PREPRINT

Continuing COVID-19 Vaccination of Front-Line Workers in BC with the AstraZeneca Vaccine: Benefits in the Face of Increased Risk for Prothrombotic Thrombocytopenia

Amin Adibi[a], Mohammad Mozafarihashjin[b,c]

[a]Respiratory Evaluation Sciences Program, Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, British Columbia; [b]Lunenfeld-Tanenbaum Research Institute, Sinai Health System, Toronto, Ontario; [c]Department of Microbiology, Sinai Health System, Toronto, Ontario

ARTICLE HISTORY
Compiled April 10, 2021

ABSTRACT

Background: On March 29th, 2021, Canada's National Advisory Committee on Immunization (NACI) recommended against using the AstraZeneca COVID-19 vaccine in younger adults pending further review of the risk for Vaccine-Induced Prothrombotic Immune Thrombocytopenia (VIPIT). As a result, the province of British Columbia halted its front-line workers vaccination program which used the AstraZeneca vaccine. The province is expected to receive an additional 246,700 doses of AstraZeneca vaccine through US and COVAX until April 11th, enough to provide the first dose of vaccine to all unvaccinated front-line workers. It is unclear whether the alternative, mRNA vaccines can be immediately made available to front-line workers. We evaluated the harms and benefits of delaying vaccination of front-line workers in BC.

Methods: We reviewed the latest available evidence and used compartmental modelling to *a)* compare the expected number of deaths due to COVID-19 and VIPIT under the scenarios of immediately continuing vaccination of front-line workers with the AstraZeneca vaccine or delaying it in favour of mRNA vaccines, and *b)* compare the mortality risk of immediately receiving the AstraZeneca vaccine and delaying vaccination at an individual risk level for different age groups.

Results: We estimate that if British Columbia continues the front-line worker vaccination program with the AstraZeneca vaccine, we expect to see approximately 27,000 fewer cases of COVID-19, 500 fewer hospitalizations, 80 fewer COVID-related deaths, and 1,400 fewer cases of Long COVID, for an expected number of VIPIT-related deaths of 0.674 [95% CI 0.414-0.997]. In areas of high transmission, projected risk for COVID-related death from April 1st, to July 1st, 2021 was 4.63 per 100,000 in 60-69 years old, 2.49 per 100,000 in 50-59, 2.29 per 100,000 in 40-49 years old, 1.21 per 100,000 in 30-39 years old and 0 per 100,000 for 20-29 years old, compared to 0.26 (95% CI 0.16-0.39) per 100,000 due to VIPIT.

Conclusions: The benefits of immediately continuing immunization of front-line workers with AstraZeneca far outweigh the risk both at a societal level and at an individual risk level for those over 40, and those over 30 in high-risk areas.

KEYWORDS
COVID19; vaccination; front-line workers; blood clots; vaccine-induced prothrombotic immune thrombocytopenia; harm-benefit; BC

CONTACT Amin Adibi. Email: amin.adibi@ubc.ca, Mohammad Mozafarihashjin. Email: mohammad.mozafarihashjin@sinaihealth.ca

1. Background

On March 29th, 2021, Canada's National Advisory Committee on Immunization (NACI) recommended against using the AstraZeneca (AZ) COVID-19 Vaccine for Canadians under the age of 55, due to concerns about Vaccine-Induced Prothrombotic Immune Thrombocytopenia (VIPIT) based on European reports (NACI 2021). On Match 18, 2021, the European Medicines Agency estimated the incidence of VIPIT at approximately 1 per 1,000,000 people vaccinated with the AZ vaccine (EMA 2021). A higher estimated rate of 1 per 100,000 by the Paul-Ehrlich Institut in Germany was published on March 19th (PEI 2021). It was this higher rate reported by the Paul-Ehrlich Institut that led NACI to recommend against using this vaccine in adults under 55 years old (NACI 2021).

On April 1st, the UK Medicines & Healthcare Products Regulatory Agency (MHRA) updated its own previously reported data to report a total of 22 cerebral venous sinus thrombosis (CVST) and 8 other clot-related events from 18.1 million doses of the AZ vaccine (total incidence rate 1 in 600,000) (MHRA 2021a). On April 7th, MHRA concluded a possible link between the AZ vaccine and extremely rare clotting events and updated its data to report 79 UK cases of VIPIT (51 in women and 28 in men, all of them between 18 to 79 years old), including 44 cases of CVST and 35 cases of thrombosis in other major veins (incidence rate 1 in 250,000)(MHRA 2021b).

On the same day, the Pharmacovigilance Risk Assessment Committee (PRAC) of the European Medicines Agency (EMA) concluded that VIPIT should be listed as a very rare side effect of the AZ vaccine. PRAC noted that as of March 22nd, a total of 86 cases of VIPIT (62 cases of CVST and 24 cases of splanchnic vein thrombosis) and 18 fatalities out of about 25 million vaccine doses were reported in EudraVigilance, the EU drug safety database (EMA 2021). As of April 4th, 2021, 222 cases of VIPIT (169 cases of CVST and 53 cases of splanchnic vein thrombosis) had been reported to EudraVigilance out of around 34 million people who had received the AZ vaccine (EMA 2021).

