AGE-DEPENDENCE OF HOSPITALIZATION AND FATALITY FOR DIFFERENT SARS-COV-2 VARIANTS OF CONCERN IN ONTARIO, CANADA

AGE-DEPENDENCE OF HOSPITALIZATION AND FATALITY FOR DIFFERENT SARS-COV-2 VARIANTS OF CONCERN IN ONTARIO, CANADA

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Abstract

Age plays a crucial role in the severity of COVID-19 infections. This study aims to compare the severe effects of the dominant variants of concern in Ontario, Canada, and examine how the relationship between age and serious outcomes evolved throughout the pandemic. We analyzed 1,526,024 incidence records of SARS-CoV-2, collected by Public Health Ontario from January 23, 2020, to December 6, 2022, to construct age distributions for known infections (KIs), hospitalizations, and fatalities. By examining hospitalization and fatality probabilities across different age groups during the periods when the Ancestral, Alpha, Delta, and Omicron variants were dominant, we found that older age groups consistently faced higher risks. The Alpha and Delta periods exhibited the highest probabilities of hospitalization and fatality among older individuals, while the Omicron epoch showed the lowest. The roll-out of vaccines and the implementation of varying restrictions during different waves of the pandemic likely influenced these outcomes, highlighting the relationship between age, variant transmissibility, and public health measures.

Résumé

L'âge joue un rôle essentiel dans l'évaluation de la gravité des infections par COVID-19. Cette analyse a pour but de comparer les effets graves des variantes dominantes préoccupantes en Ontario, Canada, et d'examiner comment la relation entre l'âge et les conséquences graves a évolué tout au long de la pandémie. Nous avons analysé 1 526 024 dossiers d'incidence du SARS-CoV-2, recueillis par Santé publique Ontario entre le 23 janvier 2020 et le 6 décembre 2022, afin de construire des distributions d'âge pour les infections connues, les hospitalisations et les fatalités. En examinant les probabilités d'hospitalisation et de décès dans différents groupes d'âge au cours des périodes où les variantes Alpha, Delta et Omicron étaient dominantes, nous avons constaté que les groupes d'âge plus élevés étaient constamment confrontés à des risques plus élevés. Les périodes Alpha et Delta présentaient les probabilités les plus élevées d'hospitalisation et de décès chez les personnes âgées, tandis que l'époque Omicron présentait les probabilités les plus faibles. Le déploiement des vaccins et la mise en œuvre de restrictions variables au cours des différentes vagues de la pandémie ont probablement influencé ces résultats, mettant en évidence la relation entre l'âge, la transmissibilité de la variante et les mesures de santé publique.

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Notation and Abbreviations

COVID-19	Coronavirus Disease 2019
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus 2
LTC	Long-term Care
KI	Known Infection
GAM	Generalized Additive Model
GCV	Generalized-Cross Validation
ICU	Intensive Care Unit

Chapter 1

Introduction

Coronavirus Disease 2019 (COVID-19) is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), a virus that was first identified in Wuhan, China, in late 2019 [48]. The first cases of the virus appeared in Ontario, Canada, in January, 2020, brought by individuals returning to Canada from international travels [20]. As a result, the virus began to spread throughout the province, and by mid-March, there were over 100 active cases [14].

Over the course of the pandemic, the provincial government enacted various restrictions to mitigate disease spread (Table B.1). Figure 1.1 depicts known infections (KIs), i.e., infections confirmed by a positive test, over time, with more detailed information on when restrictions were implemented or relaxed in the province. On March 17 of 2020, six days after the World Health Organization (WHO) declared the epidemic to be a pandemic, the province of Ontario declared a state of emergency [21]. This resulted in closures of non-essential businesses, schools, and public spaces. The provincial government also introduced a series of measures intended to prevent the spread of the virus, such as recommending self-isolation to those experiencing

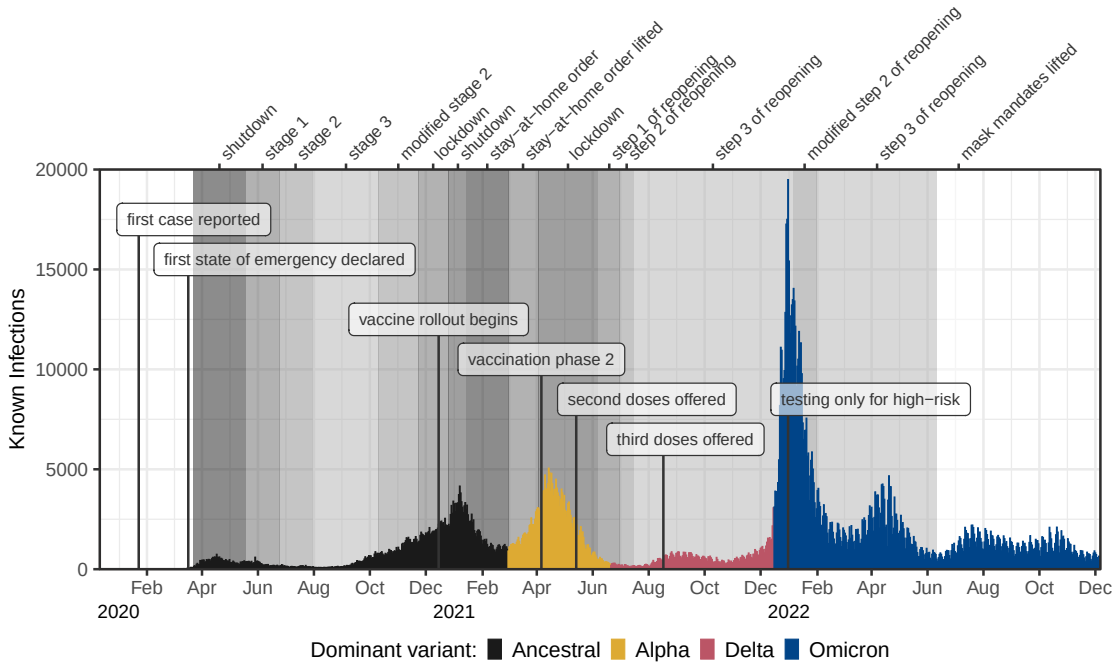

Figure 1.1: Known infections (KIs) in Ontario over time, coloured by time period when each variant was dominant. Shaded regions roughly represent different stages of lockdown and reopening in Ontario (exact dates varied by public health units across Ontario), where darker shades correspond to the tightening of restrictions. Vertical lines mark specific dates important to the start of the pandemic, vaccine roll-out, and testing eligibility in Ontario. See Table B.1 for details on measures implemented. [18, 19, 21–25, 27–42]

symptoms or those returning from travel abroad. Most people were required to work from their homes, children were schooled online, and all social activities were reduced to close family circles or became virtual [21]. In May 2020, test eligibility expanded from only symptomatic individuals (specifically, only health care workers, international travellers, individuals in remote communities, and hospitalized patients) to both symptomatic and asymptomatic individuals [26]. As the number of new active cases per day decreased in May 2020, the province reopened in stages in the summer of 2020 [18, 24, 25]. However, a new rise in cases in September 2020 prompted

stricter restrictions to be put in place again, and a province-wide shutdown with a strict stay-at-home-order was enacted on December 21, 2020 [19, 27].

COVID-19 case numbers in Ontario continued to rise until the beginning of 2021. Ontario implemented policies to curb the rise of COVID-19 cases in January 2021, such as a province-wide shutdown and a stay-at-home-order, followed by another lockdown after the week-long March break [31, 39]. Additionally, vaccine roll-out in Ontario began in December 2020, prioritizing the vaccination of frontline workers (such as healthcare workers, grocery store employees, and public safety personnel), residents of congregate living settings, adults in remote communities, and individuals with high-risk chronic conditions [22]. Following the emergence of the Alpha variant, eligibility to book vaccination appointments opened to high-risk individuals and those residing in COVID-19 hot-spots in March 2021 [35]. This variant's spread in Ontario resulted in a spike in KIs and prompted another province-wide lockdown in April, including moving schools to an online learning format [32]. By the time schools opened (in a hybrid format) in September 2021, 90% of individuals over 70 were fully vaccinated, and 80% of 12–18-year-olds had at least one dose of a vaccine [44]. However, children under 12 were not eligible for vaccination until November 2021 [30]. We note that the definition of being fully vaccinated evolved over time; at this stage, it was defined as having received two doses of a Health Canada-approved vaccine. Counts of KIs remained comparatively low during the time period when the Delta variant was dominant in Ontario (June–December, 2021). The emergence of the Omicron variant, however, caused an unprecedented spike in KIs compared to the other epochs. The province did not lock down when Omicron was spreading, and instead moved to a Modified Stage 2 of reopening in January 2022, which limited

capacity in public spaces, moved schools to remote learning, and closed recreation spaces such as museums and fitness facilities [23]. On December 31, 2021, testing eligibility changed significantly to only allow high-risk individuals (workers and residents in high risk settings and vulnerable populations) who were symptomatic or with severe risk of illness [36]. This may have contributed to the sharp decrease in KIs seen through January 2022. As vaccination rates in Ontario increased, with more people receiving at least two doses, and the Omicron variant proved to be less severe, the province maintained eased restrictions throughout 2022, and lifted mask mandates in most public spaces by June [40, 41].

