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Supplemental methods

Data sources

Data on personal characteristics: This dataset provides data on personal characteristics (i.e., year of birth, sex, and immigration background) collected from the Personal Records Database (in Dutch “Basisregistratie Personen”, BRP)¹. It includes all persons who have been registered in the BRP since October 1994, both residents (i.e., individuals who were registered in the population register of a Dutch municipality) and non-residents (i.e., individuals who had a relationship with the Dutch government)². In the Netherlands, individuals who would stay in the Netherlands for more than four months are compulsory to register at a Dutch municipality and therefore their demographic characteristics would be recorded in the BRP. For the current study, data from the calendar years 2013 to 2019 were used.

Data on household income: Data on household income were collected from the Tax and Customs administration and the student grant registration of the Education Executive Agency (in Dutch “Dienst Uitvoering Onderwijs”, DUO)^{2,3}.

Data on mortality and causes of death: Mortality data includes information on the dates of death for all persons who have been registered in the BRP since October 1994⁴. Data on underlying causes of death of persons who were registered in the BRP and died since the 2013 statistical year were collected from the nationwide Dutch Registry of Causes of Death statistics⁵. This registry also contains information on the most important injury and the location of the accident for those who died of non-natural death. For all deceased persons, the location of death and the statistical year, or the year in which the deceased was included in the statistics, are also present.

Data on diagnoses registered during hospitalizations: Data on diagnoses registered with hospital admissions in Dutch hospitals were collected from the Dutch Hospital Data registry, which includes all general and academic Dutch hospitals and two short-stay categorical hospitals (i.e., a cancer clinic and an eye hospital)² and includes data from individuals registered in the BRP⁶⁻⁹. The data contain diagnoses retrieved from discharge letters, length of hospital stay, and date of admission/discharge. The variable main diagnosis indicated which diagnosis was the main reason for the corresponding hospital admission, and the variable primary diagnosis indicated whether a diagnosis was the main reason for providing the corresponding care¹⁰.

Data on outpatient medication prescriptions: Data on outpatient medication prescriptions for which costs were reimbursed under the basic health insurance in the Netherlands. The data included information on medications for individuals in residential homes for elderly, whereas information on medications in hospitals and in nursing homes were not included^{10,11}. Only the prescription year was available.

Data on outpatient medication prescriptions of anticoagulants: Data on outpatient prescription of anticoagulants, identified by the codes from the World Health Organization’s Anatomic-Therapeutic-Chemical (ATC) system (i.e., B01A*). Data contain information on the type of anticoagulant and the prescription date, but information on the amount of medication per dispensed prescription and the anticoagulant subtypes were not available¹⁰.

Data from Dutch anticoagulation clinics: These data compromise information about VKA treatments managed by participating anticoagulation clinics, including information on start date, indication(s) for treatment, type of VKAs, dose, target INR ranges, INR values and measurement time, reason for

stop and stop date (if available). These clinics are managed by the Dutch Federation of Anticoagulation Clinics (in Dutch “Federatie Nederlandse Trombosediensten”, FNT). The following anticoagulation clinics participated in the study: Leiden Anticoagulation Clinic (Leiden), Atalmedial (Amsterdam), Saltro (Utrecht), Star-shl (Rotterdam), and Isala (Zwolle).

Netherlands Cancer Registry (NCR): The NCR is provided by the Netherlands Comprehensive Cancer Organization (in Dutch “Integraal Kankercentrum Nederland”, IKNL) and comprises individual-level data of newly diagnosed patients with cancer in the Netherlands, including cancer diagnosis, tumour staging (according to the TNM-classification developed and maintained by the Union for International Cancer Control (UICC)), tumour site (topography) and morphology (histology) (according to the WHO International Classification of Diseases for Oncology (ICD-O-3)), co-morbidity at diagnosis and treatment received directly after diagnosis (source: [Netherlands Cancer Registry \(NCR\) \(iknl.nl\)](https://www.iknl.nl)).

Data linkage

Data from the anticoagulation clinics were linked to data from Statistics Netherlands by sex, date of birth, postal code, and last date known to be alive and >95% of records were successfully matched. Data from the NCR were also linked to Statistics Netherlands by sex, date of birth, and postal code with an 98.5% match.

Details about constructing treatment periods for anticoagulants

Dispensed anticoagulant prescriptions for vitamin K antagonists (VKAs), direct oral anticoagulants (DOACs) and Low-molecular-weight heparins (LMWHs) from 2012 to 2020 were used to examine VKA and anticoagulant exposure after registered VKA end dates from the anticoagulation clinics, to account for possible switching to non-VKA anticoagulants and non-participating anticoagulation clinics. Both VKA and anticoagulant exposure were modelled by constructing treatment periods of person-time exposed according to dispensed prescriptions, only considering prescriptions after VKA end dates from anticoagulation clinics. As no data were available on the amount of anticoagulant dispensed nor the prescribed dose, treatment periods for the different types of anticoagulants were constructed assuming that a dispensing lasted a fixed number of days (i.e., the exposure time) unless a refill, death or end of follow-up occurred earlier. Whenever the period between two subsequent dispensed prescription dates exceeded this fixed number of days, the next prescription was considered to belong to a new treatment period. A predefined number of days was added to the last prescription date within the treatment period to construct the end of the corresponding treatment period (*Supplemental Figure 1*). For VKAs, the exposure time of a single prescription was based on a previously performed validation study (Kempers et al. 2024, unpublished data), which resulted in 180 days allowed between subsequent VKA prescription dates and the addition of 60 days to the last prescription date to construct the end date of the corresponding treatment period. For DOACs and LMWHs, exposure times were based on the number of days between two dispensed prescriptions studied in a random sample of patients with DOAC and/or LMWH prescriptions between 2013-2019 (*Supplemental Figure 2*). We applied an exposure time of 120 days for DOAC prescriptions and 30 days for LMWH prescriptions.

As sensitivity analyses, we varied the exposure time of anticoagulant prescriptions when constructing treatment periods: 100 days for LMWH prescriptions, 150 days combined with the addition of 100 days to the last prescription date within the treatment period for VKA prescriptions.

R packages used

The following packages were used for statistical analyses and preparing figures: tidyverse¹², dplyr¹³, lubridate¹⁴, stringr¹⁵, tidyr¹⁶, foreign¹⁷, forcats¹⁸, purrr¹⁹, ggplot2²⁰, survival²¹, proclim²², epiR²³, tidycmprks²⁴, ggsurvfit²⁵, and cowplot²⁶.

Supplemental Table 1. ICD-10 codes used to identify non-cancer life-limiting diseases

Life-limiting disease	Restrictions	ICD 10 codes
Liver disease		
Esophageal varices	Primary diagnosis of hospital admission	I85.0
Alcoholic cirrhosis of liver	Primary diagnosis of hospital admission	K70.3
Secondary biliary cirrhosis	Primary diagnosis of hospital admission	K74.4
Unspecified cirrhosis of liver	Primary diagnosis of hospital admission	K74.6
Hepatorenal syndrome	Primary diagnosis of hospital admission	K76.7
Hip fracture		
Fracture of neck of femur	Primary diagnosis of hospital admission in patients >70 years	S72.0
Pertrochanteric fracture	Primary diagnosis of hospital admission in patients >70 years	S72.1
Subtrochanteric fracture	Primary diagnosis of hospital admission in patients >70 years	S72.2
Heart disease		
Hypertensive heart disease with heart failure	Primary diagnosis of hospital admission	I11.0
Hypertensive heart and chronic kidney disease with heart failure and stage 1 through stage 4 chronic kidney disease, or unspecified chronic kidney disease	Primary diagnosis of hospital admission	I13.0
Hypertensive heart and chronic kidney disease with heart failure and with stage 5 chronic kidney disease, or end stage renal disease	Primary diagnosis of hospital admission	I13.2
Ischemic cardiomyopathy	Primary diagnosis of hospital admission	I25.5
Heart failure	Primary diagnosis of hospital admission	I50.1; I50.2; I50.3; I50.4; I50.8; I50.9
Lung disease		
Mixed simple and mucopurulent chronic bronchitis	Primary diagnosis of hospital admission	J41.8
Other chronic obstructive pulmonary disease	Primary diagnosis of hospital admission	J440; J441; J449;
Other interstitial pulmonary diseases with fibrosis	Primary diagnosis of hospital admission	J84.1
Diabetes mellitus		
Type 1 diabetes mellitus with kidney complications	Primary diagnosis of hospital admission in combination with diagnosis of severity (see table S4)	E10.2

