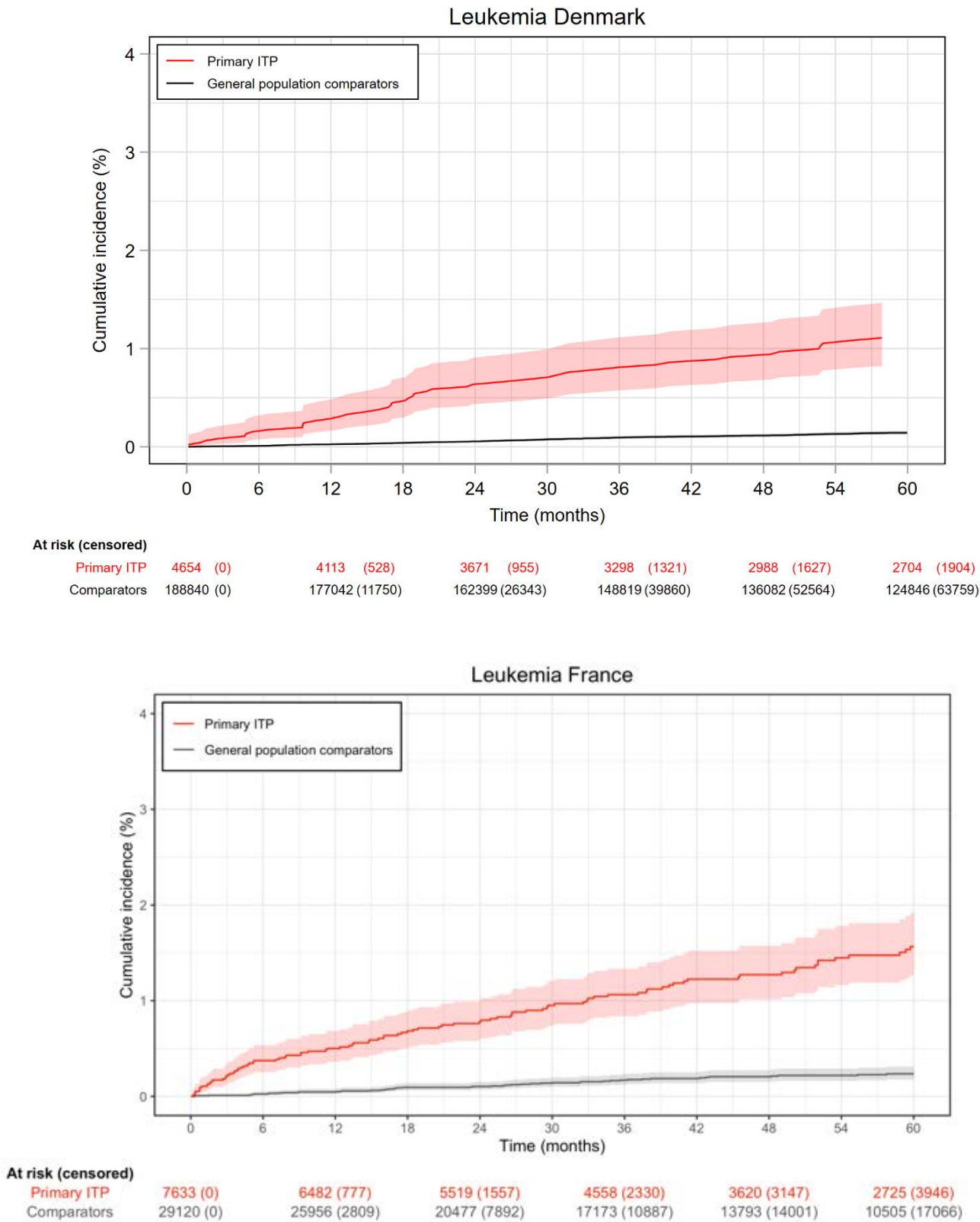
At risk (censored)

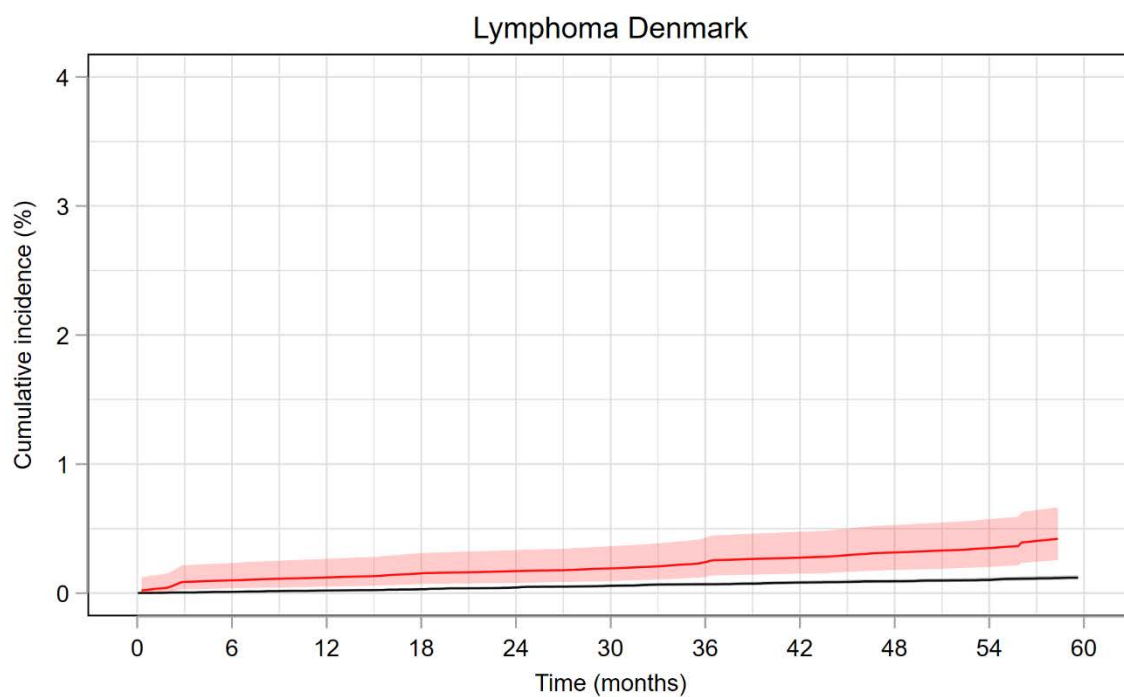
Primary ITP	7592 (0)	6465 (779)	5509 (1561)	4565 (2328)	3629 (3147)	2736 (3947)
Comparators	28938 (0)	25792 (2803)	20359 (7854)	17087 (10824)	13725 (13920)	10465 (16959)



Supplementary figure S1. Five-year cumulative incidences of subgroups of solid cancers in primary ITP and general population comparators in Denmark and France. Blue lines represent patients with ITP and grey lines represent comparators. Each page represent a specific subgroup of solid cancer as stated in the title of each graph, with the top graph on each page representing Danish estimates, and the bottom graph representing French estimates. Please also refer to the Methods section for details on the grouping of investigated cancers. We found an increased incidence of female, thorax, and upper GI cancer in patients with ITP compared to the general population in Denmark, while the incidence of colorectal, skin and CNS cancer was increased in France. Abbreviations: ITP: immune thrombocytopenia

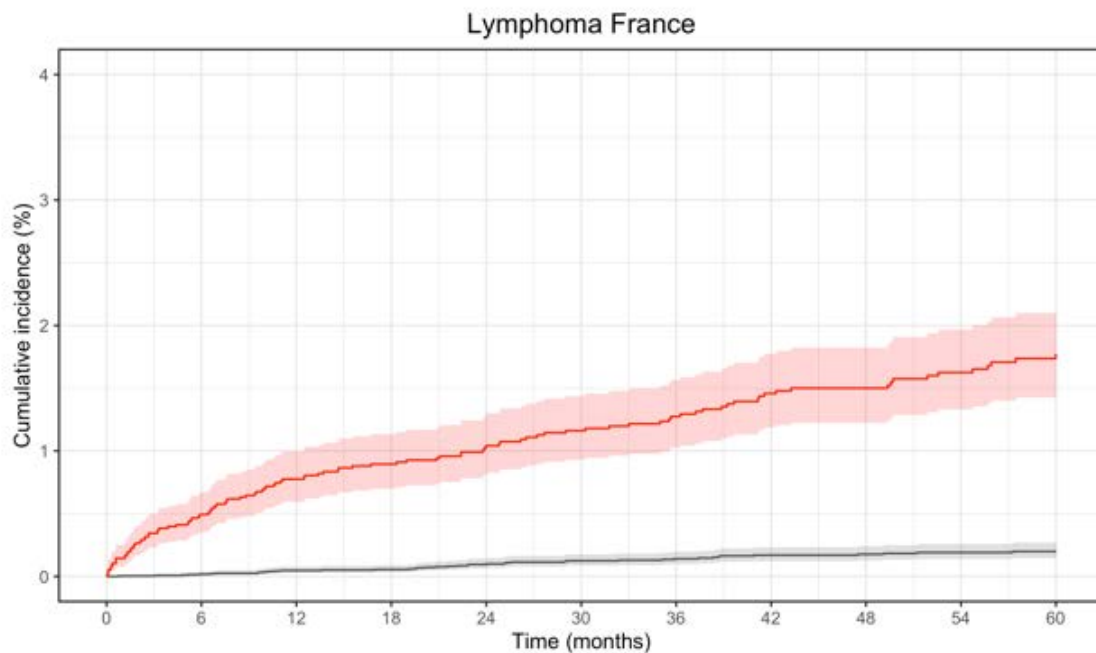
Supplementary figures S2. Five-year cumulative incidences of hematological subgroup cancers in primary ITP and general population comparators in Denmark (top) and France (bottom)





