

## Analysis

# Could Expanding the COVID-19 Case Definition Improve the UK's Pandemic Response in The Vaccination Era?

Alex Crozier<sup>1</sup>  
Jake Dunning<sup>2,3</sup>  
Selina Rajan<sup>4</sup>  
Malcolm G Semple<sup>5,6</sup>  
\*Martin McKee<sup>4,7</sup>  
\*Iain Buchan<sup>8</sup>

<sup>1</sup> Division of Biosciences, University College London, London, UK

<sup>2</sup> Royal Free London NHS Foundation Trust, London, UK

<sup>3</sup> Epidemic diseases Research Group Oxford (ERGO), University of Oxford, Oxford, UK

<sup>4</sup> Department of Health Services Research and Policy, London School of Hygiene and Tropical Medicine, London, UK

<sup>5</sup> NIHR Health Protection Research Unit in Emerging and Zoonotic Infections and Institute of Infection, Veterinary and Ecological Sciences, University of Liverpool, Liverpool, UK

<sup>6</sup> Respiratory Medicine, Alder Hey Children's Hospital, Liverpool, UK

<sup>7</sup> European Observatory on Health Systems and Policies, London, UK

<sup>8</sup> Institute of Population Health, University of Liverpool, Liverpool, UK

\*Joint senior authors

### Correspondence to:

Full name - Alex Crozier

Mailing address - University College London, Gower Street, London, WC1E 6BT.

Email: alexander.crozier.20@ucl.ac.uk

Phone: 07412411054

Word count: 1784

References: 53

### KEY MESSAGES

- There is a wide range of symptoms associated with COVID-19.
- Many patients with COVID-19 do not experience the UK official case-defining symptoms initially, or ever, and other symptoms often manifest earlier.
- Limiting the case definition and symptomatic testing to those with only the 'official' symptoms will miss, or delay the identification of, many COVID-19 cases. This is a major concern for interrupting transmission.
- We evaluate the potential opportunities and challenges of expanding: the clinical case definition; the criteria for self-isolation; and eligibility for symptomatic testing - asking whether these could improve the UK's pandemic response in the vaccination era.

## Contributors and sources

The authors have broad experience and direct involvement in COVID-19 responses. Alex Crozier has expertise in developing and troubleshooting diagnostic assays and improved COVID-19 testing programmes for sports organisations. Dr Jake Dunning is a Senior Research Fellow in the Epidemic diseases Research Group Oxford (ERGO) at the University of Oxford and formerly a National Incident Director for COVID-19 at Public Health England. Dr Selina Rajan is a Public Health Specialist Registrar who has supported the Public Health England regional response, including managing outbreaks in care homes and educational institutions, and has also contributed extensively to the COVID-19 Health Systems Response Monitor produced by the European Observatory on Health Systems and Policies in partnership with the World Health Organisation. Professor Malcolm G Semple is a professor of outbreak medicine and child health and consultant physician in paediatric respiratory medicine, and a member of NERVTAG and regularly attends SAGE COVID-19. Professor Iain Buchan is a public health physician data scientist, Dean of Liverpool's Institute of Population Health, and researcher leading the evaluation of the Liverpool community testing pilot. Professor Martin McKee is research director of the European Observatory on Health Systems and Policies, and a member of Independent SAGE.

Drawing on scientific evidence and our combined field experience, we aim to evaluate the potential opportunities and challenges of expanding the clinical case definition and the criteria for self-isolation and symptomatic testing eligibility, and ask whether this could help improve the UK's pandemic response in the vaccination era.

## Acknowledgements

Buchan is NIHR Senior Investigator.

