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DOI: [https://doi.org/10.1016/S2213-2600\(21\)00234-4](https://doi.org/10.1016/S2213-2600(21)00234-4)

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False positives in SARS-CoV-2 antigen testing should be weighed against the costs of failing to control transmission

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Lateral flow device (LFD) rapid tests for SARS-CoV-2 antigen are used for asymptomatic testing (which in practice includes those who are pre-symptomatic or pauci-symptomatic) in a variety of settings in the UK. On April 9 2021, LFDs were made available for twice weekly rapid testing to everyone in England. A recent news article reported pressures within the government to rescind asymptomatic testing due to concerns that despite very high specificity (estimated to be approximately 99.9%¹), the positive predictive value (PPV) was falling in line with reducing prevalence, leading to greater proportions of individuals having to 'unnecessarily isolate' on false positive test results². Asking people to isolate on the basis of what might be a "false" positive is associated with a perceived unfairness and, in some cases, moral indignation.

The risk of uninfected people self-isolating due to false positive test results is a cost to the individual, their household and their workplace that needs consideration and mitigation. However, this cost should be considered in the context of the costs of *failing to identify true positives*. The epidemic control strategies implemented over the past year, including 'lockdowns', have all, to varying extents, required people who are not infected to isolate or quarantine and greatly restrict their social contacts, whilst shutting down entire economic sectors. These restrictions have had massive implications for the education and wellbeing of many, including children and young people³. Any discussions concerning LFD testing policy should incorporate the trade-offs between the negative impact of false positives and the onwards transmission prevented. This is particularly pertinent when we consider the contribution that LFD testing might make to preventing the triggering of more widespread restrictive measures.

Keeping Covid-19 prevalence low is a great *public* benefit. During the pandemic we in the UK have all been asked to take measures that might be challenging personally in order to mitigate risk to others, even when not experiencing symptoms and with low likelihood of transmitting virus. We commonly wear a mask over our nose and mouth in enclosed spaces; we self-isolate if we are a contact of a known case, even when the proportion of contacts who become cases has been previously estimated at just 10-15% during a period of high prevalence⁴. These could be considered measures in response to "false positives" but we recognise the value of the reduction in transmission they give. Most people also recognise that reducing the risk of transmission to others is of benefit to ourselves, and the same applies to asymptomatic or community testing.

No measures to control transmission are without cost or harm, and these are not experienced equally across society. If asymptomatic testing is to work and be more equitable, it is imperative that more is done to ensure that isolation or quarantine is not an undue sacrifice that disproportionately harms people who cannot work from home and might lose their jobs, incomes or ability to care for family members^{5,6}. A critical part of the problem is distinguishing between "false" and "true" positives and their consequences as an end-to-end system. Much of the harm of false positives can be mitigated by taking a second test if the first is positive; if this is performed via LFD, it would add only 30 minutes, and varying test batches (or even tests that detect different antigens) could help address concerns that the chance of receiving a false positive might be correlated across tests delivered together^{7,8}. Although, it should be borne in mind that while this increases specificity of the testing procedure, a second test can only lower

overall *sensitivity* as neither LFD nor PCR testing is 100% sensitive. This accompanying reduction in true positives could also have an impact on transmission.

If prevalence is low and the proportion of false positives is judged too high for mass asymptomatic population testing when considered within the appropriate trade-offs, then LFD testing may be well suited to other applications, including: testing subpopulations with higher prevalence such as contacts of a case^{9,10}; testing in high-transmission settings or where social distancing is impossible; and testing in areas where variants of concern have been detected. The role of LFD testing in society can, and should, be subject to continuous study (including cost-effectiveness), review, and communication, with policy-modifications made accordingly. Moreover, messaging around LFD test accuracy, interpretation, and importance should be clear, reach underserved groups, and be based on the most up-to-date evidence.

Asymptomatic testing interventions should not be dismissed on the basis of numbers isolating on false positive test results alone, without assessing their worth in preventing both onward transmission and more widespread restrictive interventions.

Author contributions

EF drafted the manuscript. All authors contributed by commenting on and/or directly editing the draft. All authors read and approved the final draft. All authors accept responsibility to submit for publication.

Role of funding source

EF, GFM, MF, TH, TW, CJ, TDH, and ELD are supported by UKRI (MRC)/DHSC (NIHR) to investigate Test, Trace and Isolate strategies for SARS-CoV-2 control in the UK (MR/V028618/1). IB is supported by NIHR as Senior Investigator and by DHSC to evaluate community rapid antigen testing. LP and HS were funded by the Wellcome Trust and Royal Society (202562/Z/16/Z). ELD, LP, TDH, TH, IH were supported by the UKRI through the JUNIPER modelling consortium (MR/V038613/1). TW is supported by grants from: the Wellcome Trust, UK (209075/Z/17/Z); the Medical Research Council, Department for International Development, and Wellcome Trust (Joint Global Health Trials, MR/V004832/1), the Academy of Medical Sciences, UK; and the Swedish Health Research Council, Sweden. MEPS is funded by the Engineering and Physical Sciences Research Council Manchester Centre for Doctoral Training in Computer Science (grant number EP/I028099/1). RD is funded by an Engineering and Physical Sciences Research Council (EPSRC) National Productivity Investment Fund (NPIF) Studentship. BJQ is supported in part by a grant from the Bill and Melinda Gates Foundation (OPP1139859). This research was partly funded by the National Institute for Health Research (NIHR) (16/137/109 & 16/136/46) using UK aid from the UK Government to support global health research. The views expressed in this publication are those of the author(s) and not necessarily those of the NIHR or the UK Department of Health and Social Care. No funding source played a role in the writing of this manuscript or decision to submit.

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