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Codes used for identifying cases
ICD-10 diagnostic codes were used to identify all patients who presented to hospitals or emergency departments in Alberta during the study period with a final diagnosis of ischemic stroke for their episode of care. An episode of care refers to all contiguous inpatient hospitalizations. These case identification codes are based on the Heart and Stroke Foundation's Canadian Best Practice Recommendations (2016).

ICD-10-CA Code	Description
	Ischemic Stroke
G08	Intracranial and Intraspinal Phlebitis and Thrombophlebitis
H341	Central Retinal Artery Occlusion
I630	Cerebral Infarction Due To Thrombosis Of Precerebral Arteries
I631	Cerebral Infarction Due To Embolism Of Precerebral Arteries
I632	Cerebral Infarction Due To Unspecified Occlusion Or Stenosis Of Precerebral Arteries
I633	Cerebral Infarction Due To Thrombosis Of Cerebral Arteries
I634	Cerebral Infarction Due To Embolism Of Cerebral Arteries
I635	Cerebral Infarction Due To Unspecified Occlusion Or Stenosis Of Cerebral Arteries
I636	Cerebral Infarction Due to Cerebral Venous Thrombosis, Nonpyogenic
I638	Other Cerebral Infarction
I639	Cerebral Infarction, Unspecified
I64***	Stroke, Not Specified As Haemorrhage Or Infarction *(see note below)*
I676	Nonpyogenic Thrombosis Of Intracranial Venous System

*** NOTE: The decision to place I64 under the Ischemic group is based on the following rationale: *Coding guidelines direct health information management systems to assume "ischemic" if hemorrhagic stroke has been ruled out (there is no supporting documentation of a hemorrhagic stroke). Hemorrhagic strokes are fairly well documented.*
From the Canadian Institutes of Health Information (CIHI) eQuery 44220: One valid circumstance [for coding I64] is when diagnostic imaging has not yet been performed and another is when any transfer information does not indicate the type of stroke. For the majority of cases, the coder can locate the information required to assign a code for hemorrhagic stroke or ischemic stroke from the documentation. Despite specific resources (CIHI eLearning Different Codes for Different Strokes, eQueries), I64 is still frequently assigned. In such cases, the stroke was most likely ischemic.

The following additional selection criteria were used: (a) All first and recurrent stroke events, (b) Age at admission 20 years and older, (c) Admission to an acute care facility, (d) Valid health care number (ULI), (e) Sex recorded as male or female, and (f) all discharge dispositions.

A patient was considered to have a minor stroke if they had suffered an ischemic stroke and were discharged home directly from the emergency department.

The following additional codes were used to identify all stroke deaths in the Vital Statistics Database maintained by Alberta Health Services:

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ICD-10-CA Code	Description
I64	Stroke, Not Specified As Haemorrhage Or Infarction
I64	Stroke, Not Specified As Haemorrhage Or Infarction
I65	Stroke, Not Specified As Haemorrhage Or Infarction
I66	Stroke, Not Specified As Haemorrhage Or Infarction
I67	Stroke, Not Specified As Haemorrhage Or Infarction
I68	Stroke, Not Specified As Haemorrhage Or Infarction

Authors AG, JMS, and MDH had full access to the database population used to create the study population. The corresponding author had full access to all data in the study and had final responsibility for the decision to submit for publication.

