APPENDIX 1

SUPPLEMENTAL TABLES

Supplemental Table 1. Description of databases at ICES used to ascertain study variables

Database	Description	Relevance
Registered Persons Database (RPDB)	Records all demographic and vital statistics of all individuals covered by the Ontario Health Insurance Plan.	Used to capture vital status and study sociodemographic characteristics of patients, including age, sex, neighbourhood income quintile, and rural residence.
Immigrant, Refugees, and Citizenship Canada Permanent Residents Database (CIC)	Provides information on permanent and temporary residents, as well as immigration and citizenship programs.	Used to determine whether a patient was a recent immigrant to Canada, captured by landing date.
Ontario Health Insurance Plan Database (OHIP)	Records data on physician service claims, including diagnostic codes.	Used for cohort identification (palliative care physician home visits), and for identification of comorbidities.
Ontario Drug Benefit Plan Database (ODB)	Captures information on drug prescriptions filled for individuals 65 and older.	Used to identify anticoagulant and other prescription medication use.
Canadian Institute for Health Information Discharge Abstract Database (DAD)	Records data from hospitalizations in acute care hospitals in Ontario.	Used to study indications for anticoagulation, comorbidities, subsequent thrombotic/bleeding events, and location of death
National Ambulatory Care Reporting System Database (NACRS)	Records data on ambulatory and emergency department visits.	Used to study indications for anticoagulation, comorbidities, subsequent thrombotic/bleeding events, and location of death.
Same Day Surgery Database (SDS)	Records information from same day surgeries/procedures.	Used to identify comorbidities and location of death.
Continuing Care Reporting System Database (CCRS)	Records information from continuing care facilities.	Used in conjunction with other databases to ascertain location of death.
Ministry of Health and Long-Term Care Institution Database (INST)	Records information from long-term care facilities.	Used in conjunction with other databases to ascertain location of death.
National Rehabilitation Reporting System Database (NRS)	Records information from rehabilitation facilities.	Used in conjunction with other databases to ascertain location of death.
Ontario Mental Health Reporting System Database	Records information from mental health facilities.	Used in conjunction with other databases to ascertain location of death.
ICES Physician Database (IPDB) and Corporate Provider Database (CPDB)	Records demographic, training, and practice characteristics of physicians in Ontario.	Used to study characteristics of palliative care physicians, including age, sex, graduation year, and training/specialty.
Drug Identification Number (DIN) File (IVQIA Solutions Canada Inc.)	Contains information on drug and product names in the ODB formulary	Used to identify an exhaustive list of prescription medications dispensed

Supplemental Table 2. Data sources and description of sociodemographic, clinical and health care variables

Variable	Source	Description	References
Sociodemographic variables			
Age	RPDB		
Sex	RPDB	*SEX*	
Neighbourhood income quintile	RPDB	*INCQUINT* variable (nearest census-based neighbourhood income quintile)	
Rural residence	RPDB	*RURAL* flag: *%getdemo* macro	
Immigrant status	CIC	1. Recent immigrant: *LANDING_DATE* within 10 years prior to index date. 2. Long-standing resident: all others	(1,2)
Vital status	RPDB	*DTHDATE*	(3)
Diagnostic and procedural variables			
Atrial fibrillation	DAD, NACRS	ICD-9: 4273 ICD-10-CA: I48 Look-back window: 10 years*	(4–7)
Venous thromboembolism	DAD, NACRS	ICD-10-CA: • Deep vein thrombosis: I801, I802, I803, I808, I809, I81, I820, I821, I822, I823, I828, I829 • Pulmonary embolism: I260, I269 Look-back window: 5 years*	(4–7)
Mechanical heart valve	DAD	CCP: 4721, 4723, 4725, 4727, 4729 CCI: 1HS780GPFE, 1HS80LAFE, 1HS90LACF, 1HT80GPFE, 1HT80LAFE, 1HT90LACF, 1HU80GPFE, 1HU80LAFE, 1HU90LACF, 1HU90PNXXK, 1HU90PNCF, 1HV80GPFE, 1HV80LAFE, 1HV90LACF, 1HV90LACFA, 1HV90LACFL, 1HV90LACFN, 1HV90WJCFN Look-back window: 10 years*	(4–7)
Cancer	DAD, NACRS, OHIP	Prior diagnosis of cancer (any) identified using HSPRN macro for the presence of 18 chronic conditions. Look-back window: 10 years*	(8–10)
Congestive heart failure	DAD, NACRS, OHIP	Prior diagnosis of congestive heart failure identified using HSPRN macro for the presence of 18 chronic conditions. Look-back window: 10 years*	(8–10)
Hypertension	DAD, NACRS, OHIP	Prior diagnosis of hypertension identified using HSPRN macro for the presence of 18 chronic conditions. Look-back window: 10 years*	(8–10)
Diabetes mellitus	DAD, NACRS, OHIP	Prior diagnosis of diabetes mellitus identified using HSPRN macro for the presence of 18 chronic conditions. Look-back window: 10 years*	(8–10)
Ischemic stroke or transient ischemic attack	DAD, NACRS	ICD-10-CA: • Ischemic stroke: I630, I631, I632, I633, I634, I635, I636, I638, I639, • TIA: G450, G451, G452, G453, G454, G458, G459	(4–7)
Coronary artery disease	DAD, NACRS, OHIP	Myocardial infarction: • ICD-10-CA: I21, I22 All other coronary artery disease: • ICD-10-CA: I22, I23, I24, I25, Z955, Z958, Z959, R931, T822 • CCI: 1IJ54, 1IJ57, 1IJ50, 1IJ76 • OHIP: R741, R742, R743, G298, E646, E651, E652, E654, E655, G262, Z434 Look-back window: 5 years*	(4,6,11)
Peripheral arterial disease	DAD, NACRS, SDS, OHIP	• ICD-10-CA: I700, I702, I708, I709, I731, I738, I739, K551	(4,6,11)

