




# BMJ Open Background incidence rates of hospitalisations and emergency department visits for thromboembolic and coagulation disorders in Ontario, Canada for COVID-19 vaccine safety assessment: a population-based retrospective observational study

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## ABSTRACT

**Objective** The objective of this study was to estimate background rates of selected thromboembolic and coagulation disorders in Ontario, Canada.

**Design** Population-based retrospective observational study using linked health administrative databases. Records of hospitalisations and emergency department visits were searched to identify cases using International Statistical Classification of Diseases and Related Health Problems, 10th Revision, Canada diagnostic codes.

**Participants** All Ontario residents.

**Primary outcome measures** Incidence rates of ischaemic stroke, intracerebral haemorrhage, subarachnoid haemorrhage, deep vein thrombosis, pulmonary embolism, idiopathic thrombocytopenia, disseminated intravascular coagulation and cerebral venous thrombosis during five prepandemic years (2015–2019) and 2020.

**Results** The average annual population was 14 million with 51% female. The mean annual rates per 100 000 population during 2015–2019 were 127.1 (95% CI 126.2 to 127.9) for ischaemic stroke, 22.0 (95% CI 21.6 to 22.3) for intracerebral haemorrhage, 9.4 (95% CI 9.2 to 9.7) for subarachnoid haemorrhage, 86.8 (95% CI 86.1 to 87.5) for deep vein thrombosis, 63.7 (95% CI 63.1 to 64.3) for pulmonary embolism, 6.1 (95% CI 5.9 to 6.3) for idiopathic thrombocytopenia, 1.6 (95% CI 1.5 to 1.7) for disseminated intravascular coagulation, and 1.5 (95% CI 1.4 to 1.6) for cerebral venous thrombosis. Rates were lower in 2020 than during the prepandemic years for ischaemic stroke, deep vein thrombosis and idiopathic thrombocytopenia. Rates were generally consistent over time, except for pulmonary embolism, which increased from 57.1 to 68.5 per 100 000 between 2015 and 2019. Rates were higher for females than males for subarachnoid haemorrhage, pulmonary embolism and cerebral venous thrombosis, and vice versa for ischaemic stroke and intracerebral haemorrhage. Rates increased

## Strengths and limitations of this study

- We estimated background rates of ischaemic stroke, intracerebral haemorrhage, subarachnoid haemorrhage, deep vein thrombosis, pulmonary embolism, idiopathic thrombocytopenia, disseminated intravascular coagulation and cerebral venous thrombosis that are potential adverse events of special interest related to COVID-19 vaccine.
- Population-based rates during five prepandemic years (2015–2019) and 2020 were estimated using routinely collected health administrative data.
- We included both hospitalised cases and cases that were treated in the emergency department without requiring hospitalisation.
- Imperfect validity of administrative data without information on clinical and/or diagnostic confirmation may have resulted in under or overestimation of these rates.

with age for most of these conditions, but idiopathic thrombocytopenia demonstrated a bimodal distribution with incidence peaks at 0–19 years and ≥60 years.

**Conclusions** Our estimated background rates help contextualise observed events of these potential adverse events of special interest and to detect potential safety signals related to COVID-19 vaccines.

## INTRODUCTION

As COVID-19 vaccines are rapidly being licensed and used in mass immunisation programmes worldwide, postmarketing safety surveillance is essential to identify rare adverse events and maintain vaccine confidence.<sup>1</sup> In March 2021, there had been

reports of serious thrombotic events from the UK, the European Union and Scandinavian countries related to the ChAdOx1-S (AstraZeneca) vaccine.<sup>1</sup> The European Medicines Agency (EMA) at that time reviewed seven cases of disseminated intravascular coagulation and 18 cases of cerebral venous thrombosis (including nine deaths) following vaccination.<sup>2</sup> These events occurred predominantly in females aged <55 years. Based on pre-COVID-19 rates of these two rare conditions, the EMA's safety committee noted that observed events among vaccinated individuals were higher than expected for that age group (expected vs observed within 14 days of vaccination in those aged <50 years: 1 vs 5 for disseminated intravascular coagulation, and 1.35 vs 12 for cerebral venous thrombosis), and they recommended close safety monitoring and further analysis.<sup>2</sup> A causal relationship between these two rare events and the vaccine was neither proven nor ruled out. However, the overall number of thromboembolic events after vaccination was not deemed to be higher than expected.<sup>2</sup> The EMA mandated that information on the thrombotic events be added to AstraZeneca vaccine's summary of product characteristics and package leaflets.

This situation underscores the invaluable role of knowing background rates in vaccine safety signal assessments.<sup>3</sup> Without background rates, the occurrence of adverse events in vaccinated individuals could be misinterpreted as a vaccine safety signal.<sup>4–6</sup> However, background rates may vary by several factors, including geography, sex, age and calendar time.<sup>3,4</sup>

Following a risk assessment based on available data on the reported events in Europe, Health Canada described in public messaging that a combination of thrombosis and thrombocytopenia had been observed very rarely following vaccination with the AstraZeneca COVID-19 vaccine, although there was no overall increased risk of thrombosis and that the benefits of the vaccine outweighed the risks.<sup>7</sup> In response to the safety signal in Europe, Health Canada also updated the product monograph for AstraZeneca to include information on the reported rare events.<sup>8</sup> In its first statement on AstraZeneca vaccine, Canada's National Advisory Committee on Immunisation (NACI) initially recommended its use in adults aged 18–64 years due to insufficient evidence on efficacy in older adults available at that time, although the recommendation was later expanded to include adults aged ≥65 years.<sup>9</sup> There was considerable variability across Canadian provinces and territories in regards to the populations offered AstraZeneca vaccine. Following a review of more detailed risk information on vaccine-induced immune thrombotic thrombocytopenia, NACI ultimately recommended that AstraZeneca should not be used in individuals <30 years, and should only be offered if mRNA vaccines are contraindicated or inaccessible.<sup>10</sup>

There is a lack of Canadian data on recent background rates of potential thromboembolic and coagulation disorder adverse events of special interest (AESI) that might inform ongoing safety surveillance of AstraZeneca's

COVID-19 vaccine and others. Therefore, we sought to estimate background rates of hospitalisations and emergency department visits for selected thromboembolic and coagulation disorders during five prepandemic years (2015–2019) and 2020 in Ontario, Canada.

## METHODS

We conducted a population-based retrospective observational study using health administrative databases from Ontario, Canada. These datasets were linked using unique identifiers and analysed at ICES. We searched records of hospitalisations and emergency department visits to identify cases of ischaemic stroke, intracerebral haemorrhage, subarachnoid haemorrhage, deep vein thrombosis, pulmonary embolism, idiopathic thrombocytopenia, disseminated intravascular coagulation, and cerebral venous thrombosis using diagnostic codes from the International Statistical Classification of Diseases and Related Health Problems, 10th Revision, Canada (ICD-10-CA)<sup>11</sup> (online supplemental table S1). Where available, we used codes that have been previously validated.<sup>12–16</sup>

We used the Canadian Institute for Health Information (CIHI) Discharge Abstract Database (DAD) and CIHI's National Ambulatory Care Reporting System to identify hospitalisations and emergency department visits, respectively. We included inpatient cases where an ICD-10-CA code of interest was indicated as being present on admission and of primary relevance to the stay (as opposed to being listed as a secondary diagnosis, comorbidity or part of the medical history). We included emergency department visits where a code of interest was present in any diagnosis field. We counted only new cases after a 365-day period without the same condition (ie, group of codes) (online supplemental table S1). Information on age and sex were obtained from Ontario's Registered Persons Database, which contains all Ontarians registered under the Ontario Health Insurance Plan.

## Statistical analysis

For each AESI, we calculated annual incidence rates per 100 000 population by age and sex during each of five prepandemic years (2015–2019) and 2020, and also the overall mean annual incidence for 2015–2019. Similarly, we calculated annual and overall mean (for 2015–2019) incidence rates separately by sex, by age group (0–19, 20–29, 30–39, 40–49, 50–59, 60–69, 70–79 and ≥80 years), and by sex and age group. To examine seasonality, we calculated monthly averages (per 30 days) for 2015–2019. We used Statistics Canada Census and intercensal population estimates as denominators. The 95% CIs were calculated using a gamma distribution.<sup>17</sup>

## Patient and public involvement

There was no direct interaction with patients in this study and no direct patient involvement in the design or conduct of this study.

## Ethics approval

ICES is a prescribed entity under Ontario's Personal Health Information Protection Act (PHIPA). Section 45 of PHIPA authorises ICES to collect personal health information, without consent, for the purpose of analysis or compiling statistical information with respect to the management of, evaluation or monitoring of, the allocation of resources to or planning for all or part of the health system. Projects that use data collected by ICES under section 45 of PHIPA, and use no other data, are exempt from Research Ethics Board review. The use of the data in this project is authorised under section 45 and approved by ICES' Privacy and Legal Office.

## RESULTS

The study population included approximately 85 million person-years of observation from 2015 to 2020. The average annual population was 14 million, with 51% female. During 2015–2019, among the 8 AESI studied, overall rates of ischaemic stroke were highest at 127.1 (95% CI 126.2 to 127.9) per 100 000, whereas rates of cerebral venous thrombosis were lowest at 1.52 (95% CI 1.43 to 1.62) per 100 000 (table 1, (online supplemental tables S2–S7)). Rates of ischaemic stroke and intracerebral haemorrhage tended to be higher for males than females (table 1, (online supplemental table S2)). In contrast, rates of pulmonary embolism and cerebral venous thrombosis were higher for females aged 0–49 years than males of the same age range (table 1, (online supplemental tables S4 and S7)). Rates increased with age for most of these AESI, but idiopathic thrombocytopenia demonstrated a bimodal distribution with incidence peaks at 0–19 years and  $\geq 60$  years (table 1, online supplemental tables S5). Rates were generally consistent over time, with the exception of pulmonary embolism, which increased from 57.1 to 68.5 per 100 000 between 2015 and 2019 (table 2). Rates were lower in 2020 than during the prepandemic years for ischaemic stroke, deep vein thrombosis and idiopathic thrombocytopenia. We noted seasonality for four AESI: intracerebral haemorrhage peaked in January and December, subarachnoid haemorrhage peaked in February and December, pulmonary embolism peaked in February and October, and deep vein thrombosis peaked in April and July (online supplemental figure 1).