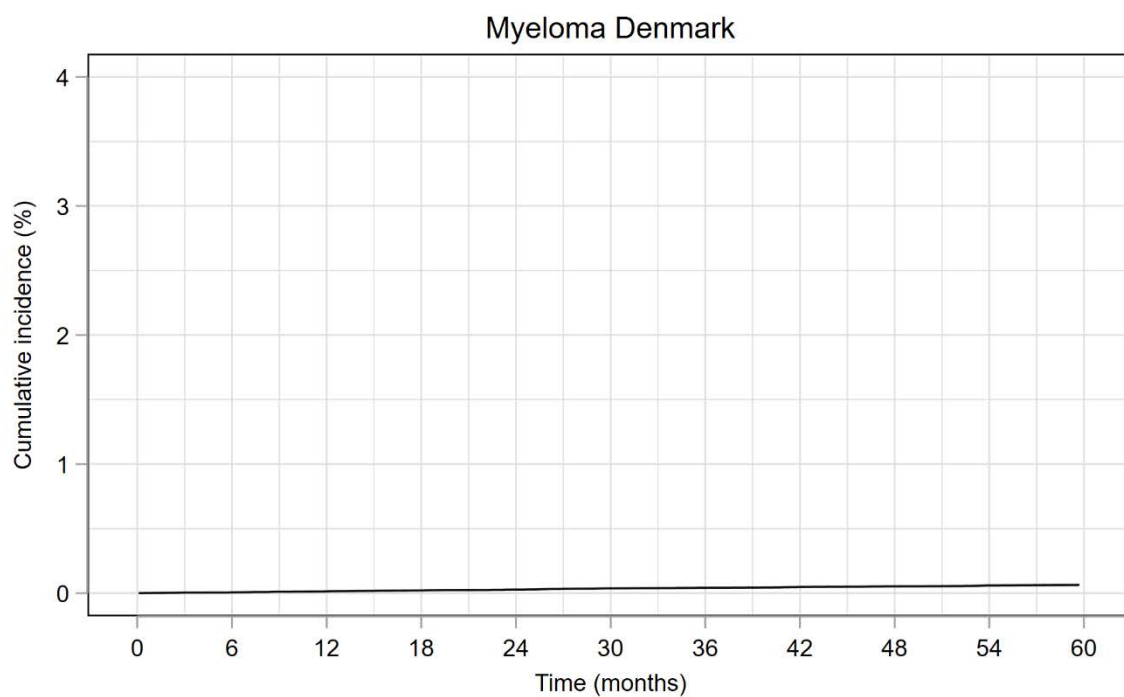
At risk (censored)

Primary ITP	4654 (0)	4115 (534)	3674 (973)	3300 (1344)	2991 (1650)	2704 (1933)
Comparators	188840 (0)	177045 (11757)	162409 (26352)	148837 (39883)	136079 (52606)	124843 (63799)



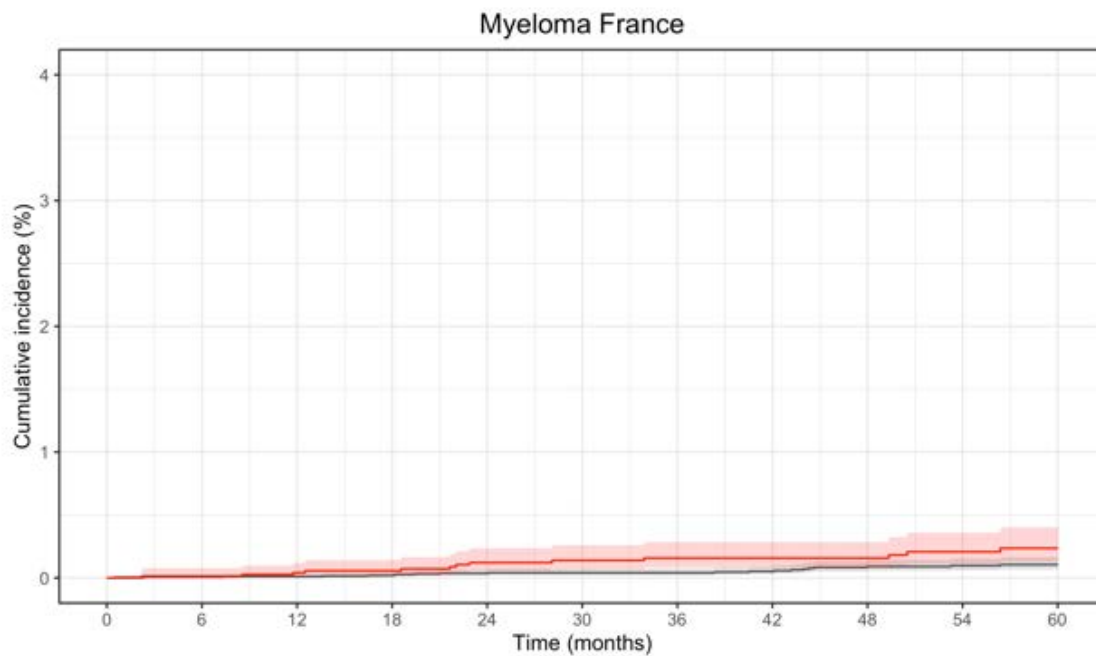
At risk (censored)

Primary ITP	7633 (0)	6457 (780)	5495 (1557)	4536 (2328)	3598 (3140)	2704 (3938)
Comparators	29120 (0)	25953 (2811)	20477 (7895)	17177 (10887)	13795 (14000)	10511 (17063)



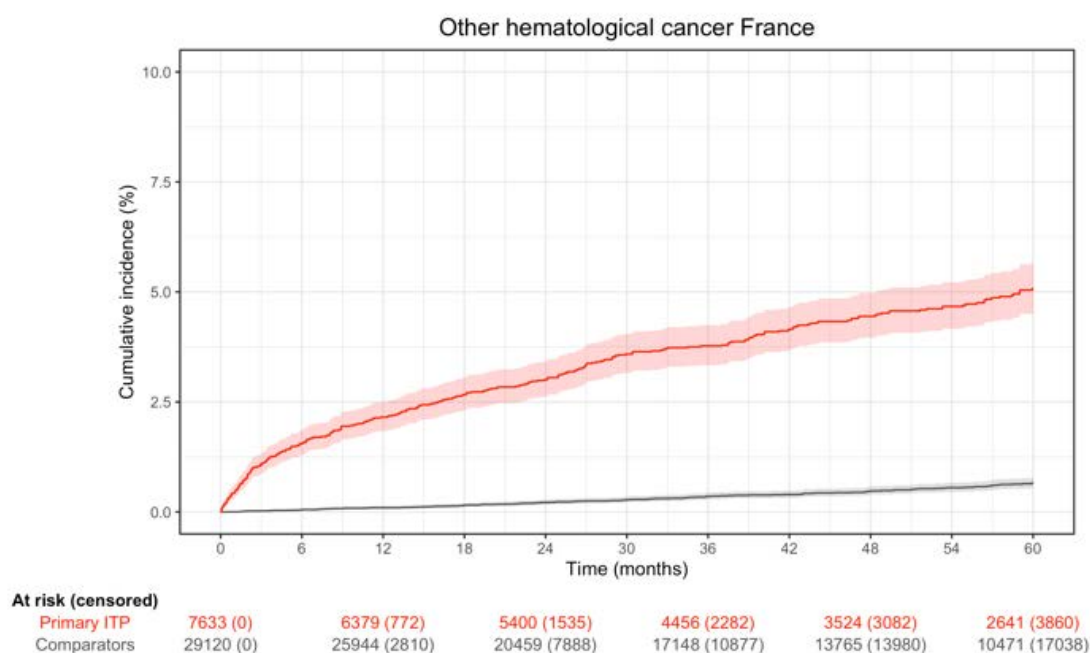
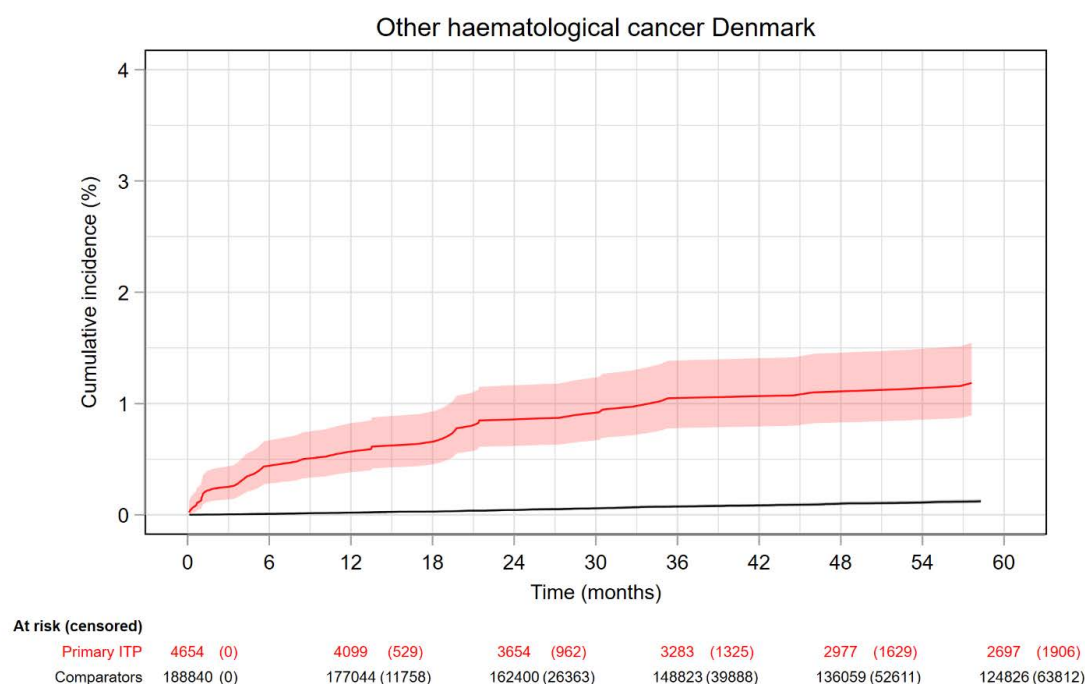
At risk (censored)

Primary ITP	4654 (0)	4120 (534)	3679 (974)	3307 (1346)	2997 (1656)	2715 (1938)
Comparators	188840 (0)	177057 (11758)	162434 (26356)	148878 (39889)	136127 (52623)	124898 (63836)



