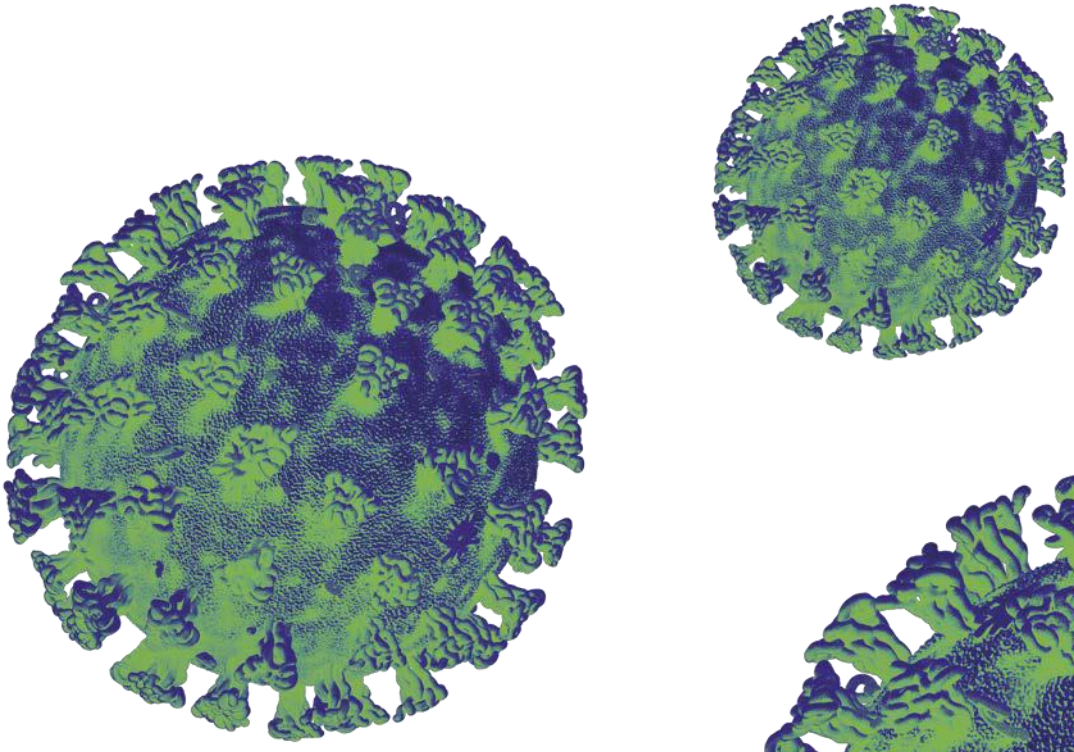
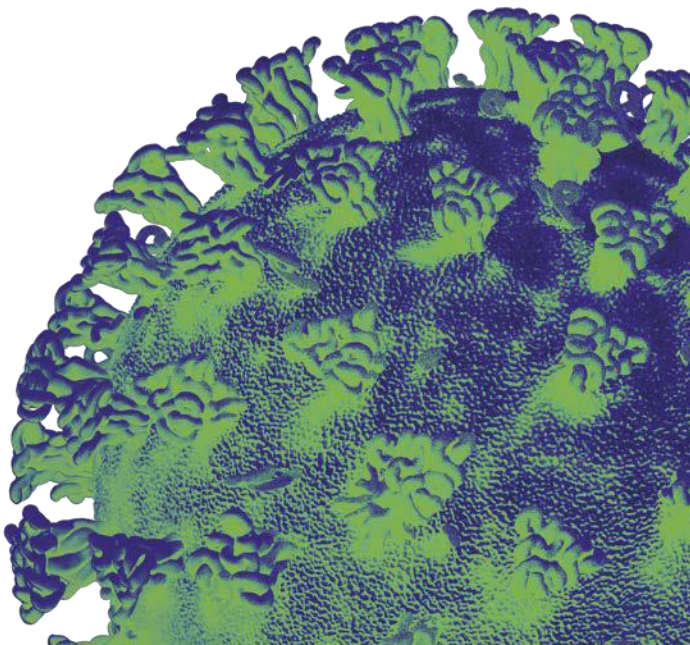
Llywodraeth Cymru
Welsh Government

# Technical Advisory Group

## Reduction in isolation period supported by lateral flow testing for cases of COVID-19

28 January 2022





# Reduction in isolation period supported by lateral flow testing for cases of COVID-19

**26 January 2022**

- On Friday 21 January 2022, the Technical Advisory Group reviewed modelling, behavioural and technical information with regard to the proposal to reduce the isolation time for COVID-19 positive individuals.

- The group is satisfied that the analysis carried out by Public Health Wales, UKHSA and NERVTAG and provided to the Chief Medical Officer is sufficiently robust that there will not be a benefit in duplicating the work (see attached PHW CMO Advice note).

- The recommendation that has been considered is to reduce the self-isolation period for positive cases in Wales to a minimum of five full days, with cases strongly advised to take two consecutive lateral flow tests on days 5 and 6 to check that they are not still infectious (positive by lateral flow test used according to manufacturer's instructions) before leaving isolation.

- The caveats are:
    - That there is a greater risk that people who undertake this shorter isolation could go on to infect others (e.g. if consecutive LFTs are not undertaken properly). This risk is considered to be offset by the benefit to other parts of society (e.g. workforce pressures), although there has not yet been a socio-economic assessment of the size of that benefit.
    - Bays et al[1] warn that "caution must still be exercised for the period following someone's release from isolation as in all scenarios there is a risk of releasing an infective person."
    - That individuals who test positive should continue to isolate beyond the minimum of 5 full days and that some individuals will remain positive, infectious (and unwell) for a longer period. Bays et al[1] caution that "It is key to this regimen that people do not end isolation early, without the two negative rapid antigen tests, as there is significant risk that they will still be infectious."
    - That there should be support for the correct consecutive testing to occur (e.g. adequate availability of LFTs), in order to minimise risk to others.
    - That the acceptability of a shorter isolation period is linked to the reduced severity of infection likely with Omicron if an individual is fully vaccinated and boosted. Ministers may wish to consider whether those who are not vaccinated should continue to isolate for a longer period.
    - That in the event of a negative step-change in the severity of Omicron, a significant reduction in the efficiency of current vaccine against hospitalisation and death, or a new variant with greater severity in its profile, the policy should be reconsidered.

