Review of “NERVTAG Paper on COVID-19 variant of concern B.1.1.7”


One-minute summary

- The New and Emerging Respiratory Virus Threats Advisory Group (NERVTAG) reported with 40% to 50% confidence that COVID-19 Variant of Concern (VOC) B.1.1.7 is associated with an increased risk of death compared to non-VOC, based on preliminary evidence from data of COVID-19 deaths linked to testing results in the community.
- Using a Cox proportional hazards model on 2,583 deaths among 1.2 million COVID-19 patients, the London School of Hygiene and Tropical Medicine (LSHTM) estimated the relative hazard of death (95% confidence interval) within 28 days of diagnosis to be:
  - 1.35 (1.08–1.68), adjusted for misclassification of S-gene target failure (SGTF)
  - 1.28 (1.06–1.56), not adjusted for misclassification of SGTF after November 1, 2020
- In a non-parametric analysis of data from all of England in epidemiological weeks 46 through 54, Imperial College London (ICL) estimated the mean ratio of case-fatality rate (CFR) to be:
  - 1.36 (1.18–1.56) by case-control weighting
  - 1.29 (1.07–1.54) by standardized CFR
- In a case-control study of death data linked to community swab test results, the University of Exeter (UE) reported a mortality hazard ratio of 1.91 (1.35–2.71).
- In a retrospective matched cohort study by Public Health England (PHE) of 184,414 COVID-19 patients (92,207 were SGTF cases) matched by age, sex, week of diagnosis and region, an increased risk ratio for 28-day case fatality at 1.65 (1.21–2.25) was reported only with additional time for follow-up and death verification.
- Using high quality data based on lineage sequencing in a single national health trust (32 VOC cases and 184 non-VOC cases), the COVID-19 Clinical Information Network (CO-CIN) did not find an increased mortality risk—odds ratio: 0.63 (0.20–1.69).

Additional information

- The relative increase in CFR’s seem to be consistent across age groups in the analyses by LSHTM, ICM, and apparent in the UE analysis.
• Sensitivity analysis considering covariates of hospital pressure did not substantially alter the results by LSHTM.
• Subsequent analysis of cases with polymerase chain reaction cycle threshold value under 30 to control for false classification as SGTF did not make any meaningful difference in the ICL results.
• Confidence in the data and generalizability of findings to the entire population are limited:
  • Short follow-up time and lags in availability of hospitalization data.
  • Small sample size—only 8% of all deaths during the study period were included in the analyses.
  • CFR in hospitalized patients does not fully address severity of illness by VOC.
  • CFR may be underestimated in analyses using SGTF as proxy for VOC as cases with low viral load may be missed and not all COVID-19 test samples were tested for VOC. On the other hand, CFR may be overestimated as SGTF can be detected in VOC’s other than B.1.1.7 lineage.

PHO reviewer’s comments
• Broader scale analysis including COVID-19 patients with no or mild symptoms would more fully inform the risk of hospitalization and death in VOC cases.
• 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 severe illness in VOC cases.
• Analyses included in this report were unpublished communications, have not been peer-reviewed, and were not publicly available for independent review; therefore, caution should be exercised when using them to inform policy decision-making.

Citation

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