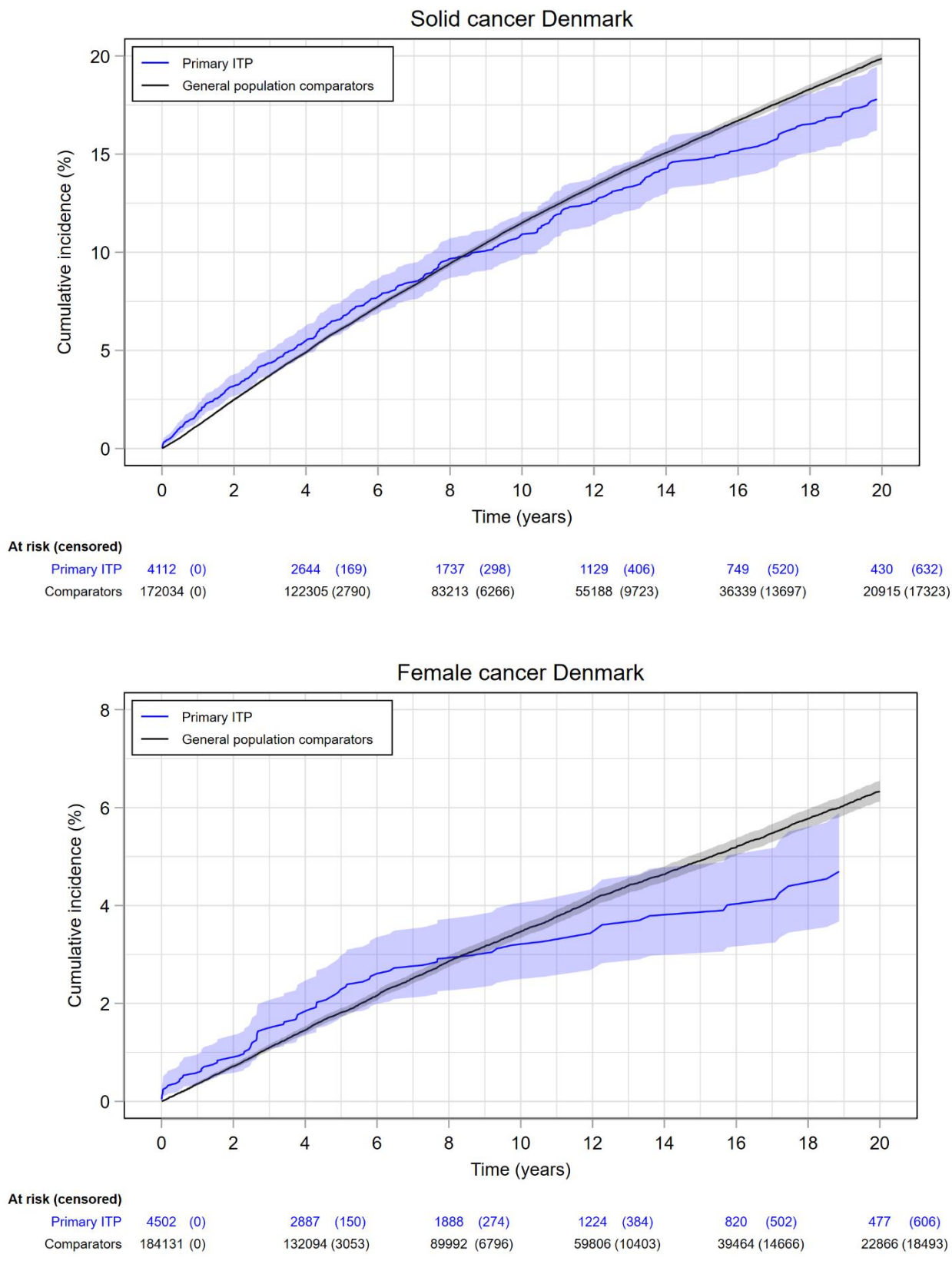
At risk (censored)

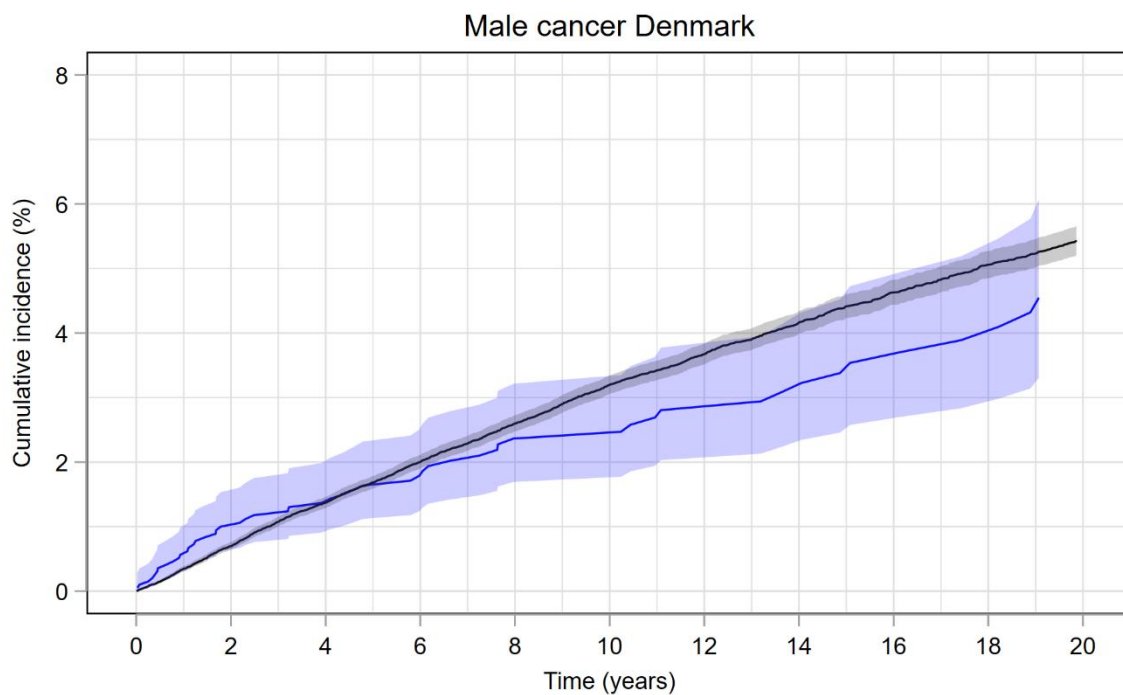
Primary ITP	7633 (0)	6504 (781)	5543 (1565)	4585 (2344)	3644 (3167)	2744 (3975)
Comparators	29120 (0)	25963 (2811)	20486 (7896)	17191 (10891)	13802 (14005)	10515 (17070)



Supplementary figure S2. Five-year cumulative incidences of subgroups of haematological cancers in primary ITP and general population comparators in Denmark and France. Red lines represent patients with ITP and grey lines represent comparators. Each page represent a specific subgroup of solid cancer as stated in the title of each graph, with the top graph on each page representing Danish estimates, and the bottom graph representing French estimates. Please also refer to the Methods section for details on the grouping of investigated cancers. We found an increased incidence of all types of haematological cancers (leukemia, lymphoma, and other haematological cancers except multiple myeloma in Denmark) in both countries.
Abbreviations: ITP: immune thrombocytopenia

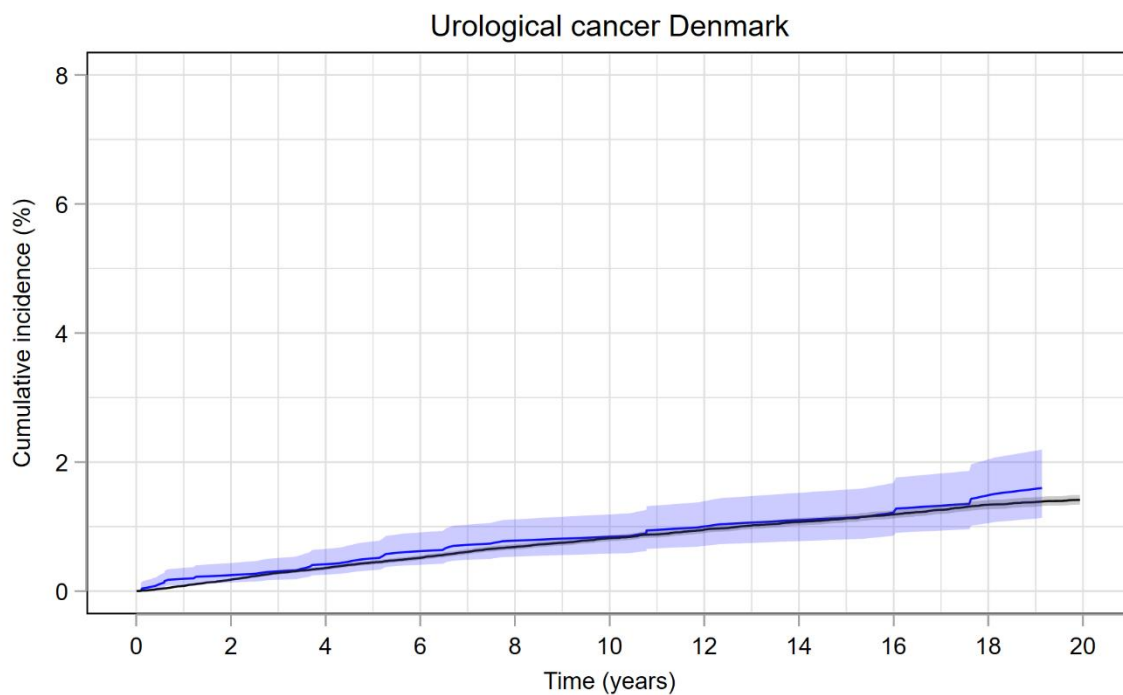
Supplementary figures S3. 20-year cumulative incidences for solid cancers in primary ITP and age-sex matched general population comparators in Denmark





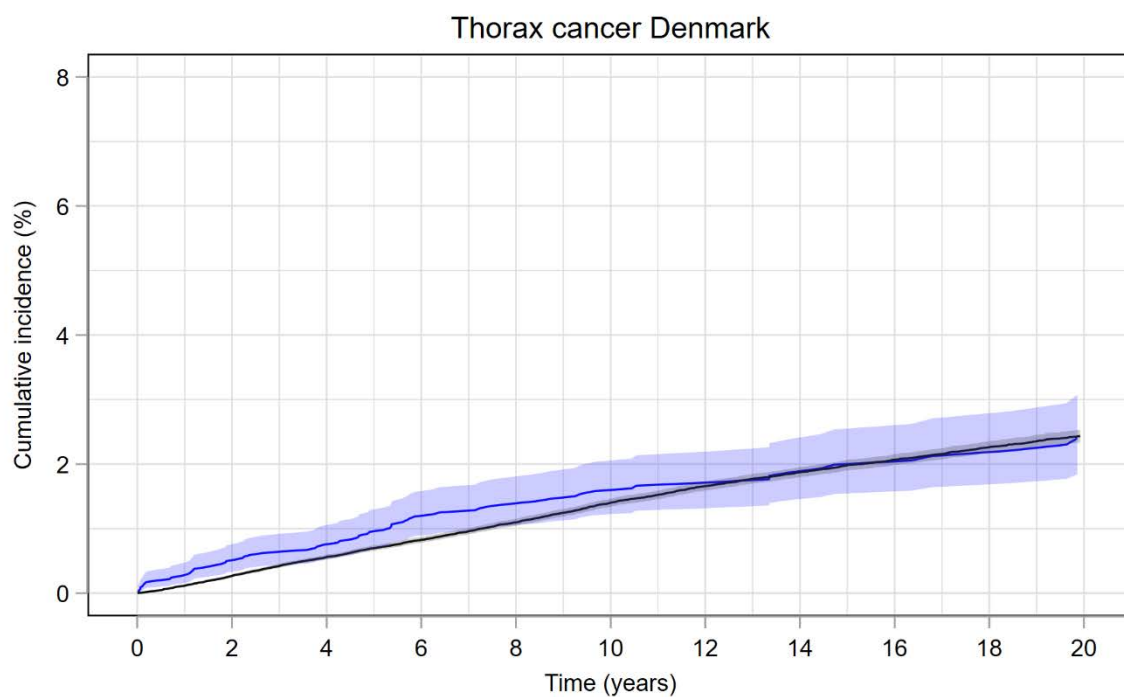
At risk (censored)