Throughout the COVID-19 pandemic, different variants have posed varying levels of threat due to differences in transmissibility and severity. The Alpha variant, first documented in the United Kingdom, was about 1.5 times more transmissible than the original strain, while the Delta variant was approximately 1.6 times more transmissible than Alpha [2, 4, 7]. Omicron was significantly more contagious, with a transmissibility 3 to 6 times higher than Delta, allowing it to spread rapidly [47]. One study on 2,779 patients in Ohio found that although there was not a substantial difference in hospitalization or fatality rates between Alpha and Delta, individuals infected with Omicron were less likely to experience severe illness or require hospitalization [8]. Another study on patients in the United States found that vaccines were effective in preventing hospitalization across all variants, though three doses were necessary to achieve the same level of protection against Omicron as two doses provided against Alpha and Delta, possibly due to waning of immunity and the biology of the variant itself [11]. For all variants, vaccinated individuals experienced reduced severity of illness in the hospital compared to those who were unvaccinated [11].

Over the course of the pandemic, people with infections or suspected infections sought medical care in hospitals. It became evident there was a strain on the health-care system, including emergency rooms in hospitals and long-term care (LTC) homes [49]. Because of the specific characteristics of these facilities and their patients, the virus spread significantly faster than in other settings [49]. The number of fatalities among elderly patients was also high, especially at the start of the pandemic and when Delta was the dominant variant of concern in Ontario [49].

Age is a key factor in predicting a COVID-19 patient's risk of hospitalization or death; studies on COVID-19 have demonstrated that severity of infection generally increases with age and is associated with comorbidities such as a weakened immune system, diabetes, and asthma – conditions that are more common in older adults [5, 12, 51]. Conversely, younger ages may have lower susceptibility to infection and less severe clinical manifestations of the disease, possibly due to their more robust immune systems [5]. Papst et al. [43] examined the relationship between COVID-19 patient age and serious outcomes as a result of infection for line-list data in Ontario between January, 2020 and February, 2021. Their study found that the majority of hospitalizations occurred among those aged 60–90, while fatalities were most common in those 80+. Additionally, they demonstrated that the probability of survival given hospitalization decreased significantly after age 60. Our study aims to further these findings by exploring how the age-dependence of serious outcomes changed across different periods of COVID-19 variant dominance in Ontario.

Ontario has experienced multiple waves of COVID-19, each posing significant challenges in implementing public health guidelines and providing adequate care to those affected. We investigate the differences in hospitalization and fatality rates between

time periods when different variants of COVID-19 were dominant, and identify the age groups most severely impacted. Additionally, we explore how external factors, such as policy changes, social behaviour, and vaccine availability, influenced the likelihood of hospitalization and mortality among different age groups.

Chapter 2

Methods and Results

2.1 Methods

This study is based on individual-level SARS-CoV-2 infection records from the province of Ontario, Canada. In order to investigate age-dependency of hospitalization and fatality probabilities for COVID-19 in Ontario, we look at age distributions of KIs, hospitalizations, and fatalities and construct a generalized additive model (GAM) to estimate conditional probabilities of these outcomes for specific ages [52].

2.1.1 Data description

We use incidence records of SARS-CoV-2 from Public Health Ontario which contain information on 1,526,024 cases between January 23, 2020, and December 6, 2022. Among these data is information on case report date, age, whether or not patients were hospitalized, ICU admission, and patient outcomes (for example, fatal, recovered, residual effects).

The data are split into four groups based on dates when different variants of SARS-CoV-2 were dominant in Ontario, Canada: i.e., that specific variant would account for more than half of cases during that week according to Public Health Ontario's weekly genomic surveillance summaries [15, 16]. We use the term *epoch* to refer to the different time periods when the Ancestral, Alpha (B.1.1.7), Delta (B.1.617.2), and Omicron (B.1.1.529) strains were dominant in Ontario (Table 2.1). This study focuses on the three dominant variants of SARS-CoV-2 between March, 2021 and December, 2022 and their differences in age-dependence of hospitalization and fatality.

Epoch	**Time period**
Ancestral	January 23, 2020* to February 28, 2021
Alpha	March 1, 2021 to June 20, 2021
Delta	June 21, 2021 to December 15, 2021
Omicron	December 16, 2021 to December 6, 2022*

* These are the first and last dates recorded in the dataset.

Table 2.1: Time periods used to define epochs where the Ancestral, Alpha, Delta, and Omicron variants were dominant in Ontario.

Most, but not all, cases occurring during a particular epoch are caused by the dominant variant. In addition to separating the data by date, unknown age data are discarded (coded as below 0 or over 120), and ages 100 to 119 are aggregated into one level named 100+. Figure A.1 shows counts of KIs, hospitalizations, and fatalities for different age groups, coloured by epoch. The Omicron epoch generally had higher total counts in each category, with the Delta epoch showing the lowest counts. The majority of KIs were recorded during the Omicron epoch, but the reduction in test eligibility to only high-risk populations in December 2021 artificially lowered the number of KIs recorded in those aged 65 and under, as these high-risk populations

generally consist of many older individuals. The most fatalities occurred in the Ancestral epoch, and they are highly concentrated in older adults. These fatalities are notably high considering the number of KIs and hospitalizations during this epoch.

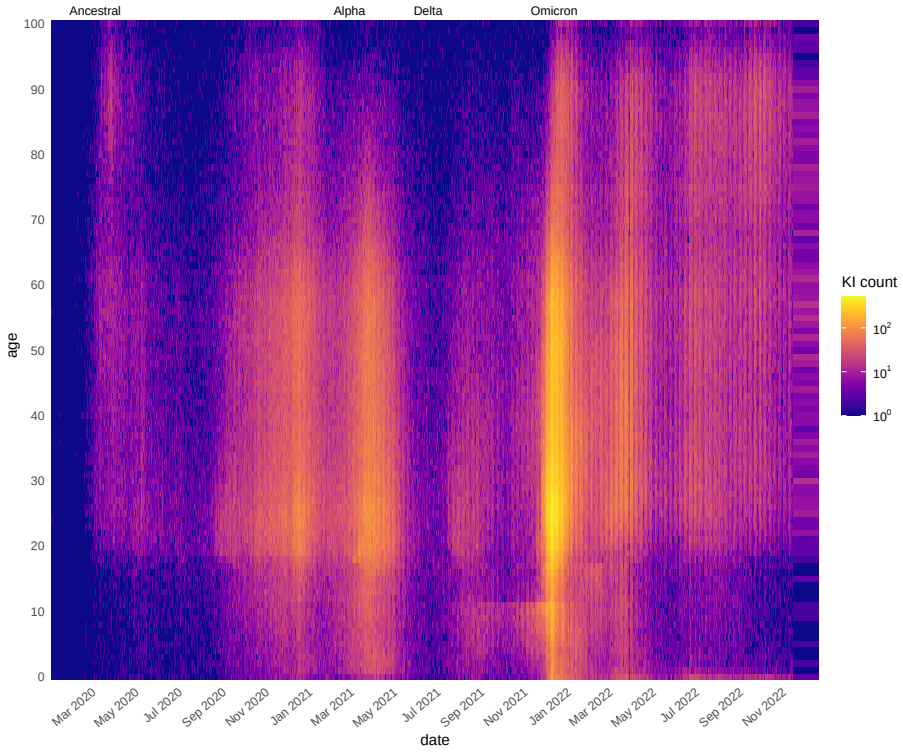

Figure 2.1: Heatmap of counts of known infections (KIs) by age and month from January 23, 2020 to December 6, 2022. KI count is on a log(10) scale, and the colour of the heatmap becomes lighter as KI count increases.

