THE BEST OF THE WEEK (08 mag – 14 mag 2023)

Linda Nab et al.

Changes in COVID-19-related mortality across key demographic and clinical subgroups in England from 2020 to 2022: a retrospective cohort study using the OpenSAFELY platform

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Abstract

COVID-19 has been shown to differently affect various demographic and clinical population subgroups. We aimed to describe trends in absolute and relative COVID-19-related mortality risks across clinical and demographic population subgroups during successive SARS-CoV-2 pandemic waves.

Methods

We did a retrospective cohort study in England using the OpenSAFELY platform with the approval of National Health Service England, covering the first five SARS-CoV-2 pandemic waves (wave one [wild-type] from March 23 to May 30, 2020; wave two [alpha (B.1.1.7)] from Sept 7, 2020, to April 24, 2021; wave three [delta (B.1.617.2)] from May 28 to Dec 14, 2021; wave four [omicron (B.1.1.529)] from Dec 15, 2021, to April 29, 2022; and wave five [omicron] from June 24 to Aug 3, 2022). In each wave, we included people aged 18–110 years who were registered with a general practice on the first day of the wave and who had at least 3 months of continuous general practice registration up to this date. We estimated crude and sex-standardised and age-standardised wave-specific COVID-19-related death rates and relative risks of COVID-19-related death in population subgroups.

Interpretation

There was a substantial decrease in absolute COVID-19-related death rates over time in the overall population, but demographic and clinical relative risk profiles persisted and worsened for people with lower vaccination coverage or impaired immune response. Our findings provide an evidence base to inform UK public health policy for protecting these vulnerable population subgroups.

Mark W Tenforde, Ruth Link-Gelles

Reduction in COVID-19-related mortality over time but disparities across population subgroups

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Abstract

More than 3 years into the pandemic, the world has made major progress in understanding, preventing, and treating COVID-19, and has experienced periods of substantial individual and societal disruption. High rates of immunity from vaccination and recovery from previous infection are now observed among populations,1 which are likely to attenuate the severity of new infections due to long-lasting cellular and

humoral immunity.2 Greater normalcy has returned as governments have ended pandemic restrictions or declared an end to COVID-19 as a public health emergency.3, 4 Despite this progress, SARS-CoV-2 continues to circulate and thousands of COVID-19-related deaths occur weekly worldwide,5 suggesting that there is further room for improvement.

In this issue of The Lancet Public Health, Linda Nab and colleagues6 report the findings of a retrospective cohort study in England that used the OpenSAFELY platform to examine COVID-19-related mortality in adults aged 18 years or older across five pandemic waves spanning almost 2·5 years. Each pandemic wave cohort included data from about 19 million adults with continuous general practice registration. COVID-19-related deaths were captured from death registry linkage and defined by citation of COVID-19 as an underlying or contributing cause of death. Crude and age-standardised and sex-standardised mortality rates and relative hazards of COVID-19-related deaths across demographic and clinical subgroups were assessed for each pandemic wave. Because of dynamic changes in public health measures, population immunity, clinical management, and transmissibility and severity of SARS-CoV-2 variants, the study could not disentangle precise contributions of individual factors but nevertheless provides valuable insights and a comprehensive picture of temporal changes.Nab and colleagues6 found that COVID-19-related mortality rates decreased over time, with crude rates per 1000 person-years declining from 4·48 deaths during wave one (March 23–May 30, 2020) to 0·67 deaths during wave five (June 24–Aug 3, 2022). Compared with wave one, wave two (Sept 7, 2020–April 24, 2021), corresponding with alpha (B.1.1.7) variant circulation and before most adults were vaccinated against COVID-19, showed broad decreases in mortality rates. This might reflect the effects of early public health efforts or improved clinical management, although this should be interpreted in the context of measuring incidence of COVID-19-related deaths over periods with varying lengths and rates of SARS-CoV-2 infection. During wave three (May 28–Dec 14, 2021; in which delta [B.1.617.2] was the dominant variant), the largest decreases in mortality rates were observed among groups who were prioritised for COVID-19 vaccination, especially older adults who had very high primary vaccine series coverage. This finding is consistent with data that have shown a lower risk of severe COVID-19-related outcomes among vaccinated adults, and highlights the fundamental importance of vaccination for all adults.7, 8

Despite overall reductions in COVID-19-related mortality rates over time, improvements were not realised equally across population subgroups. Notwithstanding higher vaccine coverage and relative reductions in COVID-19-related mortality over time, older adults continued to show higher COVID-19-related mortality rates than younger adults, although this study could not discern whether COVID-19 was the primary cause of death or a contributing factor, such as by exacerbating chronic health conditions. Furthermore, in settings of high vaccine coverage, adults with conditions associated with frailty or reduced vaccine response (eg, organ transplant, haematological malignancy, or advanced kidney disease) did not show the same reductions in mortality rates as those without these conditions, suggesting that focused efforts in key population subgroups remain crucial. These efforts might include differential vaccine schedules in groups who are at high risk of severe outcomes, a low threshold for testing and early initiation of effective but underused antiviral therapies (such as nirmatrelvir–ritonavir), and implementation of non-pharmaceutical measures, such as face masks indoors in some settings and improved ventilation.9 The broader community should also protect people who are at high risk of severe outcomes, such as through testing and avoiding public places when unwell. Using the Index of Multiple Deprivation, the Nab and colleagues6 additionally found that relative mortality in populations living in the most socially deprived areas was higher than in less deprived areas. This finding corresponded with lower vaccination coverage in areas with greater deprivation and might also reflect other differences in

access to or utilisation of health-care services, or more crowded living conditions. These findings underscore a need for improved outreach and COVID-19 vaccination among the most vulnerable groups in society.