[1] Mitigating isolation: The use of rapid antigen testing to reduce the impact of self-isolation periods

**Behavioural considerations**

- Consistent with previous advice, a clear rationale for the policy is essential if adopted in order to maximise adherence. It is essential to explain why the policy change is thought to be appropriate (i.e. the changing balance of harms, whilst recognising the likelihood a small proportion will still be infectious) and the benefits the policy will deliver.

- Consistency in policies across the UK, and particularly with England, remains a consistent theme emerging from research and would improve understanding and adherence.

- The move to a minimum of five full days in a gradual manner, supported by current scientific evidence, should be explained as part of the approach to the population taking more control over their decisions, with appropriate support (e.g.to determine risk and deal with this in a proportionate manner).

- Such an approach is more likely to result in adherence, which messaging should make clear remains important. Put simply, the shift in policy does not mean the risk has gone, rather it is being managed differently and the two consecutive negative LFT results are a critical component in the new approach.

- A degree of caution would still be advisable if leaving self-isolation after a minimum of five full days but to avoid blurring and non-adherence (i.e. is it safe to do so or not) this will need careful messaging around residual risk, emphasising the need for clarity of rationale noted above.

- To support maximum adherence messaging should confirm the accuracy of LFT; their widespread availability; advice/signposting on ease and method of use (to also maintain accuracy); and clear ‘next steps’ including reporting of all results.

- Whilst acknowledging the reporting system is gov.uk provided, the friction involved makes reporting less likely. If there is a need/desire to use these data for surveillance and TTP (in the increasing absence of PCR results), the streamlining of processes and reframed ‘attractiveness’ from individuals perspectives should be considered.

- With the change in policy, it would be an opportune time to remind people about the availability of financial and practical support, planning ahead if at all possible (e.g. food in freezer/cupboard but recognising this will be easier for some than others) and reinforcing the value of the communitarian approach in Wales such that people support family, friends and neighbours where possible.

- There is value in reinforcing the use of existing evidence to maximise the likelihood of adherence to self-isolation by understanding the main

determinants. Useful papers from SPI-B and Scottish Government summarise the literature.

GIG CYMRU NHS WALES | Iechyd Cyhoeddus Cymru Public Health Wales

# Public Health Wales COVID-19 advice to the Chief Medical Officer for Wales No. 26

## *Reduction in isolation period supported by lateral flow testing for cases of COVID-19*
## 20 January 2022

This advice note is provided by Public Health Wales to the Chief Medical Officer to inform the development of strategy and policy decisions taken by Welsh Government. As such, it is intended to be independent advice informed by evidence and should not be considered as definitive guidance or government policy.

### Context

In Wales, COVID-19 cases were required to self-isolate for 10 days from diagnosis. On 7 January 2022 the self-isolation period changed so that individuals are now required to self-isolate for 7 full days and advised to perform a Lateral Flow Test on Days 6 and 7 to test for infectivity.

On 17 January 2022, self-isolation of COVID-19 cases in England changed with the possibility of individuals to be released from isolation if they have negative LFT tests on Days 5 and 6.

### Background

Public Health Wales has developed a simple model to examine the impact of various strategies on the number of infectious individuals released to mix in society and the numbers of individuals released at different time points.

The model draws basic proportions of infectious individuals from UKHSA data as shown in Table 1.[2]

[2] Declan Bays et al. for UKHSA. Mitigating isolation: The use of rapid antigen testing to reduce the impact of self-isolation periods.

**Table 1: Percentage of individuals who are infectious on days from diagnosis.**

| Day | % Infectious |
|---|---|
| 0 | 100 |
| 1 | 92 |
| 2 | 75 |
| 3 | 58 |
| 4 | 43 |
| 5 | 31 |
| 6 | 22 |
| 7 | 16 |
| 8 | 11 |
| 9 | 7 |
| 10 | 5 |
| 11 | 3 |
| 12 | 2 |
| 13 | 2 |
| 14 | 1 |

The LFT performance characteristics used in the model are sensitivity 75%, specificity 99.9%.

When a single LFT is used, the number of individuals potentially released on a day is the number of people giving a negative LFT, composed of the number of non-infectious individuals plus the number of infectious individuals who give a false negative result.

> For example, for a population of 1,000 tested on Day 10 (5% infectious), 950 individuals would be non-infectious (and have a negative LFT) and 50 individuals would be infectious, but only 37 would be identified by an LFT with sensitivity 75% - 13 individuals would be expected to give a false negative result. So 963 individuals would be released, 13 of whom would be infectious (1.3%).

In cases of sequential testing, it is assumed that the prevalence for the first round of testing is taken as the proportion infectious expected to be infectious on that day. For the second day of testing, the prevalence is calculated from the number of expected false negatives in the first round tests, within the residual population.

> For example, for sequential testing on Day 5 and Day 6, the initial prevalence is 31% on Day 5. Testing 1,000 individuals would give an expected 767 negative results of which 78 would be expected to be false negatives. The overall prevalence in the population decreases

between 31% to 22% between Day 5 and Day 6, a drop to 71% of the prevalence on Day 5. So the prevalence on Day 6 in those who had tested negative on Day 5 is taken to be 78/767 (10.2%) decreased to 71% of the Day 5 level, making it 7.1%. The prevalence within the population who had a negative test on Day 5 is used to calculate the number of false positives if testing is repeated on Day 6. Only those who have a negative on Day 5 plus Day 6 are released from isolation. The number of false negatives on Day 6 who had had a negative result on Day 5 is taken to be the number of infectious individuals released from isolation.