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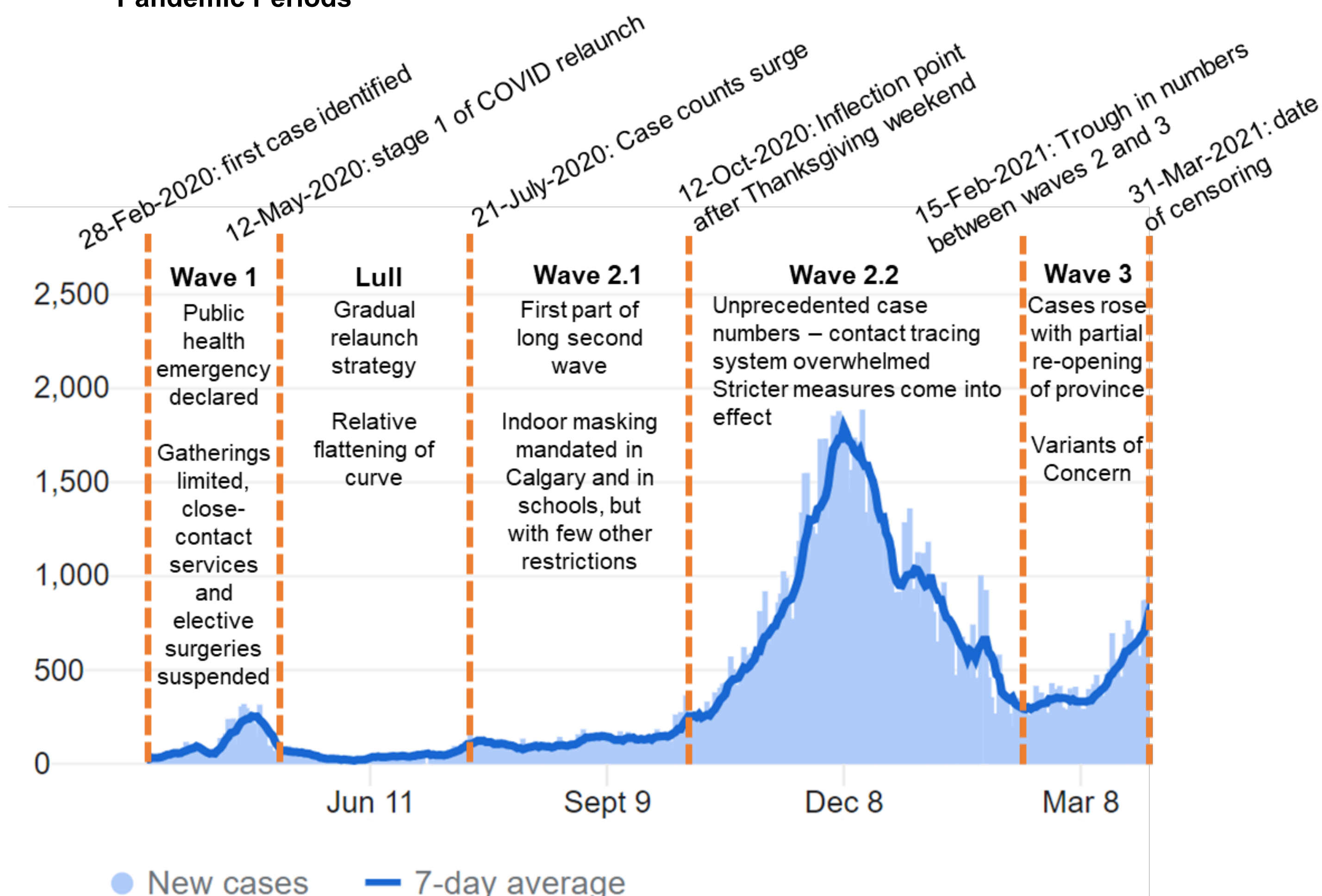
Timeline of the COVID-19 Pandemic and Public Health Orders in Alberta during our Five Pandemic Periods



Supplementary Figure 1: Summary of the new daily cases and 7-day average case counts for COVID-19 during the first year of the pandemic in Alberta, with key dates noted for relevant changes in cases and in public health restrictions by which we defined our five Pandemic Periods for the study. The original graph (before our annotations) was obtained online from publicly available data on COVID-19 cases provided by the Government of Alberta, available at: https://www.alberta.ca/stats/covid-19-alberta-statistics.htm#total-cases.

Below, we have detailed the key events and changes that characterized each of these five periods of interest, highlighting all important public health orders (both restrictions and lifting or re-opening decisions) as well as relevant changes in case numbers.

<u>PANDEMIC PERIOD #1: "WAVE 1"</u> (February 28, 2020 to May 12, 2020)

March 5, 2020: Alberta identifies its first presumptive COVID-19 case.

March 14, 2020: The Government of Alberta recommended against travel outside of Canada and instructed all Albertans currently travelling outside of Canada to self-isolate on their return for 14 days, independent of the country they were visiting.

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March 17, 2020: Government of Alberta declared a **provincial public health emergency** and cancelled in-person learning at schools.

March 25, 2020: The Government of Alberta announced that through amendments to the *Procedures Regulation* under the *Provincial Offences Procedures Act*, peace and police officers would be able to issue tickets to enforce COVID-19 Public Health Orders. Alberta's Chief Medical Officer passed a Public Health Order requiring mandatory 14-day self isolation for international travelers returning to Alberta, mandatory 14-day isolation for close contacts of persons confirmed to have COVID-19, and mandatory minimum 10-day isolation for persons with COVID-19 or experiencing symptoms such as cough and fever (link). Health care service providers were required to follow new operational protocols (link).

March 27, 2020: Alberta's Chief Medical Officer passed a Public Health Order prohibiting public gatherings in excess of 15 people, requiring all persons to maintain a minimum of 2 meters distance from one another, and mandating the closure of all non-essential businesses including personal services, wellness services, and retail stores (link); violation was subject to fines (link).