Type 1 diabetes mellitus with circulatory complications	Primary diagnosis of hospital admission in combination with diagnosis of severity	E10.5
Type 1 diabetes mellitus with multiple complications	Primary diagnosis of hospital admission in combination with diagnosis of severity	E10.7
Type 2 diabetes mellitus with kidney complications	Primary diagnosis of hospital admission in combination with diagnosis of severity	E11.2
Type 2 diabetes mellitus with circulatory complications	Primary diagnosis of hospital admission in combination with diagnosis of severity	E11.5
Type 2 diabetes mellitus with multiple complications	Primary diagnosis of hospital admission in combination with diagnosis of severity	E11.7
Malnutrition-related diabetes mellitus with renal complications	Primary diagnosis of hospital admission in combination with diagnosis of severity	E12.2
Malnutrition-related diabetes mellitus with peripheral circulatory complications	Primary diagnosis of hospital admission in combination with diagnosis of severity	E12.5
Malnutrition-related diabetes mellitus with multiple complications	Primary diagnosis of hospital admission in combination with diagnosis of severity	E12.7
Other specified diabetes mellitus with kidney complications	Primary diagnosis of hospital admission in combination with diagnosis of severity	E13.2
Other specified diabetes mellitus with circulatory complications	Primary diagnosis of hospital admission in combination with diagnosis of severity	E13.5
Other specified diabetes mellitus with multiple complications	Primary diagnosis of hospital admission in combination with diagnosis of severity	E13.7
Unspecified diabetes mellitus with renal complication	Primary diagnosis of hospital admission in combination with diagnosis of severity	E14.2
Unspecified diabetes mellitus with peripheral circulatory complications	Primary diagnosis of hospital admission in combination with diagnosis of severity	E14.5
Unspecified diabetes mellitus with multiple complications	Primary diagnosis of hospital admission in combination with diagnosis of severity	E14.7
Dementia		
Creutzfeld-Jakob disease	Primary or secondary diagnosis of hospital admission	A81.0
Subacute sclerosing panencephalitis	Primary or secondary diagnosis of hospital admission	A81.1
Progressive multifocal leukoencephalopathy	Primary or secondary diagnosis of hospital admission	A81.2

Other atypical virus infections of central nervous system	Primary or secondary diagnosis of hospital admission	A81.8
Vascular dementia, unspecified severity	Primary or secondary diagnosis of hospital admission	F01.5
Vascular dementia, severe	Primary or secondary diagnosis of hospital admission	F01.C
Dementia in other diseases classified	Primary or secondary diagnosis of hospital admission	F02.8
Dementia in other diseases classified, severe	Primary or secondary diagnosis of hospital admission	F02.C
Unspecified dementia, unspecified severity	Primary or secondary diagnosis of hospital admission	F03.9
Unspecified dementia, severe	Primary or secondary diagnosis of hospital admission	F03.C
Delirium superimposed on dementia	Primary or secondary diagnosis of hospital admission	F05.1
Alzheimer's disease	Primary or secondary diagnosis of hospital admission	G30
Frontotemporal dementia	Primary or secondary diagnosis of hospital admission	G31.0
Senile degeneration of brain	Primary or secondary diagnosis of hospital admission	G31.1

Supplemental Table 2. ICD-10 codes used to identify any diagnosis of severity to indicate the severity of diabetes mellitus.

Any diagnosis of severity in combination with diabetes mellitus	ICD-10 codes
Peripheral vascular disease	
Diabetes mellitus due to underlying condition with circulatory complications	E08.5
Drug or chemical induced diabetes mellitus with circulatory complications	E09.5
Atherosclerosis of unspecified type of bypass graft(s) of the extremities	I70.3
Atherosclerosis of autologous vein bypass graft(s) of the extremities	I70.4
Atherosclerosis of nonautologous biological bypass graft(s) of the extremities	I70.5
Atherosclerosis of nonbiological bypass graft(s) of the extremities	I70.6
Atherosclerosis of other type of bypass graft(s) of the extremities	I70.7
Other and unspecified atherosclerosis	I70.9
Other arterial dissection	I77.7
Coronary artery disease	
Angina	I20.0; I20.1; I20.8; I20.9
ST elevation (STEMI) myocardial infarction involving other sites	I21.0; I21.1; I21.2; I21.3; I21.4; I21.9
Subsequent ST elevation (STEMI) and non-ST elevation (NSTEMI) myocardial infarction	I22.0; I22.1; I22.8; I22.9
Other acute ischemic heart diseases	I24.0; I24.1; I24.8; I24.9
Atherosclerotic heart disease of native coronary artery	I25.1
Old myocardial infarction	I25.2
Coronary artery aneurysm and dissection	I25.4
Ischemic cardiomyopathy	I25.5
Silent myocardial ischemia	I25.6
Atherosclerosis of coronary artery bypass graft(s) and coronary artery of transplanted heart with angina pectoris	I25.7
Atherosclerosis of other coronary vessels without angina pectoris	I25.8
Chronic ischemic heart disease, unspecified	I25.9
Kidney failure	
Hypertensive renal disease with renal failure	I12.0
Hypertensive heart and chronic kidney disease without heart failure	I13.1
Chronic kidney disease, stage 4	N18.4
Chronic kidney disease, stage 5	N18.5
End stage renal disease	N18.6

Unspecified kidney failure	N19
Encounter for adequacy testing for haemodialysis	Z49.3
Dependence on renal dialysis	Z99.2

Supplemental Table 3. Survival rates of different cancer diagnoses

Cancer location	Stage	1 year survival	3 year survival	5 year survival	Reference
Pancreas	All stages	22%	6%	< 5%	van der Geest, L. et al. Alveesklier in Nederland, kleine stappen vooruit. IKNL (2021).
Cervix					
	IIA2-IVA (locally advanced)	86%	66%	59%	van der Aa, M. et al. (no date) Baarmoederhalskanker in Nederland. Available at: https://iknl.nl/cervixcarcinoom-in-nederland (Accessed: 17 September 2024).
	IIIB	71%	42%	37%	
	IVA	47%	24%	21%	
	IVB	38%	13%	7%	
Endometrium^a		90%	83%	80%	Soslow, Robert A et al. Clinicopathologic analysis of 187 high-grade endometrial carcinomas of different histologic subtypes: similar outcomes belie distinctive biologic differences. The American journal of surgical pathology vol. 31,7 (2007): 979-87.
	III	80%		48%	
	IV	48%		15%	
Bladder					
	T2-4a			45,7%	Ripoll, J et al. Cancer-specific survival by stage of bladder cancer and factors collected by Mallorca Cancer Registry associated to survival. BMC cancer vol. 21,1 676. 7 Jun. 2021
	T3	60%	42%	41,0%	
	T4a+b	IV: 40%	IV:20%	21% ; 12%	
Breast					
	III	96%	83%	73%	IKNL 2023. Overleving borstkanker. Available at: https://iknl.nl/kankersoorten/borstkanker/registratie/overleving (Accessed: 17 September 2024).
	IV	70%	38%	22%	
Bone and soft tissue (sarcoma)					
	Bone	83%	69%	63%	IKNL 2024. Overleving bot- en wekedelenkanker. Available at: https://iknl.nl/kankersoorten/bot-en-wekedelenkanker/registratie/overleving (Accessed: 17 September 2024).
	Soft tissue sarcoma	79%	65%	59%	
	GIST	91%	84%	80%	
Colon					
	III	88-92%		71%	Araghi, Marzieh et al. Colon and rectal cancer survival in seven high-income countries 2010-2014: variation by age and stage at diagnosis (the ICBP SURVMARK-2 project). Gut vol. 70,1 (2021): 114-126.
	IV	40-58%		12%	
Rectal					

	III	91-96%		75%	Araghi, Marzieh et al. Colon and rectal cancer survival in seven high-income countries 2010-2014: variation by age and stage at diagnosis (the ICBP SURVMARK-2 project). Gut vol. 70,1 (2021): 114-126.
	IV	52-66%		14%	
Ovary					
	III	80%	40%	25%	Gaitskell, Kezia et al. Ovarian cancer survival by stage, histotype, and pre-diagnostic lifestyle factors, in the prospective UK Million Women Study. Cancer epidemiology vol. 76 (2022): 102074.
	IV	75%	25%	12%	
Brain		54%	31%	26%	IKNL 2023. Overleving Hersentumoren. Available at: https://iknl.nl/kankersoorten/hersentumoren/registratie/overleving (Accessed: 17 September 2024)
Hepatobiliary - liver		44%	24%	18%	IKNL 2023. Overleving HPB-tumoren. Available at: https://iknl.nl/kankersoorten/hpb-tumoren/registratie/overleving (Accessed: 17 September 2024)
Hepatobiliary – gallbladder / bile duct		46%	22%	17	IKNL 2023. Overleving HPB-tumoren. Available at: https://iknl.nl/kankersoorten/hpb-tumoren/registratie/overleving (Accessed: 17 September 2024)
Lung			34%		IKNL 2024. Overleving longkanker. Available at: https://iknl.nl/kankersoorten/longkanker/registratie/overleving (Accessed: 17 September 2024)
	NSCLC III	78%	42%	30%	
	NSCLC IV	33%	< 10%	< 5%	
	SCLC III	78%	35%	24%	
	SCLC IV	25%	< 10%	< 5%	
NEC/NET (any location)^b	All stages	73%	53%	39%	Man, Da et al. "Prognosis of patients with neuroendocrine tumor: a SEER database analysis." Cancer management and research vol. 10 5629-5638. 13 Nov. 2018. Dasari, Arvind et al. "Trends in the Incidence, Prevalence, and Survival Outcomes in Patients With Neuroendocrine Tumors in the United States." JAMA oncology vol. 3,10 (2017): 1335-1342.
Primary tumor unknown					
	Treated	40%		20%	IKNL 2024. Overleving Primaire Tumor Onbekend. Available at: https://iknl.nl/kankersoorten/primaire-tumor-onbekend/registratie/overleving (Accessed: 17 September 2024)
	Untreated	5%	< 5%	< 5%	
Esophagus					
	III	65%	33%	26%	