Table 3 outlines the model as applied to a population of 1,000 and assumes 100% compliance with isolation and with testing.

**Table 3: Simple PHW model for different isolation strategies**

| Testing strategy | Day of Release | % Infectious | Number of Individuals potentially released on that day | Number of infectious individuals released | Cumulative number of released days up to day 14 | % of those released who are infectious |
|---|---|---|---|---|---|---|
| No Testing | 5 | 31 | 1,000 | 310 | 10,000 | 31.0 |
| | 6 | 22 | 1,000 | 220 | 9,000 | 22.0 |
| | 7 | 16 | 1,000 | 160 | 8,000 | 16.0 |
| | 8 | 11 | 1,000 | 110 | 7,000 | 11.0 |
| | 9 | 7 | 1,000 | 70 | 6,000 | 7.0 |
| | 10 | 5 | 1,000 | 50 | 5,000 | **5.0** |
| | 11 | 3 | 1,000 | 30 | 4,000 | 3.0 |
| | 12 | 2 | 1,000 | 20 | 3,000 | 2.0 |
| | 13 | 2 | 1,000 | 20 | 2,000 | 2.0 |
| | 14 | 1 | 1,000 | 10 | 1,000 | 1.0 |
| Single LFT | 5 | 31 | 768 | 78 | 9,250 | 10.1 |
| | 6 | 22 | 835 | 55 | 8,483 | 6.6 |
| | 7 | 16 | 880 | 40 | 7,648 | 4.5 |
| | 8 | 11 | 918 | 28 | 6,768 | 3.0 |
| | 9 | 7 | 948 | 18 | 5,850 | 1.8 |
| | 10 | 5 | 963 | 13 | 4,903 | **1.3** |
| | 11 | 3 | 978 | 8 | 3,940 | 0.8 |
| | 12 | 2 | 985 | 5 | 2,963 | 0.5 |
| | 13 | 2 | 985 | 5 | 1,978 | 0.5 |
| | 14 | 1 | 993 | 3 | 993 | 0.3 |
| Sequential LFT Day 5 &6 release Day 6 | 6 | 22 | 725 | 14 | 8,336 | 1.9 |

| Testing strategy | Day of Release | % Infectious | Number of Individuals potentially released on that day | Number of infectious individuals released | Cumulative number of released days up to day 14 | % of those released who are infectious |
|---|---|---|---|---|---|---|
| **Sequential LFT Day 6&7 release Day 7** | 7 | 16 | 803 | 10 | 7,548 | 1.2 |
| **Sequential LFT Day 6&7 release Day 8** | 8 | 11 | 803 | 7 | 6,590 | 0.8 |

As highlighted in Table 3, sequential daily LFT testing with release after 2 negative results can give better performance in terms of risk of releasing infectious individuals compared to release without testing at Day 10 in this model. In addition, sequential testing can give significant increased days of release from isolation compared with blanket isolation without testing.

As noted, the model assumes 100% compliance with both isolation and testing. If a policy of sequential LFT on Day 5 and Day 6 with release from isolation on Day 6 (assuming LFTs negative) was implemented, the best case scenario would suggest that for every 1,000 individuals, 14 individuals would be infectious when released on Day 6 (compared to 50 infectious individuals released after Day 10 without LFT testing). Worse case scenarios, for example, would be if individuals left isolation on Day 6 without any testing, in which case approximately 22% would be infectious, OR, individuals performed a single test on Day 6 and only ended isolation if negative, in which case approximately 6.6% would be infectious.

There are a number of papers dealing with options for self-isolation of COVID-19 cases and the role of LFT testing that have been developed by UKHSA. These are available in the Appendix.

There is some confusion in the UKHSA papers regarding the definition of Day 0 and the days on which testing and release form isolation might occur. This makes the information difficult to analyse with confidence. UKHSA modelling of the percentage of individuals who are released from isolation under different strategies who are infectious is shown in Table 2 (derived from two papers, both currently unpublished). This suggests that the risk of using 2 negative LFT tests from day 6 or day 5 carries a slightly higher risk than releasing after 10 days without any testing. It is not clear how these estimates are derived.

**Table 2: Percentage of individuals who are released from isolation who are infectious.**

| Isolation/testing strategy | Released Infectious (%) | |
|---|---|---|
| | Paper 1 [3] | Paper 2 [4] |
| 10-day isolation | 4.9 | 5.1 |
| 14-day isolation | 1 | 1.1 |
| 2 negative LFT tests from day 6 | 5.9 | 6.2 |
| 2 negative LFT tests from day 5 | 6.8 | 7.2 |

## Advice

Self-isolation for the general population is a balance between risk from the release and thereby mixing of infectious individuals versus socio-economic risks from exclusion of individuals from society.

Modelling suggests that the risks from release of infectious individuals with reduced isolation supported by LFT testing is similar or reduced compared to isolation for 10 days. Reducing isolation to 6, 7, or 8 days would give a significant increase in the number of individual days released from isolation. A strategy of release following 2 sequential daily LFT tests starting on Day 5 and allowing release on Day 6 would carry an acceptable risk of releasing infectious individuals, and allow individuals to be released earlier. In the PHW model a move to this strategy from the current arrangement of testing on Days 6 and 7 and releasing on Day 8 would mean an additional 7 infectious individuals/1,000 might be released.

Health and Social Care workers represent a group with significant additional concerns around avoidance of exposure of vulnerable individuals to SARS-CoV-2. In these cases, additional testing is already in place, and Health and Social Care workers should perform an LFT test prior to a shift. If the risk of potential 1.9% of individuals returning to work on Day 6 being infectious is felt to be too high, return could be delayed to Day 7 with a further LFT test – a negative test at this point would give a residual risk of 0.5%.

## Conclusions and Recommendations

The release of COVID-19 cases from isolation is a balance between risk of releasing infectious individuals, socio-economic factors, and potential issues of public compliance.