## Patient involvement

No patients were involved in the writing of this manuscript

## Conflicts of Interest

We have read and understood [BMJ policy on declaration of interests](#) and have the following interests to declare: IEB and MGS received grant funding from the UK Department of Health and Social Care to evaluate LFT in the Liverpool pilot. IEB reports fees from AstraZeneca as Chief Data Scientist adviser via Liverpool University outside the submitted work. MGS is Chair of the Infectious Disease Scientific Advisory Board and a minority shareholder in Integrum Scientific LLC, Greensboro, NC, USA, a company that has interests in COVID-19 testing but not with lateral flow technology, and reports grants from the NIHR, the Medical Research Council, and the Health Protection Research Unit in Emerging and Zoonotic Infections, University of Liverpool.

## Licence

The Corresponding Author has the right to grant on behalf of all authors and does grant on behalf of all authors, an exclusive licence (or non exclusive for government employees) on a worldwide basis to the BMJ Publishing Group Ltd ("BMJ"), and its Licensees to permit this article (if accepted) to be published in The BMJ's editions and any other BMJ products and to exploit all subsidiary rights, as set out in [The BMJ's licence](#)

## Could Expanding the COVID-19 Case Definition Improve the UK's Pandemic Response in The Vaccination Era?

Alex Crozier, Jake Dunning, Selina Rajan, Malcolm G Semple, Martin McKee, Iain Buchan

### Standfirst

*Alex Crozier and colleagues evaluate the potential opportunities and challenges of expanding the clinical case definition, linked to self-isolation and symptomatic testing, and ask whether this could help improve the UK's pandemic response in the vaccination era.*

In the COVID-19 pandemic, the British public have been instructed “If you have a high fever, a new continuous cough, or you’ve lost your sense of smell or taste or its changed, self-isolate and get a test.”<sup>1</sup> Yet these UK case-defining symptoms are just a few of many described by those infected with SARS-CoV-2.<sup>2,3,4,5</sup> Many mild-to-moderate cases don’t have these symptoms (initially), and other symptoms often manifest earlier.<sup>3,6</sup> Most spread is from symptomatic cases around the time of symptom onset<sup>7,8,9,10,11</sup> and interrupting transmission depends on early identification and isolation of contagious individuals.<sup>12,13</sup> The narrow UK case-definition therefore limits this detection, restricting the effectiveness of the test, trace and isolate programme.<sup>8,14,15</sup>

As vaccination progresses and social mixing increases, infections are now highest among young, un- or partially-vaccinated people, who are also more likely to experience ‘unofficial’ symptoms.<sup>16,17</sup> Variants are adding further to transmission, as predicted, with potential for another wave of hospitalisations and deaths.<sup>18</sup> Therefore, improvements in transmission control are needed. Here we build on calls to broaden the UK’s COVID-19 case definition,<sup>5,19</sup> analysing the potential to improve self-isolation and symptomatic testing, guided by a case definition fit for the vaccination era.

### Updating the UK’s COVID-19 Clinical Case Definition

The European Centre for Disease Prevention and Control described a breadth of symptoms associated with mild-to-moderate COVID-19, the most commonly reported being headache (70%), nasal obstruction (68%), asthenia (weakness and/or fatigue) (63%), myalgia (63%), rhinorrhoea (60%), gustatory dysfunction (54%) and sore throat (53%).<sup>20</sup> Up to half of cases don’t present with any UK case-defining symptom: loss of taste or smell (70%), cough (63%), or fever (45%) .<sup>3,21</sup> So, UK cases are less likely to seek symptomatic testing and self-isolate. While this may reduce the volume of testing, it is likely to impede control of transmission. Critically, unofficial symptoms often manifest earlier.<sup>9</sup> In a recent population-based study in Arizona, USA, the most commonly-reported first symptoms were sore throat (19.0%), headache (15.5%), cough (12.7%), runny nose/cold-like symptoms (12.1%) and fatigue (12.0%).<sup>22</sup> These unofficial symptoms are more common in school-age children<sup>16</sup> and younger people,<sup>17</sup> who now account for an even greater proportion of transmission because older people are vaccinated.