	IV	22%	4%	2%	IKNL 2023. Overleving slokdarm- en maagkanker. Available at: https://iknl.nl/kankersoorten/slokdarm-en-maagkanker/registratie/overleving (Accessed: 17 September 2024)
Gastric					
	III	60%	25%	16%	IKNL 2023. Overleving slokdarm- en maagkanker. Available at: https://iknl.nl/kankersoorten/slokdarm-en-maagkanker/registratie/overleving (Accessed: 17 September 2024)
	IV	17%	2%	1%	
<p>First, all survival rates were collected by consulting the website of the Netherlands Comprehensive Cancer Organization ('IKNL' in Dutch). If 3 or 5 year survival rates were not available on the IKNL website, epidemiological literature was used to identify the survival rates. Cancer types and stages with a 3-year survival rate of 50% or less were included in the study.</p> <p>a: Good quality epidemiological studies describing 1/3/5 year survival rates were found, hence this more pathology focused paper was used for the survival rates.</p> <p>b: 3 year survival rates for all NET/NECs in general were above 50%, however, as described in the paper from Dasari et. al, grade 3-4 patients had a much lower survival rate than grade 1-2 patients. Looking at the overall 3-year survival rate of 53%, it was chosen to include the grade 3 and 4 patients but not the grade 1 and 2 patients.</p>					

Supplemental Table 4. Description of included severe cancer diagnoses

All stages	Stage III + IV	Stage IV
Pancreas	Cervix	Breast
Primary tumor unknown	Bladder	Colon and rectum
Brain	Ovary	Endometrium
Hepatobiliary (liver and gall bladder/duct)	Lung (NSCLC and SCLC)	
	Neuro-endocrine tumors	
	Esophagus	
	Gastric	
Cancer types with a median survival time of 3 years or less at the time of first diagnosis were selected.		

Supplemental Table 5. ICD codes used to identify comorbidities

Comorbidities	Type of code	Code(s)
Asthma	ICD-10	J45, J46
	ICD-9	493
Chronic obstructive pulmonary disease	ICD-10	J44
	ICD-9	491, 492, 496
Other chronic lung diseases	ICD-10	J41, J42, J43, J47, J6, J7
	ICD-9	494, 495, 50
Heart failure	ICD-10	I50
	ICD-9	428
Hypertension	ICD-10	I10, I11, I13, I15
	ICD-9	401, 402, 404, 405
Atrial fibrillation	ICD-10	I48
	ICD-9	4273
Atherosclerosis	ICD-10	I20, I250, I251, I255, I258, I259, I70
	ICD-9	413, 4140, 4143, 4144, 4148, 4149, 4292, 440
Myocardial infarction (history)	ICD-10	I21, I22, I252
	ICD-9	410, 412, 4142
Rheumatic Heart disease	ICD-10	I05, I06, I07
	ICD-9	3941, 395, 3971
Other valvular heart disease	ICD-10	I08, I34, I35, I36, I37, I38, I39, Z952
	ICD-9	3940, 3942, 3949, 396, 3970, 424, V433
Peripheral artery disease	ICD-10	I739
	ICD-9	4439
Liver disease	ICD-10	B15, B16, B17, B18, B19, D684, I982, I983, K70, K71, K72, K73, K74, K75, K76, K77, Z944
	ICD-9	070, 4560, 4561, 4562, 571, 5722, 5723, 5724, 5728, 5731, 5732, 5733, 5735, V427
Diabetes	ICD-10	E10, E11, E12, E13, E14
	ICD-9	250
Thyroid disease	ICD-10	E00, E01, E02, E03, E04, E05, E06, E07
	ICD-9	240, 241, 242, 243, 244, 245, 246

Kidney disease	ICD-10	I12, N01, N02, N03, N04, N05, N06, N07, N08, N11, N12, N14, N150, N158, N159, N16, N18, N19, N25, N26, Q60, Q611, Q612, Q613, Q614, Q615, Q618, Q619, Z49, Z940
	ICD-9	403, 581, 582, 583, 585, 586, 587, 588, 5900, 7530, 7531, V420, V451, V56
Anemia	ICD-10	D5, D60, D61, D63, D64
	ICD-9	280, 281, 282, 283, 2840, 2848, 2849, 2850, 2852, 2858, 2859
Coagulopathy	ICD-10	D65, D66, D67, D680, D681, D682, D683, D685, D686, D688, D689, D69
	ICD-9	286, 287
Stroke/TIA (history)	ICD-10	G45, G46, I63, I64
	ICD-9	3623, 434.1, 434.9, 435, 436
(Other) arterial thromboembolism	ICD-10	H340, H341, H342, I513, I74, K550
	ICD-9	3623, 444, 5570
Venous thromboembolism (history)	ICD-10	H348, I26, I636, I676, I801, I802, I803, I808, I809, I81, I820, I822, I823, I828, I829, K765, O225, O873
	ICD-9	4340, 4376, 4511, 4512, 4518, 4519, 452, 4530, 4532, 4533, 4534, 4536, 4538, 4539, 6715
Major and clinically relevant bleeding (history)	ICD-10	D62, D683, H356, H431, I230, I312, I60, I61, I62, I850, I983, J942, K226, K250, K252, K254, K256, K260, K262, K264, K266, K270, K272, K274, K276, K280, K282, K284, K286, K290, K625, K661, K920, K921, K922, M250, N02, N837, N920, N921, N924, N938, N939, N950, R04, R31, R58, S064, S065, S066
	ICD-9	2851, 2865, 4230, 430, 431, 432, 4560, 4590, 5307, 5310, 5312, 5314, 5316, 5320, 5322, 5324, 5326, 5330, 5332, 5334, 5336, 5340, 5342, 5344, 5346, 5350, 5693, 578, 5967, 5997, 6207, 6262, 6266, 6268, 6269, 6270, 6271, 7191, 7847, 7848, 7863, 852
Parkinson's disease	ICD-10	F023, G20
	ICD-9	3320
Alzheimer's disease	ICD-10	F00, G30
	ICD-9	3310
Immune deficiency	ICD-10	D80, D81, D82, D83, D84, D89
	ICD-9	2790, 2791, 2792, 2793, 2798, 2799
Autoimmune/autoinflammatory disease	ICD-10	D86, E271, G35, K50, K51, K900, M05, M06, M07, M08, M09, M30, M31, M32, M33, M34, M35

	ICD-9	135, 2554, 2794, 340, 556, 5790, 6960, 710, 714, 725
Malignant tumor	ICD-10	C
	ICD-9	14, 15, 16, 17, 18, 19, 20

Supplemental Table 6. ATC codes used to identify medication prescription at the pharmacological subgroup level at index date

Pharmacological subgroup	ATC-code
Antihypertensives	C02, C03, C07, C08, C09
Lipid lowering drugs	C10
Non-steroid anti-inflammatory and anti-rheumatic drugs	M01A
Steroids	H02A, H02B
Antidepressants	N06A
Antacids	A02B
Antiplatelet drugs	B01AC
Data on outpatient medication prescriptions covered by the Dutch statutory basic medical insurance were obtained from Statistics Netherlands. These included the year of prescription and Anatomical Therapeutic Chemical (ATC) code. Medications received in hospitals and nursing homes were not available. Only for anticoagulants, more detailed prescription data were provided, including dispensing date and type of anticoagulant. The latter were used to identify prescriptions of antiplatelet drugs.	