BC had initially slated the AZ vaccine for outbreak control and front-line workers vaccination program. On March 29th and following NACI's recommendation, BC paused using the AZ vaccine for those under 60 and put the front-line workers vaccination program on hold.

Canadian provinces are expected to receive 1.5 million doses of the AZ vaccine from the US and another 316,800 doses from the COVAX program between now and April 11th (Government of Canada 2021). British Columbia expects to receive 246,700 doses from these two AZ deliveries, enough to finish providing the first dose to all remaining front-line workers.

The 300,690 doses of Pfizer-BioNTech and 105,900 doses of Moderna vaccines expected within the same time frame are currently allocated for the priority groups, indigenous population, and the currently ongoing age-based vaccination campaign. The AZ vaccine was initially allocated to front-line workers due to its easier handling and storage requirements. If it is not logistically possible to switch the vaccine allocation for above 55 years old age groups to the AZ vaccine and use either Pfizer-BioNTech or Moderna vaccines for younger front-line workers without delay, one might ask whether the benefits of immediately deploying the AZ vaccine for front-line workers outweigh the rare but serious risk for VIPIT.

Here, we provide a preliminary harm-benefit analysis of immediate vaccination of all front-line workers with the AZ COVID-19 vaccine. We based our analysis on mortality

alone, and explore the risk both from a societal and individual risk perspective.

2. Methods

We assumed that BC allocates all 246,700 doses to front-line workers and that there is enough uptake that BC is able to administer all these doses. We compared immediately prioritizing of front-line workers for the AZ vaccine (Scenario A) and delaying it until after those over 60 are fully vaccinated (Scenario B). For harm-benefit analysis from a societal perspective, we compared expected number of deaths under each vaccination strategy. We estimated the expected number of deaths due to VIPIT as $E(death)_{VIPIT} = d \times P(VIPIT|vaccine) \times P(death|VIPIT, vaccine)$, where d is the number of doses administered, $P(VIPIT|vaccine)$ is the risk of VIPIT after receiving each dose of the AZ vaccine, and $P(death|VIPIT, vaccine)$ is the case fatality for VIPIT. We did a probabilistic analysis where enough data was available.

We assumed that each dose of the vaccine is independently associated with the risk for VIPIT and that the risk of VIPIT is uniform across all age groups. The most recent estimate for these probabilities by EMA, and the estimates NACI used in its calculations are summarized in Table 1.

We estimated benefits of the AZ COVID-19 vaccine using a BC-specific age-structured COVID-19 compartmental model by Mulberry and colleagues that takes into account transmission, age-based contact structure, front-line worker status, and rising R_0 due to variants of concern (Mulberry et al. 2021). The model included susceptible, exposed, infectious and recovered (SEIR) status and was based on the transmission model by Bubar et al (Bubar et al. 2021).

We ran the model from January 2021 to September 2021, which is when the vaccination campaign is expected to conclude. To follow BC vaccination strategy and case counts in the first three months of 2021, we held R_0 at 1.03 from January 1, 2021 for 70 days during which people over 80 years old were eligible for vaccination. Age groups that were offered vaccination were considered to be vaccinated at a steady pace until everyone who is not vaccine-hesitant is vaccinated. Around the end of March, we raised R_0 to either 1.15 or 1.35 to account for variants of concern gaining a foothold in BC and increased the pace of the vaccination program. We validated these assumptions against observed case counts.

We assumed the first dose of the vaccine, regardless of the manufacturer, to be, on average, 80% effective against illness and 75% effective in preventing transmission. We further assume that all British Columbians will be offered a first dose before July 1st, 2021, and a second dose before the end of September 2021. We assumed the second dose to have no effect other than prolonging the immunity acquired after the first dose and posing a risk for VIPIT again. We did not consider the risk for anaphylaxis, as all vaccines seem to have a similar risk in that regard and the risk can be mitigated in the vaccination clinic. Population estimates that were used in the model are summarized in Table 2. COVID-19 age-based case fatality and hospitalization rates were obtained from BC CDC (BCCDC 2021) and Public Health Agency of Canada (Tables: 13-26-0003)(Statistics Canada 2021). For seniors, we used case fatality rates from January 1s, 2021 to April 9th, 2021 to account for the immunity already acquired in long-term care homes. Rates of Long COVID are Mulberry et al's estimations from data in Sudre et al(Sudre et al. 2021). The proportion of essential workers by age was taken from the COVID Speak survey per Mulberry et al (Mulberry et al. 2021). Population of BC in each group was obtained from Statistics Canada (Statistics Canada 2017).