WHO<sup>2</sup> and CDC<sup>4</sup> already include 9 and 11 more case-defining symptoms than the UK, respectively. Greater testing capacity is now available to address a wider case definition in the UK, particularly with rapid antigen tests, yet these are only officially available to people without symptoms.<sup>23,24</sup> Some people with wider symptoms, however, may use asymptomatic testing facilities.<sup>25</sup> Symptomatic testing with RT-PCR meanwhile is open only to those declaring a high temperature, a new continuous cough, or a loss/change in sense of smell.

The UK's narrow clinical case definition impedes not only the identification of cases but also the understanding of SARS-CoV-2 transmission. Although infected individuals without symptoms can clearly pass on the virus,<sup>26</sup> the characterisation of asymptomatic infection and transmission has been poor.<sup>3</sup> It is important to distinguish between those not experiencing symptoms throughout infection (persistently asymptomatic), becoming infectious before symptoms manifest (pre-symptomatic), or having only unofficial or subtle symptoms (pauci-symptomatic). Persistently asymptomatic cases likely account for less than 20% of infections, and they may be 3-25 times less likely than those with symptoms to pass on the virus.<sup>7,8,9,10,11</sup> Real-world evidence suggests pre-symptomatic and (official and unofficial) symptomatic cases drive transmission more than asymptomatic cases.<sup>7,8,9,10,11</sup> It seems counter-intuitive, therefore, to have no official UK guidance on wider COVID-19 symptoms, or to offer different testing routes for those with 'official' symptoms vs no symptoms, with nothing in-between. Meanwhile, people with unofficial symptoms might bypass the rules to get a test – legitimising this choice could be helpful.

There have been concerns over testing capacity, false negative rapid tests, and non-compliance with self-isolation.<sup>23,24</sup> However, the benefits of identifying more cases sooner are likely to be significant. SAGE recommended "prioritising rapid testing of symptomatic people is likely to have a greater impact on identifying positive cases and reducing transmission than frequent testing of asymptomatic people in an outbreak area."<sup>27</sup>

Testing people with a single, non-specific symptom could, of course, overwhelm and waste capacity. Indeed, NERVTAG<sup>28</sup> and SAGE<sup>29</sup> in September 2020 considered data from the First Few Hundred Study<sup>30</sup> and COVID Symptom Study App to reason against expanding symptomatic testing eligibility. The data suggested expanding the definition would decrease symptom specificity from 97% to 94%, while only marginally increasing symptom sensitivity from 85% to 95%. However, more recent evidence on symptom combinations warrants reconsidering the case definition, especially since vaccination means the population most likely to be infected and transmit will now be younger and/or one-dosed, and so less likely to experience severe disease or 'official' symptoms.

Combinations of symptoms could be used to help identify more cases sooner, without overwhelming testing capacity. An age-stratified approach derived from REACT selected chills (all ages), headache (5–17 years), appetite loss (18–54 and 55+ years), and muscle aches (18–54 years) as jointly and positively predictive of RT-PCR positivity together with the 'official' four symptoms.<sup>5</sup> The authors

concluded that triage based on these symptoms would identify more cases than the current approach, at any level of testing. The Virus Watch cohort suggested a wider symptom definition captured cases a day earlier than the current definition, on average,<sup>31</sup> a critical time-difference for preventing onwards transmission. The COVID Symptom Study App was used to identify optimal symptom combinations for capturing most cases with fewest tests, and found that within three days of symptom onset, the 'official' symptom combination (cough, dyspnoea, fever, anosmia/ageusia) identified only 69% of symptomatic cases (requiring 47 tests per case identified), while the combination with the highest coverage (fatigue, anosmia/ageusia, cough, diarrhoea, headache, sore throat) identified 96% of symptomatic cases (requiring 96 tests per case identified).<sup>32</sup> This combination of symptoms would increase the number of cases captured by symptomatic testing by over a third, and would likely result in earlier identification of many cases,<sup>22</sup> potentially containing transmission more as we re-open society.