2.1.2 Modelling

Following [43], conditional probabilities of hospitalization given KI, fatality given hospitalization, and fatality given KI are calculated independently for each age. We calculate (for each age) the number of times hospitalization or fatality occurs out of the total number of times KIs or hospitalizations occur, which are equivalent to the

maximum likelihood estimates for a binomial [1]. We then use these proportions to fit a quasibinomial GAM, which accounts for overdispersion [10, 52]. This method allows us to examine patterns in hospitalization and fatality conditional probabilities by age.

GAMs are particularly useful for capturing non-linear relationships between the outcome and the predictors. In our three models, the outcome variables are, respectively: proportion of hospitalizations out of KIs, proportion of fatalities out of hospitalizations, and proportion of fatalities out of KIs, each independently for different ages. The predictor is modelled as a smooth function of age. We use the `mgcv` package in R to fit these GAMs, which uses splines to estimate the smooth functions used in the model [46, 52]. To prevent overfitting, the method used in our code minimizes the Generalized-Cross Validation (GCV) score [52].

2.2 Results

2.2.1 Outcome trends by age

Figure 2.2 shows proportions of KIs, hospitalizations and fatalities for each age out of total KIs, hospitalizations and fatalities for all ages, separated by epoch (for example, 2.3% of recorded KIs during the Alpha epoch were from 26-year-olds). Figure A.2 shows the same plot but with the time series on a log scale. Figure A.3 shows age distributions of KIs, hospitalizations and fatalities normalized by Ontario population sizes for each age group. On the left of figure 2.2, counts for KIs, hospitalizations, and fatalities are shown over time, coloured by epoch. There is a clear, sharp spike in cases during the Omicron epoch, with KIs peaking at $19,500$ cases per day on

December 31st, 2021, after which Ontario reduced testing eligibility to only high-risk individuals, restricting testing to a limited population and cutting off KI records at this peak [36]. Alpha and Delta peaked at 5,063 and 3,078 cases on April 14th, 2021 and December 15th, 2021, respectively. However, it is important to note that this peak in cases during the Delta epoch occurred on the last date that Delta was the dominant variant in Ontario; Omicron had already begun to emerge at this time. It is likely that the rise in KIs during the end of the Delta epoch was the result of the emergence of Omicron in Ontario. Considering this, the first peak of KIs during the Delta epoch can be regarded to be on September 2nd, 2021, with 871 infections. The number of KIs during the Alpha epoch is much higher than during the Delta epoch, yet in figure 2.2, they have similar trends in proportions of KIs, hospitalizations, and fatalities for different ages.

The proportion of KIs during the Alpha epoch peaks in 26-year-olds and steadily declines as age increases, meaning most recorded KIs came from young adults. Almost 40% of all KIs during the Alpha epoch came from individuals between the ages of 15 and 35. The pattern in proportion of KIs for different ages is similar for the Omicron epoch. However, more cases occur in individuals over 70 years of age, and a smaller proportion occurs in young adults; the proportion of KIs in individuals over 70 is three times higher during the Omicron epoch than during the Alpha or Delta epochs. The change in testing criteria at the start of the Omicron epoch is likely to have driven this noticeable difference, as older individuals tend to have an elevated risk of severe illness and therefore would be more likely have been tested at that time.

The trend of higher proportions for older individuals during the Omicron epoch is also true for hospitalizations and fatalities. During the Omicron epoch, 63% of

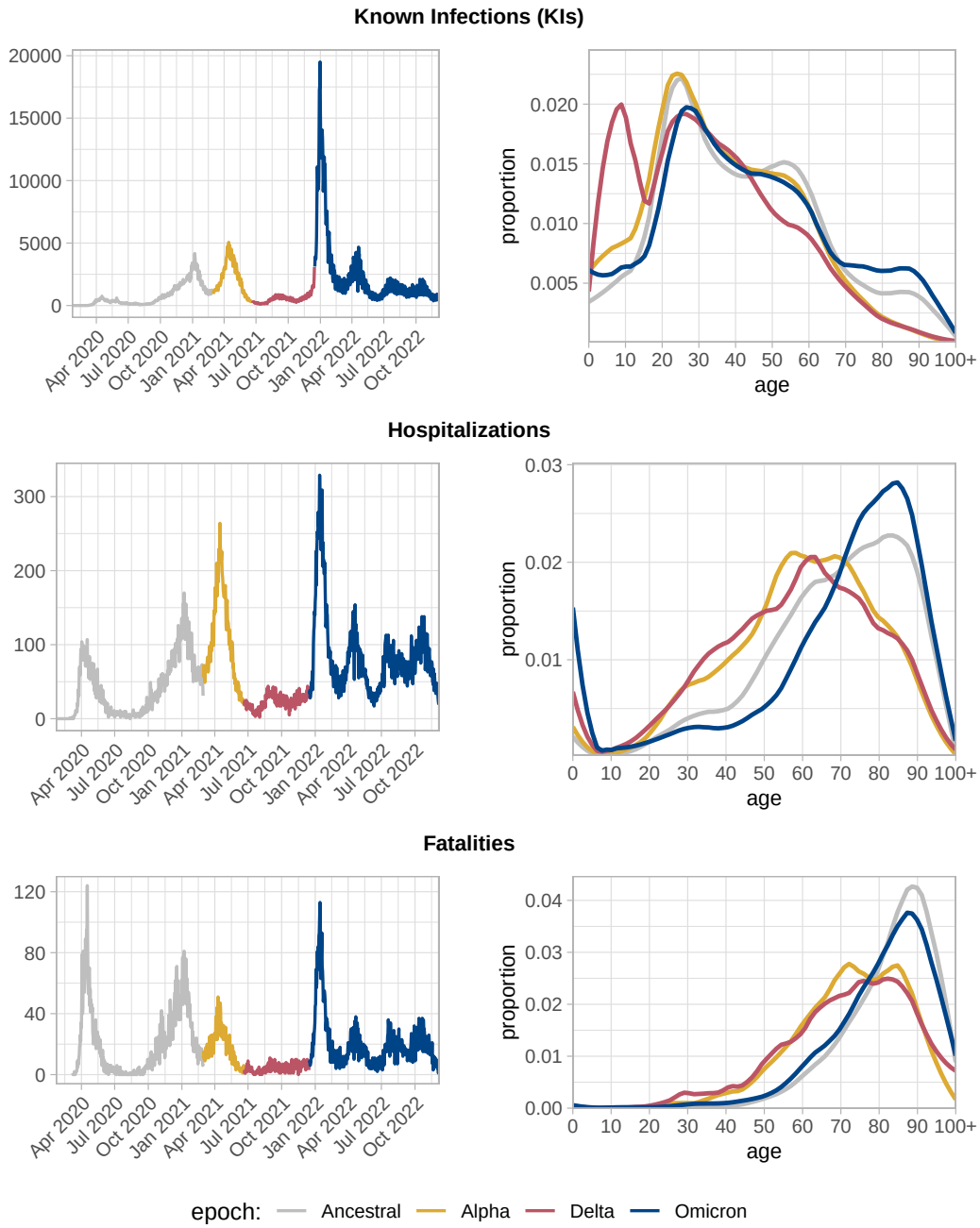

Figure 2.2: On the left are time series of known infections, hospitalizations, and fatalities between January 2020 and December 2022, coloured by epoch. On the right are age distributions for known infections, hospitalizations, and fatalities.

hospitalizations were in individuals above 70 years of age, compared to 34% and 33% during the Alpha and Delta epochs, respectively. Similarly, 81% of fatalities during the Omicron epoch occurred in the 70 and up age group, compared to 60% and 62% during the Alpha and Delta epochs, respectively. The Ancestral epoch also experienced disproportionately high numbers of fatalities in this age group.

Unlike during the Ancestral, Alpha and Omicron epochs, a high proportion of individuals between the ages of 0 and 15 had KIs during the Delta epoch (23%) (Figure 2.2). The proportion of KIs during the Delta epoch spikes in 11-year-olds at 2.5%, but decreases to 1.0% for 14-year-olds before increasing again and following a similar trend to Alpha and Omicron. In general, known infections versus hospitalizations and fatalities display opposite trends in that more KIs occur in lower age groups. KI counts peak in young adults and steadily decrease, whereas proportion of hospitalizations and fatalities increase towards older ages. However, there is also a decrease in hospitalizations from infants and children, with proportion of infants (age 0) hospitalized during the Omicron epoch being nearly equal to the proportion of 73-year-olds hospitalized (2.4%).