Primary ITP	4611 (0)	2968 (136)	1942 (259)	1263 (360)	844 (474)	491 (585)
Comparators	187076 (0)	134814 (3092)	92175 (6798)	61512 (10376)	40653 (14544)	23641 (18341)



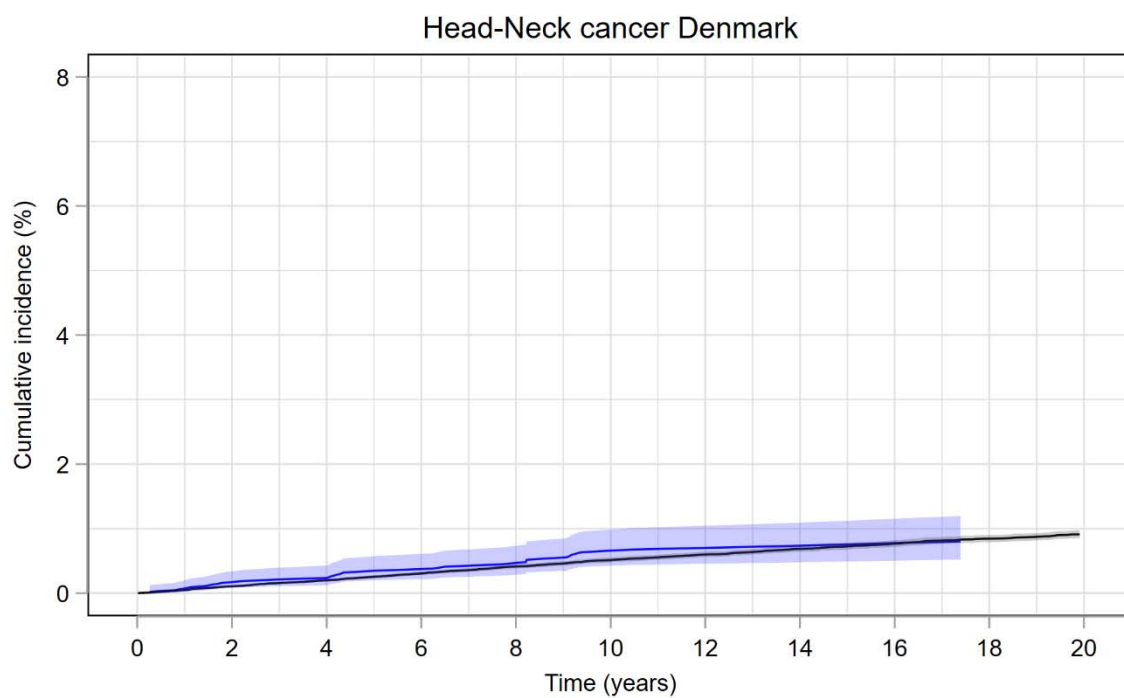
At risk (censored)

Primary ITP	4609 (0)	2978 (215)	1951 (384)	1269 (520)	843 (667)	490 (806)
Comparators	187523 (0)	135167 (3272)	92395 (7414)	61666 (11594)	40794 (16525)	23728 (21068)



At risk (censored)

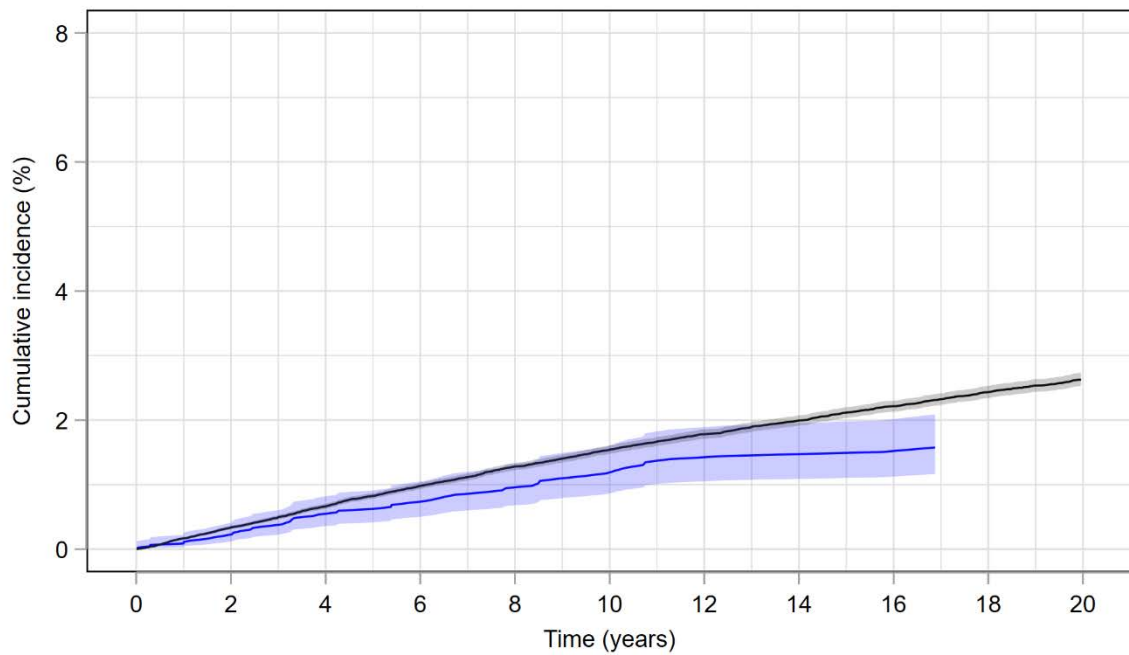
Primary ITP	4621 (0)	2987 (205)	1955 (371)	1269 (509)	845 (659)	492 (797)
Comparators	188450 (0)	135833 (3289)	92824 (7440)	61894 (11592)	40942 (16530)	23813 (21061)



At risk (censored)

Primary ITP	4635 (0)	2986 (217)	1958 (388)	1268 (529)	848 (680)	496 (823)
Comparators	188112 (0)	135605 (3287)	92646 (7451)	61810 (11656)	40886 (16637)	23784 (21213)

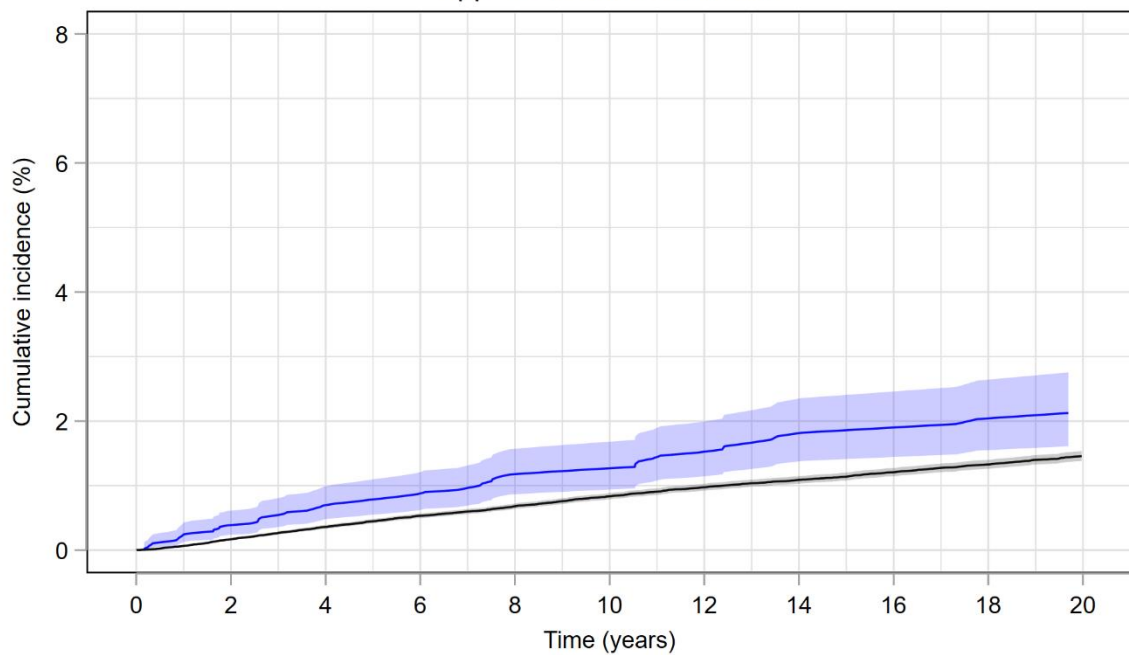
Colorectal cancer Denmark



At risk (censored)

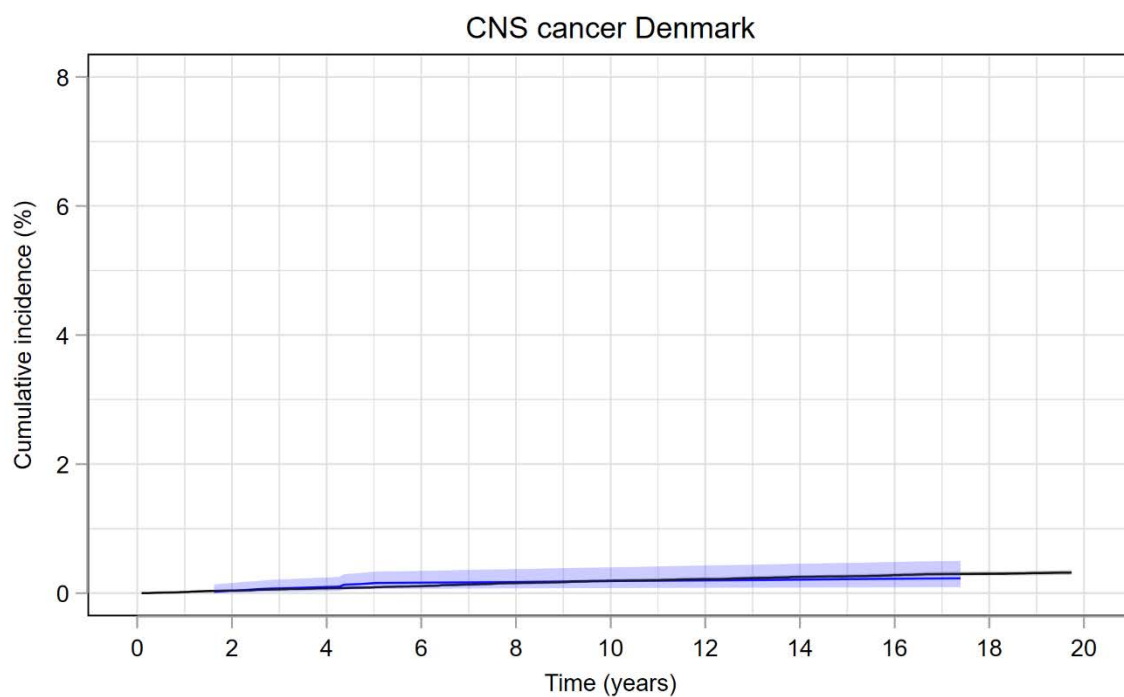
Primary ITP	4593 (0)	2958 (212)	1939 (382)	1258 (518)	839 (669)	494 (808)
Comparators	187065 (0)	134681 (3251)	92038 (7356)	61412 (11495)	40591 (16393)	23583 (20876)