### **Implementing an Updated Clinical Case Definition**

Expanding the case definition would likely increase testing demand and numbers self-isolating. The system-wide effects would be complex, requiring careful implementation.<sup>33</sup> Any change must neither overwhelm NHS Test and Trace nor impede existing symptomatic testing. Instructions such as 'isolate if you have case-defining symptoms, regardless of test status' must not lose clarity despite more complex lists of symptoms. Potential harms from false negative or positive results need mitigation. While it is essential to consider the pre-test probability (based on background prevalence, epidemiological history, and clinical presentation) and the performance of the test,<sup>34,35</sup> there is likely to be a substantial net-reduction in transmission if more symptomatic cases are identified and isolate sooner.

The initial UK decision to adopt a narrow case definition was based on ease of communication, avoiding confusion with other infections, and preserving testing capacity. This situation is now different - testing capacity is high. The emergence of Delta variant and the potential evolution of more transmissible and/or vaccine resistant variants means that, even with vaccination, further waves of cases, hospitalisations, and deaths may ensue.<sup>18</sup> Mitigating waves, and potentially enduring transmission,<sup>36</sup> requires agile intervention to minimise the risks of vaccine escape variants, long-COVID, further NHS disruption and further harms from restrictions. To realise the benefits of a wider case definition it will be necessary to revise testing and self-isolation policies.

Recognising RT-PCR capacity is limited, and quick turnaround is vital, we suggest targeting this capacity dynamically, guided by continuous review of symptoms, transmission patterns, variants, vaccination uptake, and circulation of other respiratory viruses. Routinely-collected data could be used to adapt testing eligibility, access and communications systematically.<sup>37,38,39</sup> Communication is particularly important considering only half the public correctly identify the official COVID-19 symptoms.<sup>40</sup> Intelligence-led adaptation of the test, trace, and isolate system could make an

important contribution to UK COVID-19 responses while we wait for direct COVID harms to abate as all eligible adults become fully vaccinated.

### **Test, Trace, and Isolate in the Vaccination Era**

Given the heterogeneity in SARS-CoV-2 transmission,<sup>8,14,15</sup> where fewer than 20% of cases may account for more than 80% of transmission, re-opening society ahead of maximum vaccination coverage requires more identification and self-isolation of infectious cases to contain emerging clusters. To achieve this, the UK's Test and Trace system must increase the proportion of cases tested (and isolated) early in their infection and trace more contacts before onwards transmission. Early, active case-finding combined with enhanced (forwards/backwards) contact tracing,<sup>14</sup> effective symptom monitoring,<sup>41</sup> and prompt contact-testing<sup>42</sup> can also reduce transmission.<sup>13</sup> Repeat testing of contacts may usefully replace isolation of asymptomatic contacts.<sup>43,44</sup> Viral sequencing can also help trace clusters back to their source,<sup>45</sup> as well as targeting resources to identify and contain more transmissible or vaccine-resistant variants. Hyper-local approaches are also key.

Testing uptake among symptomatic individuals has been low, and engagement with testing and isolation has been lowest in the communities with the highest SARS-CoV-2 prevalence and gravest COVID-19 consequences.<sup>23,24,40</sup> Effective support to isolate is key to controlling transmission.<sup>46,47</sup> To make the most of an expanded case definition, public health and NHS systems need to integrate more at/across local and national levels<sup>48,49</sup>, enabling nimbler, more equitable targeting of test-trace-isolate<sup>50,51</sup> and surge vaccination.<sup>52</sup> In addition, combinations of RT-PCR and rapid antigen tests may be helpful in reducing delays to self-isolation.<sup>39</sup>

Vaccinations alone are unlikely to end the pandemic. New, more transmissible and (partially) vaccine-resistant variants may spread through susceptible populations with high hospitalisation rates. Inequalities in vaccination are also shifting the burdens to the most disadvantaged, who are also the most harmed by COVID-19 restrictions. To reopen society with greater alacrity and fairness, transmission control must improve. This starts with a fuller case definition and rests on adaptive, locally grounded, and intelligence-led public health responses.