Supplemental Table 7. ICD-10 codes used to identify bleeding and thromboembolic events

Major & clinically relevant bleeding		
D62: Acute posthaemorrhagic anaemia	K256: Gastric ulcer, chronic or unspecified with both haemorrhage and perforation	K920: Haematemesis
D683: Haemorrhagic disorder due to circulating anticoagulants	K260: Duodenal ulcer, acute with haemorrhage	K921: Melaena
H356: Retinal haemorrhage	K262: Duodenal ulcer, acute with both haemorrhage and perforation	K922: Gastrointestinal haemorrhage, unspecified
H431: Vitreous haemorrhage	K264: Duodenal ulcer, chronic or unspecified with haemorrhage	M250: Haemarthrosis
I230: Haemopericardium as current complication following acute myocardial infarction	K266: Duodenal ulcer, chronic or unspecified with both haemorrhage and perforation	N02: Recurrent and persistent haematuria
I312: Haemopericardium, not elsewhere classified	K270: Peptic ulcer, site unspecified, acute with haemorrhage	N837: Haematoma of broad ligament
I60: Subarachnoid haemorrhage	K272: Peptic ulcer, site unspecified, acute with both haemorrhage and perforation	N920: Excessive and frequent menstruation with regular cycle
I61: Intracerebral haemorrhage	K274: Peptic ulcer, site unspecified, chronic or unspecified with haemorrhage	N921: Excessive and frequent menstruation with irregular cycle
I62: Other nontraumatic intracranial haemorrhage	K276: Peptic ulcer, site unspecified, chronic or unspecified with both haemorrhage and perforation	N924: Excessive bleeding in the premenopausal period
I850: Oesophageal varices with bleeding	K280: Gastrojejunal ulcer, acute with haemorrhage	N938: Other specified abnormal uterine and vaginal bleeding
I983: Oesophageal varices with bleeding in diseases classified elsewhere	K282: Gastrojejunal ulcer, acute with both haemorrhage and perforation	N939: Abnormal uterine and vaginal bleeding, unspecified
J942: Haemothorax	K284: Gastrojejunal ulcer, chronic or unspecified with haemorrhage	N950: Postmenopausal bleeding
K226: Gastro-oesophageal laceration-haemorrhage syndrome	K286: Gastrojejunal ulcer, chronic or unspecified with both haemorrhage and perforation	R04: Haemorrhage from respiratory passages
K250: Gastric ulcer, acute with haemorrhage	K290: Acute haemorrhagic gastritis	R31: Unspecified haematuria
K252: Gastric ulcer, acute with both haemorrhage and perforation		R58: Haemorrhage, not elsewhere classified
K254: Gastric ulcer, chronic or unspecified with haemorrhage		S064: Epidural haemorrhage
		S065: Traumatic subdural haemorrhage
		S066: Traumatic subarachnoid haemorrhage

K625: Haemorrhage of anus and rectum

K661: Haemoperitoneum

Venous thromboembolism

PE/DVT+thrombophlebitis

I26: Pulmonary embolism

I801: Phlebitis and thrombophlebitis of femoral vein

I802: Phlebitis and thrombophlebitis of other deep vessels of lower extremities

(Deep vein thrombosis NOS)

I803: Phlebitis and thrombophlebitis of lower extremities, unspecified

(Embolism or thrombosis of lower extremity NOS)

VTE other

H348: Other retinal vascular occlusions

I808: Phlebitis and thrombophlebitis of other sites

I809: Phlebitis and thrombophlebitis of unspecified site

I820: Budd-Chiari

I821: thrombophlebitis migrans

I822: Embolism and thrombosis of vena cava

I823: Embolism and thrombosis of renal vein

I828: Embolism and thrombosis of other specified veins

I829: Embolism and thrombosis of unspecified vein

K765: Hepatic veno-occlusive disease

O223: Deep phlebothrombosis in pregnancy (Deep-vein thrombosis, antepartum)

O229: Venous complication in pregnancy, unspecified

Cerebral sinus thrombosis

I636: Cerebral infarction due to cerebral venous thrombosis, nonpyogenic

I676: Nonpyogenic thrombosis of intracranial venous system

O225: Cerebral venous thrombosis in pregnancy

O873: Cerebral venous thrombosis in the puerperium

Portal vein thrombosis

I81: Portal vein thrombosis

O871: Deep phlebothrombosis in the puerperium (Deep-vein thrombosis, postpartum/Pelvic thrombophlebitis, postpartum)
 O879: Venous complication in the puerperium, unspecified
 O882: Obstetric blood-clot embolism (Obstetric (pulmonary) embolism NOS/Puerperal (pulmonary) embolism NOS)

Arterial thromboembolism

Ischemic stroke/TIA

I63: Cerebral infarction
 G45: Transient cerebral ischaemic attacks and related syndromes
 G46: Vascular syndromes of brain in cerebrovascular diseases
 I64: Stroke, not specified as haemorrhage or infarction

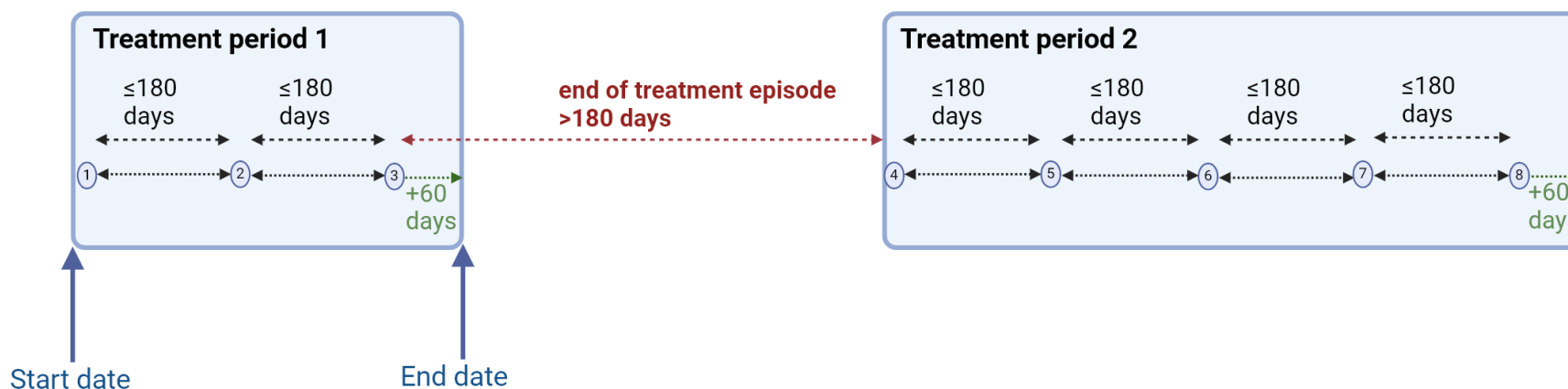
Other arterial thromboembolism

H340: Transient retinal artery occlusion
 H341: Central retinal artery occlusion
 H342: Other retinal artery occlusions
 I513: intracardial thrombosis
 I74: Arterial embolism and thrombosis
 K550: acute vascular disorder intestine

Myocardial infarction

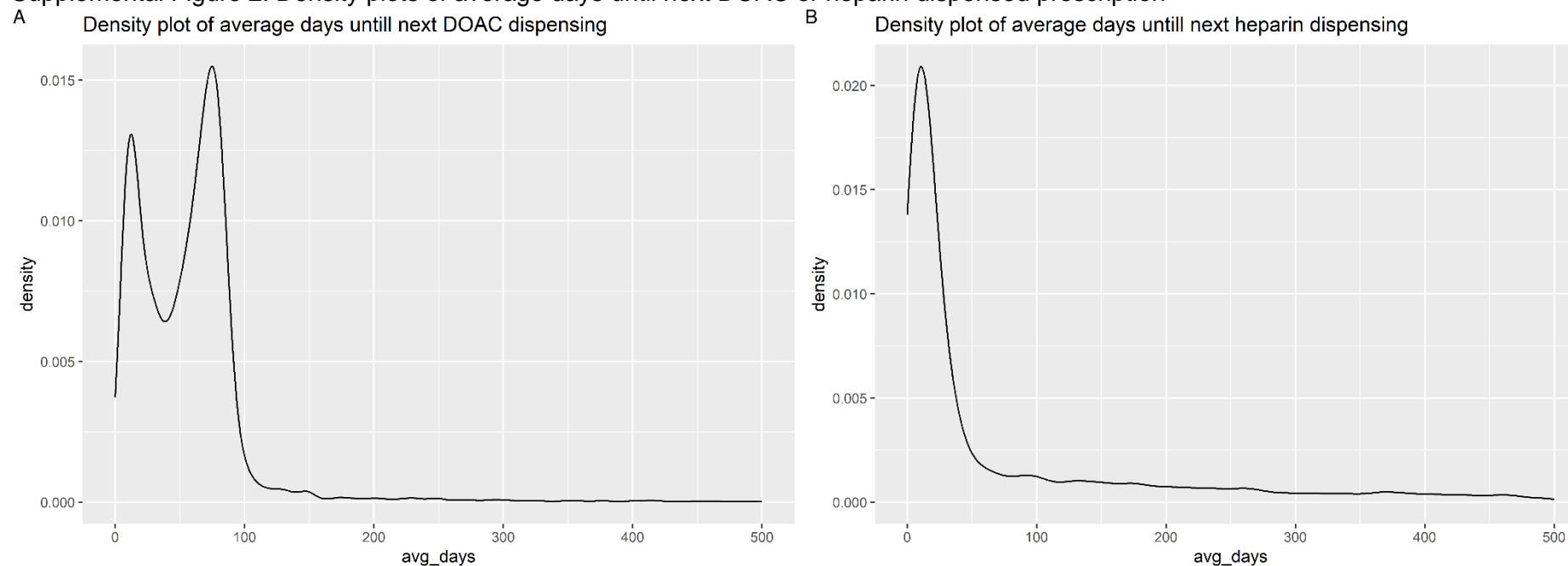
I21: Acute myocardial infarction
 I22: Subsequent myocardial infarction