Upper GI cancer Denmark



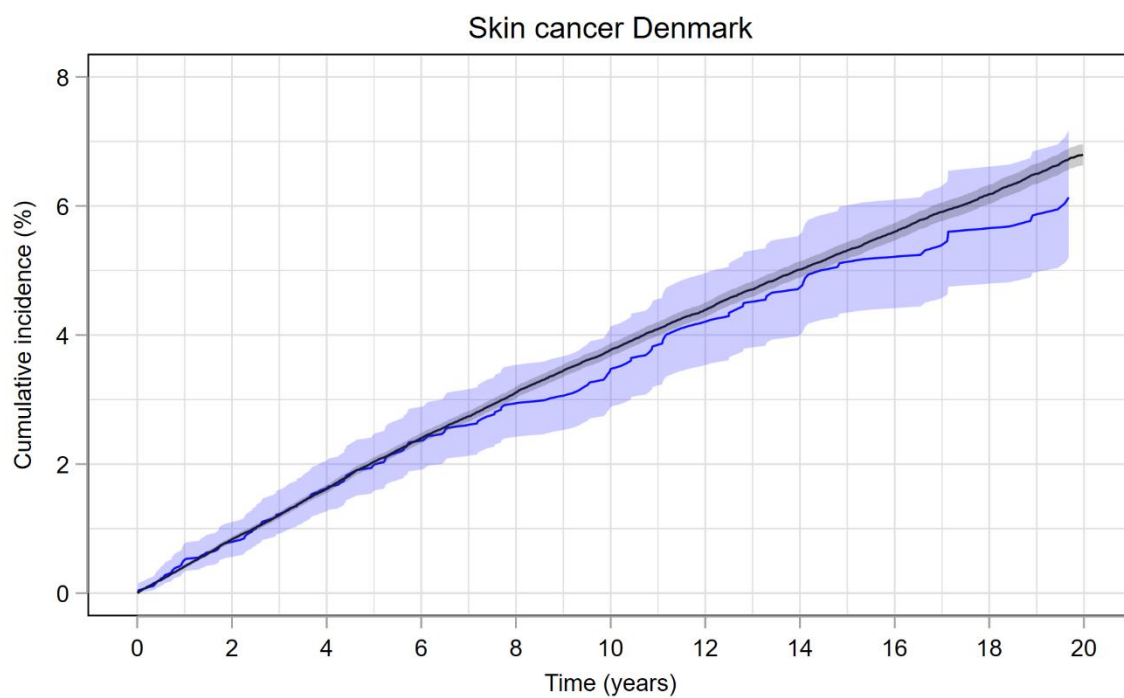
At risk (censored)

Primary ITP	4634 (0)	2985 (213)	1957 (382)	1273 (520)	848 (665)	494 (806)
Comparators	188628 (0)	135956 (3299)	92940 (7468)	62012 (11674)	41015 (16663)	23846 (21237)



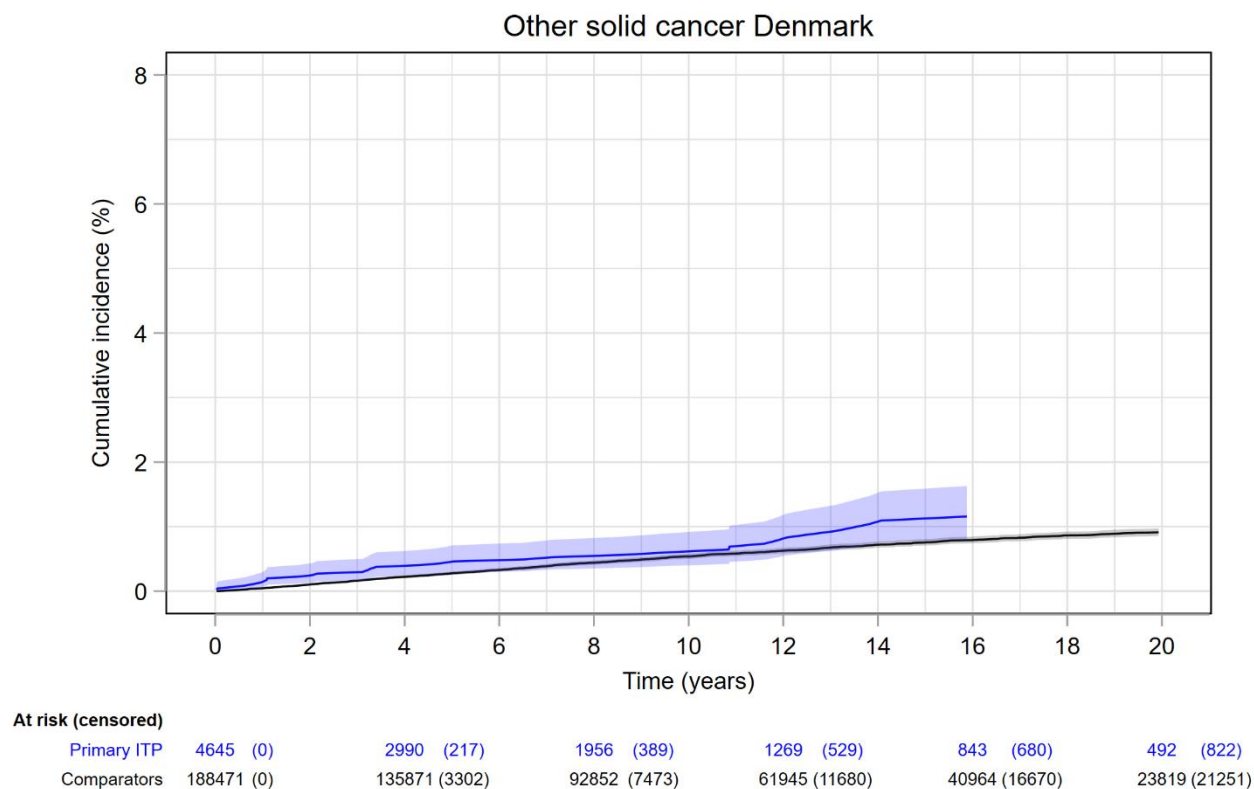
At risk (censored)

Primary ITP	4648 (0)	2994 (218)	1961 (391)	1272 (532)	849 (685)	497 (828)
Comparators	188707 (0)	136048 (3307)	92961 (7500)	62023 (11727)	41018 (16752)	23860 (21361)



At risk (censored)

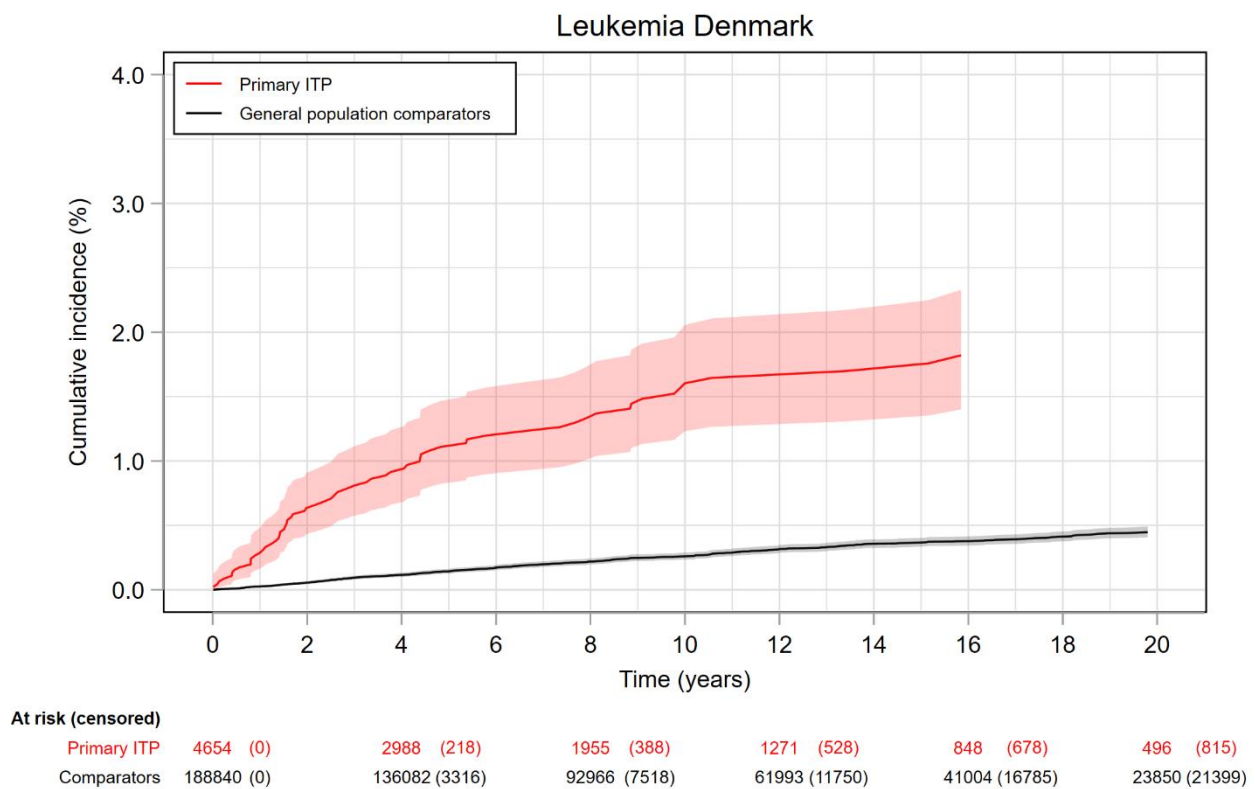
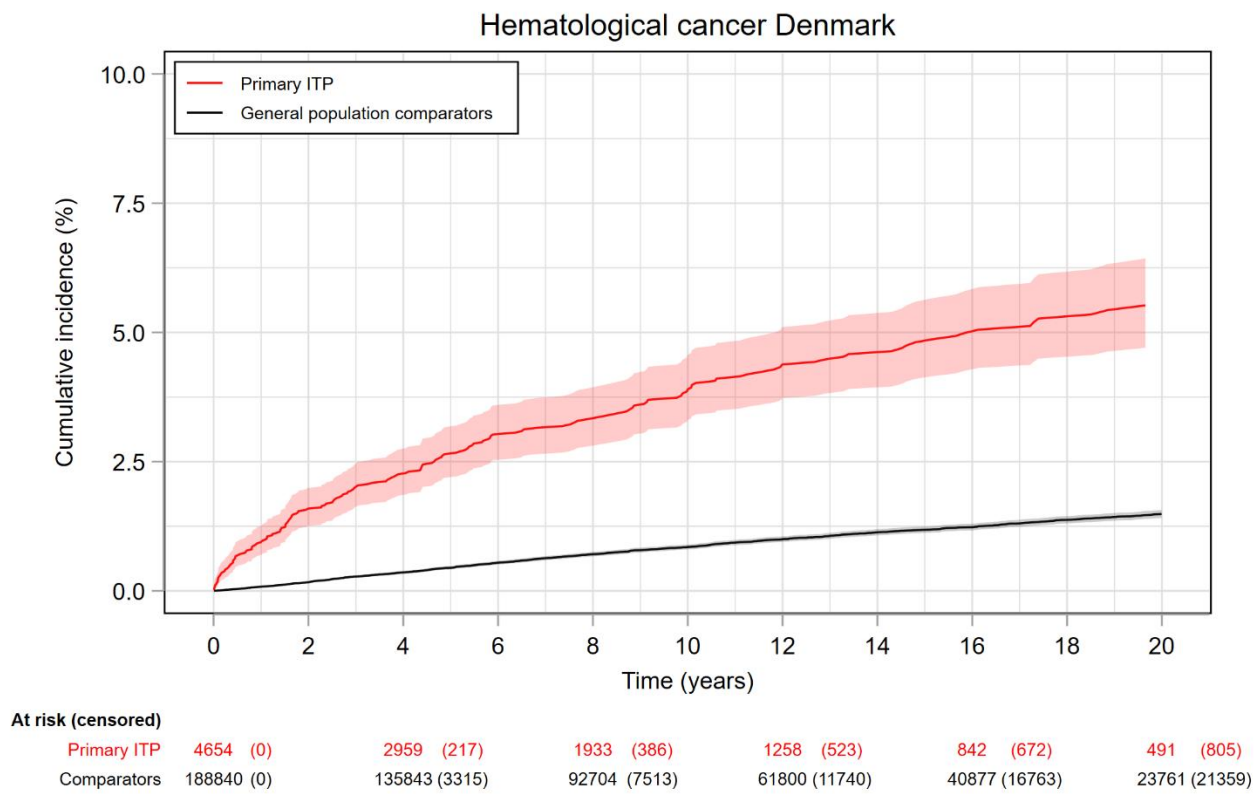
Primary ITP	4456 (0)	2860 (207)	1881 (363)	1214 (495)	807 (640)	473 (775)
Comparators	181918 (0)	130403 (3091)	88933 (7033)	59210 (10998)	39112 (15662)	22670 (19911)