## DISCUSSION

In this study, we estimated background rates of hospitalisations and emergency department visits for selected thromboembolic and coagulation disorders during 2015–2020 in Ontario. Our findings suggest that the rates were relatively stable during the prepandemic period but were lower in 2020 for three AESI. We observed high rates for some AESI and low rates for others. Females had higher rates of pulmonary embolism and cerebral venous thrombosis while males had higher rates of ischaemic stroke and intracerebral haemorrhage.

We also observed an increasing trend in the incidence of pulmonary embolism starting before the pandemic that warrants further investigation to elucidate the cause. However, it is possible that the observed trend may have resulted from changes in clinical or coding practices over time and does not reflect a true increase in the underlying disease pattern. Lack of recent data on the trends of pulmonary embolism incidence precluded other rate comparisons.

Our estimated rates of stroke and the observed higher rates in males are comparable to previously reported global rates.<sup>18–20</sup> However, higher stroke incidence was reported in females aged 18–44 years than their male counterparts (incidence rate ratio of females compared with males ranging from 1.14 to 1.93) in the Netherlands during 1998–2010.<sup>21</sup> Another study in China also reported a higher age-adjusted incidence of stroke in females than males (309 vs 280 per 100 000 population) in 2014.<sup>22 23</sup> Our crude rates of ischaemic stroke and intracerebral haemorrhage during 2015–2017 were approximately 1.5–2 times the age- and sex-standardised rates during the same period in a previous study in Ontario.<sup>24</sup> However, that study included only the first-ever episode whereas we included episodes occurring after a 365-day period.

There are limitations in the estimated rates of deep vein thrombosis in recent years. Lower rates reported in older studies<sup>25</sup> are likely because they included only the first incident case, whereas we included recurrent cases at least 1 year apart. On the other hand, the overall rate of deep vein thromboses in our study is much lower than the adult hospitalisation rate reported in the USA during 2007–2009.<sup>26</sup> The higher USA rates are likely because that study included multiple hospitalisations in a year, and they also included cases that developed during hospitalisation from other conditions whereas our study looked at deep vein thrombosis on admission only.

There is a lack of data on the incidence of disseminated intravascular coagulation, a systemic coagulopathy that is always secondary to an underlying clinical condition, such as sepsis, malignancy, trauma, acute pancreatitis, burns or obstetric complications.<sup>27</sup> As such, studies often estimate the burden of disseminated intravascular coagulation for the underlying conditions separately. The incidence of the first episode of disseminated intravascular coagulation in ICU admitted adult patients in the USA was 18.6 per 100 000 person-years in 2010,<sup>28</sup> which is far higher than the rates we have estimated.

The estimated overall incidence of cerebral venous thrombosis in our study is similar to the overall hospitalisation rate of 1.75 per 100 000/year in Norway during 2011–2020<sup>29</sup> and 1.32 per 100 000/year in Finland during 2005–2014.<sup>30</sup> However, these rates are much higher than previously reported rates of 0.1–0.5 per 100 000 population/year.<sup>16 31</sup> These differences are primarily attributable to increased use of routine vascular neuroimaging.<sup>31</sup> Females in the USA had a higher incidence than males (2.69–3.02/100 000 in females vs 0.68–1.68/100 000 in males) during 2006–2016; females aged



**Table 1** Mean background rates of hospitalisations and emergency department visits for selected thromboembolic and coagulation disorders in Ontario from 2015 to 2019

Age group, years	Incidence per 100 000 population (95% CI)							Cerebral venous thrombosis
	Ischaemic stroke	Intracerebral haemorrhage	Subarachnoid haemorrhage	Deep vein thrombosis	Pulmonary embolism	Idiopathic thrombocytopenia	Disseminated intravascular coagulation	
All sexes								
All ages	127.07 (126.24 to 127.91)	21.96 (21.62 to 22.31)	9.43 (9.20 to 9.66)	86.79 (86.10 to 87.48)	63.68 (63.09 to 64.27)	6.08 (5.90 to 6.26)	1.55 (1.46 to 1.65)	1.52 (1.43 to 1.62)
0–19	1.78 (1.57 to 2.00)	1.01 (0.86 to 1.19)	0.68 (0.56 to 0.83)	4.22 (3.91 to 4.56)	2.25 (2.02 to 2.50)	6.17 (5.79 to 6.58)	0.45 (0.35 to 0.57)	1.12 (0.96 to 1.30)
20–29	4.68 (4.27 to 5.13)	2.28 (1.99 to 2.60)	1.80 (1.55 to 2.09)	26.66 (25.65 to 27.70)	18.83 (17.98 to 19.71)	2.99 (2.66 to 3.36)	0.96 (0.77 to 1.17)	1.30 (1.09 to 1.55)
30–39	13.07 (12.35 to 13.83)	3.91 (3.52 to 4.33)	3.96 (3.57 to 4.39)	53.73 (52.25 to 55.23)	31.34 (30.21 to 32.49)	3.76 (3.38 to 4.17)	1.07 (0.87 to 1.30)	1.62 (1.38 to 1.90)
40–49	36.88 (35.66 to 38.14)	8.27 (7.70 to 8.88)	7.90 (7.34 to 8.49)	80.49 (78.68 to 82.34)	45.68 (44.32 to 47.07)	3.78 (3.39 to 4.19)	1.04 (0.84 to 1.27)	1.51 (1.27 to 1.78)
50–59	97.01 (95.13 to 98.93)	17.59 (16.80 to 18.42)	13.97 (13.26 to 14.71)	107.32 (105.34 to 109.34)	70.85 (69.24 to 72.49)	4.70 (4.29 to 5.13)	1.77 (1.53 to 2.05)	1.60 (1.37 to 1.86)
60–69	210.41 (207.28 to 213.58)	33.67 (32.42 to 34.95)	16.49 (15.62 to 17.39)	152.79 (150.12 to 155.49)	122.76 (120.37 to 125.18)	6.53 (5.99 to 7.11)	2.63 (2.29 to 3.01)	1.76 (1.49 to 2.08)
70–79	457.78 (451.84 to 463.79)	78.12 (75.67 to 80.62)	24.24 (22.88 to 25.65)	228.42 (224.22 to 232.67)	198.19 (194.28 to 202.15)	12.19 (11.23 to 13.20)	3.52 (3.02 to 4.09)	2.19 (1.79 to 2.64)
≥80	1127.67 (1115.77 to 1139.65)	181.74 (176.98 to 186.59)	41.59 (39.33 to 43.95)	344.83 (338.27 to 351.49)	274.19 (268.34 to 280.13)	23.31 (21.63 to 25.09)	5.32 (4.53 to 6.20)	2.04 (1.56 to 2.61)
Females								
All ages	121.52 (120.38 to 122.67)	20.68 (20.21 to 21.16)	10.56 (10.23 to 10.90)	86.46 (85.50 to 87.43)	67.33 (66.48 to 68.18)	6.27 (6.01 to 6.53)	1.52 (1.40 to 1.66)	1.67 (1.54 to 1.81)
0–19	1.64 (1.36 to 1.95)	0.86 (0.66 to 1.10)	0.52 (0.37 to 0.70)	4.84 (4.36 to 5.36)	3.37 (2.97 to 3.81)	5.72 (5.20 to 6.29)	0.44 (0.30 to 0.61)	0.97 (0.76 to 1.21)
20–29	5.46 (4.82 to 6.17)	2.09 (1.70 to 2.54)	1.67 (1.32 to 2.08)	32.68 (31.07 to 34.35)	26.33 (24.89 to 27.84)	3.88 (3.34 to 4.48)	1.18 (0.89 to 1.53)	1.88 (1.51 to 2.31)
30–39	13.77 (12.74 to 14.87)	3.16 (2.68 to 3.71)	4.41 (3.83 to 5.05)	60.19 (58.00 to 62.44)	39.25 (37.48 to 41.07)	5.10 (4.48 to 5.79)	1.37 (1.06 to 1.75)	2.15 (1.75 to 2.61)
40–49	30.84 (29.28 to 32.46)	6.24 (5.55 to 6.99)	8.53 (7.72 to 9.40)	80.35 (77.83 to 82.94)	47.06 (45.13 to 49.05)	4.31 (3.74 to 4.94)	1.01 (0.74 to 1.34)	1.93 (1.56 to 2.37)
50–59	71.20 (68.93 to 73.53)	14.33 (13.32 to 15.40)	15.56 (14.51 to 16.67)	90.50 (87.93 to 93.11)	63.81 (61.66 to 66.01)	4.89 (4.30 to 5.52)	1.61 (1.28 to 1.99)	1.42 (1.11 to 1.78)