## References

1. Get a free PCR test to check if you have coronavirus. <https://www.gov.uk/get-coronavirus-test>.
2. WHO. WHO COVID-19 : Case Definitions. World Health Organization 2020. WHO reference number: WHO/2019-nCoV/Surveillance\_Case\_Definition/2020.1. 2020 (2020).
3. Meyerowitz, E. A., Richterman, A., Bogoch, I. I., Low, N. & Cevik, M. Towards an accurate and systematic characterisation of persistently asymptomatic infection with SARS-CoV-2. *The Lancet Infectious Diseases* (2020) doi:10.1016/S1473-3099(20)30837-9.
4. Centers for Disease Control and Prevention. *Coronavirus Disease 2019 (COVID-19) 2020 Interim Case Definition, Approved August 5, 2020*. <https://www.cdc.gov/nndss/conditions/coronavirus-disease-2019-covid-19/case-definition/2020/08/05/> (2020).
5. Joshua Elliott, Matthew Whitaker, Barbara Bodinier, Steven Riley, Helen Ward, Graham Cooke, Ara Darzi, Marc Chadeau-Hyam, P. E. Symptom reporting in over 1 million people: community detection of COVID-19. [https://spiral.imperial.ac.uk/bitstream/10044/1/85969/5/COVID\\_19\\_symptoms\\_REACT\\_1\\_v2.pdf](https://spiral.imperial.ac.uk/bitstream/10044/1/85969/5/COVID_19_symptoms_REACT_1_v2.pdf) (2021).
6. Sudre, C. H. *et al.* Symptom clusters in Covid19: A potential clinical prediction tool from the COVID Symptom study app. *medRxiv* (2020) doi:10.1101/2020.06.12.20129056.
7. Qiu, X. *et al.* Defining the role of asymptomatic and pre-symptomatic SARS-CoV-2 transmission – a living systematic review. *Clin. Microbiol. Infect.* (2021) doi:10.1016/j.cmi.2021.01.011.
8. Koh, W. C. *et al.* What do we know about SARS-CoV-2 transmission? A systematic review and meta-analysis of the secondary attack rate and associated risk factors. *PLoS One* (2020) doi:10.1371/journal.pone.0240205.
9. Madewell, Z. J., Yang, Y., Longini, I. M., Halloran, M. E. & Dean, N. E. Household Transmission of SARS-CoV-2: A Systematic Review and Meta-analysis. *JAMA Netw. open* (2020) doi:10.1001/jamanetworkopen.2020.31756.
10. Cevik, M., Kuppalli, K., Kindrachuk, J. & Peiris, M. Virology, transmission, and pathogenesis of SARS-CoV-2. *BMJ* (2020) doi:10.1136/bmj.m3862.
11. Buitrago-Garcia, D. *et al.* Occurrence and transmission potential of asymptomatic and presymptomatic SARSCoV-2 infections: A living systematic review and meta-analysis. *PLoS Medicine* (2020) doi:10.1371/journal.pmed.1003346.
12. Kucharski, A. J. *et al.* Effectiveness of isolation, testing, contact tracing, and physical distancing on reducing transmission of SARS-CoV-2 in different settings: a mathematical modelling study. *Lancet Infect. Dis.* **20**, 1151–1160 (2020).
13. Crozier, A., Rajan, S., Buchan, I. & McKee, M. Put to the test: Use of rapid testing technologies for Covid-19. *BMJ* (2021) doi:10.1136/bmj.n208.
14. Endo, A. *et al.* Implication of backward contact tracing in the presence of overdispersed transmission in COVID-19 outbreaks. *Wellcome Open Res.* **5**, 239 (2020).
15. Taube, J. C., Miller, P. B. & Drake, J. M. An open-access database of infectious disease transmission trees to explore superspreader epidemiology. *medRxiv* 2021.01.11.21249622 (2021).
16. Parcha, V. *et al.* A retrospective cohort study of 12,306 pediatric COVID-19 patients in the United States. *Sci. Rep.* **11**, 1–10 (2021).
17. Swann, O. V. *et al.* Clinical characteristics of children and young people admitted to hospital with covid-19 in United Kingdom: Prospective multicentre observational cohort study. *BMJ* **370**, (2020).
18. Sub-group, (SPI-M-O) Scientific Pandemic Influenza Group on Modelling Operational. *SPI-M-O: Summary of further modelling of easing restrictions – Roadmap Step 2, 31 March 2021*. (2021).
19. Sohal, A. Open letter to Chris Whitty and Susan Hopkins: Change covid-19 case definition in line with WHO to save lives. *The BMJ* (2021) doi:10.1136/bmj.n283.
20. European Centre for Disease Prevention and Control. Clinical characteristics of COVID-19. <https://www.ecdc.europa.eu/en/covid-19/latest-evidence/clinical> (2020).
21. Wells, P. M. *et al.* Estimates of the rate of infection and asymptomatic COVID-19 disease in a population sample from SE England. *J. Infect.* **81**, 931–936 (2020).
22. Khan, S. M. *et al.* Symptoms of COVID-19 in a population-based cohort study. *medRxiv (Pre-Print)* 1–14 (2021).
23. Raffle, A., Taylor-Phillips, S. & Stitch, A. Mapping the outcomes of covid-19 testing reveals the