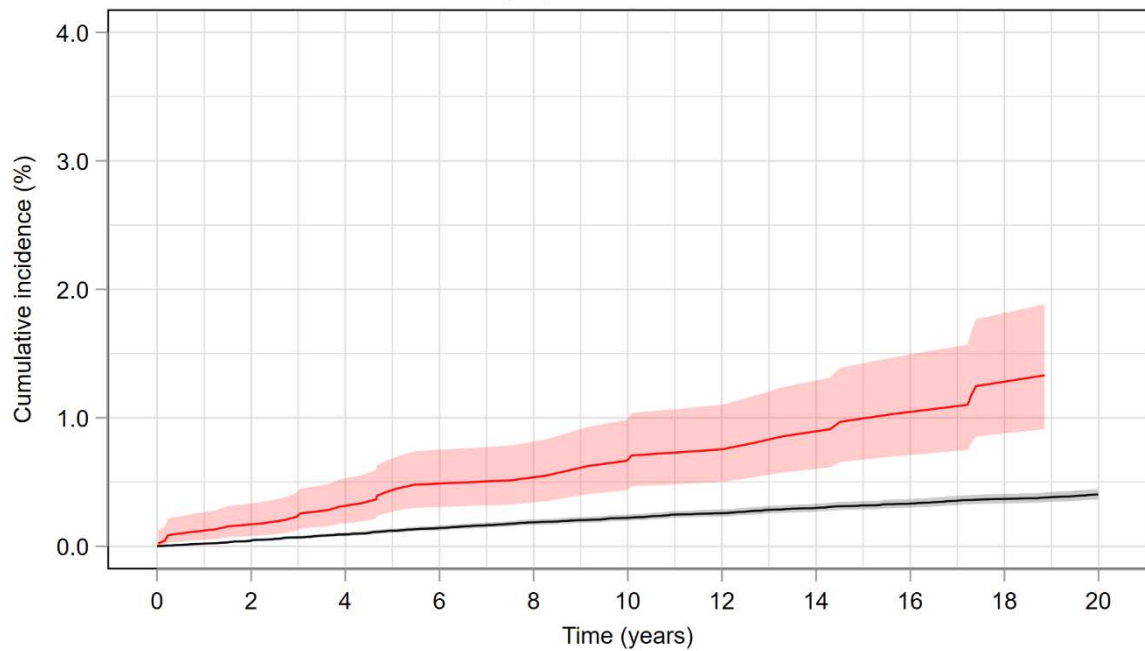
Supplementaryfigure S3. 20-year cumulative incidences of solid cancers in primary ITP and general population comparators in Denmark. Blue lines represent patients and greylines comparators. Each graph represents a subgroup of solid cancer. The graph with 'Solid cancer' represents the first-ever of any subgroup of solid cancer aggregated. In general, the risk of solid cancer in ITP compared to the general population diminished over time for most subgroups, but persisted for upper GI cancer.

Abbreviations: ITP: immune thrombocytopenia

Supplementary figures S4. 20-year cumulative incidences for solid cancers in primary ITP and age-sex matched general population comparators in Denmark



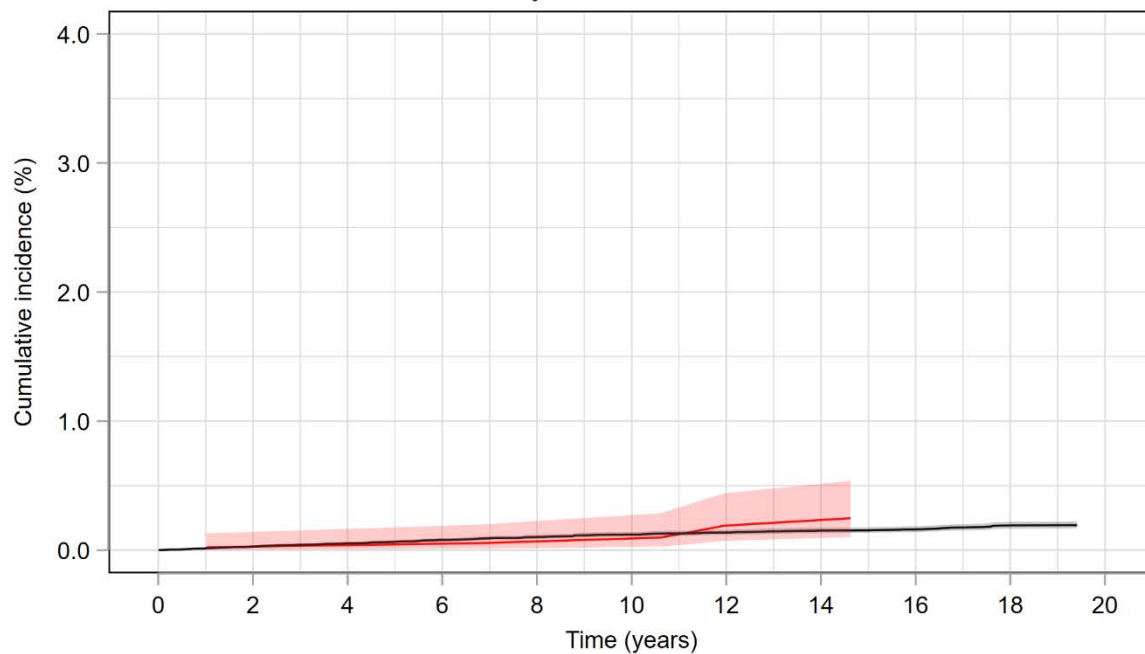
Lymphoma Denmark



At risk (censored)

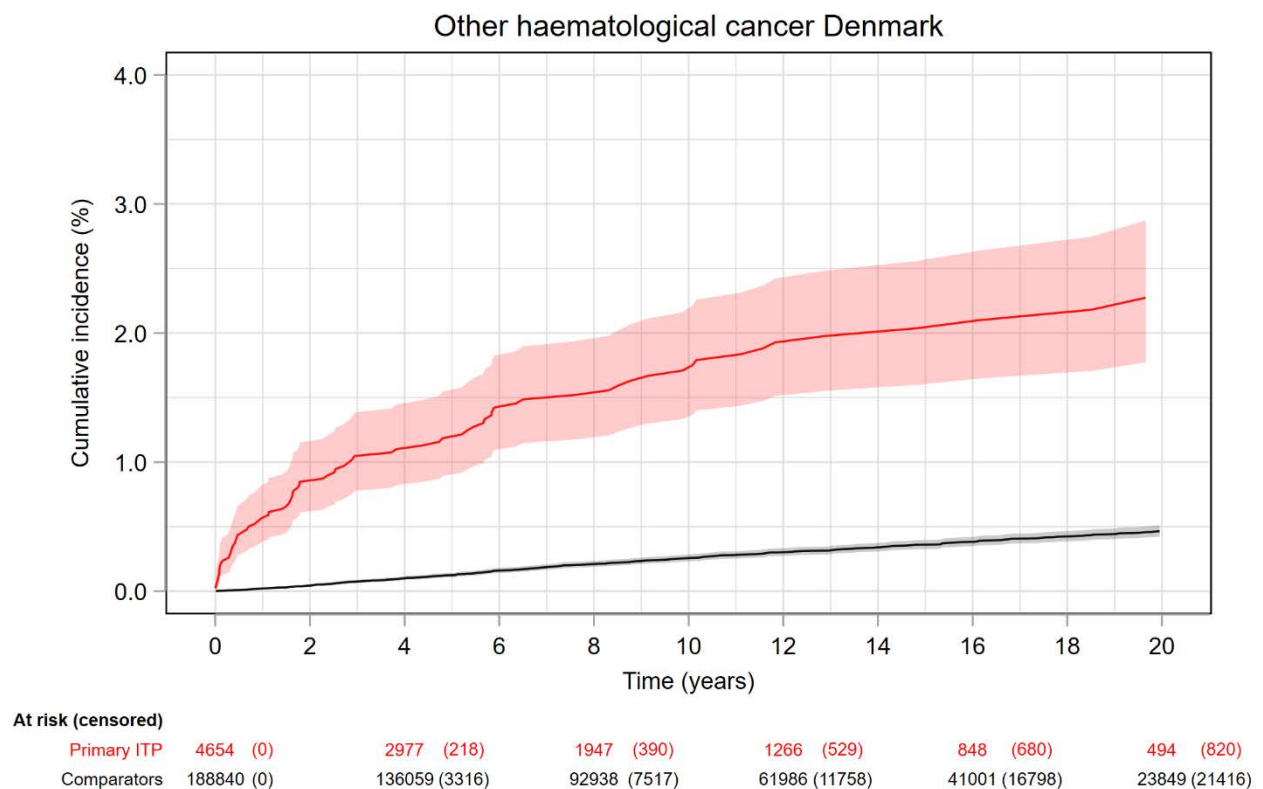
Primary ITP	4654 (0)	2991 (219)	1957 (392)	1271 (534)	848 (687)	495 (829)
Comparators	188840 (0)	136079 (3316)	92952 (7519)	62016 (11757)	41008 (16793)	23846 (21406)