Continued

**Table 1** Continued

Age group, years	Incidence per 100 000 population (95% CI)							
	Ischaemic stroke	Intracerebral haemorrhage	Subarachnoid haemorrhage	Deep vein thrombosis	Pulmonary embolism	Idiopathic thrombocytopaenia	Disseminated intravascular coagulation	Cerebral venous thrombosis
60–69	154.37 (150.65 to 158.16)	25.79 (24.28 to 27.37)	18.23 (16.96 to 19.56)	131.72 (128.28 to 135.22)	114.65 (111.45 to 117.93)	6.36 (5.62 to 7.17)	2.55 (2.09 to 3.08)	1.80 (1.42 to 2.25)
70–79	386.64 (379.18 to 394.22)	65.48 (62.43 to 68.64)	25.77 (23.87 to 27.78)	215.09 (209.53 to 220.76)	198.04 (192.71 to 203.48)	10.42 (9.23 to 11.73)	2.77 (2.17 to 3.48)	2.05 (1.54 to 2.67)
≥80	1111.20 (1096.04 to 1126.53)	174.36 (168.38 to 180.49)	42.22 (39.30 to 45.29)	343.72 (335.31 to 352.29)	274.15 (266.64 to 281.82)	20.46 (18.45 to 22.63)	4.23 (3.35 to 5.28)	2.06 (1.46 to 2.83)
Males								
All ages	132.78 (131.57 to 134.00)	23.28 (22.78 to 23.79)	8.27 (7.97 to 8.57)	87.13 (86.15 to 88.11)	59.93 (59.12 to 60.75)	5.89 (5.63 to 6.15)	1.58 (1.46 to 1.72)	1.37 (1.25 to 1.50)
0–19	1.91 (1.61 to 2.24)	1.16 (0.94 to 1.42)	0.85 (0.66 to 1.07)	3.64 (3.23 to 4.08)	1.19 (0.96 to 1.45)	6.60 (6.05 to 7.19)	0.47 (0.33 to 0.64)	1.27 (1.04 to 1.55)
20–29	3.96 (3.43 to 4.55)	2.46 (2.05 to 2.93)	1.93 (1.57 to 2.35)	21.04 (19.80 to 22.34)	11.82 (10.89 to 12.80)	2.17 (1.78 to 2.61)	0.75 (0.53 to 1.03)	0.77 (0.55 to 1.05)
30–39	12.36 (11.37 to 13.41)	4.67 (4.07 to 5.34)	3.51 (2.99 to 4.09)	47.09 (45.14 to 49.12)	23.22 (21.85 to 24.65)	2.38 (1.96 to 2.87)	0.76 (0.53 to 1.05)	1.08 (0.80 to 1.43)
40–49	43.19 (41.31 to 45.14)	10.39 (9.48 to 11.37)	7.24 (6.48 to 8.06)	80.64 (78.06 to 83.29)	44.25 (42.34 to 46.22)	3.22 (2.72 to 3.79)	1.07 (0.79 to 1.42)	1.07 (0.79 to 1.42)
50–59	123.18 (120.17 to 126.25)	20.90 (19.67 to 22.19)	12.35 (11.41 to 13.35)	124.39 (121.36 to 127.47)	78.00 (75.60 to 80.45)	4.51 (3.95 to 5.13)	1.94 (1.58 to 2.36)	1.79 (1.44 to 2.19)
60–69	270.67 (265.55 to 275.86)	42.14 (40.13 to 44.22)	14.61 (13.44 to 15.86)	175.44 (171.32 to 179.63)	131.47 (127.91 to 135.10)	6.71 (5.92 to 7.57)	2.72 (2.23 to 3.29)	1.73 (1.34 to 2.19)
70–79	539.40 (529.95 to 548.98)	92.61 (88.72 to 96.63)	22.48 (20.58 to 24.50)	243.70 (237.36 to 250.17)	198.35 (192.64 to 204.19)	14.22 (12.72 to 15.85)	4.39 (3.58 to 5.34)	2.35 (1.76 to 3.06)
≥80	1152.87 (1133.77 to 1172.22)	193.05 (185.27 to 201.06)	40.64 (37.11 to 44.40)	346.54 (336.10 to 357.22)	274.24 (264.96 to 283.76)	27.67 (24.78 to 30.81)	6.98 (5.57 to 8.64)	1.99 (1.28 to 2.97)

**Table 2** Background rates of hospitalisations and emergency department visits for selected thromboembolic and coagulation disorders for both sexes and all ages combined in Ontario, 2015–2020

Year	Incidence per 100 000 population (95% CI)							
	Ischaemic stroke	Intracerebral haemorrhage	Subarachnoid haemorrhage	Deep vein thrombosis	Pulmonary embolism	Idiopathic thrombocytopaenia	Disseminated intravascular coagulation	Cerebral venous thrombosis
2015	124.75 (122.88 to 126.63)	22.14 (21.36 to 22.94)	9.41 (8.90 to 9.94)	87.68 (86.12 to 89.26)	57.12 (55.86 to 58.40)	6.41 (6.00 to 6.85)	1.47 (1.28 to 1.69)	1.39 (1.20 to 1.61)
2016	126.89 (125.03 to 128.78)	21.58 (20.82 to 22.37)	9.37 (8.87 to 9.89)	88.01 (86.46 to 89.59)	62.34 (61.03 to 63.67)	6.31 (5.90 to 6.74)	1.59 (1.39 to 1.82)	1.43 (1.24 to 1.64)
2017	126.87 (125.02 to 128.75)	21.89 (21.12 to 22.68)	9.33 (8.83 to 9.85)	87.30 (85.76 to 88.86)	63.89 (62.57 to 65.22)	6.14 (5.74 to 6.56)	1.56 (1.36 to 1.78)	1.68 (1.47 to 1.91)
2018	127.31 (125.47 to 129.17)	21.65 (20.90 to 22.43)	9.36 (8.87 to 9.88)	86.12 (84.61 to 87.66)	66.15 (64.82 to 67.49)	5.75 (5.37 to 6.16)	1.57 (1.37 to 1.79)	1.38 (1.20 to 1.59)
2019	129.39 (127.55 to 131.26)	22.53 (21.77 to 23.32)	9.66 (9.16 to 10.18)	84.94 (83.45 to 86.46)	68.51 (67.17 to 69.87)	5.81 (5.42 to 6.21)	1.57 (1.37 to 1.78)	1.73 (1.53 to 1.96)
2020	119.63 (117.88 to 121.41)	21.04 (20.31 to 21.79)	8.95 (8.47 to 9.44)	78.67 (77.24 to 80.11)	68.39 (67.06 to 69.74)	4.45 (4.12 to 4.81)	1.59 (1.39 to 1.81)	1.60 (1.40 to 1.82)

18–44 years also had higher incidence than their male counterparts (2.4–3.3/100 000 vs 0.5–1.3/100 000).<sup>32</sup> We also observed a higher mean incidence in females than males for individuals of all ages, and for individuals aged 20–49 years.

Compared with prepandemic years, we observed lower rates in 2020 for ischaemic stroke, deep vein thrombosis and idiopathic thrombocytopaenia, but not the other AESI. While thromboembolic and coagulation disorders have been associated with severe COVID-19,<sup>33–37</sup> only approximately 1.3% (184 635 out of 14.7 million) of Ontarians were confirmed to be COVID-19 cases in 2020.<sup>38</sup> Therefore, we would not expect COVID-19 to impact the incidence of these AESI substantially. The observed decline in the rates may have resulted from decreased healthcare-seeking observed during 2020 leading to underdiagnosis and underestimation. Additionally, a population-level reduction in cerebrovascular events has been suggested based on a reported 12% reduction in stroke hospitalisation during the peak pandemic months (March through April) in 2020 globally.<sup>39</sup> This decline has been attributed to the reduced consumption of high-sodium and fast-foods, reduced exposure to ambient air pollution, improved health behaviours, and possibly from reduced exposure to other common respiratory viruses because of public health measures against COVID-19.

Our rates need to be interpreted with caution. We identified both hospitalised cases and cases that were treated in the emergency department without requiring hospitalisation. Thus, our rates may be higher than those reported in the literature that used hospitalisation data alone. We did not include cases that developed during the hospital stay. As a result, we may have underestimated the rates for conditions that frequently arise after hospitalisation, such as disseminated intravascular coagulation and idiopathic thrombocytopaenia. Additionally, we used recorded diagnostic codes in administrative data without information on clinical and/or diagnostic confirmation, and the validity of these data are imperfect, which may result in under or overestimation. However, we used previously validated codes<sup>13–16</sup> or equivalent codes<sup>12</sup> to improve the accuracy of case ascertainment in administrative data and there is no reason to believe that there would be substantial changes in the direction or magnitude of misdiagnosis between study years. The quality of DAD hospitalisation data has been previously evaluated.<sup>40</sup> Nevertheless, there may be some overlap in clinical presentations of the AESI that may have impacted our rate estimation. Our rates do not capture out-of-province care provided to Ontario residents, but we expect relatively few Ontario residents would seek care outside of Ontario, and the frequency of doing so would be consistent over time during the prepandemic years and is expected to be lower in 2020 because of reduced travel during the pandemic. As background rates are population-specific, our rates may not be generalisable to other populations/settings, including jurisdictions within Canada with different population structures,

distribution of risk factors, and diagnostic and coding practices.

Despite the limitations, our estimated background rates of hospitalisations and emergency department visits for the selected thromboembolic and coagulation disorders will help contextualise any observed apparent increase in these potential AESI in relation to Canada's mass COVID-19 immunisation programme. This will facilitate the identification of potential safety signals and help maintain vaccine confidence by preventing misinterpretation of expected baseline event rates.

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**Contributors** JCK conceived of the study and oversaw the study. JCK, SN, MS and AJC designed the study. AJC prepared the data and performed the statistical analysis. SN conducted background literature review and drafted the manuscript. SN, AJC, MS, SEM, CR, MP, TF, LWZ, SEW and JCK interpreted the results, critically reviewed and edited the manuscript, approved the final version and agreed to be accountable for all aspects of the work. JCK is the guarantor. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

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**Supplemental material:****Supplemental Table S1: ICD-10-CA diagnostic codes for selected thromboembolic and coagulation disorders**

<b>AESI</b>	<b>Diagnosis</b>	<b>ICD-10-CA code</b>
Ischemic stroke	Cerebral infarction	I63.x
	Stroke, not specified as haemorrhage or infarction	I64
	Central retinal artery occlusion	H34.1
Intracerebral haemorrhage	Intracerebral haemorrhage	I61.x
Subarachnoid haemorrhage	Subarachnoid haemorrhage	I60.x
Deep vein thrombosis	Phlebitis and thrombophlebitis	I80.1 I80.2 I80.3 I80.8 I80.9
	Deep phlebothrombosis in pregnancy	O22.3x
	Deep phlebothrombosis in the puerperium	O87.1x
Pulmonary embolism	Pulmonary embolism	I26.x
	Obstetric blood-clot embolism	O88.2x
Idiopathic thrombocytopenia (ITP)	Idiopathic thrombocytopenic purpura	D69.3x
Disseminated intravascular coagulation (DIC)	Disseminated intravascular coagulation	D65
	Premature separation of placenta with disseminated intravascular coagulation	O45.01x
	Antepartum haemorrhage with disseminated intravascular coagulation	O46.01x
Cerebral venous thrombosis	Intracranial and intraspinal phlebitis and thrombophlebitis	G08
	Cerebral infarction due to cerebral venous thrombosis, non-pyogenic	I63.6
	Non-pyogenic thrombosis of intracranial venous system	I67.6
	Cerebral venous thrombosis in pregnancy	O22.5
	Cerebral venous thrombosis in the puerperium	O87.3

**Supplemental Table S2: Background rates of hospitalizations and emergency department visits for ischemic and haemorrhagic strokes in Ontario, 2015 to 2020**