Figure 2.1 displays a heat map of KI counts by age and date. The lighter regions represent more recorded KIs on that date for that age group. The different waves of COVID-19 that appeared in Ontario are clearly visible in this representation. A rise in cases in March 2021 (Alpha epoch) shows a relatively even spread over all ages, but is mostly concentrated between 20 and 60-year-olds. There were generally fewer KIs during the Delta epoch and they were mostly concentrated in individuals under 60, with a high concentration in youths under 20. The spike in Omicron KIs in December 2021 is prominent, and there were higher concentrations in older age groups for this

epoch than previous ones, consistent with what was observed in the age distribution in Figure 2.2.

2.2.2 Probabilities of hospitalization and fatality by age

A GAM was fit to the data to estimate probabilities of various outcomes: hospitalization given a known infection (KI), fatality given hospitalization, and fatality given a KI (which is the product of the former two). Figure A.4 shows these probabilities over the entire dataset, and we observe a good fit to the data for the probability of hospitalization given a KI and probability of fatality given hospitalization. Fatality probability given a KI is underestimated for ages 60–90, and overestimated for ages 90+. To improve the GAM fit, we modelled these probabilities separately by epoch.

Figure 2.3 distinguishes these probabilities by epoch. There are notable differences in the trends seen for each variant. In general, there is an increase in probability of hospitalization and fatality as age increases. Alpha and Delta see very few hospitalizations and fatalities in general, and zero for some ages; younger ages have especially low counts of fatalities (less than 10 for most ages under 20, see figure A.1). Infants are generally more likely to be hospitalized than children, and are even more likely to be hospitalized if they were infected during the Omicron epoch than during the other epochs. In those that had known infections during the Omicron epoch, an infant had approximately the same probability of being hospitalized as a 70-year-old.

The probability of hospitalization given KI is generally very low (almost zero) for all epochs, until about the age of 70 (Figure 2.3). KIs in the Alpha epoch experience the highest probability of hospitalization for older age groups, and peaks for 90-year-olds, who have a 46% chance of being hospitalized given they had a known infection,

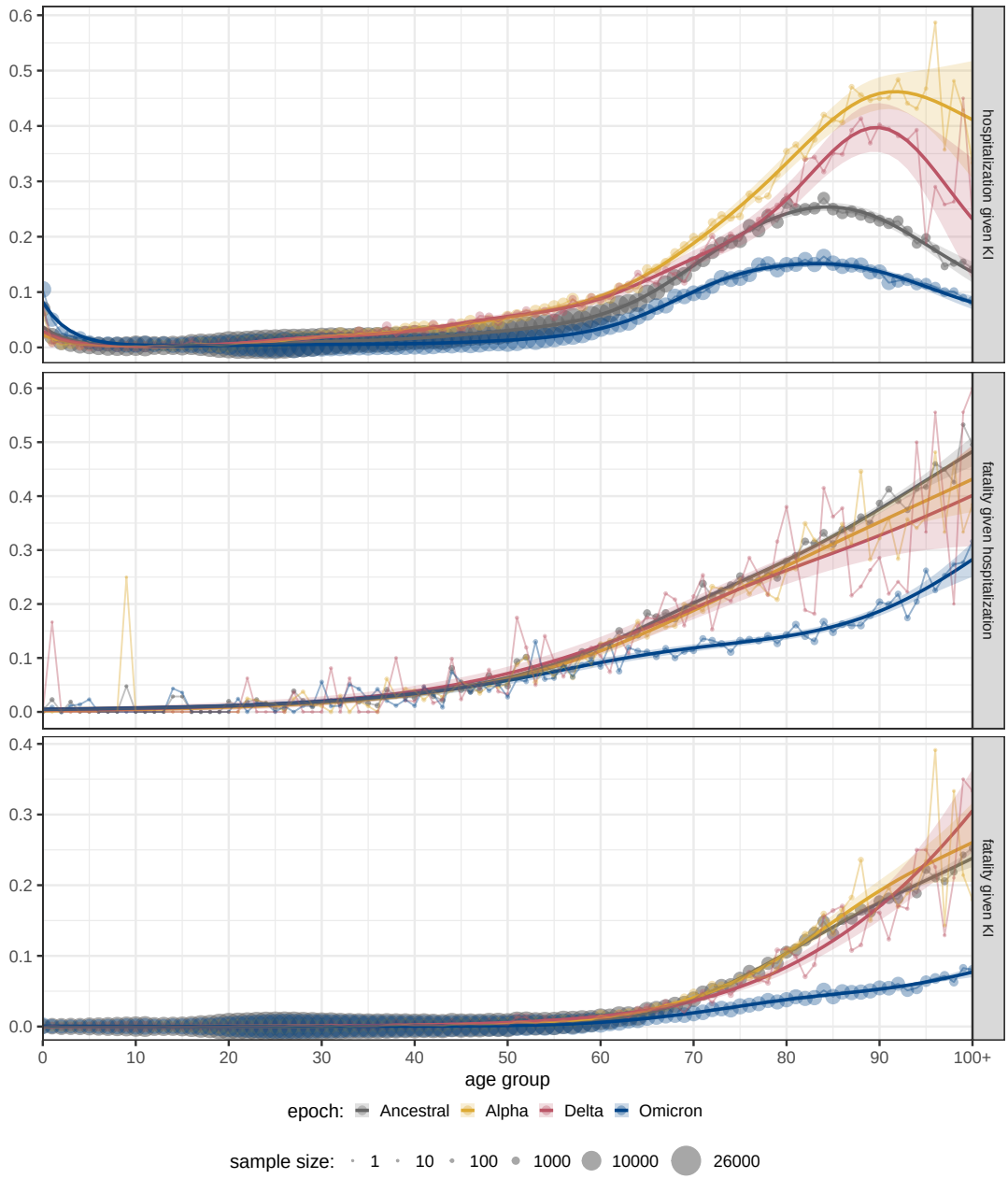

Figure 2.3: Probabilities of hospitalization given known infection (KI), fatality given hospitalization, and fatality given known infection across different epochs. Each color represents a distinct epoch. The thickest line represents the Generalized Additive Model (GAM) fit, with shaded ribbons indicating the 95% confidence intervals. Points depict the observed probabilities used for model fitting, with their size proportional to the sample size. The thinnest lines connect these data points.

compared to 40% for Delta. The probability of hospitalization given KI during the Ancestral epoch is generally lower than during the Alpha and Delta epochs, peaking at 27% for an 84-year-old. It is even lower for the Omicron epoch and does not go above 15%, which is the probability of hospitalization for an 83-year-old. For a 90-year-old infected during the Omicron epoch, the probability of hospitalization given KI is 15%, which is around 30 percentage points lower than if they were infected during the Alpha or Delta epochs. This probability begins to increase for young adults for Alpha and Delta, and for older adults for Omicron (Figure 2.3). In fact, an 83-year-old infected during the Omicron epoch has the same probability of being hospitalized as a 67-year-old or 63-year-old during the Alpha or Delta epoch, respectively. It is evident that individuals whose infections were recorded during the Omicron epoch were generally unlikely to experience severe consequences such as hospitalization or fatality. Overall, the Ancestral, Alpha and Delta epoch infections had much higher probabilities of hospitalization and fatality compared to Omicron, and thus were more likely to result in serious outcomes, especially for older individuals.

Tables B.2, B.3, and B.4 list average probabilities as percentages for different age groups (grouped by 20 years). Probability of hospitalization given KI increases significantly for the 80–100+ age group, and is highest for Alpha and Delta. Notably, the probability of hospitalization given KI for individuals over 80 is just over 40%. Probability of fatality given hospitalization does not vary greatly between the four epochs for ages below 60, but for individuals in the age groups 60–79 or 80–100 infected during either the Ancestral, Alpha or Delta epochs, this probability is about 10 percentage points higher than if they were infected during the Omicron epoch. Similarly, probability of fatality given a KI is about 13 percentage points higher for

individuals above the age of 80 infected during the Ancestral, Alpha or Delta epochs than those infected during the Omicron epoch. These results show that those infected during the first two years of the pandemic were most likely to have severe outcomes, but it is important to consider other factors, such as testing eligibility, vaccine roll-out, and changes in social behaviour that may have affected the trends seen in this data. This will be considered further in the discussion.