Myeloma Denmark



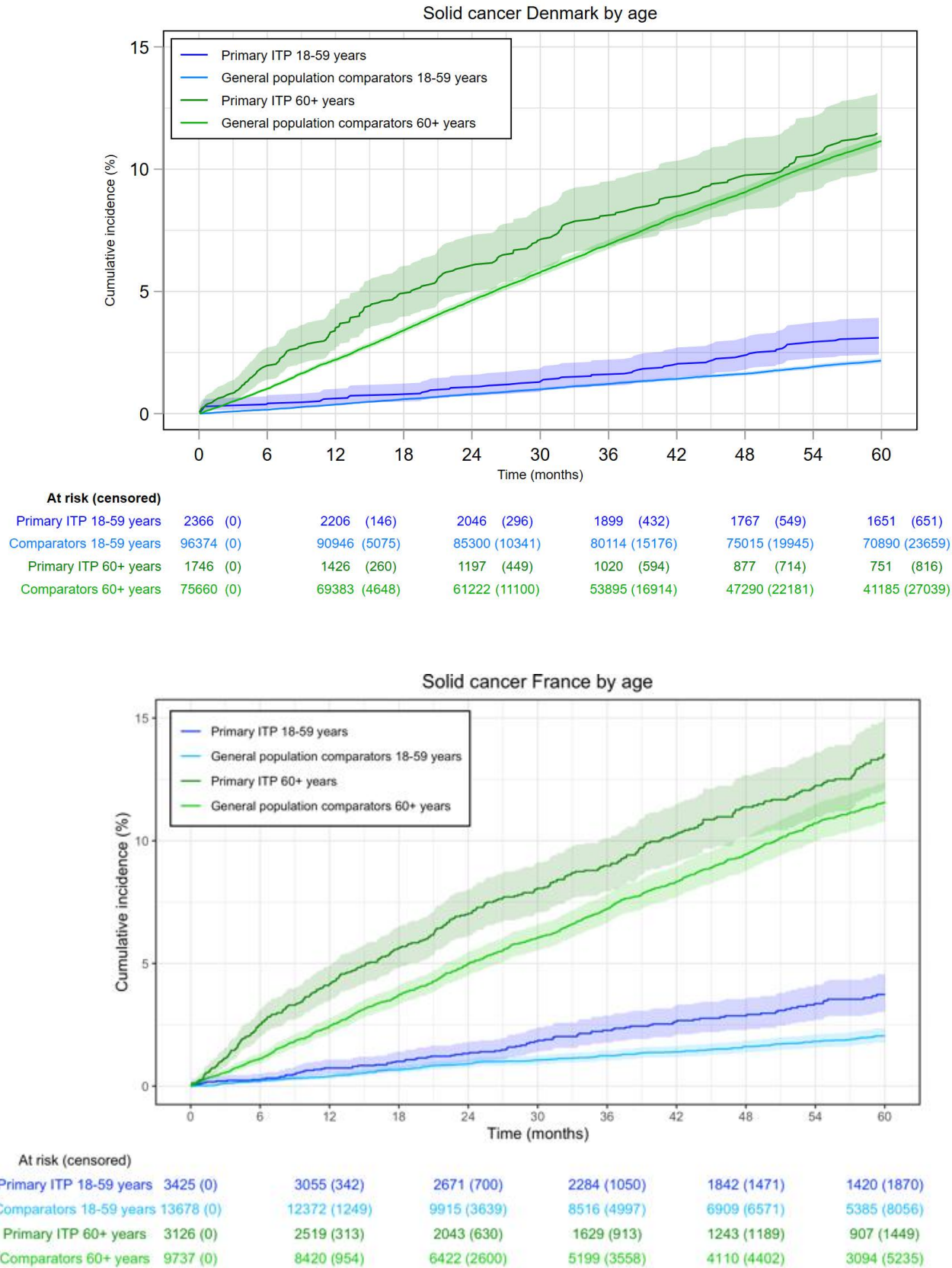
At risk (censored)

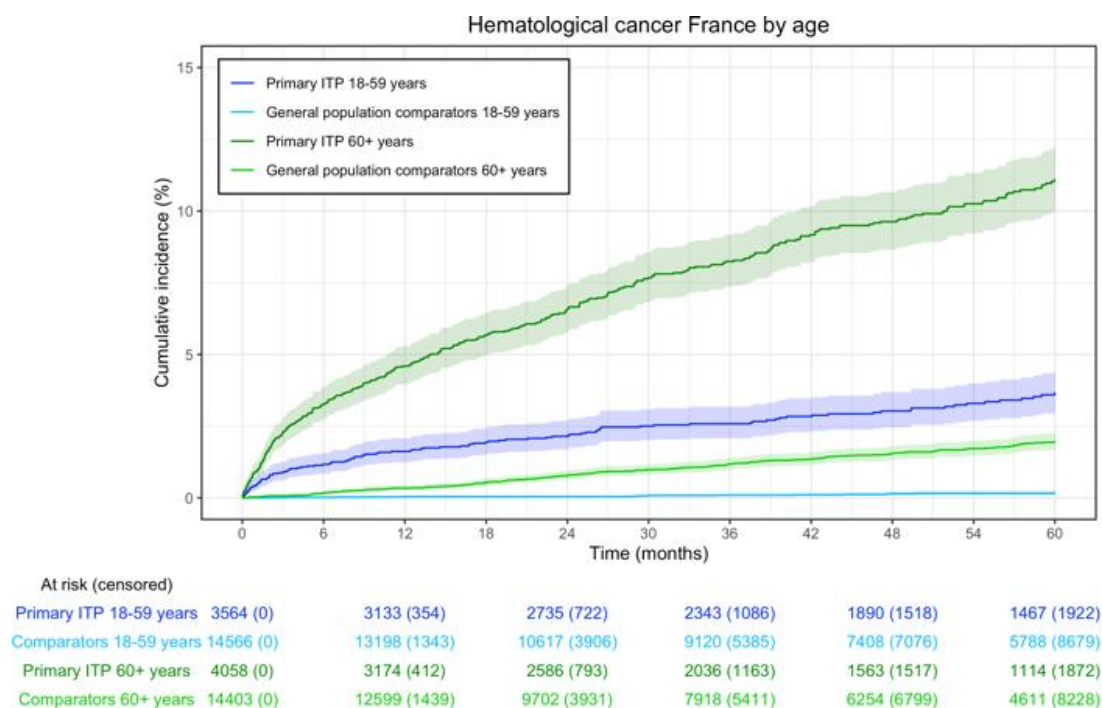
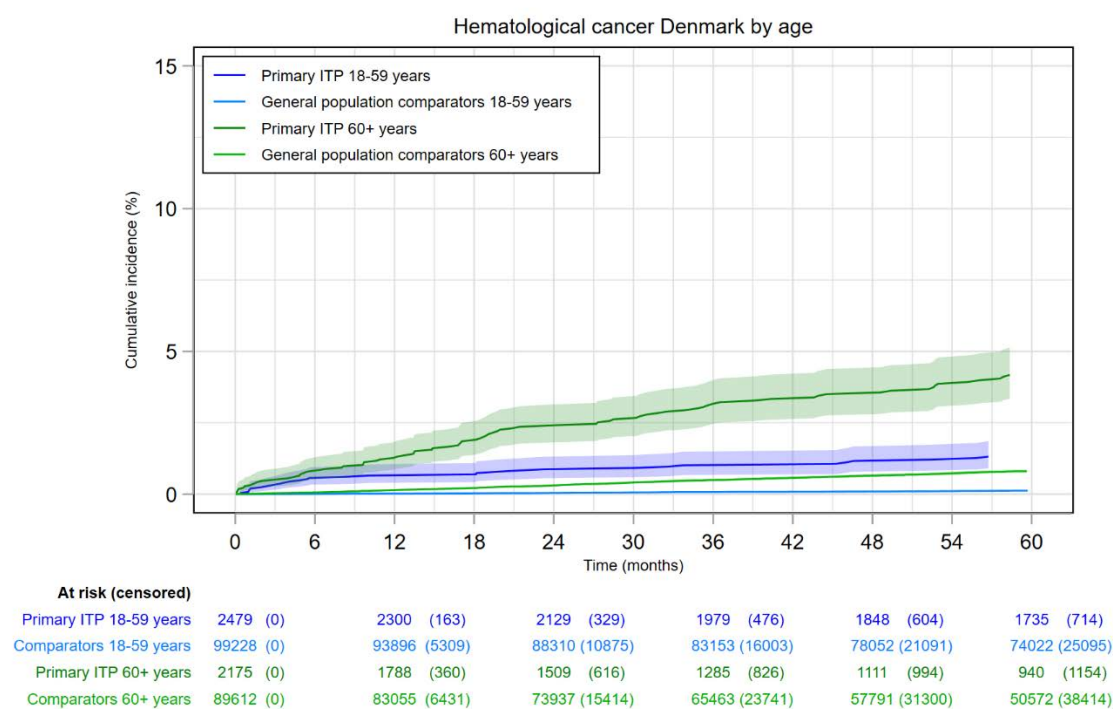
Primary ITP	4654 (0)	2997 (219)	1963 (392)	1272 (534)	848 (687)	497 (830)
Comparators	188840 (0)	136127 (3315)	93015 (7519)	62057 (11758)	41052 (16796)	23880 (21413)



Supplementaryfigure S4. 20-year cumulative incidences of hematological cancers in primary ITP and general population comparators in Denmark. Red lines represent patients and grey lines comparators. Each graph represents a subgroup of hematological cancer. The graph with 'Hematological cancer' represents the first-ever of any subgroup of hematological cancer aggregated. In general, the risk of hematological cancer in ITP was elevated compared to the general population, and persisted over time for most subgroups.
Abbreviations: ITP: immune thrombocytopenia