Table 1. Harm-benefit parameters and their distributions

	Estimates		
Variable	EMA Base Value[a]	EMA Probability Distribution	NACI Base Value[b]
$P(VIPIT\|vaccine)$	1 in 153,000	$\beta(222, 3.4 \times 10^7)$	1 in 100,000
$P(death\|VIPIT, vaccine)$	21%	$\beta(18, 68)$	40%
	Assumptions		
	Base Value	Sensitivity	
R_0	1.35	(1.15, 1.5)	
v_e	0.60	(0.60, 0.75, 0.90)	
v_p	0.80	(0.60, 0.75, 0.90)	

R_0 is the basic reproduction number. v_e is the effectiveness of vaccine against transmission. v_p is effectiveness of vaccine against severe disease

[a] EMA based values and β distributions are based on a report of 18 deaths among 68 cases of VIPIT, and 222 cases of VIPIT among 34 million vaccine recipient in Europe and the UK.

[b] NACI base values are based on NACI's rapid response published on March 29th, 2021. A probability distribution could not be calculated as numerators and denominators were not reported.

Table 2. Model parameters

Age Group	Hospitalization	Death	Long COVID	Vaccine Hesitancy	% Front-Line
Under 20	0.0062	0	0.04	NA	0
20-29	0.0106	0	0.04	0.3	17
30-39	0.0246	0.00066	0.08	0.2	20
40-49	0.0340	0.00128	0.15	0.2	17
50-59	0.0583	0.00207	0.25	0.2	15
60-69	0.1175	0.00950	0.25	0.15	16
70-79	0.2450	0.03864	0.25	0.15	10
80+	0.2736	0.16859	0.25	0.15	0

Hospitalization, death, and Long COVID rates are number of people with the outcome divided by the number of concluded cases. Hospitalization and death rates for under 50 age groups are from BCCDC Situation Report Week 12, 2021. Death rates for age groups above 50 are from the preliminary dataset on confirmed cases of COVID-19, Public Health Agency of Canada (Tables: 13-26-0003) from January 1s, 2021 to April 9th, 2021 and accounts for the immunity already acquired in long-term care homes. Rates of Long COVID are Mulberry et al's estimations from data in Sudre et al. The proportion of essential workers by age was taken from the COVID Speak survey per Mulberry et al.

For harm-benefit analysis at an individual risk level, we weighed the probability of VIPIT-related death or $P(death)_{VIPIT} = P(vaccine) \times P(VIPIT|vaccine) \times P(death|VIPIT, vaccine)$, against the average probability of contracting COVID-19 and dying from it in each age groups, or $P(death)_{delayedVaccination} = P(COVID-19) \times P(death|COVID-19)$, where $P(vaccine)$ is the probability of getting the AZ vaccine (assumed to be 1 here), and $P(COVID-19)$ is the average probability of contracting COVID-19 due to delayed vaccination from April 1st, 2021 to July 1st, 2020.

We used results from our compartmental model to project mortality risk from COVID-19 due to delayed vaccination, and conducted sensitivity analyses around model assumptions as outlined in Table 1.

All the analysis was performed using publicly-available data and code. This manuscript is produced by an open-source and reproducible R Markdown script, which is available on Github.

3. Results

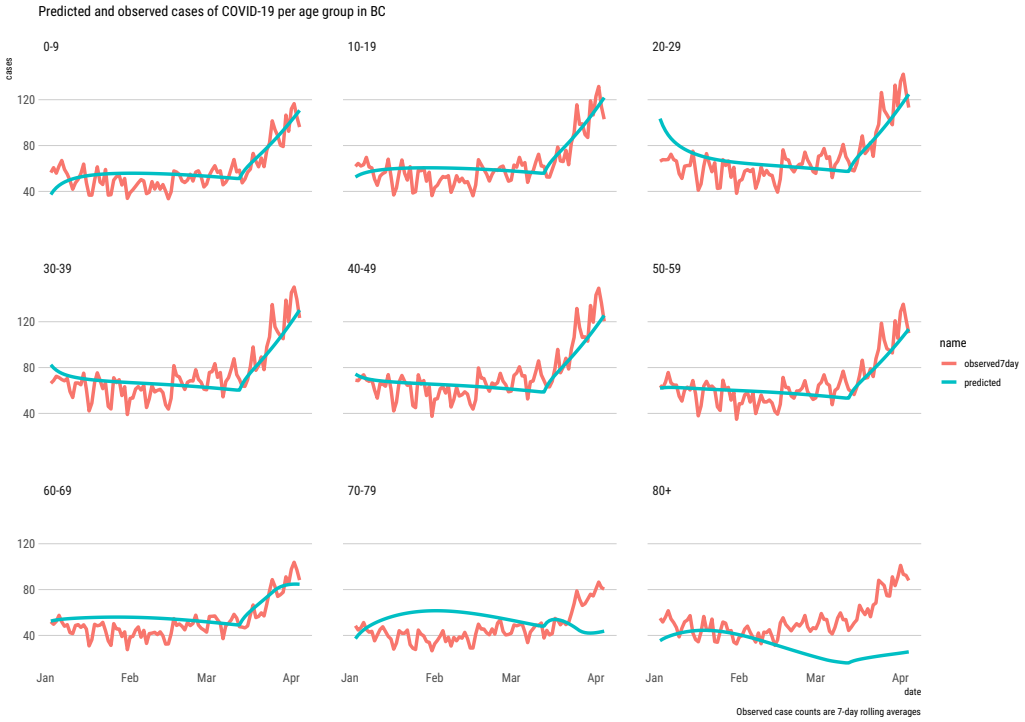

Figure 1. Face validity of model case counts

3.1. *Model validation*

Predicted epidemiological curve and age-stratified case counts showed good agreement with observed counts reported by BC CDC, except for the 80 and above age category where the model underestimated case counts (Figure 1).