Supplemental Figure 1. Construction of treatment periods for anticoagulants



Treatment episodes for anticoagulants were constructed assuming that a dispensed prescription lasted a fixed number of days, unless a refill, death or end of follow-up occurred earlier. Whenever the period between two subsequent dispensed prescription dates exceeded this fixed number of days, the next prescription was considered to belong to a new treatment period. A predefined number of days was added to the last prescription date within the treatment period to construct the end of the corresponding treatment period. Different exposure times were applied to the different types of anticoagulants: 180 days for VKA prescriptions, 120 days for DOAC prescriptions, and 30 days for LMWH prescriptions. The end date of each treatment period was constructed by adding a fixed number of days to the last dispensing date within the treatment period. This was 60 days for VKA prescriptions, 120 days for DOAC prescriptions and 30 days for LMWH prescriptions. Created in BioRender. Kruij, M. (2024) <https://BioRender.com/y81a190>

Supplemental Figure 2. Density plots of average days until next DOAC or heparin dispensed prescription



Density plots of average days until next DOAC (A) or heparin (B) dispensing per patient studied in two random samples of 10,000 patients with DOAC or heparin prescriptions between 2013-2019, respectively. For patients with DOAC prescriptions, the median number of days until the next DOAC dispensing per patient was 58 days with a 95th percentile of 117 days. For heparin the median was 22 days.

Supplemental Results

Supplemental Table 8. Additional baseline characteristics

	Total	Cancer	Non-cancer
	(N=18145)	(N=2457)	(N=15688)
Standardized household income, quintile^a, No. (%)			
First (lowest)	4207 (23.2)	589 (24.0)	3618 (23.1)
Second	6401 (35.3)	787 (32.0)	5614 (35.8)
Third	3009 (16.6)	471 (19.2)	2538 (16.2)
Fourth	1923 (10.6)	295 (12.0)	1628 (10.4)
Fifth (highest)	1408 (7.8)	261 (10.6)	1147 (7.3)
Institutional household/unknown	1197 (6.6)	54 (2.2)	1143 (7.3)
≥1 comorbidity present at index date^b, No. (%)	8195 (45.2)	956 (38.9)	7239 (46.1)
Autoimmune disease or immune deficiency	326 (1.8)	31 (1.3)	296 (1.9)
Thyroid disease	286 (1.6)	22 (0.9)	264 (1.7)
COPD	1696 (9.3)	162 (6.6)	1534 (9.8)
Asthma and other chronic lung diseases	338 (1.9)	25 (1.0)	313 (2.0)
History of major and clinically relevant bleeding	811 (4.5)	98 (4.0)	713 (4.5)
History of VTE	287 (1.6)	59 (2.4)	228 (1.5)
History of ATE	193 (1.1)	32 (1.3)	161 (1.0)
History of stroke	479 (2.6)	52 (2.1)	427 (2.7)
History of MI	1666 (9.2)	134 (5.5)	1532 (9.8)
Anemia	1440 (7.9)	136 (5.5)	1304 (8.3)
Coagulopathy	391 (2.2)	38 (1.5)	353 (2.3)
Heart failure	2380 (13.1)	93 (3.8)	2287 (14.6)
Valvular heart disease	1660 (9.1)	108 (4.4)	1552 (9.9)
Atrial fibrillation	4332 (23.9)	420 (17.1)	3912 (24.9)
Atherosclerosis	1622 (8.9)	161 (6.6)	1461 (9.3)
Peripheral artery disease	331 (1.8)	41 (1.7)	290 (1.8)
Diabetes mellitus	2292 (12.6)	198 (8.1)	2094 (13.3)
Hypertension	3119 (17.2)	295 (12.0)	2824 (18.0)
Kidney disease	1982 (10.9)	138 (5.6)	1844 (11.8)
Liver disease	247 (1.4)	31 (1.3)	216 (1.4)
ATE: Arterial Thrombotic Event; COPD: Chronic Obstructive Pulmonary Disease; MI: Myocardial Infarction; VTE: Venous Thromboembolic Event.			
^a Percentile groups were determined based on disposable income of private households of the complete Dutch population in the Statistics Netherlands database.			
^b Comorbidities were identified by examining data on hospitalizations within 3 years before the index date using ICD-10 codes and ICD-9 codes restricting to main or primary diagnosis of hospital admission. One or more comorbidities can be present.			

Supplemental Table 9. Cancer-specific baseline characteristics

		Cancer (N=2457)
Differentiation grade^a, No. (%)		
	Grade I	36 (1.5)
	Grade II	286 (11.6)
	Grade III	380 (15.5)
	Grade IV	83 (3.4)
	<i>Unknown or not applicable</i>	1672 (68.1)
Treatment of cancer, No. (%)		
	Chemotherapy	675 (27.5)
	Radiotherapy	405 (16.5)
	Surgery ^b	321 (13.1)
	Hormonal therapy	49 (2.0)
	Targeted therapy	119 (4.8)
^a The differentiation grade was identified by using the 6th number of the ICD-O-3 codes ^b Surgery was defined as any surgical procedure involving the removal of (a portion of) an organ.		

Supplemental Table 10. Median survival and follow-up times for different life-limiting diseases

	N at t=0	Number of deaths	Median survival time (95%CI)	Median follow-up time (IQR)
Total	18145	10948	2.03 (1.97, 2.10)	3.59 (1.95, 5.22)
Type of life-limiting disease				
Cancer	2457	2072	0.35 (0.32, 0.38)	3.41 (2.06, 5.07)
Non-cancer	15688	8876	2.50 (2.43, 2.59)	3.60 (1.95, 5.22)
Type of non-cancer life-limiting disease				
COPD	547	251	2.10 (1.72, 2.43)	1.93 (1.09, 2.64)
Dementia	387	275	2.14 (1.84, 2.57)	4.75 (2.80, 6.00)
Diabetes mellitus	327	203	2.28 (1.88, 2.94)	4.64 (2.20, 5.69)
Heart disease	10879	6185	2.57 (2.46, 2.68)	3.80 (2.07, 5.32)
Hip fracture	3277	1792	2.53 (2.40, 2.67)	3.20 (1.77, 4.80)
Interstitial lung disease	107	76	2.14 (1.26, 2.71)	3.58 (2.61, 5.62)
Liver disease	164	94	2.09 (1.09, 3.50)	3.57 (1.88, 5.57)

CI = confidence interval; COPD = Chronic obstructive pulmonary disease; IQR = Interquartile range. A life-limiting disease was defined according to the definition of a severe medical condition by Kelley et al. as “a diagnosis that carries an increased risk of mortality, hospitalization and emergency room visits”²⁷. These diseases were identified by ICD-10 codes of diagnoses registered as either main or primary diagnosis of the hospital admission or registered cancer diagnosis by the Netherlands Cancer Registry. Median survival and follow-up time were estimated by the Kaplan-Meier estimator.

