

SYNOPSIS

04/08/2021

Review of “Case Fatality Risk of the SARS-CoV-2 Variant of Concern B.1.1.7 in England, 16 November to 5 February.”

Article citation: Grint DJ, Wing K, Williamson E, McDonald HI, Bhaskaran K, Evans D, et al. Case fatality risk of the SARS-CoV-2 variant of concern B.1.1.7 in England, 16 November to 5 February. *Euro Surveill.* 2021;26(11):2100256. Available from: <https://doi.org/10.2807/1560-7917.ES.2021.26.11.2100256>

One-Minute Summary

- In this cohort analysis of individuals with confirmed infection of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in England, the authors compared the risk of all-cause mortality between those infected with the B.1.1.7 variant of concern (VOC) and non-VOC.
- Included in the analyses were:
 - 184,786 persons with spike gene target failure (SGTF) (used as proxy for identification of B.1.1.7) status known (42% of 441,161 confirmed SARS-CoV-2 infections): 93,011 with VOC vs. 91,775 with non-VOC.
 - 867 all-cause deaths before data censoring on February 5, 2021: 419 VOC vs. 448 non-VOC.
- Infection with the VOC vs. non-VOC was found to have higher risk of all-cause mortality:
 - **Adjusted hazard ratio (HR) = 1.67** (95% confidence interval [CI]: 1.34–2.09); $P < 0.0001$.
 - Restricting to those **diagnosed \geq 28 days before data censoring:**
 - **HR (n=112,981) = 1.71** (95% CI: 1.36–2.15; $P < 0.0001$).
 - **Adjusted odds ratio using data with \geq 28 days of follow-up from diagnosis (n=112,979) = 1.73** (95% CI: 1.34–2.23; $P < 0.0001$).
- **Absolute 28-day all-cause mortality risks are consistently higher for VOC cases in all groups (age, sex, comorbidities), albeit relatively low for those <65 years of age. Risks increase with age and the presence of comorbidities and are consistently higher for males:**
 - <65 years of age with:
 - No comorbidities: 0.07% vs. 0.05% (females); 0.14% vs. 0.09% (males).
 - One comorbidity: 0.18% vs. 0.11% (females); 0.35% vs. 0.22% (males).
 - ≥ 2 comorbidities: 0.34% vs. 0.21% (females); 0.64% vs. 0.40% (males).
 - ≥ 65 years of age with:
 - No comorbidities: 3.75% vs. 2.36% (females); 6.87% vs. 4.38% (males).
 - One comorbidity: 8.64% vs. 5.54% (females); 15.1% vs. 9.94% (males).
 - ≥ 2 comorbidities: 14.68% vs. 9.65% (females); 24.34% vs. 16.65% (males).
- **The increase in mortality due to VOC was consistent across each epidemiological week of diagnosis**, suggesting that other confounding factors (e.g., hospitals exceeding capacity) would be unlikely to explain this finding.