Age group, years	Incidence per 100,000 population (95% confidence interval)					
	2015	2016	2017	2018	2019	2020
<b>Ischemic stroke</b>						
<b>All sexes</b>						
All ages	124.75 (122.88, 126.63)	126.89 (125.03, 128.78)	126.87 (125.02, 128.75)	127.31 (125.47, 129.17)	129.39 (127.55, 131.26)	119.63 (117.88, 121.41)
0–19	1.96 (1.50, 2.52)	2.05 (1.57, 2.62)	1.68 (1.25, 2.20)	1.60 (1.19, 2.11)	1.60 (1.19, 2.11)	1.31 (0.94, 1.78)
20–29	4.70 (3.77, 5.79)	5.89 (4.85, 7.09)	5.19 (4.22, 6.30)	4.11 (3.28, 5.10)	3.65 (2.88, 4.57)	3.54 (2.79, 4.44)
30–39	12.75 (11.15, 14.52)	11.22 (9.74, 12.87)	12.85 (11.28, 14.59)	14.04 (12.41, 15.82)	14.35 (12.73, 16.13)	12.19 (10.72, 13.80)
40–49	34.05 (31.47, 36.79)	38.05 (35.31, 40.96)	35.88 (33.21, 38.71)	37.91 (35.16, 40.82)	38.57 (35.79, 41.50)	35.56 (32.89, 38.38)
50–59	95.19 (91.03, 99.48)	95.02 (90.88, 99.30)	92.53 (88.44, 96.76)	99.45 (95.20, 103.84)	102.94 (98.61, 107.42)	93.09 (88.95, 97.37)
60–69	211.35 (204.17, 218.72)	211.97 (204.89, 219.24)	204.16 (197.29, 211.22)	212.98 (206.04, 220.10)	211.55 (204.73, 218.55)	199.86 (193.32, 206.57)
70–79	469.04 (454.96, 483.46)	471.76 (457.89, 485.95)	467.79 (454.39, 481.48)	442.69 (430.00, 455.67)	441.97 (429.57, 454.64)	414.70 (402.93, 426.72)
≥80	1149.95 (1122.45, 1177.94)	1141.30 (1114.29, 1168.80)	1135.95 (1109.33, 1163.03)	1102.51 (1076.62, 1128.86)	1111.62 (1085.96, 1137.72)	986.53 (962.63, 1010.87)
<b>Females</b>						
All ages	118.80 (116.26, 121.39)	121.12 (118.56, 123.71)	122.77 (120.21, 125.37)	121.23 (118.71, 123.80)	123.53 (121.01, 126.10)	111.18 (108.80, 113.60)
0–19	1.74 (1.14, 2.55)	1.93 (1.29, 2.77)	1.19 (0.71, 1.88)	1.64 (1.06, 2.42)	1.70 (1.11, 2.49)	1.11 (0.65, 1.78)
20–29	6.26 (4.74, 8.11)	6.63 (5.07, 8.52)	5.53 (4.13, 7.25)	5.25 (3.91, 6.90)	3.80 (2.69, 5.22)	3.83 (2.72, 5.24)
30–39	13.05 (10.82, 15.60)	11.61 (9.52, 14.02)	12.84 (10.65, 15.34)	14.24 (11.96, 16.83)	16.91 (14.45, 19.68)	12.03 (9.99, 14.36)
40–49	30.27 (26.89, 33.97)	30.55 (27.14, 34.27)	32.22 (28.71, 36.03)	30.02 (26.64, 33.72)	31.14 (27.69, 34.90)	30.57 (27.16, 34.29)
50–59	72.88 (67.79, 78.25)	65.67 (60.86, 70.77)	70.02 (65.04, 75.28)	69.21 (64.25, 74.45)	78.28 (72.99, 83.85)	62.20 (57.47, 67.20)
60–69	151.31 (142.92, 160.07)	155.07 (146.70, 163.79)	154.32 (146.07, 162.93)	157.61 (149.36, 166.20)	153.36 (145.32, 161.72)	145.67 (137.94, 153.72)
70–79	389.51 (372.04, 407.58)	392.58 (375.33, 410.41)	399.58 (382.69, 417.01)	377.74 (361.75, 394.26)	376.00 (360.39, 392.10)	341.43 (326.87, 356.47)
≥80	1114.26 (1079.71, 1149.63)	1141.09 (1106.50, 1176.48)	1117.36 (1083.48, 1152.03)	1091.55 (1058.40, 1125.47)	1093.67 (1060.86, 1127.24)	964.71 (934.21, 995.96)
<b>Males</b>						
All ages	130.88 (128.16, 133.64)	132.84 (130.13, 135.60)	131.09 (128.41, 133.81)	133.54 (130.86, 136.26)	135.40 (132.72, 138.12)	128.29 (125.70, 130.92)
0–19	2.17 (1.50, 3.03)	2.16 (1.50, 3.02)	2.15 (1.49, 3.00)	1.57 (1.01, 2.31)	1.50 (0.96, 2.23)	1.50 (0.96, 2.23)
20–29	3.22 (2.19, 4.57)	5.20 (3.87, 6.84)	4.87 (3.60, 6.43)	3.06 (2.09, 4.32)	3.52 (2.49, 4.83)	3.28 (2.29, 4.53)
30–39	12.44 (10.21, 15.01)	10.82 (8.78, 13.20)	12.87 (10.65, 15.41)	13.84 (11.57, 16.42)	11.78 (9.74, 14.13)	12.35 (10.28, 14.70)
40–49	37.96 (34.10, 42.14)	45.86 (41.58, 50.46)	39.70 (35.71, 44.02)	46.19 (41.87, 50.84)	46.38 (42.05, 51.04)	40.82 (36.75, 45.21)
50–59	117.79 (111.25, 124.61)	124.71 (118.00, 131.71)	115.33 (108.87, 122.07)	130.12 (123.24, 137.29)	128.01 (121.17, 135.14)	124.57 (117.79, 131.65)
60–69	275.97 (264.17, 288.16)	273.30 (261.74, 285.25)	257.84 (246.74, 269.32)	272.43 (261.15, 284.07)	273.89 (262.74, 285.40)	257.74 (247.08, 268.74)
70–79	560.85 (538.31, 584.11)	562.69 (540.54, 585.52)	545.95 (524.81, 567.73)	517.07 (497.03, 537.71)	517.47 (497.87, 537.64)	498.60 (479.75, 518.01)
≥80	1206.12 (1161.10, 1252.44)	1141.63 (1098.64, 1185.87)	1164.40 (1121.68, 1208.33)	1119.07 (1077.88, 1161.44)	1138.48 (1097.58, 1180.51)	1018.95 (980.79, 1058.21)

Age group, years	Incidence per 100,000 population (95% confidence interval)					
	2015	2016	2017	2018	2019	2020
<b>Intracerebral haemorrhage</b>						
<b>All sexes</b>						
All ages	22.14 (21.36, 22.94)	21.58 (20.82, 22.37)	21.89 (21.12, 22.68)	21.65 (20.90, 22.43)	22.53 (21.77, 23.32)	21.04 (20.31, 21.79)
0–19	0.85 (0.55, 1.24)	1.01 (0.68, 1.43)	0.94 (0.63, 1.35)	1.22 (0.86, 1.67)	1.05 (0.73, 1.48)	0.99 (0.67, 1.41)
20–29	2.30 (1.66, 3.09)	2.26 (1.64, 3.05)	2.26 (1.64, 3.03)	2.28 (1.67, 3.04)	2.31 (1.70, 3.06)	1.79 (1.27, 2.46)
30–39	3.84 (2.99, 4.86)	3.78 (2.94, 4.78)	3.93 (3.08, 4.94)	3.61 (2.81, 4.57)	4.36 (3.49, 5.39)	4.03 (3.21, 5.00)
40–49	8.96 (7.66, 10.42)	8.51 (7.24, 9.94)	7.80 (6.58, 9.18)	7.82 (6.60, 9.20)	8.25 (7.00, 9.67)	8.47 (7.20, 9.90)
50–59	17.52 (15.77, 19.42)	17.38 (15.64, 19.27)	15.57 (13.92, 17.37)	18.10 (16.32, 20.03)	19.41 (17.56, 21.41)	19.05 (17.20, 21.04)
60–69	32.76 (29.97, 35.74)	32.32 (29.59, 35.24)	36.21 (33.35, 39.25)	31.83 (29.18, 34.65)	35.11 (32.37, 38.03)	31.38 (28.83, 34.11)
70–79	86.52 (80.53, 92.84)	76.74 (71.21, 82.59)	80.35 (74.85, 86.14)	74.10 (68.96, 79.52)	74.20 (69.17, 79.50)	70.16 (65.37, 75.21)
≥80	187.70 (176.69, 199.22)	185.78 (174.98, 197.08)	177.50 (167.08, 188.41)	179.64 (169.28, 190.47)	178.69 (168.50, 189.35)	160.56 (151.01, 170.56)
<b>Females</b>						
All ages	21.19 (20.12, 22.30)	20.41 (19.37, 21.50)	20.45 (19.42, 21.53)	20.55 (19.52, 21.62)	20.80 (19.77, 21.87)	20.04 (19.04, 21.08)
0–19	0.67 (0.32, 1.23)	1.00 (0.56, 1.64)	0.99 (0.56, 1.64)	1.12 (0.65, 1.79)	0.52 (0.23, 1.03)	1.31 (0.80, 2.02)
20–29	2.09 (1.26, 3.26)	2.07 (1.24, 3.23)	1.70 (0.97, 2.76)	1.95 (1.18, 3.05)	2.60 (1.70, 3.81)	1.28 (0.68, 2.18)
30–39	3.04 (2.02, 4.40)	2.90 (1.91, 4.22)	2.97 (1.97, 4.29)	3.22 (2.19, 4.57)	3.65 (2.55, 5.05)	3.75 (2.65, 5.14)
40–49	7.20 (5.60, 9.12)	6.82 (5.27, 8.70)	5.58 (4.18, 7.30)	5.69 (4.27, 7.42)	5.89 (4.45, 7.65)	7.35 (5.73, 9.29)
50–59	14.48 (12.26, 16.98)	13.17 (11.07, 15.56)	13.37 (11.25, 15.78)	15.43 (13.14, 18.01)	15.21 (12.93, 17.78)	14.85 (12.59, 17.39)
60–69	27.17 (23.68, 31.03)	23.55 (20.36, 27.10)	26.59 (23.23, 30.30)	25.31 (22.06, 28.89)	26.35 (23.08, 29.95)	23.47 (20.43, 26.84)
70–79	69.89 (62.61, 77.79)	67.35 (60.32, 74.97)	67.17 (60.35, 74.54)	63.20 (56.76, 70.17)	60.92 (54.74, 67.60)	64.39 (58.16, 71.11)
≥80	182.64 (168.82, 197.30)	178.45 (164.93, 192.78)	170.48 (157.41, 184.35)	169.47 (156.56, 183.15)	171.40 (158.56, 185.00)	152.03 (140.07, 164.74)
<b>Males</b>						
All ages	23.12 (21.99, 24.30)	22.79 (21.67, 23.95)	23.37 (22.24, 24.53)	22.78 (21.68, 23.92)	24.30 (23.17, 25.47)	22.06 (21.00, 23.17)
0–19	1.02 (0.58, 1.66)	1.02 (0.58, 1.65)	0.88 (0.48, 1.48)	1.32 (0.81, 2.01)	1.56 (1.01, 2.31)	0.69 (0.34, 1.23)
20–29	2.50 (1.60, 3.71)	2.45 (1.57, 3.64)	2.78 (1.85, 4.02)	2.58 (1.70, 3.75)	2.04 (1.28, 3.08)	2.27 (1.47, 3.36)
30–39	4.68 (3.36, 6.35)	4.69 (3.38, 6.33)	4.91 (3.58, 6.57)	4.01 (2.84, 5.51)	5.08 (3.77, 6.70)	4.31 (3.13, 5.79)
40–49	10.78 (8.77, 13.12)	10.26 (8.29, 12.56)	10.12 (8.16, 12.41)	10.06 (8.10, 12.35)	10.74 (8.71, 13.10)	9.65 (7.73, 11.90)
50–59	20.60 (17.92, 23.57)	21.64 (18.90, 24.67)	17.80 (15.32, 20.57)	20.81 (18.12, 23.80)	23.68 (20.79, 26.86)	23.33 (20.45, 26.51)
60–69	38.77 (34.43, 43.51)	41.78 (37.33, 46.61)	46.58 (41.93, 51.61)	38.83 (34.65, 43.38)	44.50 (40.08, 49.28)	39.83 (35.71, 44.30)
70–79	105.72 (96.06, 116.08)	87.53 (78.93, 96.81)	95.45 (86.73, 104.81)	86.59 (78.51, 95.28)	89.40 (81.36, 98.01)	76.77 (69.48, 84.61)
≥80	195.67 (177.79, 214.86)	197.14 (179.52, 216.03)	188.25 (171.31, 206.41)	195.02 (178.05, 213.18)	189.62 (173.15, 207.23)	173.24 (157.72, 189.87)
<b>Subarachnoid haemorrhage</b>						
<b>All sexes</b>						
All ages	9.41 (8.90, 9.94)	9.37 (8.87, 9.89)	9.33 (8.83, 9.85)	9.36 (8.87, 9.88)	9.66 (9.16, 10.18)	8.95 (8.47, 9.44)
0–19	0.65 (0.40, 1.01)	0.71 (0.45, 1.08)	0.45 (0.25, 0.76)	0.90 (0.60, 1.30)	0.70 (0.44, 1.06)	0.70 (0.44, 1.06)
20–29	1.98 (1.39, 2.72)	2.05 (1.46, 2.81)	1.49 (1.00, 2.14)	1.78 (1.25, 2.47)	1.73 (1.21, 2.40)	1.75 (1.23, 2.41)
30–39	4.90 (3.93, 6.04)	3.45 (2.65, 4.41)	4.14 (3.27, 5.18)	3.93 (3.09, 4.92)	3.45 (2.68, 4.37)	3.59 (2.81, 4.51)