		• CCI: 1KA76, 1KA50, 1KE76, 1KG50, 1KG57, 1KG76MI, 1KG87, 1IA87LA, 1IB87LA, 1IC87LA, 1ID87, 1KA87LA, 1KE57 • OHIP: R787, R780, R797, R804, R809, R875, R815, R936, R783, R784, R785, E626, R814, R786, R937, R860, R861, R855, R856, R933, R934, R791, E672, R794, R813, R867, E649 Look-back window: 5 years*	
Renal disease	DAD, NACRS, OHIP	Prior diagnosis of renal disease identified using HSPRN macro for the presence of 18 chronic conditions. Look-back window: 10 years*	(8–10)
Liver disease	DAD, NACRS	ICD-10-CA: • Mild liver disease: B18x, K700-K703, K709, K713-K715, K717, K73x, K74x, K760, K762-K764, K768, K769, Z944 • Moderate or severe liver disease: I850, I859, I864, I982, K704, K711, K721, K729, K765, K766, K767 Look-back window: 5 years*	(12)
Bleeding events	DAD, NACRS	ICD-10-CA: • Intracranial: I600, I601, I602, I603, I604, I605, I606, I607, I608, I609, I610, I611, I612, I613, I614, I615, I616, I618, I619, I620, I621, I629 • Upper gastrointestinal: I850, I982, I983, K2210, K2212, K2214, K2216, K226, K250, K252, K254, K256, K260, K262, K264, K266, K270, K272, K274, K276, K280, K282, K284, K286, K290, K3180, K6380, K920, K921, K922 • Lower gastrointestinal: K5520, K625 • Other (primarily genitourinary and respiratory): D683, H113, H313, H356, H431, H450, J942, J9500, K661, M2500, M2501, M2502, M2503, M2504, M2505, M2506, M2507, M2508, M2509, N020, N021, N022, N023, N024, N025, N026, N027, N028, N029, N421, N938, N939, N950, R040, R041, R042, R048, R049, R310, R311, R318, R58 Look-back window: 5 years*	(4–7)
Dementia	DAD, NACRS, OHIP	Prior diagnosis of renal disease identified using HSPRN macro for the presence of 18 chronic conditions. Look-back window: 10 years*	(8–10)
COPD	DAD, NACRS, OHIP	Prior diagnosis of COPD identified using HSPRN macro for the presence of 18 chronic conditions. Look-back window: 10 years*	(8–10)
Comorbidity	DAD	Charlson Comorbidity Index: *%getcharlson* macro Look-back window: 10 years*	(12,13)
Health care variables			
Palliative care physician home visit (cohort identification)	OHIP	OHIP *FEECODE* (any of): • B966 (travel premium) • B998 (home visit from 07:00-24:00) • B997 (home visit from 24:00-07:00)	(14–17)
Physician characteristics	CPDB, IPDB, OHIP, ODB	Age: IPDB *BDATE* Sex: IPDB *SEX* Graduation year: IPDB *GRADYEAR* International medical graduate: IPDB *IMG* Primary certification (base specialty): IPDB *MAINSPECIALTY* 1. Family medicine	(16,18)

		2. Specialist: medical or surgical	
		Rural practice: IPDB *RURAL*	
		Palliative care specialist: Barbera et al. algorithm employing OHIP claims 1. Specialist: ≥10% of all service claims are for palliative care services. 2. Generalist: <10% of all service claims are for palliative care services.	