3.2. *Harm-benefit from a societal perspective*

EMA evidence as of April 4th, 2021 suggests that if we immediately offer a first dose of the AZ vaccine to all eligible front-line workers in BC, the expected number of VIPIT-related deaths by the end of June 2021 is 0.336 [95% CI 0.206-0.494], which means the probability of observing at least one death in the same period is almost zero. Adding the risk from the second dose, the expected number of VIPIT-related deaths until the end of summer is 0.675 [95% CI 0.41-0.991]. The probability of observing at least one VIPIT-related death till the end of the summer will be 24.8%, and the probability of observing two deaths would be almost zero.

NACI had based its analysis on the older and more pessimistic estimates of a chance of 1 in 100,000 for VIPIT, and a mortality probability of 40%, based on the data that was available in late March. In this worst-case scenario analysis, the expected number of deaths in BC would be 1 after the first dose is completed for all front-line workers and 2 after the second doses are delivered

Figure 2 shows the progression of the vaccination campaign, as well as projections for COVID-19 cases, hospitalizations, and deaths under the two scenarios of immediately prioritizing front-line workers (A) and delaying their vaccination to after all those over

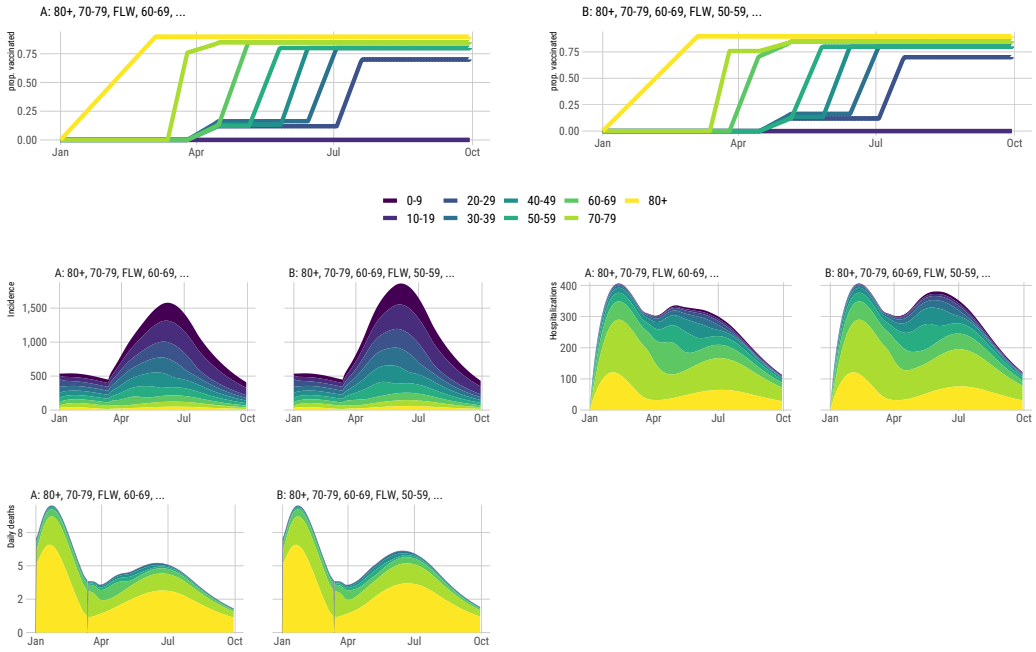

Figure 2. Projection of the progression of the vaccination for different age groups and front-line workers (FLW) as well as COVID-19 cases and outcomes

60 years of age are offered a dose of the vaccine (B).

In our analysis, Scenario A led to 27175 fewer cases of COVID-19, 506 fewer hospitalizations, 87 fewer deaths, and 1462 fewer cases of Long COVID, assuming $R_0 = 1.35$. Figure 3 shows results for a wider range of values for R_0 and the effectiveness of the vaccine against transmission, (v_e). Sensitivity analysis on vaccine effectiveness against severe disease, v_p, lead to similar results and conclusions with a slight variation in number of outcomes. As v_p increased, both the overall number of deaths and the number of deaths prevented decreased.