Supplemental Table 11. Cumulative incidence and incidence rate of VKA and anticoagulant treatment discontinuation stratified by life-limiting disease

	VKA discontinuation				Anticoagulation discontinuation			
	IR / 100 PY (95%CI)	6-month Cumulative incidence % (95%CI)	1-year Cumulative incidence % (95%CI)	3-year Cumulative incidence % (95%CI)	IR / 100 PY (95%CI)	6-month Cumulative incidence % (95%CI)	1-year Cumulative incidence % (95%CI)	3-year Cumulative incidence % (95%CI)
Cancer	63.1 (59.3- 67.0)	33.7 (31.9-35.6)	38.7 (36.7-40.6)	43.7 (41.7-45.8)	42.6 (39.7- 45.7)	23.8 (22.1- 25.5)	28.7 (26.9-30.5)	33.7 (31.7-35.6)
COPD	17.3 (14.1- 21.0)	10.8 (8.3-13.7)	13.6 (10.8-16.7)	24.7 (20.3-29.3)	10.4 (8.0-13.2)	6.4 (4.6-8.8)	8.2 (6.0-10.7)	17.3 (13.0-22.1)
Dementia	21.7 (18.4- 25.5)	16.8 (13.3-20.7)	23.2 (19.1-27.6)	35.6 (30.7-40.6)	19.9 (16.7-23.4)	15.5 (12.1- 19.4)	22.2 (18.2-26.5)	33.5 (28.7-38.3)
Diabetes mellitus	17.1 (13.9- 20.7)	12.3 (9.0-16.1)	14.9 (11.2-19.0)	27.0 (22.0-32.1)	14.1 (11.3-17.4)	10.8 (7.7- 14.4)	12.7 (9.3-16.6)	23.6 (18.8-28.6)
Heart disease	13.8 (13.3- 14.3)	11.0 (10.4-11.6)	14.4 (13.7-15.1)	23.8 (22.9-24.6)	9.4 (9.0-9.8)	7.4 (6.9-7.9)	10.1 (9.5-10.7)	17.4 (16.6-18.2)
Hip fracture	18.7 (17.6- 19.9)	14.9 (13.7-16.1)	18.4 (17.1-19.8)	30.1 (28.4-31.9)	15.5 (14.4-16.5)	12.7 (11.6- 13.9)	15.8 (14.6-17.1)	26.1 (24.4-27.7)
Interstitial lung disease	18.6 (12.7- 26.2)	12.2 (6.8-19.2)	16.9(10.5-24.7)	29.4 (20.6-38.8)	12.0 (7.5-18.1)	9.4 (4.8- 15.9)	11.3 (6.1-18.2)	19.1 (12.0-27.6)
Liver disease	29.6 (22.8- 37.9)	22.1 (16.1-28.8)	29.9 (23.0-37.2)	36.5 (28.9-44.1)	21.0 (15.5- 27.7)	17.9 (12.4- 24.1)	24.4 (18.0-31.3)	30.5 (23.3-38.0)

Cumulative incidences were computed taking the competing risk of death into account. Crude incidence rates (IR) were estimated as events per 100 person-years (PY). Abbreviations: CI = confidence interval; COPD = chronic obstructive pulmonary disease; IR = incidence rate; PY = person-years; VKA = vitamin K antagonist.

Supplemental Table 12. Mean proportion of days covered with anticoagulants during follow-up

	Number of patients, No.	Mean PDC % (SD)	Adherent* patients %
Total	18145	91.8 (22.2)	88.0
Type of life-limiting disease			
Cancer	2457	87.2 (26.4)	81.0
Non-cancer	15688	92.6 (21.4)	89.2
Type of non-cancer life-limiting disease			
COPD	547	95.3 (17.3)	93.6
Dementia	387	83.9 (30.2)	75.5
Diabetes mellitus	327	88.0 (26.4)	82.9
Heart disease	10879	94.1 (18.8)	91.3
Hip fracture	3277	88.9 (26.3)	84.3
Interstitial lung disease	107	92.7 (21.2)	87.9
Liver disease	164	82.3 (32.2)	76.8
Sex			
Females	8841	91.0 (23.4)	86.8

Males

9304

92.6 (21.1)

89.2

*Adherent was defined as a proportion of days covered (PDC) with anticoagulants >80%. Abbreviations: COPD = chronic obstructive pulmonary disease; PDC = proportion of days covered; SD = standard deviation.

Supplemental Table 13. Cumulative incidence and incidence rate of VKA and anticoagulant treatment discontinuation in sensitivity analysis
VKa exposure time

	VKa discontinuation				Anticoagulation discontinuation			
	IR / 100 PY (95%CI)	6-month Cumulative incidence % (95%CI)	1-year Cumulative incidence % (95%CI)	3-year Cumulative incidence % (95%CI)	IR / 100 PY (95%CI)	6-month Cumulative incidence % (95%CI)	1-year Cumulative incidence % (95%CI)	3-year Cumulative incidence % (95%CI)
Total	17.7 (17.2-18.2)	14.9 (14.4-15.5)	18.6 (18.1-19.2)	27.7 (27.0-28.4)	12.7 (12.3-13.1)	10.8 (10.4-11.3)	14.0 (13.5-14.5)	21.4 (20.7-22.0)
Type of life-limiting disease								
Cancer	62.8 (59.0-66.7)	33.7 (31.8-35.5)	38.5 (36.6-40.5)	43.6 (41.6-45.6)	42.4 (39.5-45.4)	23.7 (22.0-25.4)	28.5 (26.7-30.4)	33.5 (31.6-35.5)
Non-cancer	15.0 (14.5-15.5)	12.0 (11.5-12.5)	15.5 (15.0-16.1)	25.3 (24.5-26.0)	10.8 (10.4-11.2)	8.8 (8.4-9.3)	11.7 (11.2-12.2)	19.5 (18.8-20.2)
Type of non-cancer life-limiting disease								
COPD	17.1 (14.0-20.8)	10.6 (8.2-13.4)	13.4 (10.6-16.5)	24.5 (20.1-29.2)	10.2 (7.9-13.0)	6.3 (4.4-8.5)	8.0 (5.8-10.5)	17.2 (12.9-22.0)
Dementia	21.7 (18.4-25.5)	16.8 (13.3-20.7)	23.2 (19.1-27.6)	35.6 (30.7-40.6)	19.9 (16.7-23.4)	15.5 (12.1-19.4)	22.2 (18.2-26.5)	33.5 (28.7-38.3)

Diabetes mellitus	16.7 (13.6-20.3)	12.3 (9.0-16.1)	14.9 (11.2-19.0)	26.6 (21.7-31.8)	13.7 (11.0-17.0)	10.8 (7.7-14.4)	12.7 (9.3-16.6)	23.2 (18.5-28.2)
Heart disease	13.5 (13.0-14.1)	10.9 (10.3-11.5)	14.3 (13.7-15.0)	23.4 (22.5-24.2)	9.2 (8.8-9.6)	7.4 (6.9-7.9)	10.1 (9.5-10.7)	17.0 (16.3-17.8)
Hip fracture	18.5 (17.4-19.7)	14.8 (13.6-16.1)	18.3 (16.9-19.6)	29.8 (28.1-31.5)	15.2 (14.2-16.3)	12.6 (11.5-13.8)	15.7 (14.5-17.0)	25.7 (24.1-27.4)
Interstitial lung disease	18.0 (12.2-25.6)	11.3 (6.1-18.1)	16.9(10.5-24.7)	28.1 (19.5-37.4)	11.4 (7.1-17.5)	8.4 (4.1-14.7)	11.3 (6.1-18.2)	17.8 (11.0-26.0)
Liver disease	29.6 (22.7-37.8)	22.1 (16.1-28.8)	29.9 (23.0-37.2)	36.5 (28.9-44.2)	21.0 (15.5-27.7)	17.9 (12.4-24.1)	24.4 (18.0-31.3)	30.5 (23.3-38.0)
Sex								
Females	17.8 (17.1-18.5)	14.9 (14.1-15.6)	18.9 (18.0-19.7)	28.7 (27.7-29.7)	13.1 (12.6-13.7)	11.1 (10.4-11.7)	14.4 (13.6-15.1)	22.6 (21.7-23.6)
Males	17.6 (16.9-18.3)	15.0 (14.3-15.7)	18.4 (17.6-19.2)	26.8 (25.9-27.8)	12.3 (11.7-12.9)	10.6 (10.0-11.3)	13.6 (12.9-14.3)	20.2 (19.4-21.1)

This table displays the cumulative incidences and incidence rates of vitamin K antagonist (VKA) and anticoagulant treatment discontinuation calculated in a sensitivity analysis where we varied the exposure time of a VKA prescription when constructing treatment periods (150 days + 100 days added versus 180 days + 60 days added in the main analysis).

Cumulative incidences were computed taking the competing risk of death into account. Crude incidence rates (IR) were estimated as events per 100 person-years (PY). Abbreviations: CI = confidence interval; COPD = chronic obstructive pulmonary disease; IR = incidence rate; PY = person-years; VKA = vitamin K antagonist.