With respect to the fit of the GAM, the large discrepancy in KI counts for each age group may have had an effect on the quality of the fit (Figure A.1). There were significantly more records of Omicron and Ancestral KIs, and thus much less noise that affects the fit of the model, especially with older age groups (sample size represented by circle size in Figure 2.3). Alpha and Delta epochs both saw significantly fewer KIs, hospitalizations and fatalities reported, and probabilities are more erratic when there are small sample sizes, such as in ages 85 and up. As seen in Figure 2.3, the confidence intervals are wider for older age groups for the Alpha and Delta epochs. In comparison to the Ancestral and Omicron epochs, which had consistently high sample sizes, especially for hospitalizations and fatalities given KI, confidence intervals are narrow. Moreover, looking closely at the probability curves in Figure 2.3, the panel for fatality given KI (the product of the top two panels), we observe a crossing in the Alpha and Delta curves around the 95-year mark, which does not occur in the other panels (see Figure A.5 for a more detailed view). This unexpected crossover is possibly a result of the noise discussed above.

Chapter 3

Discussion

Many waves of infections occurred during the COVID-19 pandemic in Ontario, each one with different characteristics that presented new challenges in reducing the spread and the severity of the disease. In particular, we investigated four epochs representing time periods when particular strains of the virus were dominant circulating variants in Ontario: Ancestral, Alpha, Delta, and Omicron.

At the beginning of the pandemic, not much was known about COVID-19 and communities struggled to find ways to effectively mitigate disease spread. The initial phase of the pandemic (the Ancestral epoch) had many hospitalizations and fatalities. This phase of the pandemic had a significant effect on individuals above the age of 70, with 86% of fatalities occurring in this age group. Vaccine roll-out began only near the end of this epoch, on December 15, 2020, and began with high-risk individuals (frontline workers and individuals with high risk of having severe outcomes from infection) [22]. COVID-19 vaccines have been shown to significantly reduce serious outcomes and fatalities, so it is not surprising that the epoch when vaccines were not yet available has high fatality and hospitalization counts [11].

In March 2021, Alpha became the dominant variant in Ontario and was more transmissible and severe than the Ancestral. New challenges arose in rapidly and efficiently vaccinating as much of the province as possible. Despite vaccinations becoming available to more age groups during this epoch, the probability of hospitalization given a KI significantly increased for older individuals compared to the Ancestral epoch. The rise in hospitalizations in April 2021 put a strain on the healthcare system in Ontario, but a smaller proportion of individuals over 70 were being hospitalized compared to during the Ancestral epoch.

While Delta is a highly transmissible variant that led to more severe outcomes than the other variants, our results show that the Delta epoch had comparatively fewer total KIs, hospitalizations, and fatalities. For the most part, these outcomes did not disproportionately affect any particular age group (Figure 2.2). In general, the Delta epoch had very similar patterns to Alpha in age distributions of KIs, hospitalizations, and fatalities, but had significantly fewer cases reported. It is surprising that even though the Delta variant became dominant as restrictions loosened (June 2021, see Figure 1.1), case numbers did not rapidly increase as with the other variants. Apart from the characteristics of the variant itself, an explanation for this may be the increase in immunity in the population, especially in older and high-risk individuals, who were prioritized in the roll-out of vaccine eligibility; by August 2021, nearly 90% of individuals over 70 in Ontario were fully vaccinated [44]. Taking this into consideration, the estimated probability of hospitalization given a KI, probability of fatality given hospitalization, and probability of fatality given a KI are higher than what might be expected for vaccinated individuals (Figure 2.3). This is possibly the result of waning vaccine-induced immunity in the population, especially in ages 80

and over who were vaccinated first [3].

The first doses of COVID-19 vaccines became available for individuals aged 12 and older starting on May 23, 2021, with second doses becoming available in Delta hotspot regions beginning on June 26, 2021 [28, 29]. However, by the time schools had reopened in-person in September 2021, young children (under 12) had not yet been eligible for vaccination. Although there was a requirement for publicly-funded school board employees to be either immunized against COVID-19 or to perform daily rapid antigen tests, classrooms are areas where children have high contact with each other, with resources used in teaching, and secondary contact with other students' close contacts [17]. Earlier immunization of young children possibly could have prevented these high case numbers, as 80% of students attending middle or high school (ages 12 to 18) had at least one dose of a vaccine and had a lower proportion of KIs in comparison [44]. These KI counts are also likely to be underreported for this age category, as children mostly had aymptomatic cases or mild symptoms, which are often not tested or recorded [13]. Though the likelihoods of hospitalization and fatality were very low for these age groups (Figure 2.3), reducing the spread of the virus from children to others who are of higher risk of severe outcomes is also crucial [6].

Although the province did not implement a full lockdown, schools moved to online learning for two weeks in January, 2022 following the winter break, then resumed in-person [42]. The province was in the most lenient stage of its reopening plan by the end of January [41]. The sharp decrease in daily KI counts over the month of January is likely not the result of this short-term change in restrictions, but of change in testing eligibility to only high-risk individuals, who do not make up the majority

of the population.

By March 2022, 80% of Ontarians were fully vaccinated (i.e., had two doses of a vaccine) [45]. Despite high vaccination numbers in the population, the emergence of the highly transmissible Omicron variant in December, 2021 led to a huge increase in daily KIs, hospitalizations, and fatalities. Vaccinations and booster doses did help prevent severe illness in those infected, but the Omicron variant disproportionately affected older individuals. We see this result in Figure 2.3, where probability of hospitalization and fatality are considerably lower for those infected during the Omicron epoch compared to the other epochs. Hospitalizations and fatalities occurred disproportionately highly in individuals over 70 compared to other ages (Figure 2.2). As mentioned earlier, these age groups have a higher risk of severe outcomes, and so were prioritized during vaccine roll-out, but it may mean that vaccine-induced immunity waned earlier for these age groups as well if they did not receive a booster dose early enough [3]. Although these probabilities generally increase for individuals over 60, the average probability of hospitalization or fatality given KI are very low for these age groups compared to the other epochs (see Tables B.2, B.3, and B.4). We can also consider that individuals who had a higher risk of mortality from COVID-19 may have died earlier in the pandemic, resulting in a population with slightly lower mortality later in the pandemic [9]. It is evident that individuals whose infections were recorded during the Omicron epoch were generally unlikely to experience severe consequences such as hospitalization or fatality. Considering the testing bias towards high-risk individuals partway through this epoch, this conclusion highlights the lower severity of the Omicron variant and shows the importance of vaccinations.

Interestingly, the proportion of infants who were hospitalized during the Omicron

epoch was higher compared to the other epochs. This may be due to the increased transmissibility of the Omicron variant, leading to an overall increase in the number of infections in infants, and the fact that this age group is still too young to receive vaccinations. Though there were more hospitalizations in infants during the Omicron epoch, fatalities were very rare, indicating that this variant was less severe for younger age groups.

Over all epochs, we observe an unexpected decrease in the probability of hospitalization given KI in ages 90+ (Figure 2.3). We must consider that during the pandemic, many KIs occurred in older individuals residing in long-term care homes (LTC homes), particularly during the Ancestral and Alpha epochs (before vaccinations became available). At the start of the pandemic, the province restricted visits to LTC homes to only those who are essential, and continued to place restrictions on visitors (such as masking and negative test requirements) as the different waves of the pandemic persisted. These facilities are populated by older individuals who tend be more susceptible to severe outcomes and have weakened immune systems, and rooms can often have up to four residents. Healthcare workers visit multiple patients, giving more opportunity for COVID-19 to easily spread throughout one facility and cause significant effects. Because of these conditions (and the nature of the virus being more severe for older adults), LTC home residents experienced higher rates of mortality during the COVID-19 pandemic. In fact, in January, 2021, 60% of all COVID-19 deaths were accounted for by LTC home residents [49]. Because residents received medical care in LTC homes and were not recorded as hospitalizations [49], there is a downward bias in the probability of hospitalization given KI. Infections in these residents that were serious enough to need intensive care were often treated

from these facilities instead of hospitals, and the high mortality rate of COVID-19 led to many deaths in these homes [49]. Stall et al. [49] emphasizes the importance of implementing measures to minimize the risk of LTC home staff becoming infected and decrowding LTC homes as general precautions to limit the virus spreading in these facilities.