March 30, 2020: Albertans under mandatory self-isolation (such as those returning from travel, experiencing COVID-19 symptoms, or in close contact with a person who tested positive for COVID-19) were now required to remain inside and could only go for walks on their own property for the duration of their self-isolation (link).

April 6, 2020: Alberta Health Services prohibited visitors to long-term care, supportive living, congregate living, hospice care and acute care settings, with limited exceptions (link). Alberta chief medical officer of health Dr. Deena Hinshaw recommended the use of non-medical face masks when physical distancing is difficult.

April 23, 2020: The Calgary Stampede cancelled its 2020 event, as Hinshaw restricted gatherings of more than 15 people.

April 29, 2020: Peak in new daily cases of COVID-19 for Wave 1 with 315 new cases and a 7-day rolling average of 252 new cases.

May 3, 2020: Alberta recorded fewer than 100 cases of COVID-19 for the first time since mid-April, signalling the end of the province's first wave of the virus.
May 12, 2020: *Bill 13: Emergency Management Amendment Act, 2020 (No. 2)* came into force, allowing police enhanced authority during a state of emergency, allowing municipalities to declare a 90-day state of local emergency, and granting the government powers to cancel, rescind or restrict actions taken by a municipality pursuant to a state of local emergency (link).

PANDEMIC PERIOD #2: "LULL" (May 13, 2020 to July 20, 2020)

May 13, 2020: Alberta entered Stage 1 of its COVID-19 relaunch, letting businesses like restaurants and retailers reopen, but Calgary and Brooks were singled out of relaunch due to ongoing meat-plant outbreaks. Both municipalities were allowed to join in the relaunch May 25.

June 5, 2020: Alberta recorded only seven new COVID-19 cases while also conducting its highest number of tests to date. Hinshaw lauded the efforts of Albertans to flatten the curve.

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June 12, 2020: Stage 2 of Alberta's relaunch began a week ahead of schedule, with businesses like massage clinics, theatres and libraries allowed to reopen. Calgary's local state of emergency expired, with the rest of Alberta following on June 16.

PANDEMIC PERIOD #3: "WAVE 2.1" (July 21, 2020 to October 11, 2020)

July 21, 2020: Calgary made mask use mandatory in indoor public spaces effective Aug. 1 as COVID-19 case counts began to surge, with 141 new daily cases (7-day average of 117 new daily cases).

August 4, 2020: Alberta mandated mask use for its back-to-school plan for students in grades 4 to 12. The Calgary Board of Education and Calgary Catholic School District both soon expanded that mandate to include all students.

August 20, 2020: COVID-19 cases continued to rise, with the Edmonton region responsible for much of the increase. Hinshaw suggested that young people and indoor gatherings were driving the spread.

October 8, 2020: "Voluntary" COVID-19 restrictions came to the Edmonton zone amid a surge in infections. However, at this point there was no return of the prior public health restrictions that had been implemented in Wave 1.

October 9, 2020: Initial peak of the first part of Wave 2, with 277 new daily cases and a rolling average of 234 cases.

PANDEMIC PERIOD #4: "WAVE 2.2" (October 12, 2020 to February 15, 2021)

October 12, 2020: Albertans celebrated Thanksgiving. The holiday was later cited as an inflection point in the pandemic's second wave, with family gatherings driving viral spread.

October 22, 2020: The Government of Alberta announced a new pilot program in conjunction with the Government of Canada allowing people to quarantine for less than 14 days if their on-landing COVID test was negative and they received a second test on day 6-7 post-arrival (link).

October 26, 2020: Alberta imposed a mandatory 15-person limit on social gatherings for Calgary.

October 29, 2020: All social gatherings in Calgary and Edmonton (largest cities in Alberta with the province's only two comprehensive stroke centres) were limited to 15 people, including gatherings for dinner parties, wedding and funeral receptions, and banquets (link).

November 5, 2020: Alberta's contact tracing system was overwhelmed by surging case counts. The system did not recover until February 2021.
November 12, 2020: New targeted public health measures were announced to help control the spread of COVID-19 (link).

November 24, 2020: Mandatory restrictions from November 12 were now in effect province wide, including:

1. No indoor social gatherings in any setting, including workplaces

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2. Outdoor gatherings limited to no more than 10 people
3. Funeral services and wedding ceremonies to follow all public health guidance, limited to no more than 10 people, and receptions not permitted (link).

November 27, 2020: Certain Alberta peace officers and community peace officers granted temporary authority to enforce public health orders (link).

December 5, 2020: Alberta logged 1,879 cases of the coronavirus, the most ever in a single day. The peak in active cases would come a week later, when 21,135 infections were active.

