Estimating COVID-19 incidence, hospitalization, and death rates by vaccine status

Background and problem

Estimating risk estimates for COVID-19 outcomes requires flexible analytic decisions that can address issues as they arise. The ongoing nature of the COVID-19 pandemic means our analyses must be responsive to changes in disease transmission, vaccination recommendations, and overall public health guidance as well as data sources and quality. This document outlines how Public Health – Seattle & King County (PHSKC) have handled these analytic decisions and how we have modified our analyses over time.

Problem 1: measurement errors due to small numbers of individuals who are not fully vaccinated

As more people become fully vaccinated, the size of the population of not fully vaccinated individuals in some demographic and geographic groups begins to approach zero. In some King County zip codes and subgroups of King County residents, due to imprecision in official King County population estimates, we are observing more vaccinated individuals than the total population. The sources of these biases are complex. There are multiple measurement errors that combined test the limits of PHSKC's available data resources. The issues include:

- Inaccurate 2020 population estimates that are derived from models utilizing 2010 US Census and 2011-2019 American Community Surveys
- Changes to the population distribution of King County, by age, race/ethnicity, and geographic region
- Misclassification of non-King County residents as King County residents in the Washington Immunization Information system and Washington Disease Reporting System
- Other unknown potential data quality issues that occur upstream of these data resources

The result of these measurement errors is likely an overestimation of rates among individuals who are not fully vaccinated, especially in shorter and more recent time periods.

Problem 2: differential disease transmission and vaccine eligibility over time

Due to the ongoing nature of the COVID-19 pandemic, transmission of the SARS-COV-2 virus varies considerably over time, as does the number of individuals who are not fully vaccinated, vaccinated, and boosted. The number of individuals who are not fully

vaccinated, vaccinated, and boosted varies differentially over time by age group, as older age groups have become eligible for vaccinations and booster doses earlier than younger age groups. While these are not a measurement errors, they require statistical methods to minimize biased risk estimates.

Solutions

Solution to problem 1: continuity correction

To resolve measurement error issues, we have added a "continuity correction" to our estimates of the size of the population of not fully vaccinated individuals, to ensure that it would not become unrealistically small. To do this, we assume that we will not reach 100% vaccination and that at least 5% of each age group, race/ethnicity group, and zip code will always be not fully vaccinated. Adding this correction ensures that there is always a reasonable denominator for the not fully vaccinated population that would prevent incidence, hospitalizations, and death rates from growing unrealistically large.

To assess the impact of this correction, we compared setting a different minimum size for the population of not fully vaccinated individuals (at least 0% of the total population, 1%, 2%, or 5%) on our estimates of incidence, hospitalization, and death rates among people who are not fully vaccinated, as well as relative risks comparing individuals who are not fully vaccinated to individuals who are fully vaccinated. The corrections were applied **before** standardizing rates, and thus, the population correction was applied to each population age group.

The table below shows the 7-day age-standardized relative risks (RR) and rates between May and August 2021 among individuals who are not fully vaccinated, compared to individuals who are fully vaccinated.

Scenario	Incidence RR	Incidence Rate	Hospitalization Rate	Death RR	Death Rate
0%	52.1	219.3	60.8	1175.6	9.4
1%	8.7	36.7	6.7	278.9	2.2
2%	6.4	26.9	3.8	142.3	1.1
5%	5.0	20.9	2.0	60.3	0.5

The correction makes a large impact on all of the rates and relative risks. However, even in the most conservative scenario (at least 5% of the population is unvaccinated), the relative risks remain very large. In some areas of King County and some subgroups of King County residents, it is likely that we have exceeded 95% vaccination coverage, and thus, this correction will result in a conservative estimate of rates among individuals who are not fully vaccinated, and an underestimation of the relative risks comparing individuals who are not fully vaccinated to individuals who are fully vaccinated. Despite this underestimation, we continue to see high relative risks which indicates that **these measurement issues alone do not explain the large difference in incidence**, **hospitalization or deaths between individuals who are not fully vaccinated and individuals who are fully vaccinated**.

The figure below shows the impact of 5%, 2%, and 1% continuity corrections on rates of COVID-19 outcomes among fully vaccinated individuals and relative risks of COVID-19 outcomes among not fully vaccinated individuals compared to fully vaccinated individuals.