[3] UKHSA 2022; unpublished.
[4] UKHSA 2022; unpublished.

Modelling suggests that sequential testing with lateral flow tests can support earlier release from isolation to maintain an acceptable risk of release of infectious individuals and significantly increase the number of people able to have a shorter period of isolation.

Public Health Wales would be supportive of a policy of sequential daily LFT testing on Days 5 and 6 of isolation and release for any individuals having 2 negative LFT results.

The same modelling is applicable for positive returning International Travellers, and Public Health Wales would support a change to a policy of sequential daily LFT on Days 5 and 6 of isolation and release for any individuals having 2 negative LFT results in this situation also.

It is recommended that compliance with testing and isolation should be studied.

**APPENDIX: UKHSA Papers on self-isolation periods and the role of testing**

**Paper A[5]**

UK Health Security Agency

# COVID-19 self-isolation changes: scientific summary

## Background

On Wednesday 22 December 2021 new guidance for the public and health and social care staff was introduced to enable those who test positive for SARS-CoV-2 toreduce their self-isolation period from 10 days to 7 days. This change applies to bothvaccinated and unvaccinated individuals.

The self-isolation period for those who test positive for SARS-CoV-2 includes the daytheir symptoms started, or the date of their positive test if they were asymptomatic (known as day 0), and the next 10 full days. It is now advised that self-isolation can end after 7 days provided the individual has 2 consecutive negative lateral flow test (LFT) antigen tests taken 24 hours apart. The first LFT test should be taken no earlier than 6 days after symptoms started, or a positive test result if asymptomatic.

This paper briefly describes the scientific rationale for the change in guidance.

## Reduction in self-isolation period for people who test positive for COVID-19

Synthesis of data from biological studies and international literature reviews addressing periods of infectious virus shedding has been used to inform a recent UKHSA modelling study[6] estimating the impact of different isolation periods.

This study estimated that after 10 full days of self-isolation, 5% of people who testedpositive for SARS-CoV-2 are still infectious (Table 1). By comparison, reducing the 10-day isolation period to 7 days with 2 consecutive negative LFT test results from day 6 means an estimated 6% of people are still infectious when ending self- isolation. The proportion of people estimated to remain infectious 5 days after symptom onset or a positive test is 31%, and at 14 days it is 1%.

[5] COVID-19 self-isolation changes: scientific summary; UKHSA

[6] Bays et al. Mitigating isolation: The use of rapid antigen testing to reduce the impact ofself-isolation periods. 2021. Pre-print. Accessed https://www.medrxiv.org/content/10.1101/2021.12.23.21268326v1

Other scenarios modelled included 5 days of self-isolation and 5 LFT tests (on days5-9) with self-isolation ending after a single negative test result. This increased the proportion of people infectious when released from self-isolation from 5% to 15%.

**Table 1:** Output from the model of the effect of the considered scenarios on diseaserelease into the community

| Policy | Released infectious (%) | Mean time (in hours) a released person is infectious for |
|---|---|---|
| **5-day isolation** | 31.4% (23.9-38.2) | 65.6 (57.7-73.3) |
| **7-day isolation** | 15.8% (11.9-21.0) | 62.3 (56.5-69.2) |
| **10-day isolation** | 5.1% (3.4-7.6) | 59.3 (53.5-65.6) |
| **14-day isolation** | 1.0% (0.6-1.8) | 57.1 (51.4-63.1) |
| **10-day isolation, or 1 negative test from day 7** | 9.2% (6.5-12.8) | 61.1 (55.3-67.5) |
| **10-day isolation, or 2 negative tests from day 6** | 6.2% (4.2-9.0) | 60.0 (53.9-66.3) |
| **14-day isolation, or 2 negative tests from day 6** | 4.1% (2.6-6.0) | 61.3 (55.8-67.7) |

## Effectiveness of LFT tests to support reduction in isolation period

An independent national evaluation has estimated that LFT tests have a sensitivity of around 70-90%[7] for detecting SARS-CoV-2 and a temporal association has been identified between LFT reactivity and viral load as measured by plaque forming unitson cell culture[4].

During the course of a SARS-CoV-2 infection, viral load increases from 1 to 2 daysbefore symptom onset, then peaks at symptom onset and in the first 5 days, indicating that this period has highest infectiousness potential[8]. Individuals who do not develop symptoms have the same viral trajectory but without a clear timeline.

Data from the Assessment of Transmission and Contagiousness of COVID-19 in

[7] Peto et al. COVID-19: Rapid Antigen detection for SARS-CoV-2 by lateral flow assay: a national systematic evaluation for mass-testing. E Clinical Medicine 2021 May 30; DOI:10.1016/j.eclinm.2021.100924

[8] Cevik et al. SARS-CoV-2, SARS-CoV-1 and MERS-CoV viral load dynamics, duration of viral shedding and infectiousness – a living systematic review and meta-analysis. 2020 November. Lancet Microbe. doi: 10.1016/S2666-5247(20)30172-5

Contacts (ATTACCC) study[4][9] found that SARS-CoV-2 transmission occurs early during infection and is associated with peak viral loads. In the study false negative

LFT test results mostly occurred 1 to 2 days **prior** to peak viral load. LFT tests became negative at approximately the same time as viral culture became negative. After peak viral load, LFT tests were significantly more likely to predict a positive culture than PCR, supporting their use in ending isolation. The authors note there willalways be outliers in terms of infectiousness, and it is possible that a prolonged positive LFT may represent persistent infectiousness even in immunocompetent individuals.

These data do not include the Omicron variant of SARS-CoV-2 and it is currently notknown whether the characteristics of viral shedding differ with the Omicron variant.
Early evaluation of 5 LFT tests deployed by NHS Test and Trace have shown acomparable sensitivity for the Omicron variant as with previous variants[10].