Location of death	RPDB, DAD, NACRS, CCRS, SDS, NRS, OMHRS, INST	*%locationofdeath* macro
		1. Death in a health care facility, which includes:
		  a. Acute hospital (DAD)
		  b. Emergency department (NACRS)
		  c. Complex continuing care (CCRS *FACILITY_TYPE_CODE* = 3)
		  d. Same day surgery (SDS)
		  e. Inpatient rehabilitation facility (NRS)
		  f. Inpatient mental health facility (OMHRS)
		  g. Long-Term Care (CCRS *FACILITY_TYPE_CODE*=4)
		2. Death at home: death not documented at any of the above facilities
			(15,17)

*For baseline diagnostic and procedural variables, the look-back period was from the date of the index anticoagulant claim—not the index date. The index anticoagulant claim was defined as the most recent active (remaining supply at index date) anticoagulant claim dispensed prior to or on the index date.

Abbreviations:
CCI, Canadian Classification of Health Interventions
CCP, Canadian Classification of Diagnostic, Therapeutic and Surgical Procedures
CCRS, Continuing Care Reporting System Database
CIC, Immigrant, Refugees, and Citizenship Canada Permanent Residents Database
CPDB, Corporate Provider Database
DAD, Canadian Institute for Health Information Discharge Abstract Database
HSPRN, Health System Performance Research Network
ICD-9, International Statistical Classification of Diseases and Related Health Problems, 9th Revision.
ICD-10-CA, International Statistical Classification of Diseases and Related Health Problems, 10th Revision, Canada.
INST, Information on institutions from the Ontario Ministry of Health and Long-Term Care
IPDB, ICES Physician Database
NACRS, National Ambulatory Care Reporting System Database
NRS, National Rehabilitation Reporting System Database
ODB, Ontario Drug Benefit Plan Database
OHIP, Ontario Health Insurance Plan Database
OMHRS, Ontario Mental Health Reporting System Database
RPDB, Registered Persons Database
SDS, Same Day Surgery Database

Supplemental Table 3. List and classification of study medications*

Class	Subclassification[†]	Drug
Anticoagulants	Vitamin K antagonist	Warfarin
	Direct oral anticoagulants	Apixaban
		Dabigatran
		Edoxaban
		Rivaroxaban
	Low molecular weight heparins	Dalteparin
		Enoxaparin
		Nadroparin
		Tinzaparin
Nonsteroidal anti-inflammatory drugs	N/A	Celecoxib
		Diclofenac +/- misoprostol
		Flurbiprofen
		Ibuprofen
		Indomethacin
		Ketoprofen
		Ketorolac
		Mefenamic acid
		Meloxicam
		Nabumetone
		Naproxen +/- esomeprazole
		Oxaprozin
		Piroxicam
		Sulindac
		Tiaprofenic acid
		Acetylsalicylic acid & analgesic combinations
Antiplatelet agents	N/A	Acetylsalicylic acid & dipyridamole
		Clopidogrel
		Ticlopidine
		Ticagrelor

*Identified from ICES Drug Identification Number (DIN) Drug List by *DRUGNAME* and *DIN*; all relevant medications captured in the Ontario Drug Benefit Plan Database will be included.

†In this study, anticoagulants were grouped into 3 groups: 1) warfarin (the sole vitamin K antagonist captured), 2) direct oral anticoagulants, and 3) low molecular weight heparins).