3.3. *Harm-benefit from an individual risk perspective*

Figure 4 compares the risk of VIPIT-related mortality from 2 doses of the AZ vaccine with the mortality risk from COVID-19 due to delayed vaccination from April 1st to July 1st, 2021. We did the comparison under two scenarios of an R_0 of 1.15 or 1.35, to represent different intensities for the third wave, or alternatively to represent different geographical parts of the province during the third wave. We calculated the mortality risk associated with VIPIT using both the latest and most comprehensive evidence by EMA, and the worst-case scenario using older evidence considered by NACI. Using EMA estimates, we found that under both R_0 scenarios, the mortality risk due to COVID-19 to be much higher than the mortality risk associated with VIPIT in those over 40. Mortality risk from COVID-19 was also higher for 30-39 age group that the mortality risk of VIPIT, although the difference was negligible under R_0 of 1.15 scenario. For the 20-29 age group, the estimated mortality risk of vaccination with the AZ vaccine was higher than that of COVID-19. Using the worst-case VIPIT estimates considered by NACI, mortality risk from COVID-19 was considerably higher than that

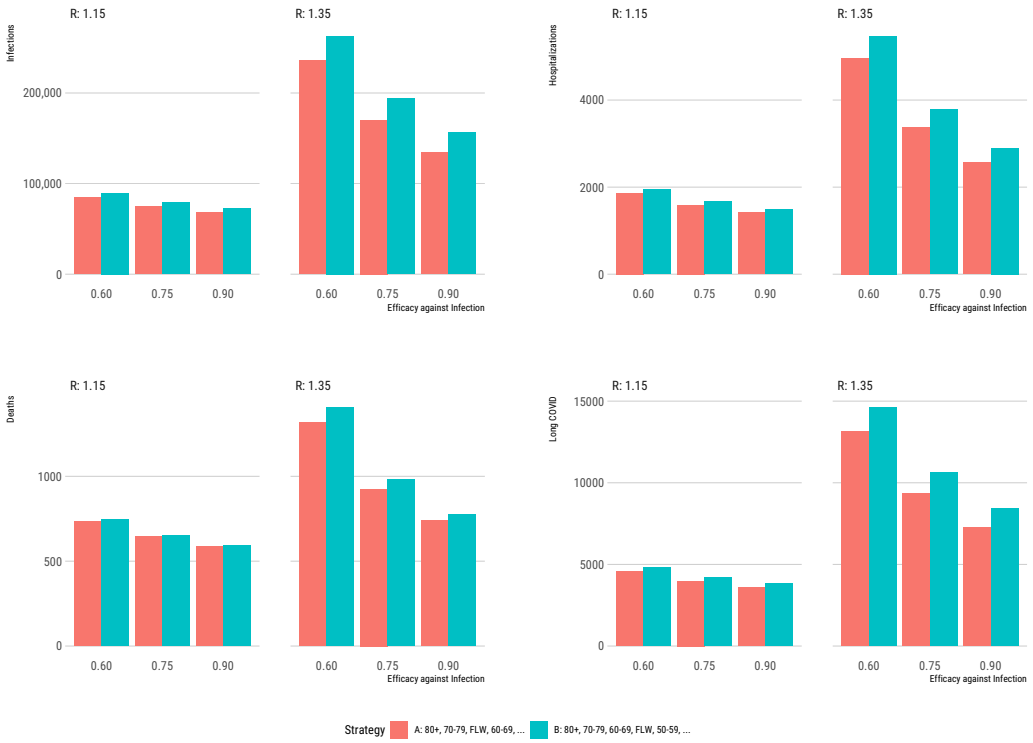

Figure 3. COVID-19 outcomes under different vaccination scenarios for different age groups and front-line workers (FLW)

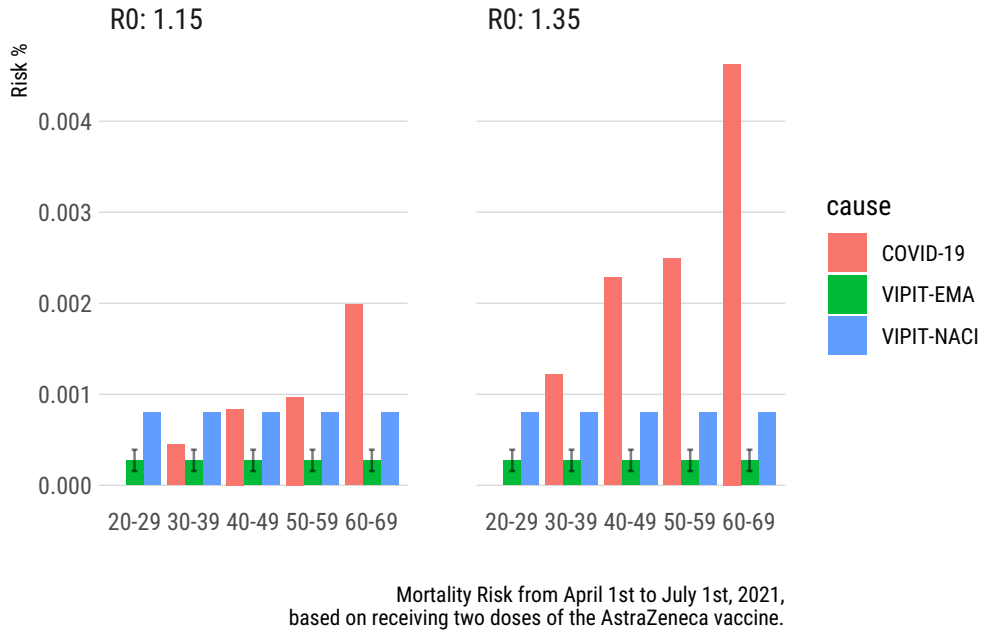

Figure 4. Mortality risk comparison for different age groups based on the estimated risk for VIPIT by the EMA and NACI