[9] DRAFT NERVTAG paper 29th Dec: UKHSA & NIHR ATTACCC study. Publication in preparation.
[10] UKHSA. SARS-CoV-2 variants of concern and variants under investigation in England. Technical briefing 32. 2021 December https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1042688/RA_Technical_Briefing_32_DRAFT_17_December_2021_2 021_12_17.pdf

**Paper B**

# Mitigating isolation: The use of rapid antigen testing to reduce the impact ofself-isolation periods

Declan Bays[1], Timothy Whiteley[1], Matt Pindar[1], Johnathon Taylor[1], Brodie Walker[1], Hannah Williams[1], Thomas J. R. Finnie[1], Nick Gent[1]

## Abstract

Isolating, either enforced or self-guided, is a well-recognised and used technique in the limitation and reduction of disease spread. This usually balances the societal harm of disease transmission against the individual harm of being isolated and is typically limited to a very small number of individuals. With the widespread transmission of SARS-CoV-2 and requirements to self-isolate when symptomatic or having tested positive, the number of people affected has grown very large causing noticeable individual cost, and disruption to the provision of essential services. With widespread access to reliable rapid antigen tests (also known as LFT or LFTs), in this paper we examine strategiesto utilise this testing technology to limit the individual harm whist maintaining the protective effect of isolation. We extend this work to examine how isolation may be improved and mitigate the release of infective individuals into the population caused by fixed time-periods.

## Introduction

Interrupting the transmission of COVID-19 has been key in limiting disease spread in the community and reducing pressure on health care services. The use of non-pharmaceutical interventions (NPIs) has played a critical role in the public health responses adopted by governments throughout the COVID-19 pandemic. We have seen that policies which impose a period of self-isolation on confirmed cases and recent contacts of confirmed cases have proved effective at reducing onward transmission, and therefore also lessening the number of more acute infections. These policies are however subject to complications and limitations, and naturally incur an economic cost (1). As such,when considering social interventions, it is important that one balances the short-term cost in productivity against the longer-term gains acquired through reduced transmission. We strive to avoid total economic shut down, but need to appreciate the detrimental effect on mental and physical well-being caused by extended periods of self-isolation (2, 3).

Guidance on self-isolation periods provided by the European Centre for Disease Prevention and Control (ECDC) and World Health Organisation (WHO) initially suggested a 14-day isolation period for any close contact of a confirmed case (4, 5). This was reduced to 10 days in the summer of 2020 (6, 7); some European nations opted to reduce this again, adopting a 7-day isolation period in September 2020. This was motivated by a deepening understand of the epidemiological characteristics of SARS-CoV-2, specifically by evidence that transmission is rare after day 7 of infection (8). The current UK guidance requires confirmed cases to self-isolate for 10 days from the receipt of a positive test result. Additionally, fully vaccinated individuals who have come into recentcontact with a confirmed case are strongly advised to undertake rapid antigen testing every day for 7days thereafter, isolating if any of these return a positive result (correct as of 21/12/2021) (9).

[1] UKHSA, Manor Farm Road, Porton Down, SP4 0JG

The recent emergence of the Omicron variant (10) has seen case numbers increase dramatically, both internationally and domestically. With this, we see an increase in the risk of debilitating healthand infrastructure services through excessive periods of self-isolation. Considering this, we present in this work an alternative strategy to manage individuals who test positive for SARS-CoV-2; utilising rapid antigen tests to facilitate an earlier end to the default isolation period. We do not consider PCRtesting in this work as the turn-round time between swabbing and result makes it impractical for the purposes envisaged.

## Background

### Impact of isolation (positive cases) on the workforce:

Across the working population, the numbers of available staff have been subject to fluctuation because of imposed self-isolation, causing an increased workload to be placed upon non-isolating staff or disruption to service provision. In the healthcare sector, academic staff have been required to work in the NHS full-time, and research fellows have returned to wards and clinics to meet demands (11), inevitably creating a backlog of work that the health service is not equipped to handle(12).

A survey conducted by the Royal College of Physicians in April 2020, at the peak of the first wave, determined that approximately 20% of healthcare staff were currently isolating due either to themselves or a household member developing COVID-19 symptoms (11) . Another study of healthcare workers, determined that 44% of staff were required to self-isolate during April-July 2020in response to developing COVID-19 symptoms, and 18% due to a household member developing symptoms (13). Additionally, a UK based survey of healthcare workers revealed that 28.9% of those surveyed had to self-isolate at least once due to developing COVID-19 symptoms or providing a positive test. Due to this, it was estimated that 11,800 – 21,000 working days were lost between February-May 2020. This equates to 71-127 working days lost per 1,000 health care workers (assuming a 40-hour working week) (14).

This reduction in staff has resulted in teams needing to revaluate risk-benefit scenarios to optimise pass-through rate, as opposed to providing care based on individual needs (11-13). In Oncology departments for example, regimens with less intensive treatments were being favoured in order toreduce the average bed-occupation time. Similarly, in radiotherapy, using fewer fractions with a higher dose per fraction was being considered, reducing the duration of treatment while simultaneously increasing the risk of toxicity (11).

Furthermore, healthcare workers from nonemergency, surgical allied health, community, and academic posts were having to be redeployed in order to meet the increase in demand that resultedfrom these pressures. Such actions also have consequences which will continue to be felt into the future, with disruption of services such as cardiology meaning fewer surgeries being performed and with it, the training capacity of new cardiac surgeons being greatly decreased.

In universities, students have found it difficult to adjust to isolation, leading to more students dropping out than usual. Staff have reported that students would refuse to participate in asymptomatic testing for fear of repercussions, including being made to isolate in the event of a positive test. University staff report “firefighting” through the pandemic, i.e., attempting to ease theburden of isolation on the student population, while simultaneously adhering to government guidelines (12).