Age group, years	Incidence per 100,000 population (95% confidence interval)					
	2015	2016	2017	2018	2019	2020
40–49	8.33 (7.08, 9.74)	8.51 (7.24, 9.94)	6.51 (5.40, 7.78)	7.93 (6.70, 9.32)	8.20 (6.95, 9.61)	7.07 (5.91, 8.39)
50–59	14.00 (12.43, 15.71)	14.16 (12.59, 15.88)	13.99 (12.43, 15.69)	13.76 (12.21, 15.45)	13.93 (12.36, 15.64)	13.61 (12.06, 15.31)
60–69	14.99 (13.12, 17.05)	16.22 (14.31, 18.32)	17.28 (15.32, 19.42)	15.85 (14.00, 17.88)	17.94 (15.99, 20.05)	14.45 (12.73, 16.33)
70–79	24.59 (21.45, 28.07)	24.14 (21.08, 27.52)	23.51 (20.58, 26.73)	23.93 (21.05, 27.10)	24.98 (22.10, 28.13)	23.71 (20.96, 26.72)
≥80	42.60 (37.44, 48.27)	40.26 (35.31, 45.70)	43.84 (38.74, 49.43)	40.83 (35.97, 46.16)	40.54 (35.76, 45.78)	38.58 (33.97, 43.63)
<b>Females</b>						
All ages	10.65 (9.89, 11.44)	10.65 (9.91, 11.44)	10.02 (9.30, 10.79)	10.28 (9.56, 11.05)	11.18 (10.43, 11.97)	10.14 (9.43, 10.89)
0–19	0.54 (0.23, 1.05)	0.53 (0.23, 1.05)	0.40 (0.15, 0.86)	0.72 (0.36, 1.29)	0.39 (0.14, 0.85)	0.78 (0.41, 1.37)
20–29	1.87 (1.09, 2.99)	1.96 (1.16, 3.09)	1.28 (0.66, 2.23)	1.54 (0.86, 2.54)	1.70 (0.99, 2.72)	1.96 (1.20, 3.03)
30–39	5.55 (4.13, 7.29)	3.87 (2.71, 5.36)	4.14 (2.94, 5.66)	4.57 (3.32, 6.14)	3.95 (2.81, 5.40)	4.14 (2.98, 5.60)
40–49	8.98 (7.18, 11.09)	9.03 (7.22, 11.15)	6.53 (5.00, 8.37)	8.64 (6.87, 10.72)	9.47 (7.61, 11.64)	7.46 (5.83, 9.41)
50–59	15.73 (13.41, 18.33)	15.94 (13.61, 18.55)	15.57 (13.27, 18.15)	14.76 (12.52, 17.29)	15.79 (13.47, 18.40)	16.30 (13.93, 18.96)
60–69	18.20 (15.37, 21.40)	18.84 (16.00, 22.04)	16.19 (13.59, 19.14)	17.56 (14.88, 20.59)	20.27 (17.41, 23.45)	15.47 (13.02, 18.24)
70–79	24.41 (20.19, 29.25)	26.41 (22.08, 31.34)	24.48 (20.43, 29.08)	24.49 (20.54, 28.97)	28.74 (24.54, 33.44)	24.44 (20.66, 28.70)
≥80	43.04 (36.47, 50.45)	41.01 (34.67, 48.18)	45.33 (38.72, 52.76)	40.17 (34.02, 47.11)	41.61 (35.42, 48.59)	39.28 (33.32, 46.00)
<b>Males</b>						
All ages	8.14 (7.47, 8.85)	8.05 (7.39, 8.75)	8.62 (7.94, 9.34)	8.42 (7.76, 9.13)	8.10 (7.46, 8.79)	7.72 (7.10, 8.39)
0–19	0.77 (0.40, 1.34)	0.89 (0.49, 1.49)	0.51 (0.22, 1.00)	1.07 (0.62, 1.71)	1.00 (0.57, 1.62)	0.62 (0.30, 1.15)
20–29	2.08 (1.27, 3.21)	2.14 (1.33, 3.27)	1.69 (0.98, 2.70)	2.01 (1.24, 3.07)	1.76 (1.06, 2.75)	1.55 (0.90, 2.48)
30–39	4.22 (2.97, 5.82)	3.01 (1.99, 4.38)	4.14 (2.93, 5.69)	3.27 (2.22, 4.65)	2.95 (1.97, 4.23)	3.04 (2.06, 4.31)
40–49	7.66 (5.98, 9.66)	7.97 (6.25, 10.02)	6.49 (4.94, 8.37)	7.18 (5.54, 9.15)	6.86 (5.26, 8.80)	6.65 (5.08, 8.57)
50–59	12.25 (10.20, 14.58)	12.37 (10.32, 14.70)	12.38 (10.33, 14.72)	12.74 (10.65, 15.12)	12.04 (10.00, 14.36)	10.88 (8.94, 13.11)
60–69	11.54 (9.23, 14.25)	13.40 (10.94, 16.26)	18.45 (15.57, 21.71)	14.02 (11.55, 16.85)	15.44 (12.88, 18.36)	13.36 (11.02, 16.04)
70–79	24.80 (20.25, 30.08)	21.54 (17.38, 26.38)	22.39 (18.28, 27.16)	23.30 (19.20, 28.01)	20.68 (16.91, 25.03)	22.88 (18.98, 27.34)
≥80	41.90 (33.86, 51.27)	39.09 (31.47, 47.99)	41.56 (33.81, 50.54)	41.82 (34.17, 50.67)	38.94 (31.68, 47.36)	37.53 (30.50, 45.69)

**Supplemental Table S3: Background rates of hospitalizations and emergency department visits for deep vein thrombosis in Ontario, 2015 to 2020**