of VIPIT for those over 60 in all areas and those over 40 in high-risk areas ($R_0 = 1.35$).

4. Discussion

In its analysis of AZ vaccine published on March 29th, 2021, NACI weighed the risk of adverse events against the age-stratified risk of mortality due to COVID-19, and concluded that the AZ vaccine should not be used in adults under 55 years of age pending an overall risk-assessment. Our analysis confirms that given the evidence available in late March (a risk of 1 in 100,000 for VIPIT and a 40% case fatality) and the lower rates of transmission (i.e. a lower R_0) at that time, suspending the use of AZ vaccine in younger adults would have been advisable. However, as of April 8th, 2021, the evidence from has evolved and the EMA is now reporting a risk of 1 in 153,000 for VIPIT and a 20% case fatality. These latest estimates together with a new wave of the disease have changed the harm-benefit landscape considerably. In addition, the benefits of the AZ vaccine go beyond preventing COVID-related mortality and include protection against more common COVID complications in younger adults including severe disease, hospitalizations, and Long COVID, as well as preventing onward transmission of the virus, as evident in the recent sharp decline of COVID-19 cases in the UK (Our World in Data 2021).

The UK vaccination program started on December 8th with the Pfizer-BioNTech vaccine and was complemented with the AZ vaccine since January 4th. The number of confirmed daily COVID-19 cases in the UK has plummeted from about 60,000 cases a day in early January 2021 when a national lockdown was imposed and about 3% of the population had received at least one vaccine dose, to about 11,000 cases per day on February 22, 2021 when a roadmap to easing the lockdown was announced, to about 6000 cases per day on March 8, 2021 when the first phase of easing public health restrictions was commenced (BBC 2021) and has continuously declined since then to just above 2589 cases as of April 10th, 2021, when 61% of the UK population had received one dose of a COVID-19 vaccine (GOV.uk 2021).

In addition to the death aversion resulting from strict public health measures, based on a recent analysis by Public Health England and the University of Warwick, it has been estimated that as of March 31, 2021, 10,400 deaths have been avoided in the UK solely due to the direct implementation of a nationwide vaccination program (indirect effects were not measured; 87.5% of these averted deaths were in the 80+ years old age group, 11.5% of them in 70-79, and 1% in 60-69 years old age group) (Public Health England 2021b). As about half of all vaccine doses administered in the UK have been AZ vaccines, and based on the estimated AZ vaccine efficacy of about 76% against symptomatic COVID-19 and 64% against any NAAT-positive COVID-19 infection between 22 and 90 days after the first dose (Voysey et al. 2021), and real-world single-dose AZ vaccine effectiveness of about 60% against symptomatic COVID-19 and 80% against COVID-19 hospitalization (Public Health England 2021a), it is suggested that the AZ vaccine is effective in reducing the overall burden of COVID-19.

Potential prevention of onward transmission with the AZ vaccine could be especially critical for front-line workers during the current wave of COVID cases. Of note, two recent studies from Toronto, Ontario have shown that neighbourhoods with the highest proportion of front-line workers had per capita COVID-19 case and death rates that were 2.5-3 folds higher than that of neighbourhoods with the lowest share of front-line workers (Chagla et al. 2021, Rao et al. (2021)).

Based on our analysis, immediately making the AZ vaccine available to front-line

workers is, assuming optimal uptake, net-beneficial by a wide margin from a societal perspective. Our analysis from an individual risk perspective shows that the risk of contracting COVID-19 and dying from it due to delayed vaccination is considerably higher than the risk of dying from VIPIT in those over 40, and also in those over 30 in high-risk areas.

For a public health intervention to be deemed ethically acceptable, being net-beneficial at a societal level is not enough in and of itself. Not all interventions that are net-beneficial at a societal level are net-beneficial for each member of the society, as those who carry the burden of the risk of adverse events may not be the same people who reap the benefits. We also recognize that many intuitively consider mortality due a public health intervention in an otherwise healthy person to be ethically worse than failing to protect someone from mortality due to COVID-19. We believe that our conclusions hold regardless of the position we take with respect to the *doing vs. allowing harm* problem (Woollard and Howard-Snyder 2016), as long as the expected benefit outweighs the harm at a personal level, as seems to be the case for most age groups in our study.