The burdens faced by key workers not based in healthcare roles mirrors the burdens faced by thehealthcare system. Self-isolation often resulted in staff shortages, increasing workloads and shift

times for staff able to go into work – often without an increase in pay as compensation (15). Some companies have refused to take on adjusted timelines for projects, causing an increased pressure onstaff (16). Additionally, staff have been required to take on tasks that they are unprepared and untrained to take on, resulting in potentially unsafe working conditions (16), additional stress/reduced wellbeing (15, 16) and increased workplace tensions amongst staff.

### Models of isolation regimes:

Studies have quantified the effect duration of quarantine/ self-isolation has on COVID-19 spread. Ashcroft et al. used mathematical modelling to explore the effect of isolation duration in both confirmed SARS-CoV-2 cases as well as returning travellers. The role of strict isolation, as well as isolation with test and release strategies was investigated. Their modelling suggests the optimal ratiobetween fraction of transmission prevented and the number of days spent in quarantine with respect to societal and economic cost is delivered with an isolation duration of 7 days. For every 1 day increase in isolation, a reduction in onwards transmission is seen. However, these gains are considered marginal past day 10. The authors also concluded that the use of rapid antigen testing at day 5 with release on day 7 had similar efficacy as a test on day 6 followed by immediate release from isolation (82.3% CI: 68.2%, 93.4%) and (80.5% CI: 67.9%, 88.7%) respectively, meaning a shorter isolation period of 6 days with the use of rapid antigen testing before release is feasible (17).

Peng et al. investigated the effectiveness of a reduced COVID-19 quarantine time-period using a publicly available outbreak simulator (18). The authors drew several conclusions from the model; using RT-PCR testing 1-2 days before the end of a 10-day self-isolation period outperformed a 14-day test free self-isolation period. To achieve a post quarantine transmission risk (PQTR) of 0.1%, comparable to a 14-day self-isolation period, a 10-day period with one QT-PCR test or 2 rapid antigen tests can be used. Similarly, a reduced duration of 6 days can be achieved with the use of
QT-PCR on days 4,5 and 6 whilst even shorter durations can be achieved using the higher PQTR of1%, which is comparable to a 10-day, test free isolation period (19).

Quilty et al. used an agent-based model to simulate viral load dynamics of exposed contacts and their onward transmission potential in different quarantine and testing strategies. Assuming moderate levels of adherence to quarantine and self-isolation on symptom onset, self-isolation alone can prevent 35% of onwards transmission. Post exposure quarantine of 14 days reduces onwards transmission by 48% (95% UI 18-79). Self-isolation with release after a negative PCR test 7 days after exposure yields comparable results (50%, 95% UI 23–80; risk ratio [RR] 1·02, 95% UI 0·88–1·41) to that of the 14-day self-isolation period. Isolation with a negative rapid antigen test 7 days after exposure (49%, 95% UI 20–78; RR 1·00, 0·82–1·28) or daily rapid antigen testing without quarantine for 5 days after tracing (50%, 95% UI 24–79; RR 1·04, 0·69–1·79) also yields similar efficacy (20).

The current literature indicates the feasibility of a shorter isolation period, especially in conjunction with multiple negative test results as a condition of release. These studies concur that a 7-day periodwith multiple tests yields similar onwards transmission to a 14-day isolation period with no testing and a 10-day isolation with testing, whilst reducing the economic and societal burdens of a longer isolation period. However, in a pilot study, close contacts of confirmed COVID-19 cases were given the option to carry out daily rapid antigen test as an alternative to self-isolation in the UK in December 2020. The participants were surveyed at the end of the study. Particularly noteworthy is that 13% of those who took part reported that they increased contacts following a negative test result (21). Although not directly related to positive cases, this study does highlight the risk of increased interactions following a single negative test result.

## Method

### Model and parameterisation

The model used within this paper is loosely based on the methodology presented in Bays et al (22). We use a Monte Carlo based model to simulate the process of 500,000 infected individuals being infected, identified and admitted into self-isolation in a given period. Depending on the scenario being considered, the isolated individuals may then undergo regular rapid antigen testing. Under some scenarios considered, a single negative test (whether true or false negative) will be sufficient to release individuals from self-isolation early. In others, we may require two consecutive negative tests. Individuals are assumed to be released at the end of their self-isolation regardless of infectiousstatus.

Testing is assumed to produce a negative result for any individual who is tested post the end of theirinfectious period. For those who are still within their infectious period, test results are evaluated using a "weighted coin-toss", where this weight is sampled according to the distribution provided in Table 1 for each individual. Each evaluation of our model will generate 100 artificial populations, each consisting of 500,000 infected individuals which are assumed to have been placed into isolation. We consider each of these populations separately to obtain confidence intervals on the values reported. For each simulated individual, we use the parameterisations given in Table 1 to sample an isolation start time, disease recovery time and rapid antigen test sensitivity. We have deliberately neglected test specificity due to current evidence suggesting this is very close to 100% (23), and omission will provide worst-case estimates for re-admission of infected individuals into the population. We assume the window of true rapid antigen test positivity coincides exactly with infectiousness (23).

Lastly, we assume that time t = 0 corresponds to the moment that each individual has fully incubated (i.e., when they would first start to test positive when tested). We define a 'day' as a 24- hour period. As individuals progress through our simulation, the model tracks the proportion whichwould be incorrectly released, how many hours on average each incorrectly released individual will remain infectious following release, and the average number of excess hours spent in isolation according to each of the self-isolation scenarios described below.

*Table 1: Parameter values and references used in the model*

| Parameter | Distribution drawn from | Reference |
|---|---|---|
| **LFT sensitivity** | Uniform (lower=0.7, upper=0.8) | (24) |
| **Infectious period distribution** | Gamma (shape=IPD_shape, scale=IPD_scale) | (25) |
| **IPD_shape** | Normal (mean=2.0, s.d.=0.1) | (25) |
| **IPD_scale** | Normal (mean=2.1, s.d.=0.1) | (25) |
| **Isolation entry** | Normal (mean=0, s.d.=0.3) | N/A |

### Scenarios

Within this work we are interested in exploring a range of scenarios which might work to reduce excess isolation in the population. As such, we do not consider all permutations of isolation and testing. Instead, we look at only those that reasonably stand a chance of easing these pressures andbeing adopted as a policy. We describe these scenarios below. Note that in all scenarios, individuals are released upon completion of their isolation period regardless of infection status:

- 7, 10, and 14-day isolation with no pre-release testing.