Supplemental Table 4. Sensitivity analysis excluding patients with recent hip or knee arthroplasty: multilevel logistic regression model for anticoagulant discontinuation[*]

Variable	Anticoagulant discontinuation
	Odds ratio (95% CI)
Patient characteristics	
Age (continuous, older)	1.00 (0.99-1.01)
Sex (female vs. male)	0.86 (0.78-0.96)
Income quintile	
First (lowest)	0.86 (0.73-1.02)
Second	0.96 (0.82-1.13)
Third	0.94 (0.80-1.11)
Fourth	0.97 (0.82 -1.14)
Fifth (highest)	1.00 (Ref)
Urban residence (vs. rural)	0.94 (0.74-1.20)
Recent immigrant[†] (vs. longstanding resident)	0.77 (0.43-1.37)
Index anticoagulant	
Warfarin	1.00 (Ref)
Direct oral anticoagulant	0.49 (0.43-0.56)
Low molecular weight heparin	0.56 (0.47-0.66)
Indication for anticoagulation[‡]	
Atrial fibrillation	0.88 (0.77-1.00)
Venous thromboembolism	0.88 (0.75-1.02)
Mechanical heart valve	0.73 (0.43-1.24)
Comorbidities and risk factors[‡]	
Cancer	1.11 (0.96-1.28)
Congestive heart failure	0.95 (0.84-1.09)
Hypertension	0.89 (0.77-1.02)
Diabetes mellitus	0.94 (0.84-1.06)
Prior stroke or transient ischemic attack	0.93 (0.78-1.12)
Coronary artery disease	0.94 (0.83-1.08)
Peripheral arterial disease	1.14 (0.90-1.44)
Renal disease	1.12 (0.99-1.27)
Liver disease	1.16 (0.83-1.62)
Prior bleeding[§]	0.98 (0.87-1.10)
Chronic obstructive pulmonary disease	1.00 (0.88-1.13)
Dementia	0.96 (0.79-1.16)
NSAID or antiplatelet agent use[¶]	1.03 (0.84-1.28)
Charlson Comorbidity Index (cont., greater)	1.02 (1.00-1.04)
Physician characteristics	
Sex (female vs. male)	1.07 (0.95-1.21)
Graduation year	
2010 or later	1.02 (0.82-1.26)
2000-2009	0.90 (0.75-1.08)
1990-1999	0.90 (0.75-1.09)
1980-1989	1.00 (0.83-1.19)
1979 or earlier	1.00 (Ref)
Primary certification (other specialty vs. family medicine)	1.20 (0.88-1.63)
Urban practice (vs. rural)	0.82 (0.61-1.10)
Palliative care specialist[**] (vs. generalist)	1.17 (1.04-1.33)

[*]Multilevel logistic regression model for anticoagulant discontinuation (primary definition) including patient and physician variables. In total, 8,125 patients and 2,018 physicians were included (498 patients were excluded due to missing Charlson Comorbidity Index and 33 were excluded for both missing rural residence and income quintile). The median number of patients per physician was 1 (IQR 1-3) and the mean discontinuation rate by physician was 23.7% (95%CI 14.6-36.1). The intraclass correlation coefficient was 0.027, indicating low proportional variance in discontinuation attributable to clustering of patients by physician.

[†]Immigrated to Canada within 10 years prior to index date.

‡Indications for anticoagulation and baseline comorbidities/risk factors occurred prior to or on the date of the index anticoagulant claim—not the index date.

§Within 1 year prior to the index anticoagulant claim.

¶Within 6 months prior to the index anticoagulant claim.

**As per Barbera et al. algorithm, in which providers are considered palliative care specialists if ≥10% of their claims are for palliative care services (18).

Abbreviations: CI, confidence interval; NSAID, nonsteroidal anti-inflammatory drug.

Supplemental Table 5. Sensitivity analysis excluding patients with recent hip or knee arthroplasty: subsequent outcomes

Outcome	Crude incidence rates		Multivariable analysis[*]
	Incidence (95% CI) per 100 person-years		Hazard ratio[†] (95% CI)
	Discontinued	Continued	
Thrombotic event[‡]	5.5 (4.3-7.0)	4.9 (4.3-5.5)	1.06 (0.81-1.39)
Bleeding event[§]	10.9 (9.1-12.9)	12.8 (11.8-13.8)	0.74 (0.61-0.90)
All-cause mortality	142.5 (136.1-149.2)	96.0 (93.5-98.6)	1.35 (1.28-1.42)
	No. (%) of patients		Odds ratio[¶] (95% CI)
	Discontinued	Continued	
Death at home (vs. in a health care facility)	1057 (57.8)	2936 (53.9)	1.22 (1.09-1.36)

*Covariates included in multivariable analyses: age, sex, income quintile, rural residence, recent immigration, index anticoagulant, atrial fibrillation, prior venous thromboembolism, mechanical heart valve, cancer, congestive heart failure, hypertension, diabetes mellitus, prior stroke or transient ischemic attack, coronary artery disease, peripheral arterial disease, renal disease, liver disease, prior bleeding, chronic obstructive pulmonary disease, nonsteroidal anti-inflammatory drug or antiplatelet use, and Charlson Comorbidity Index.