3.1 Limitations

While observing age-dependency of hospitalization and fatality of COVID-19 provides valuable insights, there are many other comorbidities that can affect probability of severe outcomes which this study did not take into account. More densely populated regions tend to experience faster spread of COVID-19 and thus higher KIs, and the age distribution in these regions may be different from more rural areas. Comorbidities such as compromised immunity and diabetes also affect severity of infection, though these tend to be more common in older adults [4, 51].

Furthermore, there is likely a vast underreporting of COVID-19 infections, meaning there were more infections in the population that were not reported in the data used in this study. Not all infections were reported to public health authorities, and asymptomatic transmission and cases are difficult to detect. Individuals with mild or no symptoms may be less inclined to go out and get a publicly-funded PCR test; they may not have reason to believe they are sick or may not feel the need to get tested unless they need to participate in contact tracing, for example. In the second half of the pandemic, rapid antigen tests became widely available. These tests were available often for free, and were used mainly for obtaining quick results in setting like schools, workplaces, and homes. Rapid test results were usually not recorded and were often

used in contact tracing or by non-vaccinated individuals. The severe underreporting of infections likely has inflated the estimated probabilities of hospitalizations and fatalities given a KI observed in this study.

The probabilities of fatality given hospitalization would not be affected by the underreporting of infections, as tests in hospitals were used as part of infection control protocols. The number of hospitalizations (and fatalities in hospitals) may have been affected by full capacity being reached in hospitals, and severe cases not being able to obtain the care needed.

Additionally, it is possible that the line-list data used in this analysis could have fields that were incorrectly reported or missed. Testing eligibility also changed according to symptoms and risk groups over the course of the pandemic.

Appendix A

Figures

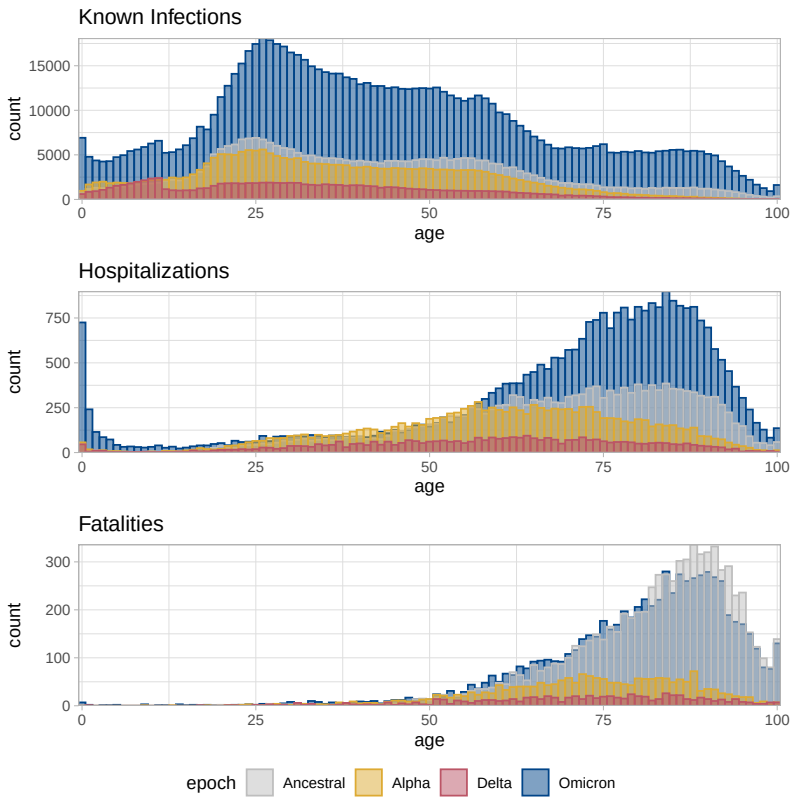

Figure A.1: Histogram of known infections, hospitalizations, and fatalities by age, coloured by epoch.

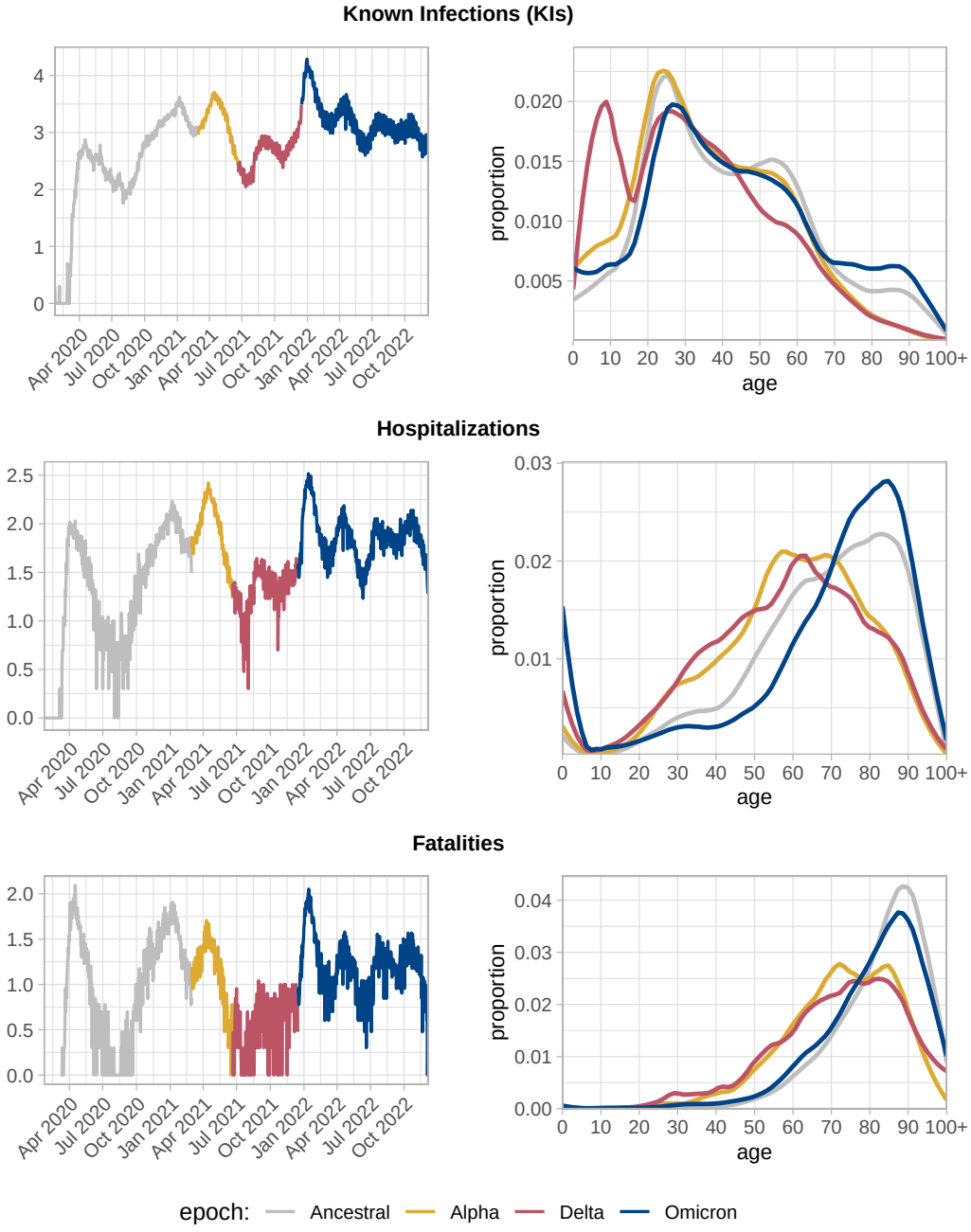

Figure A.2: On the left are time series of known infections, hospitalizations, and fatalities between January 2020 and December 2022, coloured by dominant variant and put on a log(10) scale. On the right are age distributions for known infections, hospitalizations, and fatalities.