- 10-day isolation with testing administered on days 7-9. Early release if a single negativeresult is returned.
- 10-day isolation with testing administered on days 6-9. Early release if two consecutivenegative results are returned.
- 14-day isolation with testing administered on days 6-13. Early release if two consecutivenegative results are returned.

To aid understanding, possibile pathways that an individual can proceed along under the third scenario of requring a double-negative test to end their isolation period eariler are demonstrated inTable 2. If they reach the end of the isolation period due to positive tests, then they are released regardless of whether they have had negative tests or not.

*Table 2: Potential release scenarios under 10-day isolation and double-negative test scenario*

| Day 6 | Day 7 | Day 8 | Day 9 | Day 10 |
|---|---|---|---|---|
| -ve | -ve (release) | | | |
| +ve | -ve | -ve (release) | | |
| -ve | +ve | -ve (do not release) | -ve (release) | |
| +ve | +ve | -ve | -ve(release) | |
| | No consecutive negative rapid antigen tests | | | Release as usual |

## Results:

Taking mean values, the proportion of people who are still infectious on each day is given in Table 3. This recapitulates earlier work (22) but provides a touchstone against which the reader may observe the self-isolation scenarios.

Table 4 then provides the major output from the model against the scenarios considered.

*Table 3: Percentages (rounded to integer) of people who are still infectious after each day according to their disease profile.*

| | Day | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 |
| Still infectious (%) | 100 | 92 | 75 | 58 | 43 | 31 | 22 | 16 | 11 | 7 | 5 | 3 | 2 | 2 | 1 |
| No-longer infectious (%) | 0.0 | 8 | 25 | 42 | 57 | 69 | 78 | 84 | 89 | 93 | 95 | 97 | 98 | 98 | 99 |

*Table 4: Output from the model of the effect of the considered scenarios on disease release into the community (measured in three different ways) and the self-isolation in addition to that which is necessary to contain disease spread. Intervals are the 2.5 and 97.5 quantiles from the simulations.*

| Policy | Released infectious (%) | Mean time a released person is infectious for (hours) | Mean excess isolation per person (hours) |
|---|---|---|---|
| **7-day isolation** | 15.8% [11.9 - 21.0] | 62.3 [56.5 - 69.2] | 76.8 [67.2 - 84.0] |
| **10-day isolation** | 5.1% [3.4 - 7.6] | 59.3 [53.5 - 65.6] | 141.6 [129.6 - 151.2] |
| **14-day isolation** | 1.0% [0.6 - 1.8] | 57.1 [51.4 - 63.1] | 235.2 [220.8 - 247.2] |
| **10-day isolation, or 1 negative tests from day 7** | 9.2% [6.5 - 12.8] | 61.1 [55.3 - 67.5] | 79.2 [69.6 - 86.4] |
| **10-day isolation, or 2 negative tests from day 6** | 6.2% [4.2 - 9.0] | 60.0 [53.9 - 66.3] | 81.6 [72.0 - 88.8] |
| **14-day isolation, or 2 negative tests from day 6** | 4.1% [2.6 - 6.0] | 61.3 [55.8 - 67.7] | 69.6 [64.8 - 74.4] |

# Discussion

## Overview

The current 10-day isolation period results in the release of 5% of the infected population being released from isolation whilst still being infectious. This reduces to 1% when a 14-day isolation period is considered. In comparison, 10-day isolation including 2 rapid antigen test negative resultsfrom day 6, provides a large reduction in excess isolation in return for a minimal cost of releasing those who are still infectious. Under this regime, 6% of people are released infectious. Excess isolation is reduced from 142 hours to 82 hours.

The optimal solution mathematically is unlimited mandatory isolation, which people can leave once they are no longer infectious. This is not practically possible as people's true disease status is unknowable, false negative and positive rates from tests, and the likelihood that some individuals with unusual biology (for example the immune-supressed) may never show negative. Under the considered options we introduce a ceiling on isolation time to the originally recognised 14 days and assess the course of the disease from day 7 onward with consecutive lateral flow tests. This reducesboth the average time spent isolating unnecessarily and the time that people are released whilst infectious.

Care must still be exercised for the period following someone's release from isolation as in all scenarios there is a risk of releasing an infective person. A 7-day isolation period alone is a notably poor solution as 16% of people could be released prematurely. A single negative rapid antigen test also does not appear sufficient to end isolation because there is still risk of a false negative and a 9%chance of premature release.

## Exploring 10 days isolation

We now look in more detail at when people would be released from isolation and the proportions ofthose being released correctly and falsely at each step. The breakdown according to the day of release can be seen in Table 5.

*Table 5: Breakdown of the "10-day isolation, or 2 negative rapid antigen tests from day 6" policy. The majority of people (79%) are released correctly on day 7. Conversely, there are a significant minority who end their isolation yet are still infectious (4.2%). Intervals are the 2.5 and 97.5 quantiles from the simulations.*

| | Day 6 | Day 7 | Day 8 | Day 9 | Day 10 | End of isolation |
|---|---|---|---|---|---|---|
| New false releases | 0 [0 – 0] | 1.0 [0.6 - 1.5] | 0.5 [0.3 - 0.7] | 0.3 [0.2 - 0.5] | 0.2 [0.1 - 0.3] | 4.2 [2.5 - 6.4] |
| New true release | 0 [0 – 0] | 79.0 [73.2 - 84.2] | 6.0 [5.0 - 7.0] | 4.3 [3.4 - 5.3] | 2.9 [2.1 - 3.7] | 1.6 [1.1 - 2.2] |
| Previously released | 0 [0 – 0] | 0.0 [0.0 - 0.0] | 80.0 [74.1 - 84.9] | 86.5 [81.6 - 90.4] | 91.2 [87.3 - 94.0] | N/A |
| Still in isolation | 100 [100 – 100] | 20.0 [15.1 - 25.9] | 13.5 [9.6 - 18.4] | 8.8 [6.0 - 12.7] | 5.8 [3.7 - 8.6] | N/A |

We can see that most people (79%) will be released on day 7 of their isolation. Only 6% of people will make it to the full 10 days of isolation. However, the majority of those who made it to day 10 would still need to isolate for even longer.
The biggest source of 'false releases' is caused by releasing people after 10 days. 2% of people willbe falsely released based on testing as opposed to 4% because of the end of the 10-day isolation period.