Major progress has been made and we are no longer seeing the dramatic mortality rates observed during earlier COVID-19 pandemic periods. However, COVID-19 continues to kill thousands of people, and specific population subgroups have a greater burden. The study by Nab and colleagues6 shows the value of strong national and integrated surveillance and vaccine registry data to record the implications of the pandemic and inform public health responses. It also provides robust data on groups in whom measures to reduce severe COVID-19-related outcomes could be more effectively focused, while continuing to minimise individual and societal impacts from COVID-19.

Carol A. Glaser et al.

Lessons Learned From a COVID-19 Dog Screening Pilot in California K-12 Schools

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Abstract

The California Department of Public Health sponsors a statewide, school-based COVID-19 antigen testing program. Although effective, this program requires personnel, testing resources, and sample collection and generates medical waste. Scent-trained dogs are a strategy for rapid, noninvasive, low-cost, and environmentally responsible COVID-19 screening. We conducted a dog screening program to complement a school antigen testing program.

Methods

We partnered with Early Alert Canines to train 2 medical alert dogs (eFigure 1 in Supplement 1) to identify volatile organic compounds (VOCs) emitted by people with COVID-19. Dog training was similar to that in other studies.1-3 This diagnostic study was approved as public health surveillance by California's State Committee for the Protection of Human Subjects. Electronic informed consent for testing was obtained from participants or guardians. Early Alert Canine is accredited by Assistance Dogs International to ensure ethical oversight of the dogs. We followed the STARD reporting guideline.

In-person dog screening was piloted in a subset of volunteer schools on days when antigen testing was scheduled. Participants were 6 ft apart, and the dogs, led by handlers, sniffed participants' ankles and feet (eFigure 2 in Supplement 1). Dogs alerted handlers to potential COVID-19 infection by sitting. To protect confidentiality, participants faced away from the dogs. Participants then underwent BinaxNOW (Abbott) antigen testing. Dog and antigen results were recorded in a digital platform (Primary.Health; Primary Diagnostics).

We assessed dogs' sensitivity and specificity for COVID-19 detection using antigen test results as the comparator. Antigen tests were already deployed in participating schools as their results correlate best with active infection.4 If a dog signaled positive and antigen testing results were

negative, the signal was considered falsely positive; if a dog did not signal and antigen testing results were positive, the signal was considered falsely negative. Analyses were completed in SAS, version 9.4 (SAS Institute, Inc).

Results

After 2 months of training on COVID-19 scent samples in the laboratory, the dogs achieved greater than 95% sensitivity and specificity for detection of the virus. Dog screening was then piloted in the field; 50 visits were conducted at 27 schools from April 1 to May 25, 2022. Of 1558 participants (median [IQR] age, 13 [9-17] years; 870 females [55.8%], 670 males [43.0%], and 18 nonbinary, transgender, or undisclosed gender [1.2%]), most (89%) were students and many (68%) were screened at least twice (Table 1). Overall, 3897 paired antigen-dog screenings were completed. The dogs accurately signaled 85 infections and ruled out 3411 infections (overall accuracy, 90%). However, they inaccurately signaled infection in 383 instances and missed 18 infections, resulting in sensitivity of 83% (95% CI, 75%-90%) and specificity of 90% (95% CI, 89%-91%) (Table 2).

Discussion

Studies have demonstrated dogs' impressive ability for detecting VOCs associated with COVID-19 infection using specimens collected from SARS-CoV-2–infected and uninfected individuals.2,3,5,6 After training in the laboratory, our dogs were field tested and, in more than 3500 screenings, correctly determined COVID-19 status in most instances. Unlike most other studies,2,3,5,6 our dogs directly screened people in the field, rather than specimens. Our method was associated with improved testing efficiency but had a modest decrease in sensitivity and specificity compared with laboratory results.

Dog screening for COVID-19 infection can be completed in a matter of seconds. However, dog screening directly on individuals introduced variables, such as distractions (eg, noises, young children) and environmental factors (eg, wind, smells), that likely contributed to decreased sensitivity and specificity. We considered other options, including a sample collection strategy used by other investigators2,3,5,6; however, those options would sacrifice cost and time efficiency. Study limitations included the low prevalence of SARS-CoV-2 during the study period and the consequently low number of COVID-19 infections.

The goal is for dogs to perform large-scale VOC screening with antigen testing being performed only on persons with positive dog screening results, thereby reducing antigen tests performed by approximately 85%. While modifications are needed before widespread implementation, this study supports use of dogs for efficient and noninvasive COVID-19 screening and could be used for other pathogens.

Juan Ignacio MoránBlanco et al.
Antihistamines as an early treatment for Covid-19
Cell, April 2023; doi.org/10.1016/j.heliyon.2023.e15772

Abstract

Infection with SARs-COV-2 results in COVID-19 disease.

Between March 2020 and August 2021, 468 COVID-19 patients confirmed by PCR or antigen test, in Yepes, Spain, received early treatment with antihistamines, adding azithromycin in selected cases. The primary endpoint is the hospitalization rate of COVID-19 patients, and the secondary endpoints are ICU admission and mortality rates. All endpoints are compared with the official Spanish rates during the time period of the study.

There were 20 hospital admissions (hospitalization rate 4,3%), 5 ICU admissions (ICU admission rate 1,1%) and 3 deaths (fatality rate of 0,6%). No patients in the study required follow up treatment, which suggest they did not develop long COVID. Results from this retrospective trail indicate that early treatment of SARS-COV-2 positive patients with antihistamines may reduce the odds of hospitalization (OR: 0.490, CI: 0.313–0.767, p-value: 0.001). Randomized controlled clinical trials are needed to further evaluate the effects of early antihistamine treatment of SARS-CoV-2 patients to prevent hospitalization, ICU admission, mortality and long-covid.