Additional Information

- The data cover 40% of England's population registered with a general practitioner and were linked with SARS-CoV-2 testing, vaccination and mortality records.
- SGTF, a proxy for B.1.1.7 identification, was >95% sensitive during the study period.
- All-cause death by 28 days after confirmation of SARS-CoV-2 infection is used in the analyses, as that is the standard definition of SARS-CoV-2 mortality in the United Kingdom (UK). The analysis included all individuals with at least 42 days follow-up (28 days post-COVID-19 diagnosis plus 14-days to account for the delay in the Office for National Statistics death data).
- Individuals vaccinated against SARS CoV-2 and/or those diagnosed before the study period were excluded.
- Cases are defined as those who tested positive for SARS-CoV-2 between November 16, 2020 and January 11, 2021 and SGTF data were available. Follow-up began on date of testing positive for SARS-CoV-2 and was censored on February 5 or 7 days before receipt of a SARS-CoV-2 vaccine.
- VOC (n=93,011) and non-VOC (n=91,775) groups were generally comparable except the VOC group was younger and had fewer comorbidities, and VOC cases were more frequent in epidemiological weeks 5 to 7.
 - Male: 47.7% vs. 46.1%.
 - Median (IQR) age: 37.0 (24.0-51.0) vs. 38.0 (24.0-52.0). VOC group had a lower proportion of older patients (≥80 years old).
 - Median (IQR) time to death: 14.0 (9.0-21.0) vs. 13.0 (8.0-22.0).
 - Median (IQR) follow-up time: 36.0 (30.0-45.0) vs. 57.0 (40.0-72.0). Non-VOC cases were more frequent in the first few weeks, whereas non-VOC cases occurred later.
 - Residence in care homes: 0.1% vs. 0.4%.
 - Ethnicity: white (56.7% vs. 57.4%); South Asian (10.4% vs. 12.9%); Black (3.0% vs. 1.9%); mixed (1.6% vs. 1.3%); other (1.7% vs. 1.5%); missing (26.6% vs. 25.0%).
 - Number of comorbidities: no comorbidities (86.5% vs. 84.5%); 1 comorbidity (10.6% vs. 11.7%); ≥2 comorbidities (2.9% vs. 3.8%).
 - Index of multiple deprivation quintile: 1 (least deprived) (22.1% vs. 17.4%); 2 (20.2% vs. 17.4%); 3 (20.4% vs. 17.6%); 4 (20.6% vs. 21.2%); 5 (most deprived) (16.7% vs. 26.3%). The index of multiple deprivation is the official measure of relative deprivation for small areas in England, taking into consideration income, employment, education, health, crime, barriers to housing and services, and living environment.^{1,2}
- Factors adjusted for in calculating HR for death included: age, sex, index of multiple deprivation, ethnicity, smoking status, obesity, household size, rural/urban classification, comorbidities, epidemiological week and care home status.
- Comorbidities included in the analysis were: aplastic anaemia, asplenia, asthma, bone marrow transplant, cancer, chronic cardiac disease, chronic respiratory disease, chronic liver disease, dementia, diabetes, chronic kidney disease, gastrointestinal bleed, HIV, permanent immunosuppression, temporary immunosuppression, hypertension, stroke, inflammatory bowel disease, neurological conditions, psoriasis, sickle cell disease, smoking, organ transplant.
- The analysis to calculate the absolute 28-day all-cause mortality risk was restricted to 112,979 people diagnosed with SARS-CoV-2 at least 28 days before the censoring date, with the outcome as death by 28 days after a positive test.
- Increased HR for VOC were consistent across all prespecified sensitivity analyses by National Health Service England region, imputed ethnicity, causal minimum adjustment (age, care home status, comorbidities, index of multiple deprivation and smoking status); and all prespecified

subgroup analyses, including epidemiological week, age group, categorical number of comorbidities, ethnicity and index of multiple deprivation quintile.

- Risk of death increases with age and comorbidities for VOC and non-VOC groups; therefore, the authors suggest that no change is required for vaccination priority and programs for protecting those at risk.
- The authors did not comment on the mechanism for the increased mortality risks observed in this study.
- The authors noted that the **absolute risk of death may be overestimated** as individuals with asymptomatic and mild SARS-CoV-2 infections may be less prone to go for testing. Also, risk estimates may be under- or overestimated since hospital-based testing was not included as the tests used in these settings cannot detect SGTF.

PHO Reviewer's Comments

- The findings of higher mortality risk associated with B.1.1.7 in this study are consistent with other UK analyses using community SARS-CoV-2 test data:
 - Davies et al:³ adjusted HR for 28-day mortality = 1.55 (95% CI: 1.39–1.72).
 - Patone et al (preprint):⁴ adjusted HR for 28-day mortality = 1.59 (95% CI: 1.25–2.03).
- The use of data from a general practice database facilitates controlling for potential confounders (e.g., presence of comorbidities, socioeconomic deprivation).
- Case presentation of included cases was not reported in the article and it would have been important to understand how both the VOC and non-VOC cases were comparable in terms of infection severity.
- Asymptomatic cases and those with mild symptoms might not seek testing and hence, overestimate the risk of death as mentioned by the authors. This may be true for both VOC and non-VOC cases; thus, it is unlikely to affect the HR unless there is an overrepresentation of milder cases in the non-VOC group.
- Generalization of findings to other countries should take into consideration that public health measures to control the speed and extent of COVID-19 transmission, as well as health service access and capacity, differ across jurisdictions and may impact the risk of death in VOC cases.
- As of April 4, 2021, VOCs (B.1.1.7, B.1.351 and P.1) represented ~60% of all COVID-19 cases tested for VOCs in Ontario, with the B.1.1.7 variant representing ~92% of circulating VOCs.⁵
- Available vaccines against SARS-CoV-2 available in Canada are effective against the B1.1.7 variant,^{6,7} and the overall increase in mortality risk mainly among elderly with comorbid conditions can still be mitigated through Ontario's vaccination strategy⁸ that prioritizes vaccines for those at greatest risk of severe illness.