## Comparing mandatory isolation days

Lastly, we look at different days from which people begin testing. We plot the percentage of false releases in each case in Figure 1. This figure accounts for all the people who leave isolation at different points and does not necessarily mean people will leave after the minimum isolation periodhas ended but when they have had two negative rapid antigen tests.

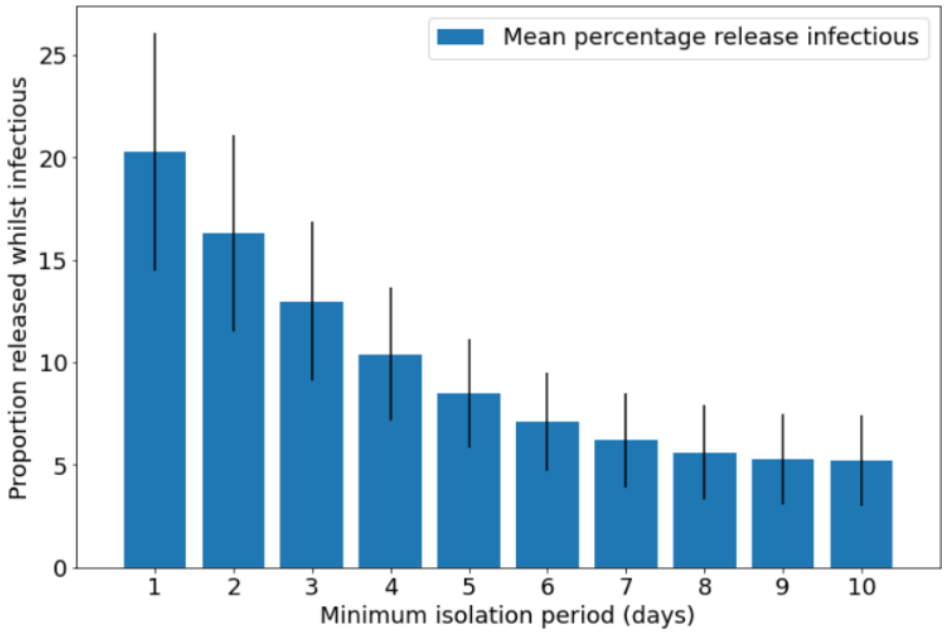



*Figure 1: Sensitivity of the model to different testing regimes. People will not necessarily be released on the first day possible but when they have two consecutive negative LFT tests, or when they reach 10 days. We are measuring the cumulative effects over all* releases over all the days

We can see that removing a mandatory isolation period and relying only on 2 rapid antigen tests alone appears unwise due to the risk of false negatives. The risk of which will increase with the number of tests taken, and hence increase over time. A mandatory isolation period of longer than 7 days will not provide much more safety but lowering this mandatory isolation point will increase thepercent of 'false releases' dramatically.

### Limitations

We have not considered compliance in this model. This is explicit as compliance is a complex andmultifaceted behavioural science problem which is far beyond the scope of this simple physical- system model.

Secondly, while the sensitivity of rapid antigen tests is well known within laboratory conditions, quantifying this in real-world situations is not trivial. To overcome this, we have incorporated someuncertainty into the model by using a random variable based on real-world conditions to describe the rapid antigen test sensitivity assigned to each simulated individual.

Lastly, we have considered time within this system from a purely mathematical viewpoint. That is, days are 24-hour periods and the testing/releasing of simulated individuals occurs exactly at unit periods. In conversion to the real-world we understand that should someone begin what they consider day 0 at 23.59 and conducts their tests at 07:00 this will shorten the time window compared to the model. Figure 1 shows the results are still reasonably robust in this scenariohowever care is required in translation of time periods.

## Conclusion

With this modelling work we can see that there is a way to reduce the period of self-isolationrequired to prevent disease transmission with the use of high-specificity, rapid antigen testing.

Within the bounds of current UK guidance, taking rapid antigen tests from day 6, and requiring 2 consecutive negative tests 24 hours apart, a regime is generated that would release 79% of people correctly on day 7, with 6% of people requiring to stay in isolation until day 10. The total percentageof people released whilst still infectious will be approximately equivalent whereas the excess isolation time will drop from 6 days to 3 days. Note that it is key to this regimen that people should not end isolation early without the two negative rapid antigen tests as there is significant risk that they will still be infectious.

In the absence of available tests, the system should revert to a simple upper-bound on isolation period. Such a bound should be set dependent on risk appetite where, say, 5% of infected individuals would be released with 10 days of plain isolation and 1% with 14 days. In all cases, we urge caution as there is still a chance of residual infectiousness. In particular, should a person be stillpositive with a rapid antigen test at, for example, day 10 then we would encourage further isolation until two clear tests are obtained.

Outside of the current guidance the most beneficial scenario is one where we both reduce the mandated minimum isolation period but allow for an unconstrained maximum isolation period whilst evidence of infection is still present. Thus, by allowing the release of each individual based ontheir own disease course and hence risk profile. Practically, some constraint on isolation period may be desirable. In which case we have shown here that 14 days may provide a sensible upper bound.

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