Supplemental Table 14. Cumulative incidence and incidence rate of anticoagulant treatment discontinuation in sensitivity analysis heparin exposure time

	Anticoagulation discontinuation			
	IR / 100 PY (95%CI)	6-month Cumulative incidence % (95%CI)	1-year Cumulative incidence % (95%CI)	3-year Cumulative incidence % (95%CI)
Total	12.7 (12.3-13.1)	10.7 (10.3-11.2)	13.8 (13.3-14.3)	21.2 (20.6-21.9)
Type of life-limiting disease				
Cancer	39.9 (37.1- 42.8)	22.9 (21.3-24.6)	27.2 (25.5-29.0)	31.4 (29.5-33.3)
Non-cancer	10.9 (10.6-11.3)	8.8 (8.4-9.3)	11.7 (11.2-12.2)	19.7 (19.0-20.3)
Type of non-cancer life-limiting disease				
COPD	10.1 (7.8-12.9)	6.4 (4.6-8.8)	7.9 (5.8-10.5)	15.9 (12.2-20.1)
Dementia	19.9 (16.7-23.4)	15.5 (12.1-19.4)	22.2 (18.2-26.5)	33.5 (28.7-38.3)
Diabetes mellitus	13.9 (11.1-17.2)	10.8 (7.7-14.4)	12.7 (9.3-16.6)	22.8 (18.1-27.7)
Heart disease	9.3 (8.9-9.7)	7.3 (6.9-7.8)	10.0 (9.5-10.6)	17.2 (16.5-18.0)
Hip fracture	15.4 (14.4-16.4)	12.7 (11.6-13.9)	15.7 (14.5-17.0)	26.0 (24.3-27.6)

Interstitial lung disease	12.0 (7.5-18.1)	9.4 (4.8-15.9)	11.3 (6.1-18.2)	19.1 (12.0-27.6)
Liver disease	20.9 (15.5- 27.7)	17.9 (12.4-24.1)	24.4 (18.0-31.3)	29.5 (22.5-36.9)
Sex				
Females	13.1 (12.6-13.7)	11.0 (10.4-11.7)	14.3 (13.6-15.1)	22.5 (21.6-23.5)
Males	12.2 (11.6-12.8)	10.5 (9.9-11.1)	13.3 (12.6-14.0)	20.0 (19.2-20.9)

This table displays the cumulative incidences and incidence rates of anticoagulant treatment discontinuation calculated in a sensitivity analysis where we varied the exposure time of a heparin (i.e. LMWH) prescription when constructing treatment periods (100 days added versus 30 days in the main analysis). Cumulative incidences were computed taking the competing risk of death into account. Crude incidence rates (IR) were estimated as events per 100 person-years (PY). Abbreviations: CI = confidence interval; COPD = chronic obstructive pulmonary disease; IR = incidence rate; PY = person-years.

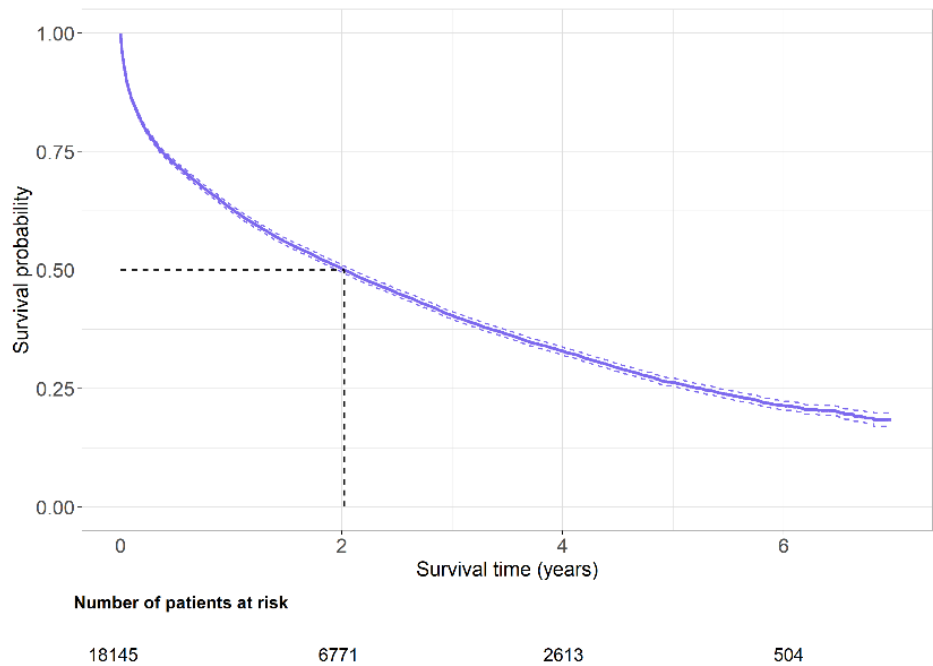
Supplemental Table 15. Incidence rates of bleeding and thromboembolic events stratified by anticoagulation exposure in sensitivity analyses

	Extending AC exposed period by 7 days		Sensitivity analysis heparin exposure time		Sensitivity analysis VKA exposure time	
	IR/100 PY AC exposed (95%CI)	IR/100 PY unexposed (95%CI)	IR/100 PY AC exposed (95%CI)	IR/100 PY unexposed (95%CI)	IR/100 PY AC exposed (95%CI)	IR/100 PY unexposed (95%CI)
Major and clinically relevant bleeding	2.6 (2.4-2.8)	1.9 (1.4-2.7)	2.6 (2.4-2.8)	2.1 (1.5-2.8)	2.6 (2.4-2.8)	2.0 (1.5-2.7)
Venous thromboembolism	0.2 (0.1-0.2)	0.4 (0.2-0.8)	0.2 (0.1-0.2)	0.4 (0.2-0.7)	0.2 (0.1-0.2)	0.4 (0.2-0.8)
Arterial thromboembolism	3.1 (2.9-3.3)	3.0 (2.3-3.8)	3.1 (2.9-3.3)	3.2 (2.5-4.1)	3.1 (2.9-3.3)	3.3 (2.5-4.1)
Myocardial infarction	1.1 (1.0-1.3)	0.8 (0.5-1.3)	1.1 (1.0-1.3)	0.8 (0.5-1.3)	1.1 (1.0-1.3)	0.9 (0.5-1.4)
Stroke	1.6 (1.5-1.7)	1.8 (1.3-2.4)	1.6 (1.4-1.7)	2.0 (1.5-2.7)	1.6 (1.4-1.7)	2.0 (1.4-2.7)
Other	0.4 (0.4-0.5)	0.5 (0.2-0.8)	0.4 (0.4-0.5)	0.4 (0.2-0.8)	0.4 (0.4-0.5)	0.5 (0.2-0.9)

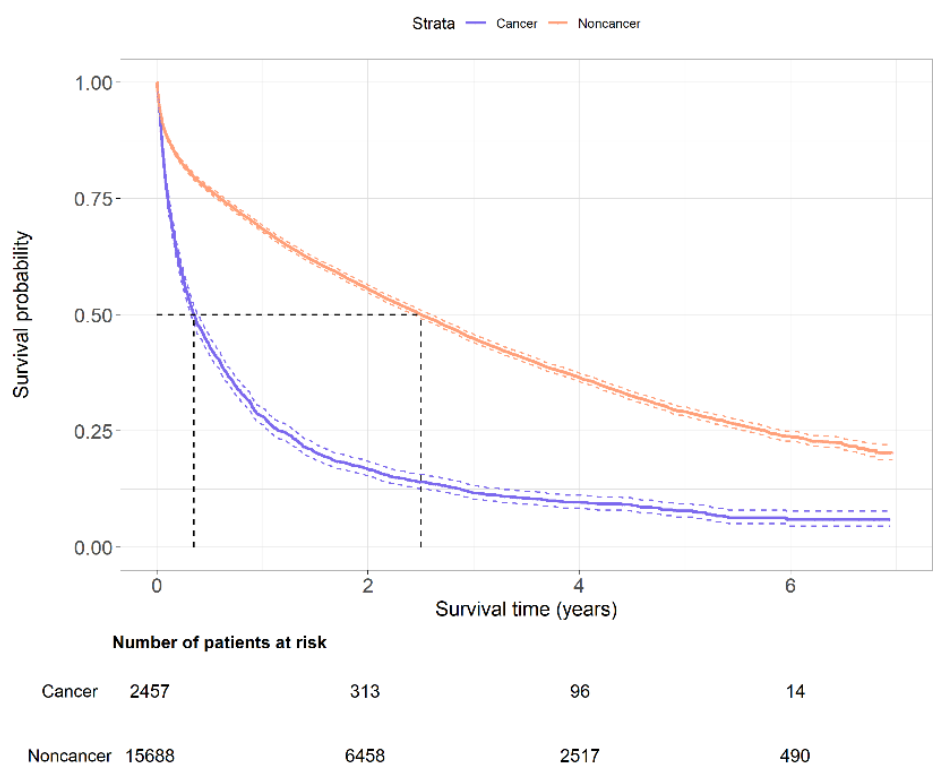
This table displays the incidence rates of first bleeding and thromboembolic events stratified by anticoagulant exposure, estimated in three sensitivity analyses. The following sensitivity analyses were performed: (1) extending the period exposed to anticoagulants by seven days, (2) varying the exposure time of a heparin (i.e. LMWH) prescription when constructing treatment periods (100 days added versus 30 days in the main analysis), (3) varying the exposure time of a VKA prescription when constructing treatment periods (150 days + 100 days added versus 180 days + 60 days added in the main analysis). Incidence rates were estimated as events per 100 PYs, where the observation time was categorized according to anticoagulant exposure. AC = anticoagulant; CI = confidence interval; IR = incidence rate; PY = person-years.