References

1. United Kingdom. Department for Communities and Local Government. The English index of multiple deprivation (IMD) 2015 [Internet]. London: Crown Copyright; 2015 [cited 2021 Apr 06]. Available from: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/464431/English_Index_of_Multiple_Deprivation_2015_-_Infographic.pdf
2. United Kingdom. Department for Communities and Local Government. The English index of multiple deprivation (IMD) 2015 – guidance [Internet]. London: Crown Copyright; 2015 [cited 2021 Apr 06]. Available from: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/464430/English_Index_of_Multiple_Deprivation_2015_-_Guidance.pdf
3. Davies NG, Jarvis CI, van Zandvoort K, Clifford S, Sun FY, Funk S, et al. Increased mortality in community-tested cases of SARS-CoV-2 lineage B.1.1.7. *Nature*. 2021 Mar 15 [Epub ahead of print]. Available from: <https://doi.org/10.1038/s41586-021-03426-1>
4. Patone M, Thomas K, Hatch R, Tan PS, Coupland C, Liao W, et al. Analysis of severe outcomes associated with the SARS-CoV-2 variant of concern 202012/01 in England using ICNARC Case Mix Programme and QResearch databases. medRxiv 21253364 [Preprint]. 2021 Mar 12 [cited 2021 Mar 15]. Available from: <https://doi.org/10.1101/2021.03.11.21253364>
5. Ontario Agency for Health Protection and Promotion (Public Health Ontario). Daily epidemiologic summary: COVID-19 in Ontario: January 15, 2020 to April 4, 2021. Toronto, ON: Queen's Printer for Ontario; 2021.
6. Bernal JP, Andrews N, Gower C, Robertson C, Stowe J, Tessier J, et al. Early effectiveness of COVID-19 vaccination with BNT162b2 mRNA vaccine and ChAdOx1 adenovirus vector vaccine on symptomatic disease, hospitalisations and mortality in older adults in England. medRxiv 21252652 [Preprint]. 2021 Mar 2 [cited 2021 Mar 16]. Available from: <https://doi.org/10.1101/2021.03.01.21252652>
7. Lumley SF, Rodger G, Constantinides B, Sanderson N, Chau KK, Street TL, et al. An observational cohort study on the incidence of SARS-CoV-2 infection and B.1.1.7 variant infection in healthcare workers by antibody and vaccination status. medRxiv 21253218 [Preprint]. 2021 Mar 12 [cited 2021 Mar 15]. Available from: <https://doi.org/10.1101/2021.03.09.21253218>
8. Government of Ontario. Ontario's COVID-19 vaccination plan [Internet]. Toronto, ON: Queen's Printer for Ontario; 2021 [updated 2021 Mar 22; cited 2021 Mar 29]. Available from: <https://covid-19.ontario.ca/ontarios-covid-19-vaccination-plan>

Citation

Ontario Agency for Health Protection and Promotion (Public Health Ontario). Review of “Case fatality risk of the SARS-CoV-2 variant of concern B.1.1.7 in England, 16 November to 5 February”. Toronto, ON: Queens’s Printer for Ontario; 2021.

Disclaimer

This document was developed by Public Health Ontario (PHO). PHO provides scientific and technical advice to Ontario’s government, public health organizations and health care providers. PHO’s work is guided by the current best available evidence at the time of publication.

The application and use of this document is the responsibility of the user. PHO assumes no liability resulting from any such application or use.

This document may be reproduced without permission for non-commercial purposes only and provided that appropriate credit is given to PHO. No changes and/or modifications may be made to this document without express written permission from PHO.

Public Health Ontario

Public Health Ontario is a Crown corporation dedicated to protecting and promoting the health of all Ontarians and reducing inequities in health. Public Health Ontario links public health practitioners, front-line health workers and researchers to the best scientific intelligence and knowledge from around the world.

For more information about PHO, visit publichealthontario.ca.