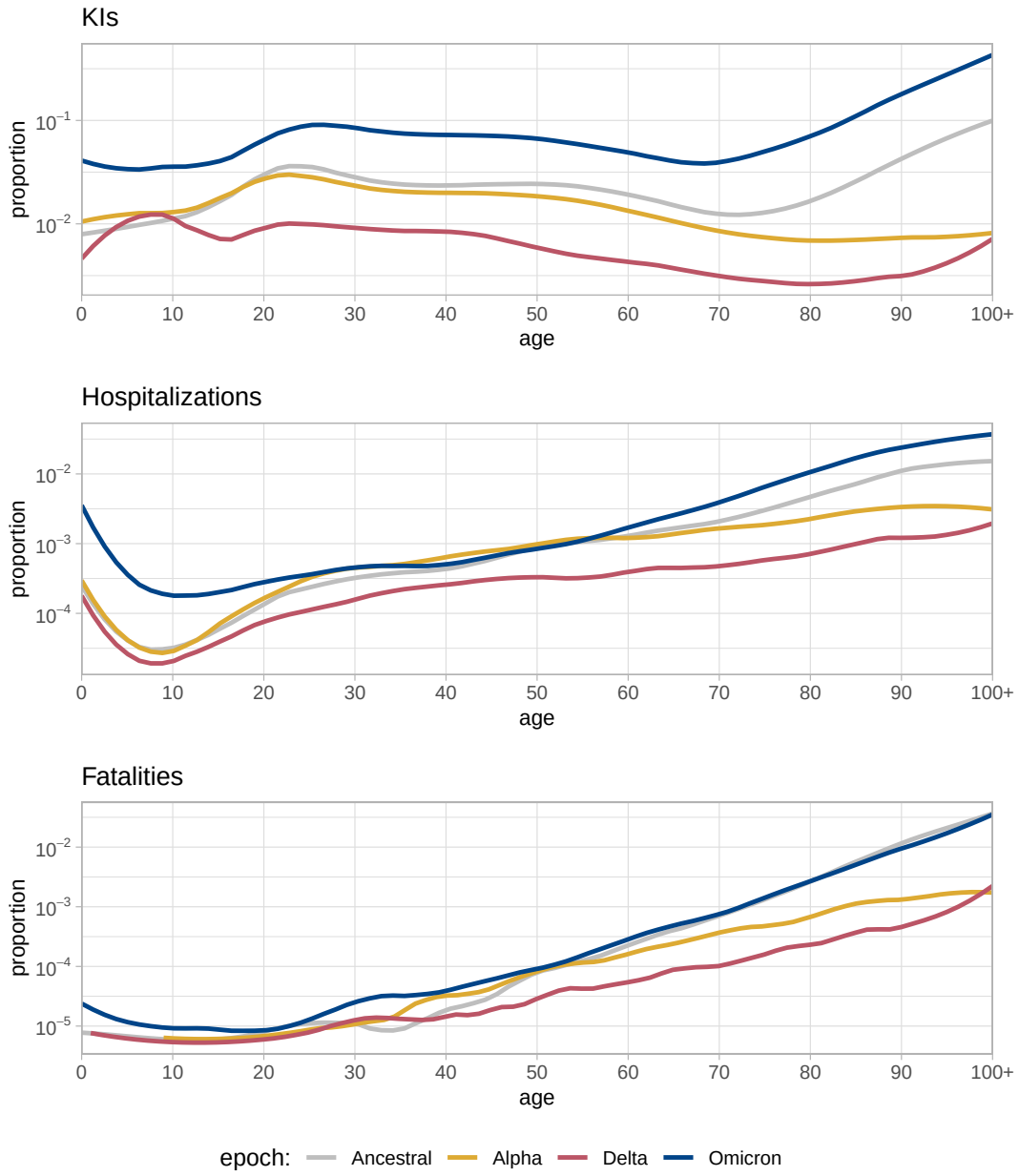

Figure A.3: Age distribution of known infections, hospitalizations and fatalities normalized by age group population in Ontario, coloured by epoch and shown on a log(10) scale. Population data were sourced from the 2021 Canadian Census [50].

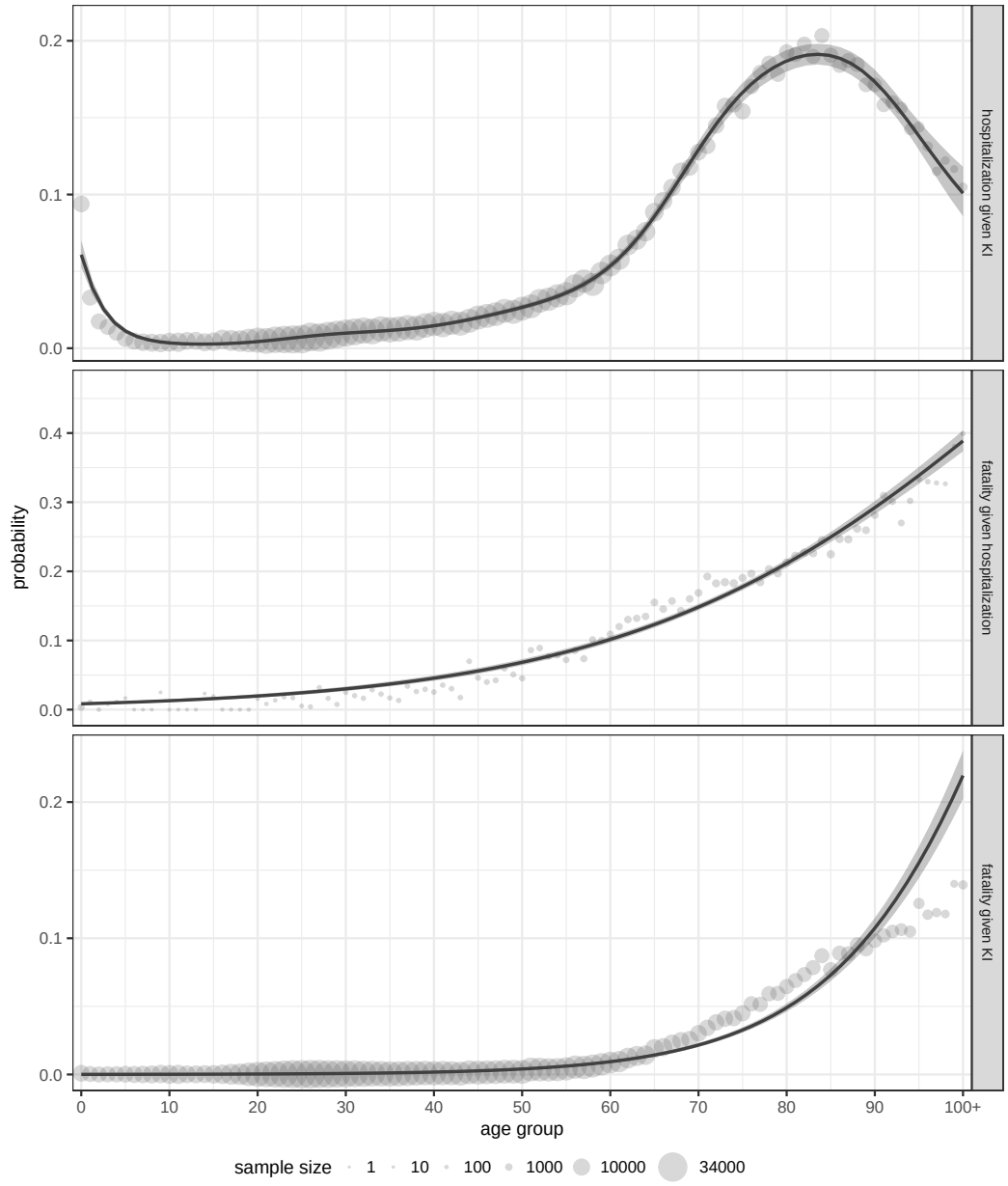

Figure A.4: Probabilities of hospitalization given known infection (KI), fatality given hospitalization, and fatality given known infection for all records between January 2020 and December 2022. The thickest line represents the Generalized Additive Model (GAM) fit, with shaded ribbons indicating the 95% confidence intervals. Points depict the observed probabilities used for model fitting, with their size proportional to the sample size.