Age group, years	Incidence per 100,000 population (95% confidence interval)					
	2015	2016	2017	2018	2019	2020
<b>All sexes</b>						
All ages	87.68 (86.12, 89.26)	88.01 (86.46, 89.59)	87.30 (85.76, 88.86)	86.12 (84.61, 87.66)	84.94 (83.45, 86.46)	78.67 (77.24, 80.11)
0–19	4.54 (3.82, 5.36)	4.45 (3.74, 5.26)	4.30 (3.60, 5.09)	3.94 (3.28, 4.71)	3.90 (3.24, 4.65)	3.10 (2.51, 3.78)
20–29	26.65 (24.37, 29.10)	24.42 (22.24, 26.74)	28.75 (26.42, 31.23)	26.46 (24.26, 28.80)	26.96 (24.78, 29.29)	22.20 (20.24, 24.30)
30–39	54.96 (51.59, 58.50)	58.09 (54.65, 61.70)	51.41 (48.21, 54.78)	51.28 (48.12, 54.60)	53.10 (49.93, 56.42)	48.46 (45.48, 51.58)
40–49	80.89 (76.88, 85.05)	82.37 (78.31, 86.59)	81.44 (77.38, 85.64)	77.61 (73.65, 81.72)	80.15 (76.13, 84.33)	74.19 (70.32, 78.21)
50–59	107.78 (103.36, 112.35)	110.00 (105.54, 114.59)	109.45 (105.00, 114.04)	106.88 (102.48, 111.43)	102.46 (98.13, 106.93)	101.22 (96.90, 105.68)
60–69	155.59 (149.43, 161.93)	158.10 (152.00, 164.39)	152.57 (146.64, 158.68)	147.95 (142.18, 153.90)	150.24 (144.50, 156.15)	136.64 (131.24, 142.21)
70–79	240.78 (230.72, 251.17)	233.67 (223.94, 243.72)	223.81 (214.58, 233.34)	229.42 (220.31, 238.81)	216.99 (208.33, 225.92)	195.58 (187.53, 203.89)
≥80	358.96 (343.67, 374.75)	341.58 (326.88, 356.78)	352.05 (337.30, 367.27)	348.08 (333.60, 363.02)	325.11 (311.30, 339.37)	299.62 (286.52, 313.17)
<b>Females</b>						
All ages	87.65 (85.47, 89.88)	87.96 (85.78, 90.18)	87.77 (85.61, 89.97)	85.89 (83.77, 88.05)	83.18 (81.11, 85.29)	76.10 (74.13, 78.11)
0–19	5.22 (4.12, 6.51)	5.58 (4.45, 6.91)	5.56 (4.43, 6.88)	3.61 (2.72, 4.70)	4.25 (3.28, 5.42)	3.53 (2.65, 4.60)
20–29	33.39 (29.74, 37.36)	28.93 (25.56, 32.62)	36.35 (32.59, 40.41)	32.30 (28.83, 36.08)	32.40 (28.97, 36.13)	25.54 (22.53, 28.84)
30–39	62.74 (57.73, 68.08)	64.18 (59.13, 69.54)	56.76 (52.05, 61.78)	58.21 (53.48, 63.23)	59.25 (54.55, 64.25)	53.34 (48.94, 58.03)
40–49	80.69 (75.10, 86.59)	82.94 (77.25, 88.93)	80.54 (74.93, 86.45)	80.80 (75.18, 86.73)	76.79 (71.32, 82.57)	72.18 (66.88, 77.78)
50–59	90.81 (85.12, 96.79)	95.74 (89.90, 101.85)	91.80 (86.09, 97.79)	87.90 (82.31, 93.78)	86.18 (80.62, 92.01)	80.44 (75.05, 86.10)
60–69	133.36 (125.49, 141.60)	139.12 (131.21, 147.40)	132.34 (124.71, 140.33)	126.53 (119.14, 134.25)	127.80 (120.47, 135.45)	113.31 (106.51, 120.44)
70–79	224.90 (211.67, 238.74)	213.13 (200.47, 226.37)	222.56 (210.00, 235.67)	215.34 (203.31, 227.90)	201.68 (190.30, 213.56)	180.95 (170.40, 191.99)
≥80	360.75 (341.21, 381.12)	344.43 (325.55, 364.13)	347.75 (328.96, 367.33)	351.17 (332.48, 370.64)	316.27 (298.74, 334.56)	299.21 (282.33, 316.83)
<b>Males</b>						
All ages	87.70 (85.48, 89.96)	88.07 (85.85, 90.32)	86.82 (84.64, 89.04)	86.36 (84.21, 88.55)	86.75 (84.61, 88.93)	81.30 (79.24, 83.40)
0–19	3.89 (2.98, 5.00)	3.37 (2.52, 4.40)	3.09 (2.29, 4.09)	4.26 (3.31, 5.40)	3.56 (2.70, 4.61)	2.69 (1.94, 3.62)
20–29	20.27 (17.53, 23.33)	20.19 (17.47, 23.20)	21.65 (18.87, 24.73)	21.03 (18.34, 24.00)	21.93 (19.23, 24.91)	19.11 (16.61, 21.87)
30–39	46.79 (42.37, 51.55)	51.78 (47.17, 56.71)	45.92 (41.63, 50.52)	44.25 (40.12, 48.70)	46.93 (42.75, 51.42)	43.60 (39.65, 47.85)
40–49	81.09 (75.40, 87.10)	81.78 (76.03, 87.85)	82.37 (76.58, 88.49)	74.25 (68.75, 80.09)	83.68 (77.82, 89.87)	76.31 (70.71, 82.23)
50–59	124.98 (118.24, 132.00)	124.42 (117.72, 131.41)	127.33 (120.54, 134.39)	126.14 (119.36, 133.19)	119.01 (112.41, 125.89)	122.40 (115.68, 129.41)
60–69	179.51 (170.02, 189.39)	178.56 (169.23, 188.26)	174.36 (165.25, 183.84)	170.95 (162.04, 180.22)	174.27 (165.40, 183.50)	161.56 (153.14, 170.32)
70–79	259.12 (243.86, 275.07)	257.26 (242.36, 272.85)	225.25 (211.74, 239.40)	245.54 (231.80, 259.90)	234.52 (221.38, 248.22)	212.34 (200.10, 225.13)
≥80	356.13 (331.86, 381.71)	337.16 (313.99, 361.60)	358.63 (335.10, 383.38)	343.40 (320.75, 367.23)	338.35 (316.23, 361.62)	300.23 (279.68, 321.88)

**Supplemental Table S4: Background rates of hospitalizations and emergency department visits for pulmonary embolism in Ontario, 2015 to 2020**

Age group, years	Incidence per 100,000 population (95% confidence interval)					
	2015	2016	2017	2018	2019	2020
<b>All sexes</b>						
All ages	57.12 (55.86, 58.40)	62.34 (61.03, 63.67)	63.89 (62.57, 65.22)	66.15 (64.82, 67.49)	68.51 (67.17, 69.87)	68.39 (67.06, 69.74)
0–19	1.83 (1.38, 2.37)	2.05 (1.57, 2.62)	2.16 (1.68, 2.75)	2.56 (2.03, 3.19)	2.65 (2.11, 3.29)	1.92 (1.46, 2.47)
20–29	16.02 (14.26, 17.94)	20.26 (18.29, 22.39)	19.10 (17.21, 21.14)	18.83 (16.98, 20.82)	19.80 (17.94, 21.81)	18.33 (16.55, 20.24)
30–39	29.35 (26.89, 31.96)	33.95 (31.33, 36.73)	30.60 (28.14, 33.22)	31.74 (29.27, 34.38)	31.04 (28.63, 33.60)	31.40 (29.02, 33.94)
40–49	41.37 (38.52, 44.38)	45.65 (42.64, 48.82)	44.91 (41.92, 48.07)	46.38 (43.33, 49.59)	50.16 (46.99, 53.49)	50.93 (47.73, 54.29)
50–59	65.60 (62.16, 69.18)	68.95 (65.43, 72.61)	71.72 (68.12, 75.45)	74.15 (70.49, 77.95)	73.87 (70.21, 77.68)	77.37 (73.60, 81.28)
60–69	110.23 (105.06, 115.59)	122.90 (117.52, 128.46)	121.94 (116.64, 127.41)	126.89 (121.55, 132.41)	130.67 (125.32, 136.19)	129.16 (123.92, 134.58)
70–79	188.58 (179.69, 197.80)	189.16 (180.41, 198.22)	199.60 (190.88, 208.61)	201.36 (192.83, 210.17)	209.46 (200.95, 218.24)	202.02 (193.83, 210.46)
≥80	244.85 (232.25, 257.95)	265.45 (252.50, 278.89)	278.16 (265.07, 291.73)	286.11 (273.00, 299.69)	293.30 (280.20, 306.86)	288.79 (275.93, 302.10)
<b>Females</b>						
All ages	60.20 (58.39, 62.05)	65.79 (63.90, 67.71)	66.97 (65.08, 68.89)	70.01 (68.09, 71.96)	73.26 (71.32, 75.24)	70.36 (68.47, 72.29)
0–19	2.48 (1.74, 3.41)	3.12 (2.29, 4.15)	3.31 (2.45, 4.36)	4.01 (3.06, 5.14)	3.92 (2.99, 5.05)	2.48 (1.76, 3.41)
20–29	23.07 (20.05, 26.41)	27.08 (23.82, 30.66)	26.89 (23.68, 30.41)	25.51 (22.43, 28.89)	28.90 (25.66, 32.43)	25.35 (22.35, 28.63)
30–39	35.12 (31.40, 39.17)	43.97 (39.81, 48.44)	37.77 (33.95, 41.91)	39.70 (35.82, 43.89)	39.60 (35.77, 43.73)	41.21 (37.36, 45.36)
40–49	42.49 (38.46, 46.82)	46.93 (42.68, 51.49)	45.90 (41.69, 50.42)	48.56 (44.23, 53.21)	51.44 (46.98, 56.21)	53.16 (48.63, 58.00)
50–59	60.70 (56.06, 65.62)	62.04 (57.37, 67.00)	64.29 (59.52, 69.34)	64.61 (59.82, 69.68)	67.40 (62.50, 72.59)	66.46 (61.58, 71.63)
60–69	102.70 (95.81, 109.96)	116.54 (109.30, 124.13)	112.14 (105.12, 119.51)	116.01 (108.95, 123.42)	124.76 (117.52, 132.32)	115.62 (108.74, 122.81)
70–79	187.76 (175.70, 200.44)	181.67 (170.00, 193.93)	202.63 (190.66, 215.16)	205.98 (194.21, 218.27)	208.73 (197.15, 220.82)	194.66 (183.70, 206.09)
≥80	242.39 (226.42, 259.19)	266.84 (250.26, 284.25)	269.30 (252.80, 286.59)	292.37 (275.34, 310.18)	297.02 (280.04, 314.76)	282.37 (265.98, 299.51)
<b>Males</b>						
All ages	53.94 (52.20, 55.72)	58.79 (56.99, 60.64)	60.72 (58.90, 62.58)	62.19 (60.36, 64.06)	63.65 (61.82, 65.52)	66.38 (64.52, 68.28)
0–19	1.21 (0.73, 1.89)	1.02 (0.58, 1.65)	1.07 (0.63, 1.72)	1.19 (0.72, 1.86)	1.44 (0.91, 2.16)	1.37 (0.86, 2.08)
20–29	9.36 (7.52, 11.50)	13.86 (11.63, 16.40)	11.82 (9.79, 14.14)	12.62 (10.56, 14.96)	11.38 (9.46, 13.58)	11.83 (9.88, 14.04)
30–39	23.28 (20.20, 26.71)	23.54 (20.47, 26.94)	23.23 (20.22, 26.57)	23.66 (20.66, 26.97)	22.45 (19.59, 25.61)	21.66 (18.89, 24.71)
40–49	40.22 (36.24, 44.52)	44.33 (40.12, 48.86)	43.88 (39.68, 48.40)	44.09 (39.87, 48.63)	48.82 (44.37, 53.59)	48.58 (44.14, 53.35)
50–59	70.56 (65.52, 75.88)	75.93 (70.71, 81.43)	79.24 (73.90, 84.86)	83.83 (78.33, 89.62)	80.45 (75.04, 86.14)	88.49 (82.78, 94.48)
60–69	118.33 (110.65, 126.41)	129.75 (121.82, 138.06)	132.49 (124.56, 140.78)	138.57 (130.56, 146.94)	137.01 (129.16, 145.21)	143.63 (135.70, 151.90)
70–79	189.52 (176.51, 203.24)	197.75 (184.71, 211.47)	196.12 (183.53, 209.34)	196.06 (183.80, 208.93)	210.30 (197.87, 223.30)	210.45 (198.26, 223.18)
≥80	248.71 (228.50, 270.23)	263.29 (242.86, 284.98)	291.72 (270.54, 314.13)	276.65 (256.36, 298.12)	287.73 (267.36, 309.25)	298.33 (277.85, 319.92)



