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Estimating SARS-CoV-2 seroprevalence in long-term care: a window of opportunity

Published Online
December 16, 2021
https://doi.org/10.1016/S2666-7568(21)00304-4

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In the UK, USA, and Canada, the majority of deaths and a high proportion of SARS-CoV-2 infections occurred in long-term care facilities (LTCFs) during the first waves of the pandemic. Administrative factors, such as poor infection control practices, overcrowding, and movement of staff between sites were associated with the likelihood of outbreaks in LTCFs,[1] and excessive burnout among front-line staff[2] probably played a role as well.[3] Short-term and long-term planning and policy requires us to understand when and where infections occurred, which is particularly difficult to do in the LTCF population because the rate of asymptomatic infections is surprisingly high.[4]

Serological testing for antibodies directed against SARS-CoV-2 has played a prominent role in estimating infection rates at both the individual and population level. Before vaccination programmes were implemented, anti-spike antibodies were a reliable predictor of both asymptomatic and symptomatic infections that occurred even months earlier. However, all currently approved vaccines induce antibodies against the SARS-CoV-2 spike antigen, so they are no longer useful for estimating infection rates. Concentration of nucleocapsid-antigen specific antibodies, which are not induced by the vaccines currently used in the UK, is therefore the most reliable estimate of seroprevalence. Unfortunately, circulating nucleocapsid antibodies wane much faster than their anti-spike counterparts,[5] and so measuring them for this purpose might lead to a gross underestimation of seroprevalence. In *The Lancet Healthy Longevity*, Maria Krutikov and colleagues report findings from VIVALDI,[6] a prospective cohort study in which seropositivity for nucleocapsid-binding antibodies was measured between June 2020 and May 2021 in nearly 1500 residents and more than 3000 staff from 201 LTCF across England. Time of infection was estimated three ways: through linkage to a national registry housing PCR test results and hospitalisation records, as the midpoint between a negative and positive test, or 14 days following the peak of cases during the first wave (ie, before August, 2020). Cumulative incidence of seropositivity and therefore infection in the previous 11-month testing period was 34·6% (29·6–40·0) for residents and 26·1% (23·0–29·5) for staff, and the overall prevalence tended to be higher in for-profit LTFCs than in not for profit or independent LTFCs, higher in larger facilities than smaller facilities, and higher in LTFCs in London and northeast England than in the east of England and East Midlands. To estimate the rate of waning of anti-nucleocapsid antibodies, the authors calculated the incidence of seroreversion, which is the loss of antibody detection after a positive test is identified. They found that seroreversion was as high as 2·4 cases per 1000 person-days at risk in residents and only 1·5 cases per 1000 person-days at risk in staff, which corresponded to a median time to seroreversion of approximately 8 months. The authors also reported a sensitivity analysis done on 116 individuals (73 residents and 43 staff who had PCR-confirmed infection, had been hospitalised, or had seroconverted) in which seroreversion was estimated to be 1·5 cases per 1000 person-days at risk in residents and 0·9 cases per 1000 person-days at risk in staff, with a median time to seroreversion of 3 months.

Given the generalisability afforded by their repeated sampling design of a large number of residents and staff from a diverse array of facilities across England, the findings reported by Krutikov and colleagues are particularly valuable for understanding the rate of infections in LTCFs and the intervals required to yield reliable seroprevalence estimates in future surveys. Of particular importance, the authors show that the incidence of infection was approximately 35% in residents and 26% in staff, which is two to three times higher than previous estimates for LTCFs facilitates in England.[7,8] Their findings will aid in predicting future outbreaks, inform vaccination strategies, and help uncover immune correlates of protection in what is arguably our most vulnerable population with respect to severe outcomes of SARS-CoV-2.[9] Although it remains unclear the degree to which previous infection will affect future infection risk or severe outcomes in LTCFs, this protection appears to be significant for at least 4 months.[10] If previous infection boosts vaccination responses (and vice versa) in LTCFs residents as it does in the general population, previous infection might skew our estimates of vaccine effectiveness in this vulnerable

population. Furthermore, considering that community-dwelling older adults have considerably lower rates of infection than older adults in LTCFs,[11] it is possible that their risk of infection might increase substantially, more so than those who are currently in care, when they transition to LTCFs. As a whole, the present study shows that we do not fully understand the penetrance of infections in LTCFs, nor do we know how well staff and residents are protected from future outbreaks.

We declare no competing interests.

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