Our analysis was based on the assumption that immediate deployment of alternative mRNA vaccines for front-line workers was not logistically feasible. If feasible, and assuming that the effectiveness of mRNA vaccines are 10-15% higher than the AZ vaccine, offering mRNA vaccines to front-line workers will be more in line with the principle of reciprocity outlined in the BC COVID-19 Ethical Decision-Making Framework (BCCDC 2020), and the more general principle of justice in bioethics (McCormick and Min 2021).

Our findings are corroborated by the the recent recommendation of the UK Joint Committee on Vaccination and Immunisation (JCVI) that the benefits of the AZ vaccine far outweigh the risk in 30 years old or older recipients (JCVI 2021).

5. Limitations

Our analysis from an individual risk perspective was based on average rates of COVID-19 and its related outcomes per age group. However, the true risk within age groups is still heterogeneous and is affected by many factors including but not limited to exposure, medical history, work environment, and socioeconomic status.

Our analysis did not consider social aspects of vaccine roll-out such as the effect of different roll-out strategies on uptake and vaccine hesitancy, as they were beyond our expertise. However, we recognize that each time a recommendation for vaccine safety is reversed, there might be a penalty in public trust which could fuel vaccine hesitancy. Potential for these effects should be weighed carefully by policy makers.

Our analysis is based on currently available estimated rates of 1 in million to 1 in 100,000 for VIPIT and might need correction should higher rates of this complication be reported.

We have not considered potential sex differences in the risk for VIPIT. Although cases identified to date have been predominantly female, it remains unclear whether this was due to more females receiving the AZ vaccine or due to an intrinsic difference in risk.

6. Conclusions

Current evidence suggests that benefits of immediate prioritization of front-line workers for vaccination with the AZ vaccine far outweigh the risk, both at a societal and at a personal level for those over 40 years of age, and those over 30 years of age in high-risk areas. Ultimately, in dynamic situations like this where the evidence is uncertain and evolving, vaccine roll-out decision are judgment calls that need to take a complex network of medical, epidemiological, ethical, logistics, and societal considerations into account.

References

BBC. 2021. "Lockdown: Boris Johnson unveils plan to end England restrictions by 21 June." Accessed 2021-04-04. https://www.bbc.com/news/uk-56158405.

BCCDC. 2020. *COVID-19 Ethical Decision-Making Framework*. Technical Report. BC Ministry of Health. Accessed 2021-04-09. https://www2.gov.bc.ca/assets/gov/health/about-bc-s-health-care-system/office-of-the-provincial-health-officer/covid-19/ethics_framework_for_covid_march_28_2020.pdf.

BCCDC. 2021. *British Columbia (BC) COVID-19 Situation Report. Week 12: March 21–March 27, 2021*. Technical Report. Accessed 2021-04-10. http://www.bccdc.ca/Health-Info-Site/Documents/COVID_sitrep/Week_12_2021_BC_COVID-19_Situation_Report.pdf.

Bubar, Kate M., Kyle Reinholt, Stephen M. Kissler, Marc Lipsitch, Sarah Cobey, Yonatan H. Grad, and Daniel B. Larremore. 2021. "Model-informed COVID-19 vaccine prioritization strategies by age and serostatus." *Science (New York, N.Y.)* 371 (6532): 916–921.

Chagla, Zain, Huiting Ma, Beate Sander, Stefan D. Baral, and Sharmistha Mishra. 2021. "Characterizing the disproportionate burden of SARS-CoV-2 variants of concern among essential workers in the Greater Toronto Area, Canada." *medRxiv* 2021.03.22.21254127. Publisher: Cold Spring Harbor Laboratory Press, Accessed 2021-04-04. https://www.medrxiv.org/content/10.1101/2021.03.22.21254127v1.

EMA. 2021. "AstraZeneca's COVID-19 vaccine: EMA finds possible link to very rare cases of unusual blood clots with low platelets." Apr. Accessed 2021-04-08. https://bit.ly/3s3ikJu.

EMA. 2021. *COVID-19 Vaccine AstraZeneca: benefits still outweigh the risks despite possible link to rare blood clots with low blood platelets*. Technical Report. European Medicines Agency. Accessed 2021-04-02. https://bit.ly/3s0pM8j.

Government of Canada. 2021. *Vaccines for COVID-19: Shipments and deliveries*. Technical Report. Government of Canada. Accessed 2021-04-03. https://www.canada.ca/en/public-health/services/diseases/2019-novel-coronavirus-infection/prevention-risks/covid-19-vaccine-treatment/vaccine-rollout.html#a4e.

GOV.uk. 2021. "Official UK Coronavirus Dashboard." Apr. Accessed 2021-04-10. https://coronavirus.data.gov.uk.

JCVI. 2021. "JCVI statement on use of the AstraZeneca COVID-19 vaccine: 7 April 2021." Apr. Accessed 2021-04-08. https://www.gov.uk/government/publications/use-of-the-astrazeneca-covid-19-vaccine-jcvi-statement/jcvi-statement-on-use-of-the-astrazeneca-covid-19-vaccine-7-april-2021.