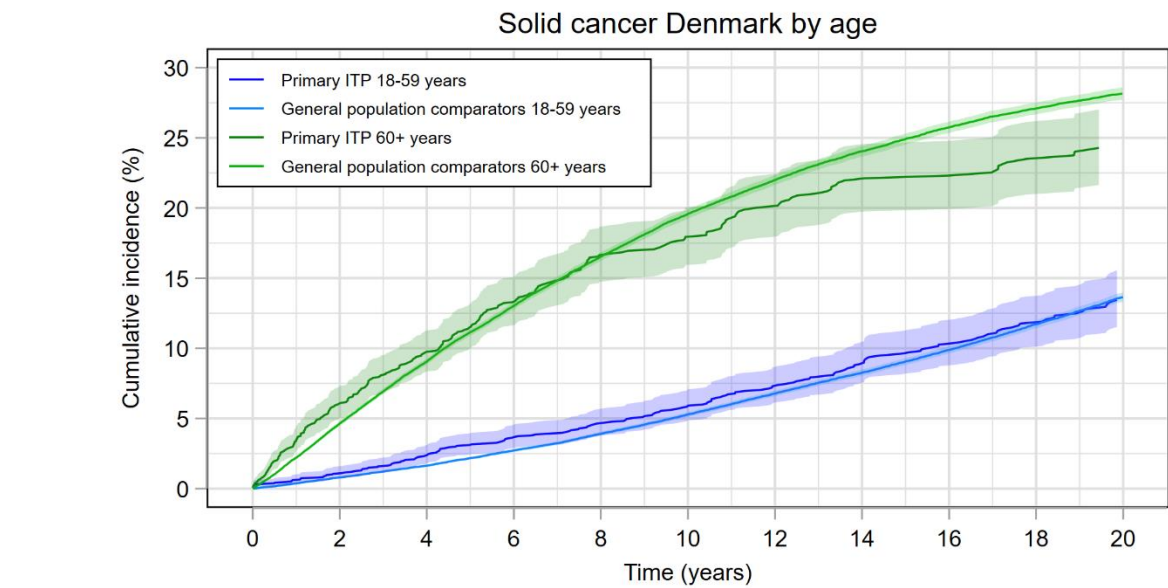
Supplementary figures S5. Five-year cumulative incidences of solid and hematological cancer in primary ITP and general population comparators in Denmark (top) and France (bottom)



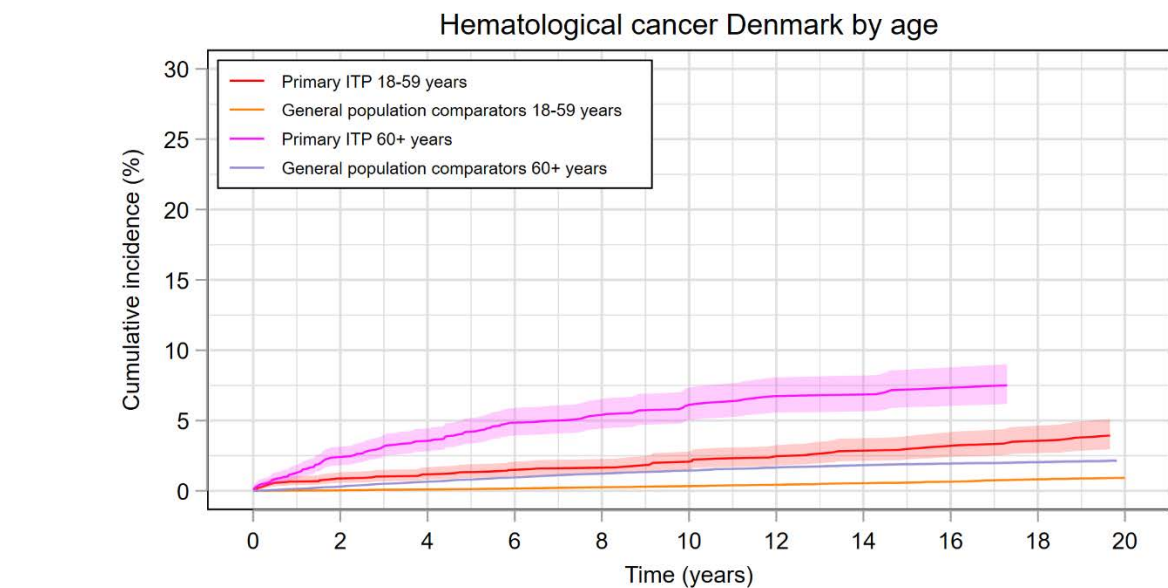


Supplementaryfigure S5. Five-year cumulative incidences for solid and hematological cancers in patients and comparators stratified by age (18-59 years; 60+ years) . Each page represent the cumulative incidence of the first- ever any solid and hematological cancer respectively, with the top graph on each page representing Danish estimates, and the bottom graph representing French estimates. Both young (18-59 years) and older patients (60 years) are represented on each graph. The cumulative incidences of both solid and hematological cancer were generally higher in the older population compared to the younger, in both countries.
Abbreviations: ITP: immune thrombocytopenia

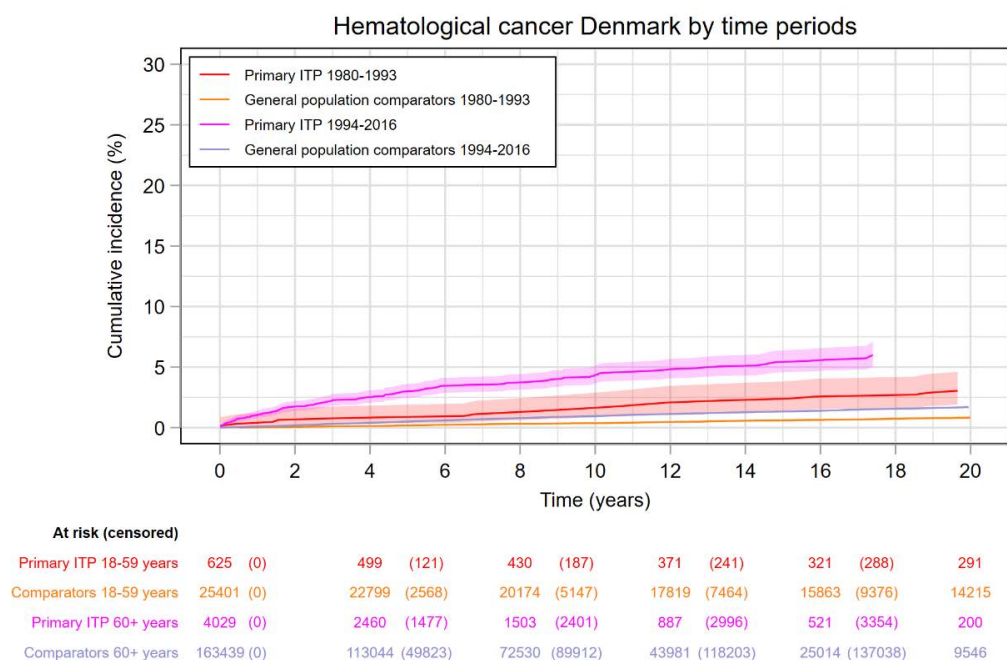
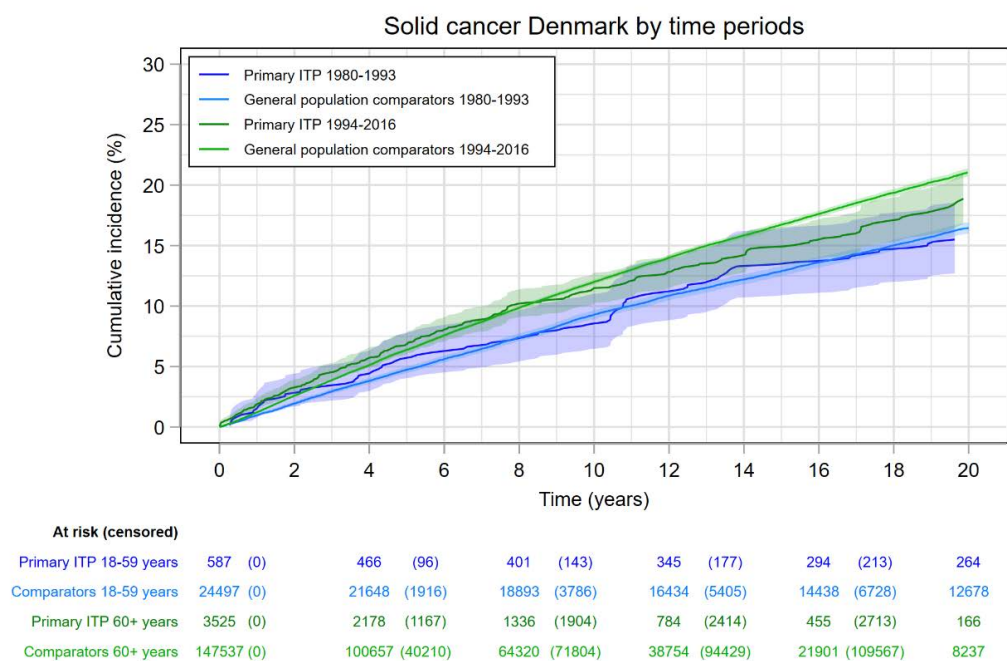
Supplementary figure S6. 20-year cumulative incidences for solid cancers in primary ITP and age-sex matched general population comparators in Denmark by age groups (18-59, 60+ years) and period of diagnosis (1980-1993, 1994-2016)



At risk (censored)						
Primary ITP 18-59 years	2366 (0)	1767 (549)	1310 (967)	938 (1304)	670 (1542)	400
Comparators 18-59 years	96374 (0)	75015 (19945)	57233 (36141)	42070 (49742)	30177 (60356)	18340
Primary ITP 60+ years	1746 (0)	877 (714)	427 (1080)	191 (1287)	79 (1384)	30
Comparators 60+ years	75660 (0)	47290 (22181)	25980 (39449)	13118 (50092)	6162 (55939)	2575



At risk (censored)						
Primary ITP 18-59 years	2479 (0)	1848 (604)	1385 (1059)	1007 (1425)	733 (1692)	448
Comparators 18-59 years	99228 (0)	78052 (21091)	60363 (38665)	45088 (53839)	32809 (66030)	20308
Primary ITP 60+ years	2175 (0)	1111 (994)	548 (1529)	251 (1812)	109 (1950)	43
Comparators 60+ years	89612 (0)	57791 (31300)	32341 (56394)	16712 (71828)	8068 (80384)	3453



Supplementaryfigure S6. Illustration of the differences in the cumulative incidences of cancer in patients with primary ITP and general population comparators when comparing across study periods and age-groups across a 20-year study period.

The top page and graphs illustrate differences in age, and the bottom page and graphs illustrate differences over study period. We estimated solid and hematological cancer as the first-ever of any of the respective subgroups of cancer. Of note, the median age at diagnosis of ITP increased from 55.0 years (IQR, 33.6-72.7) in 1980-1993 to 58.9 years (IQR, 38.4-73.1) in 1994-2016, which could (partly) explain the increase over study period.

Abbreviations: ITP: immune thrombocytopenia

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