best opportunities for system improvement. *BMJ* (2021).

24. *Liverpool Covid-19 Community Testing Pilot - Interim Evaluation Report*. (2020).

25. Dagli, M. & Practitioner, G. Covid-19: MHRA is concerned over use of rapid lateral flow devices for mass testing Rapid Response: Inappropriate use of lateral flow tests by symptomatic patients. *BMJ* <https://www.bmj.com/content/373/bmj.n1090/rr> (2021).

26. Johansson, M. A. *et al.* SARS-CoV-2 Transmission From People Without COVID-19 Symptoms. *JAMA Netw. open* **4**, e2035057 (2021).

27. *SAGE 56th meeting on covid-19, 10 Sep 2020*.  
[https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment\\_data/file/928699/S0740\\_Fifty-sixth\\_SAGE\\_meeting\\_on\\_Covid-19.pdf](https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/928699/S0740_Fifty-sixth_SAGE_meeting_on_Covid-19.pdf) (2020).

28. SAGE. Analyses of FF100 and Covid-19 Tracker App data. *Sage* **57** **53**, 1689–1699 (2020).

29. SAGE 57 minutes: Coronavirus (COVID-19) response, 17 September 2020.

30. Boddington, N. L. *et al.* COVID-19 in Great Britain: Epidemiological and clinical characteristics of the first few hundred (FF100) cases: A descriptive case series and case control analysis. *medRxiv* (2020) doi:10.1101/2020.05.18.20086157.

31. Fragaszy, E. *et al.* Symptom profiles and accuracy of clinical definitions for COVID-19 in the community. Results of the Virus Watch community cohort. *medRxiv* 2021.05.14.21257229 (2021).

32. Antonelli, M. *et al.* Optimal symptom combinations to aid COVID-19 case identification: Analysis from a community-based, prospective, observational cohort. *J. Infect.* **82**, 384–390 (2021).

33. John Tulloch, Massimo Micocci, Peter Buckle, Karen Lawrenson, Patrick Kierkegaard, Anna McLister, Adam Gordon, Marta Garcia-Fiñana, Steve Peddie, Matthew Ashton, Iain Buchan, P. P. Enhanced Lateral Flow Testing Strategies in Care Homes Are Associated with Poor Adherence and Were Insufficient to Prevent COVID-19 Outbreaks: Results from a Mixed Methods Implementation Study. *SSRN Electron. J.* (2021).

34. Watson, J., Whiting, P. F. & Brush, J. E. Interpreting a covid-19 test result. *The BMJ* (2020) doi:10.1136/bmj.m1808.

35. Peeling, P. R. W., Olliaro, P. P. L., Boeras, D. I. & Fongwen, N. Scaling up COVID-19 rapid antigen tests : promises and challenges. *Lancet Infect. Dis.* **3099**, 21–26 (2021).