Supplemental Figure 3. Kaplan-Meier survival curve for the total cohort and for patients with cancer versus non-cancer diseases

A Survival curve for the total cohort

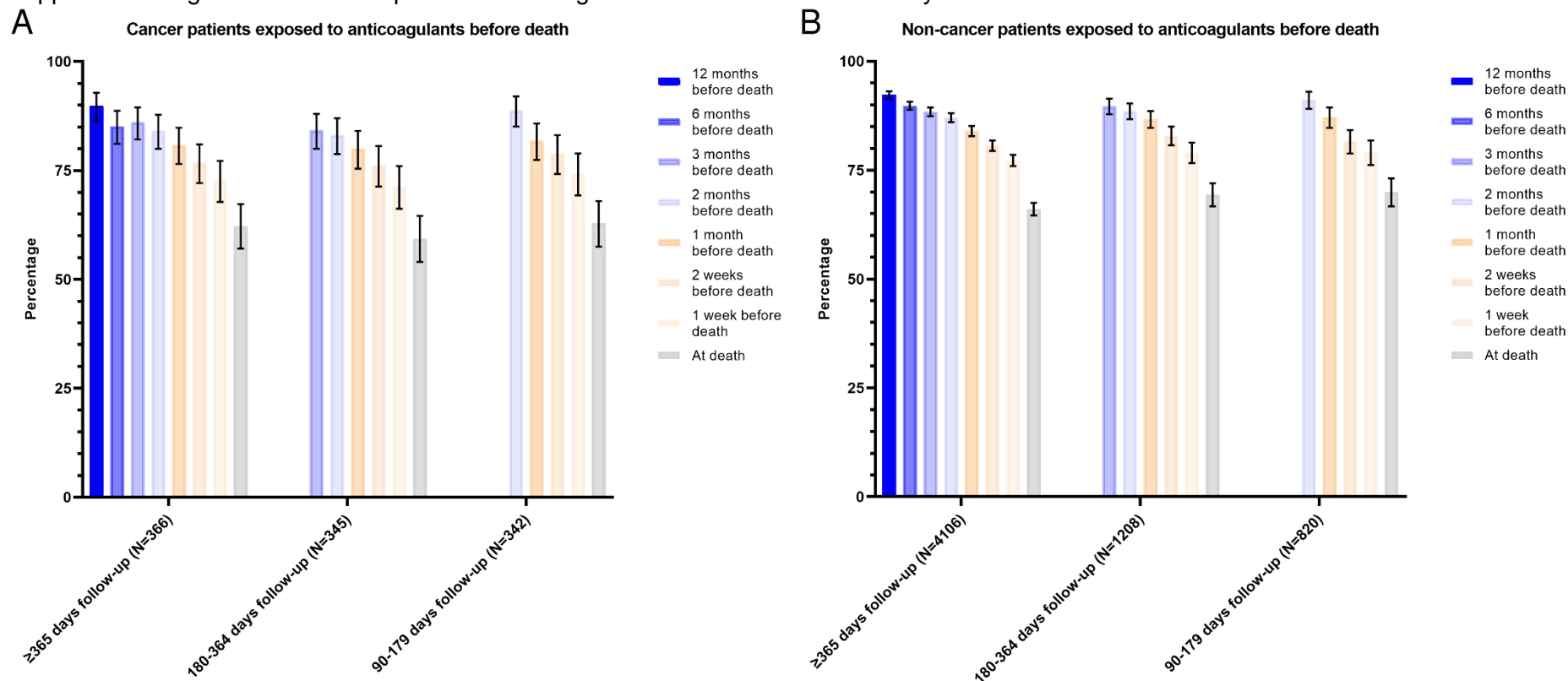


B Survival curve for cancer and noncancer patients



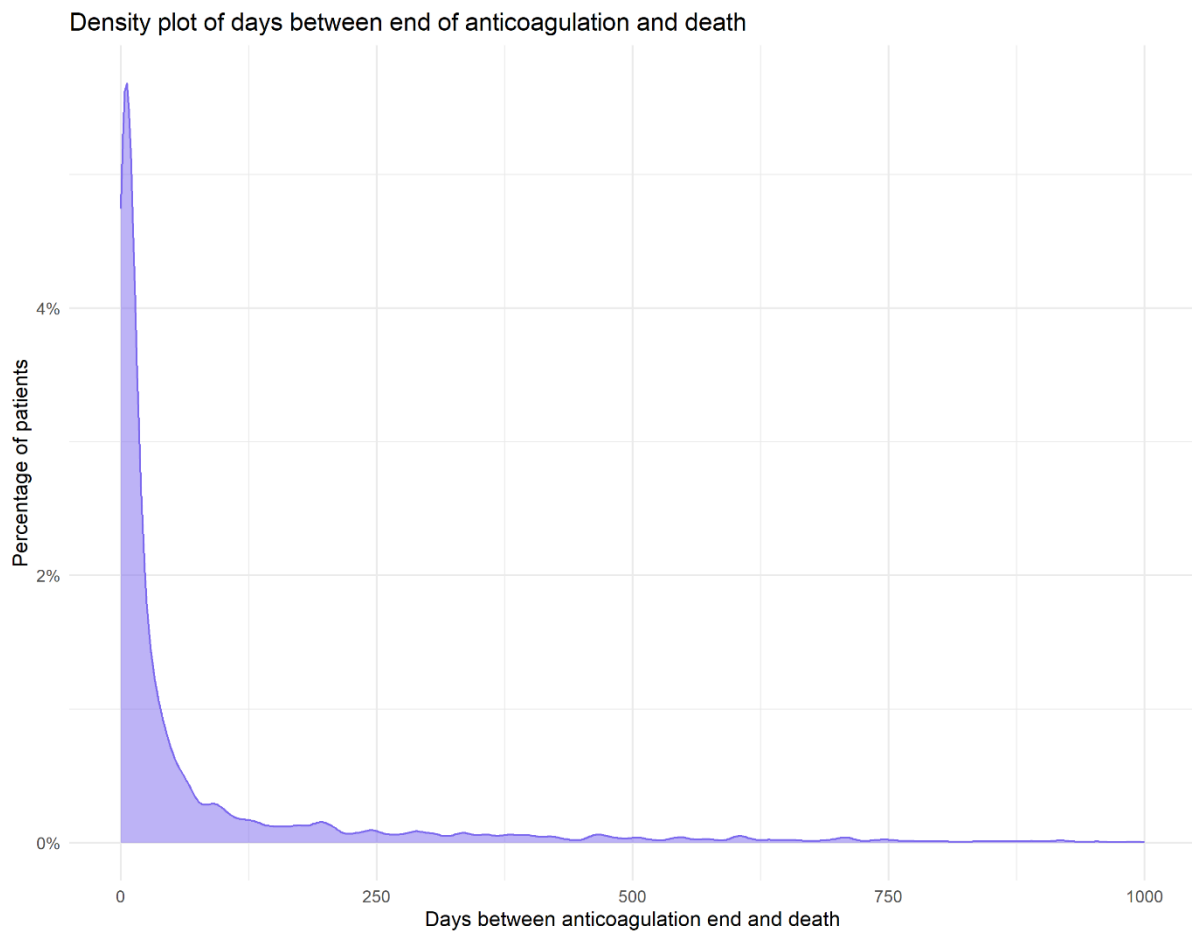
Kaplan-Meier survival curves for the total cohort (A) and patients with cancer versus non-cancer diseases separately (B). Median survival was estimated by the Kaplan-Meier estimator.

Supplemental Figure 4. Patients exposed to anticoagulants before death stratified by cancer versus non-cancer diseases



Percentage of patients exposed to anticoagulants with corresponding 95% confidence intervals at different time points before death, stratified according to the amount of follow-up time between index date and date of death and by cancer versus non-cancer diseases. This analysis was restricted to patients who died during follow-up.

Supplemental Figure 5. Density plot of days between end of anticoagulant treatment and death



Calculated among patients who died during follow-up and discontinued anticoagulant treatment before death (N=3372).

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