McCormick, Thomas R., and D. Min. 2021. "Principles of Bioethics." Apr. Accessed 2021-04-09. https://depts.washington.edu/bhdept/ethics-medicine/bioethics-topics/articles/principles-bioethics.

MHRA. 2021a. *Coronavirus vaccine - weekly summary of Yellow Card reporting*. Technical Report. Medicines & Healthcare Products Regulatory Agency. Accessed 2021-04-03. https://bit.ly/3dOW80z.

MHRA. 2021b. "MHRA issues new advice, concluding a possible link between COVID-19 Vaccine AstraZeneca and extremely rare, unlikely to occur blood clots." Apr. Accessed 2021-04-08. https://bit.ly/39XSDUu.

Mulberry, N., P. Tupper, E. Kirwin, C. McCabe, and C. Colijn. 2021. "Vaccine Rollout Strategies: The Case for Vaccinating Essential Workers Early." *medRxiv* 2021.02.23.21252309. Publisher: Cold Spring Harbor Laboratory Press, Accessed 2021-04-03. https://www.medrxiv.org/content/10.1101/2021.02.23.21252309v1.

NACI. 2021. *NACI rapid response: Recommended use of AstraZeneca COVID-19 vaccine in younger adults*. Technical Report. National Advisory Committee on Immunization (NACI). Accessed 2021-04-03. https://www.canada.ca/en/public-health/services/immunization/national-advisory-committee-on-immunization-naci/rapid-response-recommended-use-astrazeneca-covid-19-vaccine-younger-adults.html.

Our World in Data. 2021. *COVID-19 Data Explorer: Daily new confirmed COVID-19 cases per million people*. Technical Report. University of Oxford. Accessed 2021-04-04. https://ourworldindata.org/explorers/coronavirus-data-explorer?zoomToSelection=true&time=40..latest&pickerSort=asc&pickerMetric=location&Metric=Confirmed+cases&Interval=7-day+rolling+average&Relative+to+Population=true&Align+outbreaks=false&country=~GBR.

PEI. 2021. *COVID-19 Vaccine AstraZeneca - Safety assessment result: The vaccine is safe and effective in the fight against COVID-19*. Technical Report. Paul-Ehrlich-Institut (PEI), Federal Institute for Vaccines and Biomedicine. Accessed 2021-04-02. https://bit.ly/3dJ7OSQ.

Public Health England. 2021a. *1Public Health England vaccine effectiveness report*. Technical Report. Accessed 2021-04-04. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/971017/SP_PH__VE_report_20210317_CC_JLB.pdf.

Public Health England. 2021b. *Impact of COVID-19 vaccines on mortality in England*. Technical Report. Public Health England. Accessed 2021-04-09. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/977249/PHE_COVID-19_vaccine_impact_on_mortality_March.pdf.

Rao, Amrita, Huiting Ma, Gary Moloney, Jeff Kwong, Peter Juni, Beate Sander, Rafal Kustra, Stefan Baral, and Sharmistha Mishra. 2021. *A disproportionate epidemic: COVID-19 cases and deaths among essential workers in Toronto, Canada*.

Statistics Canada. 2017. "Census Profile, 2016 Census - British Columbia [Province] and Canada [Country]." Feb. Last Modified: 2019-06-18, Accessed 2021-04-09. https://www12.statcan.gc.ca/census-recensement/2016/dp-pd/prof/details/page.cfm?Lang=E&Geo1=PR&Code1=59&Geo2=PR&Code2=01&SearchText=Canada&SearchType=Begins&SearchPR=01&B1=All&type=0.

Statistics Canada. 2021. "Preliminary dataset on confirmed cases of COVID-19, Public Health Agency of Canada Tables: 13-26-0003." Apr. Last Modified: 2021-04-09, Accessed 2021-04-10. https://www150.statcan.gc.ca/n1/en/catalogue/13260003.

Sudre, Carole H., Benjamin Murray, Thomas Varsavsky, Mark S. Graham, Rose S. Penfold, Ruth C. Bowyer, Joan Capdevila Pujol, et al. 2021. "Attributes and predictors of long COVID." *Nature Medicine* .

Voysey, Merryn, Sue Ann Costa Clemens, Shabir A. Madhi, Lily Y. Weckx, Pedro M. Folegatti, Parvinder K. Aley, Brian Angus, et al. 2021. "Single-dose administration and the influence of the timing of the booster dose on immunogenicity and efficacy of ChAdOx1 nCoV-19 (AZD1222) vaccine: a pooled analysis of four randomised trials." *The Lancet* 397 (10277): 881–891. Publisher: Elsevier, Accessed 2021-04-04. https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00432-3/abstract.

Woollard, Fiona, and Frances Howard-Snyder. 2016. "Doing vs. Allowing Harm." In *The Stanford Encyclopedia of Philosophy*, edited by Edward N. Zalta, winter 2016 ed. Metaphysics Research Lab, Stanford University. Accessed 2021-04-06. https://plato.stanford.edu/

archives/win2016/entries/doing-allowing/.