36. Gruchy, J. De. Jeanelle de Gruchy: We need the tools to address Covid enduring transmission. *Local Government Chronicle* (2021).

37. Chiu, I.-M., Cheng, C.-Y., Zhang, H. & Lin, C.-H. R. Self-screening to reduce medical resource consumption facing the COVID-19 pandemic. *Emerg. Med. J.* **37**, 255 (2020).

38. Group, H. C.-19 A. T. W. *HSE COVID19 Antigen Testing Working Group Antigen Test Validation Summary Report*.  
<https://www.hse.ie/eng/services/publications/healthprotection/hse-covid-19-antigen-test-validation-report-june-2021.pdf> (2021).

39. Berger, A. *et al.* Diagnostic accuracy of two commercial SARS-CoV-2 Antigen-detecting rapid tests at the point of care in community-based testing centers. *PLOS* **1–12** (2020) doi:10.1101/2020.11.20.20235341.

40. Smith, L. E. *et al.* Adherence to the test, trace, and isolate system in the UK: Results from 37 nationally representative surveys. *BMJ* **372**, (2021).

41. Perrault, A., Charpignon, M., Gruber, J., Tambe, M. & Majumder, M. S. Designing Efficient Contact Tracing Through Risk-Based Quarantining. *medRxiv* (2020) doi:10.1101/2020.11.16.20227389.

42. Centers for Disease Control and Prevention. Options to Reduce Quarantine for Contacts of Personswith SARS-CoV-2 Infection Using Symptom Monitoring andDiagnostic Testing. *Annals of internal medicine* (2020).

43. SPI-M-O : Statement on daily contact testing. 1–10 (2021).

44. Love, N. *et al.* The acceptability of testing contacts of confirmed COVID-19 cases using serial, self-administered lateral flow devices as an alternative to self-isolation. *medRxiv* 2021.03.23.21254168 (2021).

45. Dr Dinesh Aggarwal, Dr Tom Fieldman, D. B. W. *Genomic epidemiology of SARS-CoV-2 in the University of Cambridge identifies dynamics of transmission: an interim report*.  
[https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment\\_data/file/950795/s0963-genomic-epidemiology-sars-cov-2-university-of-cambridge.pdf](https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/950795/s0963-genomic-epidemiology-sars-cov-2-university-of-cambridge.pdf) (2020).

46. Muge Cevik, Stefan D Baral, Alex Crozier, J. C. Support for self-isolation is critical in covid-19 response. *BMJ* **372**, (2021).

47. Kerkhoff, A. D. *et al.* Evaluation of a novel community-based COVID-19 ‘Test-to-Care’ model

- for low-income populations. *PLoS One* (2020) doi:10.1371/journal.pone.0239400.
48. Pettigrew, L. M., Schalkwyk, M. van, Rechel, B. & Garlick, R. Where's the integration between public health and primary care in the response to covid-19? *The BMJ Opinion* <https://blogs.bmj.com/bmj/2021/02/18/wheres-the-integration-between-public-health-and-primary-care-in-the-response-to-covid-19/> (2021).
49. Crozier, A., Mckee, M. & Rajan, S. Fixing England's COVID-19 response: learning from international experience. *Journal of the Royal Society of Medicine* (2020) doi:10.1177/0141076820965533.
50. Wasserheit, J. N. & Aral, S. O. The dynamic topology of sexually transmitted disease epidemics: Implications for prevention strategies. *J. Infect. Dis.* **174**, (1996).
51. Mishra, S. & Baral, S. D. Rethinking the population attributable fraction for infectious diseases. *Lancet Infect. Dis.* **20**, 155–157 (2020).
52. SPI-M. *SPI-M-O : Consensus Statement on COVID-19*. Sage vol. 700 (2021).
53. Harding-edgar, L., Mccartney, M. & Pollock, A. M. Test and trace strategy has overlooked importance of clinical input , clinical oversight and integration. **113**, 427–431 (2020).