†Cause-specific hazards model (n=8,125) adjusted for baseline patient characteristics. Among 8,687 patients in the study cohort, 498 patients were excluded due to missing Charlson Comorbidity Index and 33 were excluded for both missing rural residence and income quintile. In this this sensitivity analysis, 29 patients with a knee or hip arthroplasty within 30 days prior to the index anticoagulant claim were excluded. Primary discontinuation was the independent variable.

‡Hospitalization or emergency department visit with ischemic stroke, transient ischemic attack, or venous thromboembolism (see Appendix 1, Supplemental Table 2).

§Hospitalization or emergency department visit with intracranial, gastrointestinal (upper or lower), or other (primarily genitourinary and respiratory) bleeding (see Appendix 1, Supplemental Table 2).

¶Multivariable logistic regression model (n=7,276) adjusted for baseline patient characteristics. An additional 869 patients who survived beyond the study follow-up period were excluded from this model. In this this sensitivity analysis, 11 patients with a knee or hip arthroplasty within 30 days prior to the index anticoagulant claim were excluded. Primary discontinuation was the independent variable.

Abbreviations: CI, confidence interval.

Supplemental Figure 1. Inclusion criteria and primary outcome definition for anticoagulant discontinuation[*]
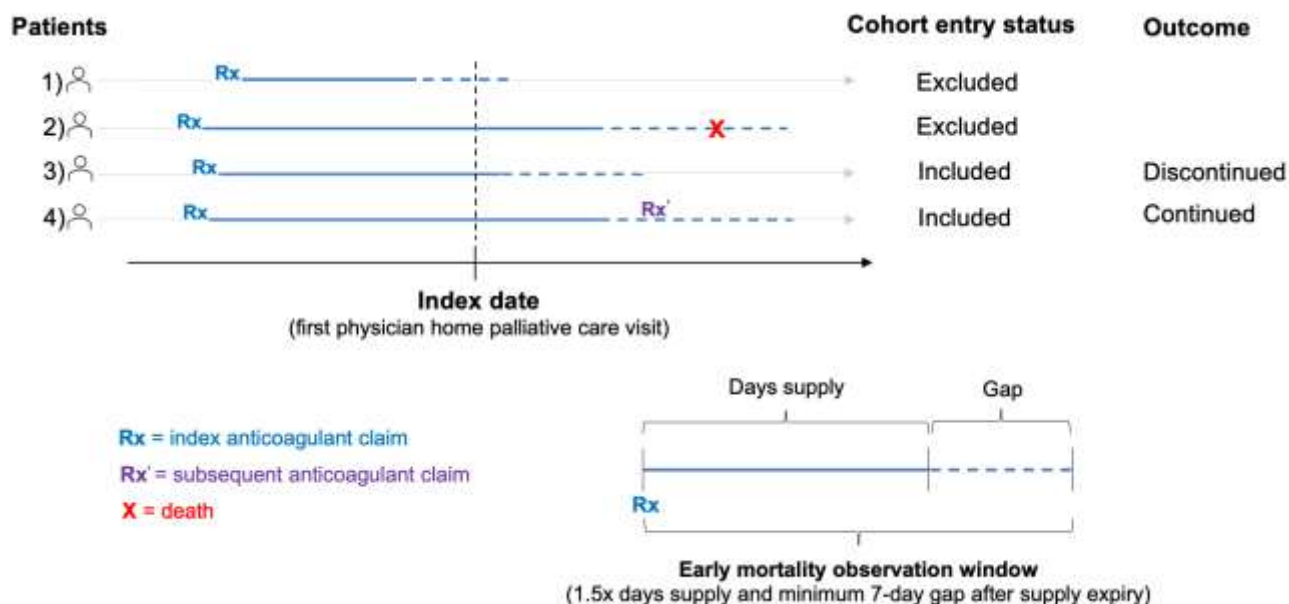
*The cohort for the study of anticoagulant discontinuation included Ontarians ≥66 years old whose first home palliative care physician visit occurred from 2010-2018 who had an active anticoagulant prescription (remaining supply from the index anticoagulant claim) at the index date. Those who died within the early mortality observation window, defined as 1.5 times the days' supply from the date of the index anticoagulant claim with a minimum gap of 7 days after supply expiry, were excluded. Patients with no subsequent anticoagulant claim within this window were considered to have discontinued (primary definition).

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