**Supplemental Table S5: Background rates of hospitalizations and emergency department visits for idiopathic thrombocytopenia in Ontario, 2015 to 2020**

Age group, years	Incidence per 100,000 population (95% confidence interval)					
	2015	2016	2017	2018	2019	2020
<b>All sexes</b>						
All ages	6.41 (6.00, 6.85)	6.31 (5.90, 6.74)	6.14 (5.74, 6.56)	5.75 (5.37, 6.16)	5.81 (5.42, 6.21)	4.45 (4.12, 4.81)
0–19	6.56 (5.69, 7.54)	6.11 (5.26, 7.04)	6.82 (5.93, 7.80)	5.67 (4.87, 6.58)	5.72 (4.91, 6.62)	3.35 (2.74, 4.06)
20–29	3.90 (3.06, 4.90)	3.05 (2.32, 3.95)	2.88 (2.17, 3.73)	2.38 (1.75, 3.15)	2.84 (2.16, 3.66)	2.65 (2.00, 3.43)
30–39	3.51 (2.70, 4.49)	4.05 (3.18, 5.09)	3.93 (3.08, 4.94)	3.77 (2.95, 4.75)	3.55 (2.77, 4.49)	2.75 (2.08, 3.57)
40–49	3.61 (2.80, 4.57)	3.91 (3.06, 4.91)	3.60 (2.79, 4.58)	3.94 (3.09, 4.95)	3.83 (2.99, 4.83)	2.48 (1.82, 3.31)
50–59	4.73 (3.84, 5.76)	4.95 (4.04, 6.00)	4.95 (4.04, 6.00)	4.30 (3.45, 5.29)	4.56 (3.69, 5.58)	4.26 (3.41, 5.26)
60–69	7.75 (6.43, 9.27)	6.58 (5.38, 7.96)	6.31 (5.15, 7.65)	6.16 (5.03, 7.47)	5.94 (4.84, 7.21)	5.10 (4.10, 6.27)
70–79	12.97 (10.71, 15.55)	13.58 (11.31, 16.17)	11.75 (9.71, 14.10)	10.28 (8.43, 12.43)	12.58 (10.56, 14.87)	9.52 (7.81, 11.49)
≥80	24.24 (20.39, 28.61)	24.93 (21.07, 29.28)	22.17 (18.59, 26.24)	24.66 (20.92, 28.87)	20.74 (17.36, 24.58)	16.47 (13.51, 19.88)
<b>Females</b>						
All ages	6.49 (5.91, 7.12)	6.45 (5.87, 7.07)	6.11 (5.55, 6.71)	6.13 (5.57, 6.72)	6.17 (5.61, 6.76)	4.68 (4.20, 5.20)
0–19	6.15 (4.96, 7.55)	5.72 (4.57, 7.06)	6.28 (5.08, 7.68)	5.06 (3.99, 6.32)	5.43 (4.32, 6.73)	3.99 (3.05, 5.12)
20–29	5.49 (4.08, 7.24)	3.70 (2.56, 5.17)	3.29 (2.24, 4.68)	2.98 (2.00, 4.28)	4.00 (2.86, 5.45)	3.73 (2.64, 5.12)
30–39	5.11 (3.76, 6.80)	5.27 (3.90, 6.96)	4.88 (3.57, 6.51)	5.72 (4.31, 7.44)	4.56 (3.32, 6.10)	3.35 (2.32, 4.68)
40–49	3.34 (2.28, 4.72)	4.41 (3.18, 5.96)	4.21 (3.01, 5.73)	4.85 (3.55, 6.46)	4.73 (3.45, 6.33)	3.15 (2.13, 4.50)
50–59	5.18 (3.89, 6.76)	4.68 (3.46, 6.18)	5.06 (3.79, 6.62)	4.79 (3.56, 6.32)	4.72 (3.49, 6.24)	3.69 (2.61, 5.06)
60–69	7.10 (5.38, 9.20)	6.76 (5.11, 8.78)	5.44 (3.98, 7.25)	6.70 (5.09, 8.66)	5.85 (4.37, 7.68)	5.05 (3.69, 6.73)
70–79	9.81 (7.20, 13.04)	11.49 (8.70, 14.89)	11.38 (8.69, 14.65)	7.56 (5.45, 10.22)	11.87 (9.24, 15.03)	7.26 (5.28, 9.75)
≥80	20.67 (16.20, 25.99)	22.44 (17.82, 27.90)	17.65 (13.62, 22.49)	23.15 (18.54, 28.55)	18.47 (14.42, 23.29)	14.79 (11.23, 19.13)
<b>Males</b>						
All ages	6.33 (5.74, 6.96)	6.16 (5.58, 6.78)	6.17 (5.60, 6.78)	5.37 (4.84, 5.93)	5.44 (4.92, 6.01)	4.22 (3.76, 4.72)
0–19	6.95 (5.71, 8.39)	6.48 (5.28, 7.86)	7.32 (6.05, 8.79)	6.27 (5.10, 7.62)	6.00 (4.86, 7.32)	2.75 (2.00, 3.69)
20–29	2.39 (1.52, 3.59)	2.45 (1.57, 3.64)	2.48 (1.61, 3.67)	1.82 (1.09, 2.84)	1.76 (1.06, 2.75)	1.64 (0.97, 2.59)
30–39	1.83 (1.04, 2.97)	2.79 (1.81, 4.12)	2.94 (1.94, 4.28)	1.80 (1.05, 2.87)	2.54 (1.64, 3.75)	2.16 (1.35, 3.26)
40–49	3.88 (2.72, 5.37)	3.38 (2.30, 4.80)	2.97 (1.96, 4.32)	2.98 (1.97, 4.34)	2.88 (1.88, 4.22)	1.77 (1.01, 2.88)
50–59	4.28 (3.11, 5.74)	5.22 (3.92, 6.81)	4.84 (3.59, 6.38)	3.79 (2.70, 5.18)	4.40 (3.21, 5.89)	4.84 (3.58, 6.40)
60–69	8.45 (6.49, 10.81)	6.38 (4.72, 8.43)	7.25 (5.49, 9.40)	5.58 (4.07, 7.47)	6.03 (4.48, 7.95)	5.15 (3.75, 6.92)
70–79	16.62 (12.93, 21.03)	15.98 (12.43, 20.22)	12.18 (9.20, 15.81)	13.40 (10.34, 17.08)	13.39 (10.40, 16.97)	12.10 (9.32, 15.45)
≥80	29.86 (23.14, 37.93)	28.78 (22.30, 36.55)	29.09 (22.68, 36.75)	26.94 (20.88, 34.21)	24.14 (18.51, 30.95)	18.95 (14.07, 24.99)

**Supplemental Table S6: Background rates of hospitalizations and emergency department visits for disseminated intravascular coagulation in Ontario, 2015 to 2020**