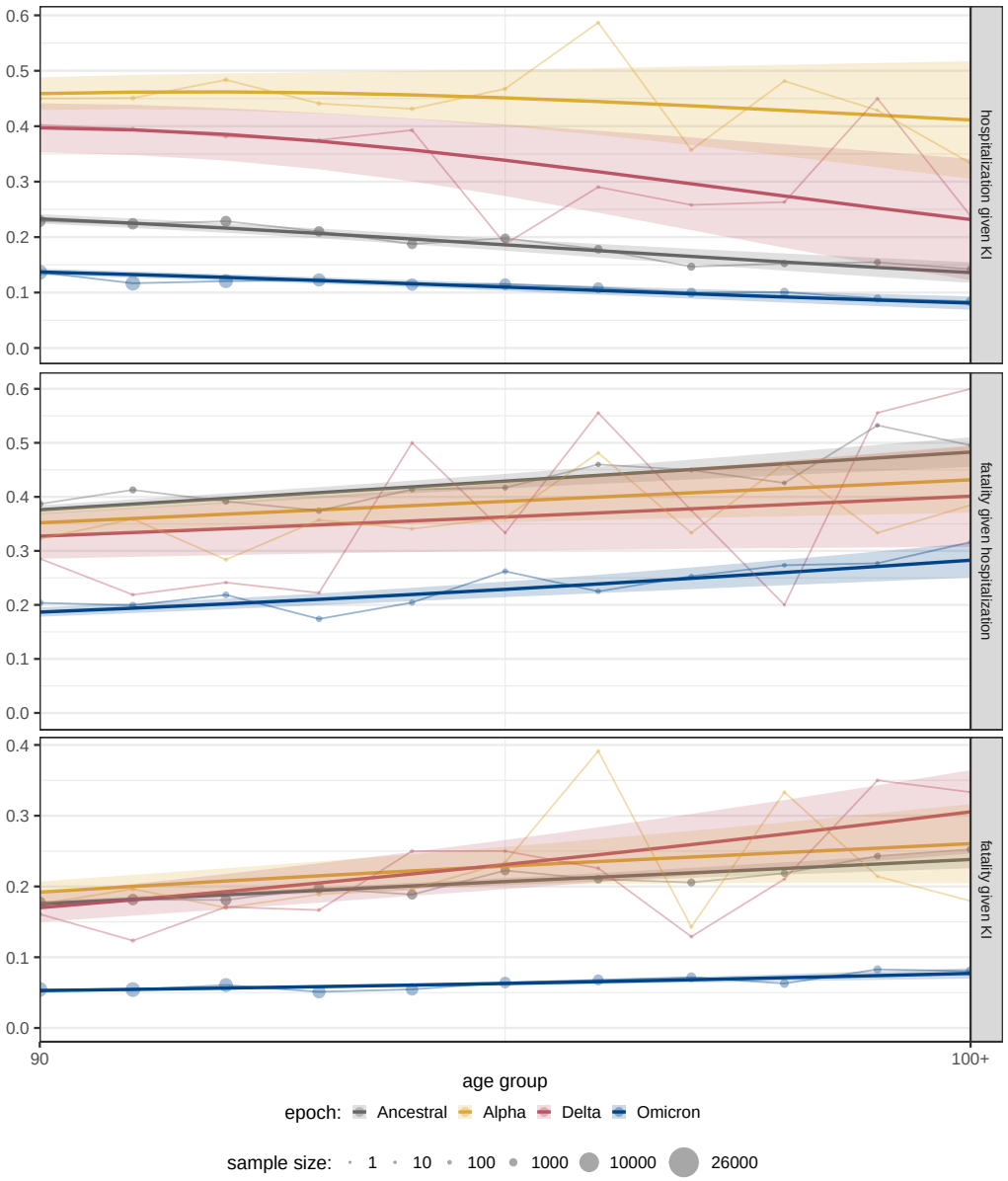

Figure A.5: Probabilities of hospitalization given known infection (KI), fatality given hospitalization, and fatality given known infection across different epochs, zoomed to show ages 90+. Each color represents a distinct epoch. The thickest line represents the Generalized Additive Model (GAM) fit, with shaded ribbons indicating the 95% confidence intervals. Points depict the observed probabilities used for model fitting, with their size proportional to the sample size. The thinnest lines connect these data points.

Appendix B

Tables

Measure	Date enacted	Details
Shutdown	March 17, 2020	Closure of all non-essential businesses, libraries, private schools, child care centres, bars and restaurants, venues. Public events over 50 people prohibited [21].
Stage 1	May 4, 2020	Certain businesses reopen: garden centres and landscaping, essential construction projects, car washes, auto dealerships (by appointment). Social gatherings limited to 5 people [18].
Stage 2	June 22, 2020*	More businesses reopen: outdoor dine-in at restaurants, shopping malls, camping, drive-in venues, weddings and funerals (limit of 10 people). Social gatherings limit increases to 10 people [24].

Measure	Date enacted	Details
Stage 3	July 29, 2020*	Almost all businesses and services able to resume operations. Social gatherings limit increases to 50 people indoors and 100 people outdoors, with physical distancing in place [25].
Modified Stage 2	October 10, 2020*	Closure of indoor fitness centres, theatres, museums, personal care services, indoor food and drink service in restaurants and bars. Social gatherings limit decreases to 10 people indoors and 25 people outdoors, with physical distancing in place [23].
Lockdown	November 20, 2020*	Retail, restaurants, and bars permitted only for curbside pick-up or delivery, personal care services closed, indoor social events prohibited except with members of the same household. Social gatherings permitted outside, limited to 10 people [27].
Shutdown	December 21, 2020	In-person shopping prohibited in retail settings, grocery stores limited to 50% capacity, indoor and outdoor dining prohibited. Schools moved to remote learning [19].

Measure	Date enacted	Details
Stay-at-home order	January 12, 2021	Everyone required to remain at home except to go to grocery stores, pharmacies, access health services, exercise, or for work where work cannot be done remotely. Masks or face coverings are required in indoor spaces. Outdoor gathering limited to 5 people. Enforcement of stay-at-home order and mask requirement by police [31].
Stay-at-home order lifted	March 5, 2021*	Stay-at-home order lifted. Different health units return to different restriction levels [39].
Lockdown	April 1, 2021	Prohibited in-person shopping in retail settings, grocery stores limited to 50% capacity, indoor and outdoor dining prohibited, day camps closed [32].
Step 1 of reopening	May 20, 2021	Begins after 60% of Ontario's adults receive at least one dose of a COVID-19 vaccine. The following is permitted: outdoor gatherings up to 10 people, outdoor dining up to 4 people, essential retail at 15% capacity, outdoor facilities with capacity limits [38].

Measure	Date enacted	Details
Step 2 of reopening	June 30, 2021	Begins if after 21 days in Step 1, 70% of adults have one dose and 20% of adults have two doses of a vaccine. The following is permitted: outdoor gatherings up to 25 people, indoor gatherings up to 5 people, outdoor sports leagues, overnight camps, essential retail at 50% capacity, non-essential retail at 25% capacity, religious services with capacity limits [34].
Step 3 of reopening	July 9, 2021	Begins if after 21 days in Step 2, 70–80% of adults have one dose and 25% of adults have two doses of a vaccine. The following is permitted: indoor and outdoor gatherings, retail with increased capacity, indoor dining, museums, art galleries and cinemas with capacity limits [33].
Modified Step 2	January 3, 2022	Reducing indoor and outdoor social gathering limits, capacity in retail settings at 50%, indoor dining closed, closed entertainment venues and sports facilities, schools temporarily move to remote learning [42].

Measure	**Date enacted**	**Details**
Step 3 of reopening	January 20, 2022	Increased capacity on social gatherings, removing capacity limits in spaces where proof of vaccination is required, increasing capacity limits in certain indoor spaces [41].
Mask mandates lifted	April 22, 2022	Mask mandates lifted in most public settings except public transit, health care settings, long-term care homes, and retirement homes [40].

Table B.1: Dates and details of measures implemented in Ontario during the COVID-19 pandemic. See Figure 1.1.

Age group	Ancestral	Alpha	Delta	Omicron
0–19	0.77	0.59	0.69	1.6
20–39	0.97	1.8	1.8	0.5
40–59	3.2	5.5	5.5	1.6
60–79	15	19	16	9.4
80–100+	22	42	33	13

Table B.2: Average probability (×100) of hospitalization given KI for different age groups.

Age group	Ancestral	Alpha	Delta	Omicron
0–19	0.70	0.48	0.60	0.71
20–39	1.9	1.8	2.1	2.0
40–59	6.7	6.3	7.2	5.9
60–79	20	19	19	12
80–100+	38	35	33	20

Table B.3: Average probability (×100) of fatality given hospitalization for different age groups.

Age group	Ancestral	Alpha	Delta	Omicron
0–19	0.01	0.01	0.01	0.02
20-39	0.04	0.06	0.09	0.03
40–59	0.33	0.49	0.62	0.19
60–79	4.3	4.4	3.9	2.0
80–100+	17	19	18	5.5

Table B.4: Average probability (×100) of fatality given KI for different age groups.

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