SARS-CoV-2: can isolation be limited to those who are truly infectious?

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At the height of the COVID-19 pandemic, public health restrictions including self-isolation of positive cases and their close contacts were vital to reduce onward transmission of SARS-CoV-2, thus preventing deaths and the potential overwhelming of health-care services. However, the requirement for prolonged and often repeated episodes of self-isolation has had an enormous impact on individuals' psychological, financial, and educational wellbeing, disproportionately affecting those on lower incomes, the self-employed, and those unable to work from home.[1, 2] Self-isolation policies have also had wider deleterious effects on national economies, infrastructure, and the delivery of public services, such as health care and education.[2]

Understanding the viral kinetics of SARS-CoV-2 infection is key to optimal self-isolation policies, which need to strike a balance between preventing onward transmission and avoiding unnecessary isolation. Lateral flow devices (LFDs) have been deployed to attempt to limit self-isolation to those who are infectious, but the guidelines for their use have been driven largely by mathematical modelling,[3] based on limited real-world data and a number of key assumptions. In two UK studies published in *The Lancet Respiratory Medicine*, Seran Hakki and colleagues[4] sought to characterise the window of SARS-CoV-2 infectiousness and correlate LFD results with infectiousness, whereas Nicola K Love and colleagues[5] assessed the use of daily LFD testing in COVID-19 contacts to circumvent the need for universal self-isolation.

Hakki and colleagues[4] recruited 57 recently exposed COVID-19 contacts who subsequently tested positive, which allowed them to measure daily viral load and degree of infectiousness (culturable virus from oropharyngeal swab) for the duration of SARS-CoV-2 infection. Median duration of infectiousness was 5 days (IQR 3–7), with both viral load and infectiousness peaking at day 3 of symptoms. LFD results correlated well with decreasing infectiousness but were unreliable in identifying infectious individuals early in the course of infection, thus supporting the use of LFD testing to guide de-isolation of COVID-19 cases but not as a screening tool to detect early infection.

This is the first community-based study to characterise infectiousness in the presymptomatic (growth) phase as well as the peak and decline phase of infectious viral shedding in naturally acquired SARS-CoV-2 infection. The results are similar to those of a recent human challenge study,[6] although with greater inter-individual variability, which is probably attributable to broader demographics and variation in infecting virus dose in the real-world setting. Nonetheless, it is important to highlight that the study, undertaken between September, 2020, and October, 2021, encompassed individuals infected with pre-alpha, alpha, or delta variants, and was underpowered to evaluate the impact of vaccination on viral kinetics. Over half of the contacts were unvaccinated, and none of the vaccinated individuals

had received a booster. A more recent longitudinal study of individuals with non-severe COVID-19 demonstrated similar viral decay kinetics between delta and omicron variants, although it also had a small sample size and a higher proportion of the omicron-infected participants had received a booster vaccine (35% *vs* 3%).[7]

Love and colleagues[5] conducted a randomised controlled trial of 54 923 adult COVID-19 contacts identified from the NHS Test and Trace programme. They concluded that daily LFD testing for 7 days, with a 24-h exemption from self-isolation if the LFD result was negative, was a safe alternative to 10 days of self-isolation in preventing community SARS-CoV-2 transmission. Attack rates (SARS-CoV-2 infections in secondary contacts) were lower in the daily testing group than in the self-isolation group (6·3% *vs* 7·5%), with a difference significantly below the non-inferiority margin. This adds to the findings of a previous study that demonstrated non-inferiority of daily LFD testing to self-isolation in COVID-19 contacts for controlling transmission within a secondary school setting.[8]

Love and colleagues[5] reported that 80% of those in the daily testing group submitted at least one LFD result, but did not report compliance with daily testing for 7 days. Behavioural change might have mitigated any effect of poor compliance with testing, with 5946 (57%) of 10 443 of participants in the daily testing group who remained negative reporting reduced non-household contacts despite this not being a requirement. This behavioural change, in addition to a higher proportion of participants in this group being able to work from home (therefore with fewer non-household contacts), meant that the two groups might have been more similar than intended. Both groups reported similar numbers of non-household contacts per case.

Free COVID-19 testing is no longer available to the majority of the population in the UK, and there is no legal requirement to self-isolate if symptomatic or COVID-19 positive,[9] which reduces the immediate impact of these findings on public health policy. Nevertheless, the two studies highlight the important part that LFDs can play in effectively targeting self-isolation to minimise secondary transmission, and the findings could have an impact in countries where LFDs are still in use. Currently, there are still substantial numbers of patients with COVID-19 in hospital in the UK and elsewhere. LFDs could potentially be used to guide earlier de-isolation of hospitalised patients, thereby facilitating patient investigations and management, and improving patient flow through the hospital. Both studies were conducted before the emergence of the omicron subvariants, and further research is needed to confirm that these findings remain true in the context of subvariants with considerably higher transmissibility, and in a highly vaccinated population.[10]

We declare no competing interests. AH receives funding from the UK Medical Research Council (ISARIC 4C: Coronavirus Clinical Characterisation Consortium; March, 2020, to September, 2022) and Public Health Scotland (CHARISMA—Clinical Characterisation of Respiratory Viral Infections among Patients with Hospitalised Severe Acute Respiratory Illness using Point-of-Care Multiplex Assays; October, 2021, to September, 2022); she was a member of the UK National Institute for Health and Care Research Urgent Public Health Group (June, 2020, to March, 2021).

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