December 8, 2020: Lockdown-style restrictions returned to Alberta, with many businesses forced to close and all indoor and outdoor social gatherings banned. The Government of Alberta announced that:

1. Effective immediately, all indoor and outdoor social gatherings were prohibited
2. Effective immediately, mandatory indoor public masking extended province wide (link)
3. Effective December 13, 2020, there would be additional operational restrictions on places of worship and retail businesses across the province.
4. Other kinds of businesses ordered to close. Full list of restrictions and closures here.
5. Mandatory work from home measures implemented unless physical presence deemed essential for operational effectiveness

December 15, 2020: Long-term care residents received the first doses of COVID-19 vaccine in Alberta, the Pfizer-BioNTech jab. Moderna's vaccine would be approved later in the month.

December 24, 2020: Alberta reported its first case of a variant strain of the coronavirus thought to be more contagious. The B.1.1.7 strain, first detected in the United Kingdom, was found in a sample from December 15.

January 14, 2020: Alberta eased restrictions for outdoor gatherings and allowed personal services businesses to reopen as case counts began to slowly decline.

January 29, 2020: Alberta announced that it would ease some restrictions on restaurants, indoor fitness and kids' sport later in February.

February 15, 2021: Trough in case numbers between waves 2 and 3, with 251 new cases and 7-day rolling average of 291 cases.

PANDEMIC PERIOD #5: WAVE 3 (February 16, 2021 onwards)

March 1, 2021: Gyms and libraries were allowed to reopen in Alberta. Other businesses were left out of the plans.

March 8, 2021: Retail permitted to operate at 25% capacity, banquet and conference halls to open for allowed activities, and collegiate sports programs allowed to conduct practices with 10 participants per-group, with three metres of social distancing between them and masks mandatory (games were prohibited).

March 22, 2021: Due to a major surge of cases brought upon by variants of concern, Health Minister Tyler Shandro stated Alberta had no plans to move to further reopening at that time.

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March 31, 2021: Date of stroke data censoring for our study, at which time wave 3 was still raging. A return to mid-February levels in new cases would only be seen by June 2021.

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Sample Size Calculation

Sample size calculations were performed using G*Power 3.1.9.7. Between April-2015 and March-2018, 576 patients received EVT for acute stroke (about 16 patients/month) of whom 326(56.6%) received alteplase (9.3/month), with the median onset-to-treatment time being 140 minutes (IQR 90-250).[16] Using these numbers, if we estimate a 25% drop in the acute treatment volume during the COVID-19 pandemic, we would need 38 acute stroke patients in each of the five Pandemic periods of interest to achieve 80% power using a Poisson regression analysis. Similarly, estimating a 25% greater delay in onset-to-treatment time (140 to 175 minutes, standard deviation 80 minutes) and assuming the size of the Pandemic sample is only 10% of the pre-pandemic sample, we would need at least 375 EVT patients in the Pre-Pandemic period (already accomplished) and 37 in each Pandemic period to achieve 80% power. We therefore planned to gather data until we had accrued at least 40 treated patients in the QuICR registry in each Pandemic period (particularly for wave 3 which was ongoing as of the end of March). Upon extracting data until 31-March-2021, we had already accrued complete data on 147 treated patients in QuICR for Wave 1, 163 for the Lull period, 144 for Wave 2.1, 228 for Wave 2.2, and 61 for Wave 3. As we had well exceeded our minimal threshold of case numbers for wave 3, we proceeded with our analyses.

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Supplementary Table 1 – Adjusted odds ratios (aORs) for in-hospital mortality among patients who received and did not receive acute stroke therapies in each pandemic period compared to the pre-pandemic period.

Time Period	Received acute stroke therapies - aOR (95%CI) N=3,028	Did not receive acute stroke therapies – aOR (95%CI) N=15,678	$p_{interaction}$ of time period and receipt of acute stroke therapies
Pre-Pandemic	Reference	Reference	Reference
Wave 1	0.99 (0.57-1.73)	1.00 (0.75-1.33)	0.9
Lull	1.06 (0.63-1.81)	1.05 (0.79-1.40)	0.9
Wave 2.1	0.32 (0.15-0.69)*	0.93 (0.71-1.23)	0.01*
Wave 2.2	1.49 (1.04-2.13)*	1.45 (1.21-1.75)*	0.8
Wave 3	1.44 (0.71-2.91)	1.47 (1.03-2.09)*	0.9

Note that these analyses exclude non-hospitalized patients with minor stroke. Adjusted odds-ratios are from logistic regressions adjusted for age, sex, pre-stroke continuing care needs, and comorbidities.

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