Age group, years	Incidence per 100,000 population (95% confidence interval)					
	2015	2016	2017	2018	2019	2020
<b>All sexes</b>						
All ages	1.47 (1.28, 1.69)	1.59 (1.39, 1.82)	1.56 (1.36, 1.78)	1.57 (1.37, 1.79)	1.57 (1.37, 1.78)	1.59 (1.39, 1.81)
0–19	0.62 (0.37, 0.97)	0.36 (0.18, 0.64)	0.55 (0.32, 0.88)	0.45 (0.25, 0.75)	0.29 (0.13, 0.55)	0.51 (0.29, 0.83)
20–29	0.69 (0.37, 1.19)	1.05 (0.64, 1.63)	1.23 (0.79, 1.83)	0.89 (0.53, 1.41)	0.91 (0.55, 1.43)	0.76 (0.43, 1.23)
30–39	0.95 (0.55, 1.52)	0.77 (0.42, 1.29)	1.40 (0.91, 2.05)	1.15 (0.72, 1.74)	1.07 (0.66, 1.63)	1.28 (0.83, 1.87)
40–49	0.90 (0.53, 1.44)	1.34 (0.87, 1.98)	1.08 (0.66, 1.66)	1.19 (0.74, 1.80)	0.70 (0.37, 1.20)	1.46 (0.96, 2.12)
50–59	1.88 (1.34, 2.57)	2.21 (1.62, 2.95)	1.15 (0.74, 1.72)	1.88 (1.34, 2.57)	1.75 (1.22, 2.42)	1.62 (1.11, 2.27)
60–69	2.52 (1.79, 3.44)	2.69 (1.95, 3.63)	2.33 (1.65, 3.20)	2.45 (1.76, 3.33)	3.14 (2.36, 4.10)	2.15 (1.52, 2.95)
70–79	3.58 (2.45, 5.05)	2.80 (1.83, 4.11)	4.46 (3.24, 5.98)	3.08 (2.10, 4.34)	3.67 (2.62, 5.00)	4.05 (2.97, 5.41)
≥80	4.50 (2.94, 6.60)	6.06 (4.25, 8.39)	4.43 (2.92, 6.45)	5.92 (4.17, 8.17)	5.61 (3.93, 7.77)	4.88 (3.34, 6.89)
<b>Females</b>						
All ages	1.38 (1.12, 1.68)	1.55 (1.27, 1.87)	1.46 (1.19, 1.77)	1.56 (1.29, 1.87)	1.67 (1.39, 1.99)	1.57 (1.30, 1.88)
0–19	0.87 (0.46, 1.49)	0.33 (0.11, 0.78)	0.26 (0.07, 0.68)	0.39 (0.14, 0.86)	0.33 (0.11, 0.76)	0.65 (0.31, 1.20)
20–29	0.99 (0.45, 1.88)	1.41 (0.75, 2.42)	1.17 (0.58, 2.09)	1.13 (0.56, 2.02)	1.20 (0.62, 2.10)	1.08 (0.54, 1.93)
30–39	1.41 (0.75, 2.42)	0.75 (0.30, 1.55)	1.70 (0.97, 2.76)	1.46 (0.80, 2.44)	1.52 (0.85, 2.51)	1.38 (0.75, 2.32)
40–49	0.94 (0.43, 1.78)	0.73 (0.30, 1.51)	0.95 (0.43, 1.80)	1.37 (0.73, 2.34)	1.05 (0.50, 1.93)	1.58 (0.88, 2.60)
50–59	1.44 (0.81, 2.37)	2.10 (1.32, 3.18)	1.05 (0.52, 1.88)	1.73 (1.02, 2.73)	1.73 (1.03, 2.74)	1.65 (0.96, 2.64)
60–69	1.99 (1.14, 3.24)	2.54 (1.57, 3.88)	2.48 (1.54, 3.79)	2.31 (1.41, 3.57)	3.38 (2.28, 4.82)	1.76 (1.00, 2.85)
70–79	1.67 (0.72, 3.29)	2.82 (1.54, 4.74)	3.79 (2.32, 5.86)	2.88 (1.65, 4.68)	2.58 (1.44, 4.26)	2.97 (1.76, 4.70)
≥80	3.68 (1.96, 6.29)	5.54 (3.39, 8.56)	3.26 (1.68, 5.69)	3.99 (2.23, 6.58)	4.68 (2.77, 7.40)	4.08 (2.33, 6.63)
<b>Males</b>						
All ages	1.57 (1.29, 1.90)	1.64 (1.35, 1.97)	1.67 (1.38, 2.01)	1.59 (1.31, 1.91)	1.46 (1.20, 1.77)	1.61 (1.33, 1.93)
0–19	0.38 (0.14, 0.83)	0.38 (0.14, 0.83)	0.82 (0.44, 1.40)	0.50 (0.22, 0.99)	0.25 (0.07, 0.64)	0.37 (0.14, 0.82)
20–29	0.42 (0.11, 1.06)	0.71 (0.29, 1.47)	1.29 (0.69, 2.21)	0.67 (0.27, 1.38)	0.65 (0.26, 1.33)	0.45 (0.15, 1.06)
30–39	0.46 (0.12, 1.17)	0.78 (0.31, 1.61)	1.09 (0.52, 2.01)	0.84 (0.36, 1.66)	0.61 (0.22, 1.33)	1.18 (0.61, 2.05)
40–49	0.86 (0.37, 1.70)	1.97 (1.16, 3.11)	1.21 (0.60, 2.16)	0.99 (0.45, 1.89)	0.33 (0.07, 0.97)	1.33 (0.69, 2.32)
50–59	2.33 (1.49, 3.47)	2.32 (1.49, 3.45)	1.26 (0.67, 2.15)	2.04 (1.26, 3.12)	1.76 (1.04, 2.78)	1.58 (0.90, 2.57)
60–69	3.09 (1.96, 4.63)	2.86 (1.79, 4.33)	2.16 (1.26, 3.46)	2.61 (1.61, 3.98)	2.89 (1.85, 4.31)	2.58 (1.62, 3.90)
70–79	5.78 (3.70, 8.60)	2.78 (1.44, 4.85)	5.22 (3.34, 7.76)	3.30 (1.89, 5.36)	4.92 (3.19, 7.27)	5.29 (3.52, 7.65)
≥80	5.79 (3.09, 9.91)	6.87 (3.93, 11.16)	6.23 (3.49, 10.28)	8.85 (5.54, 13.39)	7.01 (4.15, 11.08)	6.07 (3.47, 9.85)

**Supplemental Table S7: Background rates of hospitalizations and emergency department visits for cerebral venous thrombosis in Ontario, 2015 to 2020**

Age group, years	Incidence per 100,000 population (95% confidence interval)					
	2015	2016	2017	2018	2019	2020
<b>All sexes</b>						
All ages	1.39 (1.20, 1.61)	1.43 (1.24, 1.64)	1.68 (1.47, 1.91)	1.38 (1.20, 1.59)	1.73 (1.53, 1.96)	1.60 (1.40, 1.82)
0–19	1.18 (0.82, 1.63)	1.01 (0.68, 1.43)	1.26 (0.90, 1.72)	0.87 (0.57, 1.26)	1.31 (0.94, 1.78)	0.80 (0.52, 1.18)
20–29	0.96 (0.57, 1.52)	1.26 (0.81, 1.88)	1.49 (1.00, 2.14)	1.29 (0.84, 1.89)	1.49 (1.01, 2.11)	1.56 (1.07, 2.19)
30–39	1.78 (1.22, 2.52)	1.81 (1.24, 2.54)	1.77 (1.22, 2.49)	1.20 (0.76, 1.81)	1.57 (1.07, 2.23)	1.23 (0.80, 1.81)
40–49	1.64 (1.12, 2.33)	1.45 (0.95, 2.10)	1.45 (0.96, 2.11)	1.13 (0.70, 1.73)	1.89 (1.31, 2.63)	1.51 (1.00, 2.18)
50–59	1.35 (0.90, 1.95)	1.54 (1.05, 2.17)	1.59 (1.09, 2.23)	1.79 (1.26, 2.46)	1.75 (1.22, 2.42)	1.96 (1.40, 2.67)
60–69	1.36 (0.84, 2.07)	1.38 (0.86, 2.09)	2.02 (1.39, 2.84)	1.50 (0.97, 2.21)	2.50 (1.81, 3.37)	2.15 (1.52, 2.95)
70–79	1.56 (0.86, 2.63)	1.94 (1.15, 3.07)	2.84 (1.89, 4.10)	2.40 (1.55, 3.55)	2.11 (1.34, 3.17)	2.73 (1.86, 3.88)
≥80	1.90 (0.95, 3.41)	1.85 (0.92, 3.32)	2.30 (1.26, 3.86)	2.24 (1.23, 3.76)	1.87 (0.97, 3.27)	2.44 (1.39, 3.96)
<b>Females</b>						
All ages	1.55 (1.27, 1.87)	1.51 (1.23, 1.82)	1.77 (1.47, 2.10)	1.59 (1.31, 1.90)	1.94 (1.64, 2.29)	1.74 (1.46, 2.07)
0–19	0.94 (0.51, 1.57)	0.86 (0.46, 1.48)	0.79 (0.41, 1.39)	1.12 (0.65, 1.79)	1.11 (0.65, 1.78)	0.85 (0.45, 1.45)
20–29	1.43 (0.76, 2.44)	1.63 (0.91, 2.69)	2.66 (1.72, 3.92)	1.54 (0.86, 2.54)	2.10 (1.30, 3.21)	2.16 (1.35, 3.27)
30–39	2.39 (1.50, 3.62)	2.15 (1.31, 3.32)	2.44 (1.55, 3.66)	1.66 (0.95, 2.70)	2.13 (1.32, 3.25)	2.17 (1.36, 3.28)
40–49	1.98 (1.19, 3.10)	1.89 (1.12, 2.99)	1.68 (0.96, 2.74)	1.90 (1.12, 3.00)	2.21 (1.37, 3.38)	1.89 (1.12, 2.99)
50–59	1.15 (0.59, 2.01)	1.05 (0.52, 1.88)	1.34 (0.73, 2.24)	1.63 (0.95, 2.61)	1.93 (1.18, 2.97)	1.84 (1.11, 2.88)
60–69	1.74 (0.95, 2.93)	1.33 (0.66, 2.38)	1.77 (0.99, 2.92)	1.50 (0.80, 2.57)	2.59 (1.64, 3.89)	1.43 (0.76, 2.44)
70–79	1.25 (0.46, 2.72)	1.81 (0.83, 3.44)	2.47 (1.31, 4.22)	2.16 (1.12, 3.77)	2.41 (1.32, 4.04)	2.48 (1.39, 4.08)
≥80	2.27 (0.98, 4.46)	2.49 (1.14, 4.73)	2.17 (0.94, 4.28)	1.86 (0.75, 3.84)	1.56 (0.57, 3.40)	2.04 (0.88, 4.02)
<b>Males</b>						
All ages	1.23 (0.98, 1.53)	1.35 (1.08, 1.65)	1.59 (1.30, 1.91)	1.18 (0.94, 1.46)	1.52 (1.25, 1.83)	1.46 (1.19, 1.76)
0–19	1.40 (0.88, 2.12)	1.14 (0.68, 1.81)	1.70 (1.12, 2.48)	0.63 (0.30, 1.15)	1.50 (0.96, 2.23)	0.75 (0.39, 1.31)
20–29	0.52 (0.17, 1.21)	0.92 (0.42, 1.74)	0.40 (0.11, 1.02)	1.05 (0.52, 1.88)	0.93 (0.44, 1.70)	1.00 (0.50, 1.79)
30–39	1.14 (0.55, 2.10)	1.45 (0.77, 2.48)	1.09 (0.52, 2.01)	0.74 (0.30, 1.52)	1.02 (0.49, 1.87)	0.29 (0.06, 0.86)
40–49	1.29 (0.67, 2.26)	0.98 (0.45, 1.87)	1.21 (0.60, 2.16)	0.33 (0.07, 0.97)	1.55 (0.85, 2.60)	1.11 (0.53, 2.04)
50–59	1.55 (0.89, 2.53)	2.03 (1.26, 3.10)	1.84 (1.11, 2.87)	1.95 (1.19, 3.00)	1.57 (0.90, 2.54)	2.08 (1.29, 3.17)
60–69	0.94 (0.38, 1.93)	1.43 (0.71, 2.56)	2.29 (1.36, 3.62)	1.49 (0.77, 2.60)	2.41 (1.47, 3.73)	2.93 (1.90, 4.32)
70–79	1.93 (0.83, 3.80)	2.08 (0.95, 3.96)	3.26 (1.83, 5.38)	2.68 (1.43, 4.58)	1.77 (0.81, 3.36)	3.03 (1.73, 4.91)
≥80	1.34 (0.28, 3.91)	0.86 (0.10, 3.10)	2.49 (0.92, 5.43)	2.81 (1.13, 5.80)	2.34 (0.86, 5.08)	3.03 (1.31, 5.98)



**Supplemental Figure 1: Monthly average incidence rates of hospitalization and emergency department visits in Ontario, 2015 to 2020: A. Stroke, B. Deep vein thrombosis, C. Pulmonary embolism, D. Idiopathic thrombocytopenia, E. Disseminated intravascular coagulation, F. Cerebral venous thrombosis**