Solution to problem 2: adjusted Poisson models

To address the variation in transmission of the SARS-COV-2 virus over time and the differential eligibility for vaccination and booster by age group, we calculated our relative risk and incidence rate estimates using Poisson regression models adjusted for age group and time (by month). The inclusion of the age group and time covariates creates flexibility in the models to allow for the variations in age and transmission over time that we see in these data. Trend graphs continue to use age-standardized rates rather than modeled estimates because these rates are averaged over 7- or 14-day periods which do not include sufficient sample sizes for regression analyses.

The table below shows unadjusted, age-adjusted, and age- and time-adjusted relative risk estimates comparing not fully vaccinated individuals to boosted individuals during the Omicron surge (November 2021 to February 2022). Adjusting for age substantially changes estimates because the models take into account the amount of time that each age group has been eligible for COVID-19 vaccination and boosters. Adjusting for time further changes the estimates because the models take into account the variation in disease transmission of the SARS COV-2 virus over time.

Comparison	RR unadjusted	RR adjusted for age	RR adjusted for age and time
Unvaccinated cases	2.2	2.1	2.8
Unvaccinated hospitalizations	3.8	22.8	26.0
Unvaccinated deaths	3.3	32.3	36.6

Limitations

There are some limitations to these data and methodologies that are important to note and should lead to caution in interpretation of estimates. First, these data are for surveillance purposes and reflect COVID-related outcomes among individuals who have received a PCR or antigen COVID-19 test in which the results were reported to PHSKC, and therefore should not be used by themselves to draw conclusions about vaccine effectiveness (more information about vaccine effectiveness can be found here: https://covid.cdc.gov/coviddata-tracker/#vaccine-effectiveness). Second, as with any surveillance data, there are unmeasurable factors that may introduce bias into our estimates. These factors may include: differences in testing behavior between populations, including the effects of the introduction of free and over-the-counter antigen tests from the federal government and WA state in January 2022, as well as differences in actions by group subsequent to positive antigen tests (i.e., differences in reporting, subsequent PCR tests); differences in social behavior (leading to differences in virus exposure); possible variation of natural immunity levels between unvaccinated and vaccinated individuals, due to immunity through previous infection; differences in comorbidities by population, possibly leading to differential outcome severity. This list is not definitive and other unmeasured confounding may also exist.

Future directions and other potential solutions

As our data systems evolve in response to the changing landscape of COVID-19 and COVID-19 vaccinations, new data collection, measurement, and analysis challenges will emerge. We are routinely monitoring the validity of our analytic and informatic methodologies, and exploring ways to improve the accuracy of our reports. We are working with other jurisdictions, the CDC, and institutional partners to explore more complex solutions to these estimation issues. We are exploring options to improve our estimation of the size of the not fully vaccinated population. We are also examining solutions to improve the precision of our population estimates. Finally, because such a large proportion of King County residents are fully vaccinated, we are examining approaches to estimate vaccine effectiveness in a fully vaccinated population.

In addition to improving our estimates of the not fully vaccinated population (i.e., improvements to our denominators), we are also working with the WA Department of Health to improve identification of fully vaccinated people who test positive for COVID (i.e., improvements to our numerators). To do this, we are working on improving the linkage between immunization and case reporting data, improving data collection and outbreak

investigation tools used to identify vaccine breakthroughs, and partnering with other jurisdictions to ensure complete capture of the vaccination status of King County residents.

Conclusion

Due to the high proportion of people vaccinated in King County, there are several challenges to obtaining accurate estimates of the size of the population of people who are not fully vaccinated. Also, due to variations in transmission of the SARS-COV-2 virus over time as well as changing vaccination uptake and eligibility guidelines, statistical adjustment must be made to prevent biased risk estimates. Not accounting for these issues leads to misleading estimates of COVID-19 incidence, hospitalization, and death rates among people who are not fully vaccinated, as well as misleading relative risk estimates. To correct this, PHSKC has added a "continuity correction" to our estimates of the not fully vaccinated population, which prevents the size of this population from dropping below 5%. We also calculate our risk estimates using age- and time-adjusted Poisson models. These corrections result in a more accurate estimate of rates among people who are not fully vaccinated to individuals who are fully vaccinated.